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略号一覧表

略語・用語	定義（英語）	定義（日本語）
AG	Acylglucuronide	アシルグルクロニド
ALT	Alanine aminotransferase	アラニンアミノトランスフェラーゼ
AST	Aspartate aminotransferase	アスパラギン酸アミノトランスフェラーゼ
ATTRm-CM	Mutant transthyretin amyloid cardiomyopathy (referred to as ATTRv-CM)	遺伝性 ATTR-CM
ATTRv-CM	Variant transthyretin amyloid cardiomyopathy	遺伝性 ATTR-CM
ATTRwt-CM	Wild-type transthyretin amyloid cardiomyopathy	野生型 ATTR-CM
COVID-19	Coronavirus disease 2019	新型コロナウイルス感染症
CSR	Clinical study report	治験総括報告書
CTCAE	Common Terminology Criteria for Adverse Events	有害事象共通用語規準
EAIR	Exposure-adjusted incidence rate	曝露量で調整した有害事象（患者数）の発現率
eGFR	Estimated glomerular filtration rate	推算糸球体濾過量
FAS	Full Analysis Set	最大の解析対象集団
ISS	Integrated Summary of Safety	安全性の統合解析
MedDRA	Medical Dictionary for Regulatory Activities	ICH 国際医薬用語集
NYHA	New York Heart Association	-
OAT	Organic anion transporter	有機アニオントランスポーター
OLE	Open-label extension	オープンラベル継続投与
PT	Preferred term	MedDRA の基本語
QTc	Corrected QT interval	補正 QT 間隔
QTcF	QT interval corrected using Fridericia’s formula	Fridericia 式を用いた補正 QT 間隔
SAP	Statistical Analysis Plan	統計解析計画書
SD	Standard deviation	標準偏差
SOC	System organ class	MedDRA の器官別大分類
ULN	Upper limit of normal	正常範囲上限

2.7.4 臨床的安全性の概要

1 医薬品への曝露

1.1 総括的安全性評価計画及び安全性試験の記述

1.1.1 安全性評価対象試験

アコラミジス塩酸塩（ALXN2060；以下、アコラミジス）は、強力かつ選択的な低分子トランスサイレチン安定化薬であり、現在トランスサイレチン型心アミロイドーシス（ATTR-CM）の治療薬として臨床開発が進められている。

アコラミジスの安全性は、2 つの第 3 相試験、1 つの第 2 相試験及び 7 つの第 1 相試験で評価した。本申請でのアコラミジスの安全性評価のための臨床データパッケージを Table 1 に示す。

第 3 相試験としては、外国人 ATTR-CM 患者を対象とした AG10-301 試験（以下、海外 301 試験）及び日本人 ATTR-CM 患者を対象とした ALXN2060-TAC-302 試験（以下、国内 302 試験）を実施しており、これらの試験を ATTR-CM 患者に対するアコラミジスの安全性評価を行う上での主要な試験と位置付けた。海外 301 試験は、外国人の ATTR-CM 患者を対象とした第 3 相多施設共同ランダム化並行群間試験であり、アコラミジス 800 mg を 1 日 2 回投与したときの有効性、安全性をプラセボと比較した。また、国内 302 試験は、日本人の ATTR-CM 患者を対象とした第 3 相多施設共同オープンラベル試験であり、アコラミジス 800 mg を 1 日 2 回投与したときの有効性、安全性等を評価した。

第 2 相試験としては、外国人 ATTR-CM 患者を対象にアコラミジスの用量を設定する AG10-201 試験（以下、海外 201 試験）を実施し、アコラミジス 400 mg 又は 800 mg を 1 日 2 回投与したときの安全性等をプラセボと比較した。

第 1 相試験では、外国人健康被験者を対象とした AG10-001 試験、AG10-003 試験、AG10-005 試験及び ALXN2060-HV-101 試験並びに日本人及び外国人健康被験者を対象とした AG10-004 試験を実施した。また、外国人健康被験者を対象にアコラミジスの吸収、代謝、排泄及びマスバランスを評価した AG10-007 試験及び薬物相互作用を評価した AG10-008 試験を実施しており、これら 2 試験は参考資料として提出する。

以上の試験を本申請での安全性評価のための臨床データパッケージとし、本概要にて安全性を評価した。

個々の試験の詳細は M2.7.6 項に示す。

Table 1: アコラミジスの安全性評価の臨床データパッケージ

試験番号	試験デザイン	治験対象集団	検討した投与レジメン	健康成人又はATTR-CM 患者数			試験の状況
				アコラミジス	プラセボ	合計	
第 3 相試験							
AG10-301	アコラミジスの有効性及び安全性を評価するランダム化、二重盲検、プラセボ対照試験	ATTR-CM 患者	アコラミジス塩酸塩 800 mg 又はプラセボ BID	421	211	632	完了
ALXN2060-TAC-302	アコラミジスの有効性、安全性、PK 及び PD を評価するオープンラベル、2 パート試験	日本人 ATTR-CM 患者	アコラミジス塩酸塩 800 mg BID	25	0	25	継続中

試験番号	試験デザイン	治験対象集団	検討した投与レジメン	健康成人又はATTR-CM 患者数			試験の状況
				アコラミジス	プラセボ	合計	
第 2 相試験							
AG10-201	アコラミジスの安全性、忍容性、PK 及び PD を評価するランダム化、プラセボ対照、用量設定試験	ATTR-CM 患者	アコラミジス塩酸塩 400 mg、800 mg 又はプラセボ BID を 28 日間	32	17	49	完了
第 1 相試験							
AG10-001	アコラミジスの安全性、忍容性、PK 及び PD を評価するランダム化、プラセボ対照、単回及び反復投与用量漸増試験	健康成人被験者	単回投与:アコラミジス塩酸塩 50, 150, 300, 800 mg 又はプラセボ	24	8	32	完了
			反復投与:アコラミジス塩酸塩 100, 300, 800 mg q12h 又はプラセボを 12 日間	18	6	24	
AG10-003	空腹時にアコラミジスの異なる 2 製剤の生物学的同等性を評価するオープンラベル、単回投与、2 期クロスオーバー試験	健康成人被験者	アコラミジス塩酸塩 200 mg 錠 2 錠又はアコラミジス塩酸塩 400 mg 錠 1 錠を単回投与	24	0	24	完了
AG10-004	アコラミジスの安全性、忍容性、PK を評価するランダム化、オープンラベル、2 期クロスオーバー、単回投与試験	日本人及び外国人の健康成人被験者	第 1 期にアコラミジス塩酸塩 400 mg 又は 800 mg を単回投与した後、7 日間のウォッシュアウト期間を設け、第 2 期にもう一方の用量にクロスオーバー	19	0	19	完了
AG10-005	治療用量を超える用量のアコラミジスの安全性、忍容性、PK 及び PD を検討するランダム化、プラセボ対照、単回漸増投与試験	健康成人被験者	アコラミジス塩酸塩 1200、1600 及び 2000 mg 又はプラセボの単回投与	18	9	27	完了
AG10-007	経口［^{14}C］-アコラミジスの吸収、代謝、排泄及びマスバランスを評価するオープンラベル試験	健康成人男性被験者	［^{14}C］-アコラミジス塩酸塩 800 mg（450 µCi）の単回経口投与	6	0	6	完了
AG10-008	OAT1/OAT3 の基質であるアデホビル及びオセルタミビルカルボン酸の PK に対するアコラミジスの影響を評価するオープンラベル、2 パート、2 期試験	健康成人被験者	Part 1： 第 1 期の Day 1 にアデホビル 10 mg を単回投与 第 2 期の Day 1～8 にアコラミジス塩酸塩 800 mg q12h を 8 日間反復投与、Day 7 にアデホビル 10 mg を併用投与 Part 2： 第 1 期の Day 1 にオセルタミビル 75 mg を単回投与 第 2 期の Day 1～9 にアコラミジス塩酸塩 800 mg q12h を 8 日間反復投与、Day 7 にオセルタミビル 75 mg を併用投与	32（Part 1：14 Part 2：18）	0	32	完了
ALXN2060-HV-101	アコラミジスの PK に対する食事の影響を評価するランダム化、オープンラベル、2 期、2 順序、2 方向クロスオーバー試験	健康成人被験者	空腹時又は食後にアコラミジス塩酸塩 800 mg を単回投与	18	0	18	完了

略語：ATTR-CM = トランスサイレチン型心アミロイドーシス；BID = 1 日 2 回；OAT = 有機アニオントランスポーター；PD = 薬力学的作用；PK = 薬物動態；q12h = 12 時間間隔

1.1.2 総括的安全性評価計画

ATTR-CM 患者に対する本概要でのアコラミジスの安全性評価計画としては、まず主要な試験である 2 つの第 3 相試験の海外 301 試験及び国内 302 試験の安全性の結果を示し、次に第 2 相試験の海外 201 試験の安全性の結果を示すこととした。

海外 301 試験では二重盲検投与期（30 ヵ月間）に治験薬（アコラミジス塩酸塩 800 mg 又はプラセボ）が 1 日 2 回 30 ヵ月間投与された。また、二重盲検投与期での 30 ヵ月間の投与及び最終評価を完了した患者は、アコラミジスの長期投与を評価するオープンラベル継続投与（OLE）試験（AG10-304 試験）へ移行できることとした。本概要では二重盲検投与期での安全性データを示す。

国内 302 試験は日本人 ATTR-CM 患者を対象とした第 3 相多施設共同オープンラベル試験であり、治療期（30 ヵ月間）及び継続投与期で構成されており、治療期に治験薬（アコラミジス塩酸塩 800 mg）が 1 日 2 回 30 ヵ月間投与された。また、治療期での 30 ヵ月間の投与及び最終評価を完了した患者は継続投与期に移行し、アコラミジス塩酸塩の投与を継続できることとした。本概要では治療期での安全性データを示す。

海外 201 試験は ATTR-CM 患者を対象とした第 2 相多施設共同ランダム化プラセボ対照用量設定試験であり、二重盲検投与期に治験薬（アコラミジス塩酸塩 400、800 mg 又はプラセボ）が 1 日 2 回 28 日間投与された。また、28 日間の投与及び最終評価を完了した患者は、アコラミジスの長期投与を評価する OLE 試験（AG10-202 試験）へ移行できることとした。本概要では二重盲検投与期での安全性データを示す。

上記 3 試験の安全性及び忍容性は、有害事象（有害事象、治験薬との関連性が否定できない有害事象、重症度別の有害事象、死亡に至った有害事象、重篤な有害事象、治験薬の投与中止に至った有害事象）、臨床検査値（血液学的検査、血液生化学的検査、尿検査）、バイタルサイン、身体所見及び 12 誘導心電図パラメータの変化によって評価した。なお、各臨床試験の有害事象名は医薬品規制調和国際会議（ICH）国際医薬用語集（MedDRA）を用いてコーディングし、その重症度は軽度、中等度、重度の 3 段階又は米国国立がん研究所の有害事象共通用語規準（CTCAE）を用いて Grade 1～5 で判定した。また、治験薬との関連性は治験責任医師等が 2 段階（関連あり／関連なし）又は 4 段階（「probable」、「possible」、「unlikely」及び「unrelated」）で判定し、2 段階の「関連あり」及び 4 段階のうち「probable」又は「possible」と判定された事象を治験薬との関連性が否定できない有害事象として集計した（併合解析を含む各試験で用いた MedDRA、CTCAE の version、治験薬との関連性基準は Table 2 のとおり）。

Table 2: **各臨床試験で用いた MedDRA の version、重症度判定基準、治験薬との関連性基準**

試験名	MedDRA Ver.	重症度判定基準	治験薬との関連性基準
AG10-001	20.0	軽度／中等度／重度	「probable」、「possible」、「unlikely」及び「unrelated」の 4 段階で判定、このうち「probable」又は「possible」を関連性が否定できない有害事象として集計
AG10-003	21.0	軽度／中等度／重度	関連あり／関連なし
AG10-004	21.1	軽度／中等度／重度	関連あり／関連なし
AG10-005	21.1	軽度／中等度／重度	「probable」、「possible」、「unlikely」及び「unrelated」の 4 段階で判定、このうち「probable」又は「possible」を関連性が否定できない有害事象として集計
AG10-007	24.0	軽度／中等度／重度	関連あり／関連なし

試験名	MedDRA Ver.	重症度判定基準	治験薬との関連性基準
AG10-008	24.1	軽度／中等度／重度	関連あり／関連なし
ALXN2060-HV-101	24.0	CTCAE Ver. 5.0	関連あり／関連なし
AG10-201	21.0	軽度／中等度／重度	「probable」、「possible」、「unlikely」及び「unrelated」の 4 段階で判定、このうち「probable」又は「possible」を関連性が否定できない有害事象として集計
AG10-301	24.1	軽度／中等度／重度	関連あり／関連なし
ALXN2060-TAC-302	26.1	CTCAE Ver. 5.0	関連あり／関連なし
併合解析	24.1	軽度／中等度／重度	関連あり／関連なし

その他の総括的安全性評価計画として、海外 301 試験と現在継続中の 2 つの OLE 試験である AG10-202 試験（海外 201 試験を完了した患者が移行）、AG10-304 試験（海外 301 試験を完了した患者が移行）を含めた安全性の併合解析を実施し、その結果を示すこととした（各 OLE 試験の概要は Table 3 参照、併合解析方法の概要は 1.1.2.1 項参照）。なお、AG10-202 試験及び AG10-304 試験の併合解析のためのデータカットオフ日はそれぞれ 20[redacted] 年 [redacted] 月 [redacted] 日及び 20[redacted] 年 [redacted] 月 [redacted] 日とした。

Table 3: 併合解析に含めたアコラミジスの臨床試験

試験番号	治験デザイン	治験対象集団	検討した投与レジメン	ATTR-CM 患者数 アコラミジス	試験の状況
第 3 相試験					
AG10-304	アコラミジスの OLE 安全性評価試験	AG10-301 試験完了の ATTR-CM 患者	アコラミジス塩酸塩 800 mg BID	312	継続中
第 2 相試験					
AG10-202	アコラミジスの OLE 安全性評価試験	AG10-201 試験完了の ATTR-CM 患者	アコラミジス塩酸塩 800 mg BID	47	継続中

略語：ATTR-CM = トランスサイレチン型心アミロイドーシス；BID = 1 日 2 回；OLE：オープンラベル継続投与

また、健康被験者を対象とした第 1 相試験（AG10-001、AG10-003、AG10-004、AG10-005、AG10-007、AG10-008、ALXN2060-HV-101 試験）での安全性の結果は、5.9 項にまとめて示すこととした。

1.1.2.1 併合解析方法

併合解析計画の詳細を 5.3.5.3.1 項 ISS SAP に示す。

海外 301 試験及び現在継続中の OLE 試験 2 試験（AG10-202 試験及び AG10-304 試験）の集積データ（アコラミジスの曝露データ及び有害事象データ）を用いて、アコラミジスが投与された「アコラミジス治療集団」での併合解析を実施した。なお、海外 301 試験でプラセボが投与され、AG10-304 試験に移行した患者では、海外 301 試験でのプラセボ投与時と AG10-304 試験でのアコラミジス投与時に発現した有害事象とを分けて要約した。

また、アコラミジスの長期安全性プロファイルを評価する目的で、2 つの OLE 試験を併合した「OLE 集団」での併合解析も実施した。なお、「OLE 集団」での安全性データには、移行前の試験で収集した安全性データは含まれない。

併合解析結果は 5.3.5.3.1 項 ISS に示し、必要に応じて本概要に要約した。

1.2 全般的な曝露状況

1.2.1 海外 301 試験

海外 301 試験の患者の内訳を Table 4 に示す。本試験には 632 名（アコラミジス群 421 名、プラセボ群 211 名）がランダム割付けされ、全員に治験薬が投与された。全体でアコラミジス群 70.5%、プラセボ群 66.8%が二重盲検投与期を完了した。治験薬が投与されたすべての患者を安全性解析対象集団とし、当該集団を対象に安全性を評価した。

Table 4: 海外 301 試験の患者の内訳（安全性解析対象集団）

	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)	全体 N = 632 n (%)
試験完了[a]	331 (78.6%)	154 (73.0%)	485 (76.7%)
投与完了 [b]	297 (70.5%)	141 (66.8%)	438 (69.3%)
投与中止 [b,c]	34 (8.1%)	13 (6.2%)	47 (7.4%)
試験中止[d]	90 (21.4%)	57 (27.0%)	147 (23.3%)
試験中止の理由			
同意の撤回	15 (3.6%)	6 (2.8%)	21 (3.3%)
死亡	75 (17.8%)	51 (24.2%)	126 (19.9%)
COVID-19対策関連	0	0	0
二重盲検投与期完了	297 (70.5%)	141 (66.8%)	438 (69.3%)
二重盲検投与期中止	124 (29.5%)	70 (33.2%)	194 (30.7%)
二重盲検投与期中止の理由			
有害事象／心血管症状に関連する入院／臨床的に注目すべき事象	40 (9.5%)	18 (8.5%)	58 (9.2%)
治験実施計画書からの逸脱	1 (0.2%)	3 (1.4%)	4 (0.6%)
試験治療又は試験手順不遵守	5 (1.2%)	2 (0.9%)	7 (1.1%)
同意の撤回	9 (2.1%)	3 (1.4%)	12 (1.9%)
試験で許容されていない治療の必要性	8 (1.9%)	1 (0.5%)	9 (1.4%)
追跡不能	0	1 (0.5%)	1 (0.2%)
医師の判断	2 (0.5%)	4 (1.9%)	6 (0.9%)
患者の意思	18 (4.3%)	13 (6.2%)	31 (4.9%)
死亡	39 (9.3%)	22 (10.4%)	61 (9.7%)
その他	2 (0.5%)	3 (1.4%)	5 (0.8%)
COVID-19対策関連	0	0	0

注：割合（%）は各投与群に基づく。
[a] 30 ヵ月前に死亡した患者は「試験完了」に含めないこととした。
[b] 二重盲検投与期は治験薬の初回投与から Month 30 来院までと定義した。30 ヵ月前に死亡した患者は「投与中止」に含めた。
[c] 投与を早期中止した患者は、同意を撤回せず、生存状況の確認のために試験を継続した場合は、試験完了とみなした。
[d] 試験完了に含まれない患者はすべて試験中止とみなした。
略語：COVID-19 = 新型コロナウイルス
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.1.1.6

海外 301 試験の安全性解析対象集団での治験薬の曝露状況を Table 5 に示す。二重盲検投与期での治験薬投与期間の中央値（範囲）は、アコラミジス群：29.47 ヵ月（0.2～30.8 ヵ月）、プラセボ群：29.44 ヵ月（2.6～31.7 ヵ月）であった。

Table 5: 海外 301 試験の二重盲検期での治験薬の曝露状況（安全性解析対象集団）

	アコラミジス群 N = 421	プラセボ群 N = 211
投与期間（月）		
n	421	211
平均値（標準偏差）	24.64 (8.881)	24.90 (8.115)
中央値（Q1、Q3）	29.47 (22.31, 29.63)	29.44 (22.05, 29.63)
最小値、最大値	0.2, 30.8	2.6, 31.7

略語：Q＝ 四分位
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.1.11

1.2.2 国内 302 試験

国内 302 試験の安全性解析対象集団は最大の解析対象集団（FAS）と同一であり、その患者の内訳は M2.7.3-2.2.2 項に示す。本試験では 25 名が組み入れられ、全員に治験薬（アコラミジス）が投与された。このうち、22 名（88.0%）が治療期（Month 30）を完了し、3 名（12.0%）が早期中止した。治験薬が投与されたすべての患者を安全性解析対象集団とし、当該集団を対象に安全性を評価した。

国内 302 試験の安全性解析対象集団の治療期での治験薬の曝露状況を Table 6 に示す。治療期での治験薬投与期間の中央値（範囲）は 29.90 ヵ月（0.5～30.2 ヵ月）であった。

Table 6: 国内 302 試験の治療期での治験薬の曝露状況（安全性解析対象集団）

	アコラミジス N = 25
投与期間（月）	
n	25
平均値（標準偏差）	27.02 (8.319)
中央値（Q1、Q3）	29.90 (29.90, 29.90)
最小値、最大値	0.5, 30.2

略語：Q＝ 四分位
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.1

1.2.3 海外 201 試験

本試験には 49 名（アコラミジス 400 mg 群 16 名、800 mg 群 16 名、プラセボ群 17 名）がランダム割付けされた。全員に治験薬が投与され、いずれの患者も治験薬の投与を完了した。治験薬が投与されたすべての患者を安全性解析対象集団とし、当該集団を対象に安全性を評価した。

海外 201 試験の安全性解析対象集団での治験薬の曝露状況を Table 7 に示す。海外 201 試験での治験薬の曝露状況としては、服薬コンプライアンスによる評価が行われており、服薬コンプライアンスの中央値（範囲）はアコラミジス 400 mg 群 100.00%（96.49%～100.00%）、800 mg 群 100.00%（98.18%～100.00%）、プラセボ群 100.00%（98.18%～100.00%）であった。

Table 7: 海外 201 試験での治験薬の曝露状況（安全性解析対象集団）

	アコラミジス 400 mg 群 N = 16	アコラミジス 800 mg 群 N = 16	プラセボ群 N = 17
服薬コンプライアンス（%）			
n	16	16	17
平均値（標準偏差）	99.228 (1.2753)	99.784 (0.5918)	99.893 (0.4414)
中央値（Q1、Q3）	100.00 (98.21, 100.00)	100.00 (100.00, 100.00)	100.00 (100.00, 100.00)
最小値、最大値	96.49, 100.00	98.18, 100.00	98.18, 100.00

略語：Q＝ 四分位
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.1.1

1.2.4 併合解析

1.2.4.1 アコラミジス治療集団

アコラミジス治療集団には、AG10-202 試験でアコラミジスが投与された 47 名、海外 301 試験でアコラミジスが投与された 421 名（AG10-304 試験でアコラミジスが継続投与された 205 名を含む）、海外 301 試験でプラセボが投与され AG10-304 試験でアコラミジスが投与された 95 名、の計 563 名が含まれた。当該 563 名をアコラミジス治療集団として安全性を評価した。

アコラミジス治療集団の曝露状況を Table 8 に示す。アコラミジス治療集団全体（563 名）でのアコラミジスの曝露期間の中央値（範囲）は 2.467 年（0.00～4.42 年）であり、このうち 60.9%が 2 年以上投与され、4.4%が 4 年以上投与された。

Table 8: アコラミジス治療集団の曝露状況

	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468	**AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95**	**全体（アコラミジス治療集団） N = 563**
投与期間（年）			
n	468	95	563
平均値（標準偏差）	2.376 (1.0467)	0.456 (0.3276)	2.052 (1.2027)
中央値（Q1、Q3）	2.491 (1.814, 3.044)	0.476 (0.167, 0.695)	2.467 (0.860, 2.951)
最小値、最大値	0.01, 4.42	0.00, 1.32	0.00, 4.42
投与期間カテゴリー			
1 年以上	402 (85.9%)	6 (6.3%)	408 (72.5%)
2 年以上	343 (73.3%)	0 (0.0%)	343 (60.9%)
2.5 年以上	231 (49.4%)	0 (0.0%)	231 (41.0%)
3 年以上	127 (27.1%)	0 (0.0%)	127 (22.6%)
4 年以上	25 (5.3%)	0 (0.0%)	25 (4.4%)
5 年以上	0 (0.0%)	0 (0.0%)	0 (0.0%)

略語：Q＝ 四分位
Source: 5.3.5.3.1 項 ISS Table 2.1.2.1

1.2.4.2 OLE 集団

OLE 試験である AG10-202 試験及び AG10-304 試験の OLE 集団での曝露状況を Table 9 に示す。

OLE 集団全体では、データカットオフ時点で 347 名にアコラミジス 800 mg が投与され、投与期間の中央値（範囲）は 0.534 年（0.00～4.42 年）であった。

試験別の曝露状況では、AG10-202 試験ではデータカットオフ時点で 47 名にアコラミジス 800 mg が投与され、投与期間の中央値（範囲）は 4.211 年（0.09～4.42 年）であり、AG10-304 試験ではデータカットオフ時点で 300 名（海外 301 試験でプラセボ群であった 95 名を含む）にアコラミジス 800 mg が投与され、投与期間の中央値（範囲）は 0.496 年（0.00～1.34 年）であった。

Table 9: OLE 集団での曝露状況

	AG10-202 試験 N = 47	AG10-304 試験 N = 300	全体 N = 347
投与期間（年）			
n	47	300	347
平均値（標準偏差）	3.077 (1.6186)	0.485 (0.3403)	0.836 (1.1125)
中央値（Q1、Q3）	4.211 (1.257, 4.339)	0.496 (0.153, 0.750)	0.534 (0.189, 0.879)
最小値、最大値	0.09, 4.42	0.00, 1.34	0.00, 4.42
投与期間カテゴリー			
1 年以上	37 (78.7%)	21 (7.0%)	58 (16.7%)
2 年以上	32 (68.1%)	0 (0.0%)	32 (9.2%)
2.5 年以上	31 (66.0%)	0 (0.0%)	31 (8.9%)
3 年以上	31 (66.0%)	0 (0.0%)	31 (8.9%)
4 年以上	25 (53.2%)	0 (0.0%)	25 (7.2%)
5 年以上	0 (0.0%)	0 (0.0%)	0 (0.0%)

略語：Q = 四分位
Source: 5.3.5.3.1 項 ISS Table 1.1.2.1

1.3 治験対象集団の人口統計学的特性及びその他の特性

1.3.1 人口統計学的特性及びベースライン特性

1.3.1.1 海外 301 試験

海外 301 試験の安全性解析対象集団での人口統計学的特性及びベースライン特性を Table 10 に示す。

全体で、ランダム割付け時の平均年齢（標準偏差［SD］）は 77.27（6.552）歳であり、患者の多くが男性（90.2%）で、白人（87.8%）であった。また、多くの患者が野生型 ATTR-CM（ATTRwt-CM：90.3%）で、New York Heart Association（NYHA）心機能分類 II（72.0%）であり、スクリーニング時の推算糸球体濾過量（eGFR）は 45 mL/min/1.73 m^2 以上（81.8%）であった。

アコラミジス群とプラセボ群との間で、人口統計学的特性及びベースライン特性に大きな違いは認められなかった。

Table 10: 海外 301 試験での人口統計学的特性及びベースライン特性（安全性解析対象集団）

	アコラミジス群 N = 421	プラセボ群 N = 211	全体 N = 632
年齢（ランダム割付け時）（歳）			
n	421	211	632
平均値（標準偏差）	77.37 (6.450)	77.09 (6.763)	77.27 (6.552)
中央値（Q1、Q3）	78.00 (73.00, 82.68)	78.00 (72.87, 82.00)	78.00 (73.00, 82.00)
最小値、最大値	50.3, 90.8	55.0, 91.0	50.3, 91.0
年齢分布（歳）			
65未満	12 / 421 (2.9%)	9 / 211 (4.3%)	21 / 632 (3.3%)
65以上78未満	190 / 421 (45.1%)	95 / 211 (45.0%)	285 / 632 (45.1%)
78以上	219 / 421 (52.0%)	107 / 211 (50.7%)	326 / 632 (51.6%)
性別			
男性	384 / 421 (91.2%)	186 / 211 (88.2%)	570 / 632 (90.2%)
女性	37 / 421 (8.8%)	25 / 211 (11.8%)	62 / 632 (9.8%)

	アコラミジス群 N = 421	プラセボ群 N = 211	全体 N = 632
民族			
ヒスパニック／ラテン系	8 / 421 (1.9%)	4 / 211 (1.9%)	12 / 632 (1.9%)
ヒスパニック／ラテン系以外	401 / 421 (95.2%)	199 / 211 (94.3%)	600 / 632 (94.9%)
報告なし	11 / 421 (2.6%)	7 / 211 (3.3%)	18 / 632 (2.8%)
不明	1 / 421 (0.2%)	1 / 211 (0.5%)	2 / 632 (0.3%)
人種			
アメリカ／アラスカ先住民	0 / 421	1 / 211 (0.5%)	1 / 632 (0.2%)
アジア人	10 / 421 (2.4%)	3 / 211 (1.4%)	13 / 632 (2.1%)
黒人／アフリカ系アメリカ人	20 / 421 (4.8%)	10 / 211 (4.7%)	30 / 632 (4.7%)
ハワイ先住民／太平洋諸島住民	0 / 421	1 / 211 (0.5%)	1 / 632 (0.2%)
白人	368 / 421 (87.4%)	187 / 211 (88.6%)	555 / 632 (87.8%)
その他	5 / 421 (1.2%)	1 / 211 (0.5%)	6 / 632 (0.9%)
多様人種	2 / 421 (0.5%)	0 / 211	2 / 632 (0.3%)
報告なし	16 / 421 (3.8%)	8 / 211 (3.8%)	24 / 632 (3.8%)
BMI（kg/m^2）			
n	420	209	629
平均値（標準偏差）	27.07 (3.793)	27.01 (3.766)	27.05 (3.781)
中央値（Q1、Q3）	26.72 (24.46, 29.20)	26.53 (24.22, 29.32)	26.68 (24.42, 29.21)
最小値、最大値	18.1, 42.7	19.3, 40.0	18.1, 42.7
ATTR-CM の罹病期間（年）			
n	420	211	631
平均値（標準偏差）	1.24 (1.203)	1.12 (1.195)	1.20 (1.201)
中央値（Q1、Q3）	0.84 (0.40, 1.72)	0.71 (0.31, 1.54)	0.79 (0.38, 1.65)
最小値、最大値	0.0, 10.1	0.0, 7.4	0.0, 10.1
NYHA 心機能分類			
I	51 / 421 (12.1%)	17 / 211 (8.1%)	68 / 632 (10.8%)
II	293 / 421 (69.6%)	162 / 211 (76.8%)	455 / 632 (72.0%)
III	77 / 421 (18.3%)	32 / 211 (15.2%)	109 / 632 (17.2%)
割付け因子			
ATTRm-CM	41 / 421 (9.7%)	20 / 211 (9.5%)	61 / 632 (9.7%)
ATTRwt-CM	380 / 421 (90.3%)	191 / 211 (90.5%)	571 / 632 (90.3%)
NT-proBNP ≤ 3000 pg/mL	272 / 421 (64.6%)	136 / 211 (64.5%)	408 / 632 (64.6%)
NT-proBNP > 3000 pg/mL	149 / 421 (35.4%)	75 / 211 (35.5%)	224 / 632 (35.4%)
eGFR が 45 mL/min/1.73 m^2 以上	344 / 421 (81.7%)	173 / 211 (82.0%)	517 / 632 (81.8%)
eGFR が 45 mL/min/1.73 m^2 未満	77 / 421 (18.3%)	38 / 211 (18.0%)	115 / 632 (18.2%)

注：カテゴリカル変数では欠測値でない値の割合を示す。
略語：ATTR-CM = トランスサイレチン型心アミロイドーシス；ATTRm-CM（= ATTRv-CM）= 遺伝性 ATTR-CM；ATTRwt CM = 野生型 ATTR-CM；BMI = 体格指数；eGFR = 推算糸球体濾過量；NT-proBNP = 脳性ナトリウム利尿ペプチド前駆体 N 端フラグメント；NYHA = New York Heart Association；Q = 四分位
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.1.4.2

1.3.1.2 国内 302 試験

国内 302 試験の安全性解析対象集団は FAS と同一であり、その人口統計学的特性及びベースラインの疾患特性は M2.7.3-2.2.3 項に示す。

全体で、平均年齢（SD）は 76.5（6.31）歳であり、男性の割合が高かった（男性 88.0%、女性 12.0%）。また、ATTR-CM の遺伝子型は遺伝性 ATTR-CM（ATTRv-CM）が 8.0%、ATTRwt-CM が 92.0%、NYHA 心機能分類は I が 0%、II が 96.0%、III が 4.0%、eGFR は 45 mL/min/1.73 m^2 以上が 100.0%、45 mL/min/1.73 m^2 未満が 0%であった。

1.3.1.3 海外 201 試験

海外 201 試験の安全性解析対象集団での人口統計学的特性及びベースライン特性を Table 11 に示す。

各群の年齢の平均値（SD）の範囲は 73.2～75.4（5.65～7.35）歳であり、いずれの群でも白人の割合が高く（62.5%～76.5%）、男性の割合が高かった（87.5%～100%）。

Table 11: 海外 201 試験での人口統計学的特性及びベースライン特性（安全性解析対象集団）

	アコラミジス 400 mg 群 N = 16	アコラミジス 800 mg 群 N = 16	プラセボ群 N = 17
年齢（年）			
n	16	16	17
平均値（標準偏差）	73.8 (5.65)	75.4 (6.81)	73.2 (7.35)
中央値（Q1、Q3）	73.5 (71.0, 78.0)	76.0 (69.0, 80.0)	72.0 (67.0, 79.0)
最小値、最大値	60, 83	67, 86	60, 85
年齢分布（歳）			
65未満	1 (6.3%)	0	1 (5.9%)
65以上75未満	9 (56.3%)	8 (50.0%)	9 (52.9)
75以上	6 (37.5%)	8 (50.0%)	7 (41.2)
性別			
男性	14 (87.5)	14 (87.5%)	17 (100%)
女性	2 (12.5%)	2 (12.5)	0
民族			
ヒスパニック／ラテン系	1 (6.3%)	1 (6.3%)	2 (11.8%)
ヒスパニック／ラテン系以外	14 (87.5%)	14 (87.5%)	15 (88.2%)
報告なし	1 (6.3%)	0	0
不明	0	1 (6.3%)	0
人種			
アジア系	1 (6.3%)	0	0
黒人／アフリカ系アメリカ人	4 (25.0%)	3 (18.8%)	3 (17.6%)
白人	10 (62.5%)	12 (75.0%)	13 (76.5%)
その他	1 (6.3)	1 (6.3%)	1 (5.9%)
BMI（kg/m^2）			
n	16	16	17
平均値（標準偏差）	25.42 (3.284)	26.29 (3.705)	27.05 (3.604)
中央値（Q1、Q3）	25.70 (23.25, 27.50)	25.80 (23.05, 29.45)	26.40 (24.70, 29.20)
最小値、最大値	19.5, 30.8	20.5, 32.3	22.0, 34.4
ATTR-CM 遺伝子型			
ATTRm-CM	6 (37.5%)	5 (31.3%)	3 (17.6%)
ATTRwt-CM	10 (62.5%)	11 (68.8%)	14 (82.4%)

略語：ATTR-CM = トランスサイレチン型心アミロイドーシス；ATTRm-CM（= ATTRv-CM）= 遺伝性 ATTR-CM；ATTRwt CM = 野生型 ATTR-CM；BMI = 体格指数；Q = 四分位
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.1.2.2

1.3.1.4 併合解析

1.3.1.4.1 アコラミジス治療集団

アコラミジス治療集団での人口統計学的特性及びベースライン特性を Table 12 に示す。

全体で、アコラミジス治療集団の平均年齢（SD）は 77.55（6.581）歳であった。大部分は男性（92.2%）、白人（87.2%）、ATTRwt-CM（90.1%）、NYHA 心機能分類 II（61.6%）であった。

Table 12: アコラミジス治療集団での人口統計学的特性及びベースライン特性

	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468	**AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95**	**全体（アコラミジス治療集団） N = 563**
年齢（歳）			
n	468	95	563
平均値（標準偏差）	77.17 (6.531)	79.44 (6.534)	77.55 (6.581)
中央値（Q1、Q3）	78.00 (73.00, 82.00)	80.00 (75.00, 84.00)	78.00 (73.00, 83.00)
最小値、最大値	50.0, 90.0	59.0, 93.0	50.0, 93.0
年齢分布（歳）			
65未満	14 (3.0%)	3 (3.2%)	17 (3.0%)
65以上78未満	214 (45.7%)	33 (34.7%)	247 (43.9%)
78以上	240 (51.3%)	59 (62.1%)	299 (53.1%)
性別			
男性	427 (91.2%)	92 (96.8%)	519 (92.2%)
女性	41 (8.8%)	3 (3.2%)	44 (7.8%)
民族			
ヒスパニック／ラテン系	12 (2.6%)	2 (2.1%)	14 (2.5%)
ヒスパニック／ラテン系以外	443 (94.7%)	90 (94.7%)	533 (94.7%)
報告なし	12 (2.6%)	3 (3.2%)	15 (2.7%)
不明	1 (0.2%)	0	1 (0.2%)
人種			
アジア系	11 (2.4%)	3 (3.2%)	14 (2.5%)
黒人／アフリカ系アメリカ人	29 (6.2%)	0	29 (5.2%)
白人	403 (86.1%)	88 (92.6%)	491 (87.2%)
その他	7 (1.5%)	0	7 (1.2%)
多様人種	2 (0.4%)	0	2 (0.4%)
報告なし	16 (3.4%)	4 (4.2%)	20 (3.6%)
BMI（kg/m^2）			
n	420	95	515
平均値（標準偏差）	27.07 (3.793)	26.04 (3.723)	26.88 (3.798)
中央値（Q1、Q3）	26.72 (24.46, 29.20)	25.42 (23.48, 28.60)	26.47 (24.24, 29.17)
最小値、最大値	18.1, 42.7	20.0, 37.8	18.1, 42.7
ATTR-CM 型			
ATTRm-CM	53 (11.3%)	3 (3.2%)	56 (9.9%)
ATTRwt-CM	415 (88.7%)	92 (96.8%)	507 (90.1%)
ベースラインの eGFR (mL/min/1.73 m^2)			
n	421	87	508
平均値（標準偏差）	106.38 (39.860)	119.12 (36.324)	108.56 (39.536)
中央値（Q1、Q3）	100.00 (82.10, 122.30)	111.10 (90.70, 140.50)	100.90 (83.65, 125.30)
最小値、最大値	37.0, 559.8	50.0, 224.4	37.0, 559.8
NYHA 心機能分類			
I	51 (10.9%)	9 (9.5%)	60 (10.7%)
II	293 (62.6%)	54 (56.8%)	347 (61.6%)
III	77 (16.5%)	30 (31.6%)	107 (19.0%)
IV	0	1 (1.1%)	1 (0.2%)

略語 : ATTR-CM = トランスサイレチン型心アミロイドーシス ; ATTRm-CM（= ATTRv-CM）= 遺伝性 ATTR-CM ; ATTRwt CM = 野生型 ATTR-CM ; BMI = 体格指数 ; eGFR = 推算糸球体濾過量 ; NYHA = New York Heart Association ; Q = 四分位
Source: 5.3.5.3.1 項 ISS Table 2.1.1.2

1.3.1.4.2 OLE 集団

OLE 集団（OLE 試験組入れ時）での人口統計学的特性及びベースライン特性の要約を Table 13 に示す。

全体の平均年齢（SD）は 78.37（6.861）歳であった。移行前の試験である海外 201 試験及び海外 301 試験の人口統計学的特性と同様、大部分が男性（93.4%）で白人（87.3%）であり、また、NYHA 心機能分類は 50.7%が II であった。

Table 13: OLE 集団での人口統計学的特性及びベースライン特性

	AG10-202 試験 N = 47	**AG10-304 試験 N = 300**	**全体 N = 347**
年齢（歳）			
n	47	300	347
平均値（標準偏差）	74.26 (6.758)	79.02 (6.661)	78.37 (6.861)
中央値（Q1、Q3）	73.00 (69.00, 80.00)	80.00 (75.00, 83.50)	79.00 (74.00, 83.00)
最小値、最大値	60.0, 86.0	52.0, 93.0	52.0, 93.0
年齢分布（歳）			
65未満	2 (4.3%)	8 (2.7%)	10 (2.9%)
65以上78未満	28 (59.6%)	111 (37.0%)	139 (40.1%)
78以上	17 (36.2%)	181 (60.3%)	198 (57.1%)
性別			
男性	43 (91.5%)	281 (93.7%)	324 (93.4%)
女性	4 (8.5%)	19 (6.3%)	23 (6.6%)
民族			
ヒスパニック／ラテン系	4 (8.5%)	6 (2.0%)	10 (2.9%)
ヒスパニック／ラテン系以外	42 (89.4%)	287 (95.7%)	329 (94.8%)
報告なし	1 (2.1%)	7 (2.3%)	8 (2.3%)
人種			
アジア系	1 (2.1%)	7 (2.3%)	8 (2.3%)
黒人／アフリカ系アメリカ人	9 (19.1%)	11 (3.7%)	20 (5.8%)
白人	35 (74.5%)	268 (89.3%)	303 (87.3%)
その他	2 (4.3%)	1 (0.3%)	3 (0.9%)
多様人種	0	1 (0.3%)	1 (0.3%)
報告なし	0	12 (4.0%)	12 (3.5%)
BMI（kg/m^2）			
n	0	285	285
平均値（標準偏差）	-	26.51 (4.068)	26.51 (4.068)
中央値（Q1、Q3）	-	25.86 (23.72, 28.92)	25.86 (23.72, 28.92)
最小値、最大値	-	19.5, 42.0	19.5, 42.0
ベースラインの eGFR ($mL/min/1.73\ m^2$)			
n	0	282	282
平均値（標準偏差）	-	55.78 (19.653)	55.78 (19.653)
中央値（Q1、Q3）	-	53.00 (41.00, 69.00)	53.00 (41.00, 69.00)
最小値、最大値	-	20.0, 141.0	20.0, 141.0
NYHA 心機能分類			
I	0	55 (18.3%)	55 (15.9%)
II	0	176 (58.7%)	176 (50.7%)
III	0	64 (21.3%)	64 (18.4%)
IV	0	4 (1.3%)	4 (1.2%)

略語：BMI = 体格指数；eGFR = 推算糸球体濾過量；NYHA = New York Heart Association；Q = 四分位
Source: 5.3.5.3.1 項 ISS Table 1.1.1.2

2 有害事象

2.1 有害事象の解析

2.1.1 有害事象の概要

2.1.1.1 海外 301 試験

海外 301 試験の安全性解析対象集団での有害事象の発現状況の概要を Table 14 に示す。

有害事象はアコラミジス群 98.1%、プラセボ群 97.6%に発現し、治験薬との関連性が否定できない有害事象はアコラミジス群 11.9%、プラセボ群 5.2%に認められた。また、死亡に至った有害事象はアコラミジス群 14.3%（60 名）、プラセボ群 17.1%（36 名）、重篤な有害事象はアコラミジス群 54.6%、プラセボ群 64.9%、治験薬の投与中止に至った有害事象はアコラミジス群 9.3%、プラセボ群 8.5%に発現した。

Table 14: 海外 301 試験での有害事象の発現状況の概要（安全性解析対象集団）

	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
有害事象	413 (98.1%)	206 (97.6%)
死亡に至った有害事象	60 (14.3%)	36 (17.1%)
入院に至った有害事象	212 (50.4%)	128 (60.7%)
治験薬の投与中止に至った有害事象	39 (9.3%)	18 (8.5%)
治験薬の減量に至った有害事象	4 (1.0%)	0
重篤な有害事象	230 (54.6%)	137 (64.9%)
治験薬の投与中止に至った重篤な有害事象	21 (5.0%)	15 (7.1%)
治験薬の減量に至った重篤な有害事象	2 (0.5%)	0
治験薬との関連性が否定できない有害事象	50 (11.9%)	11 (5.2%)
治験薬との関連性が否定できない重篤な有害事象	2 (0.5%)	0
重度の有害事象	157 (37.3%)	96 (45.5%)

Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.1

2.1.1.2 国内 302 試験

国内 302 試験の安全性解析対象集団での有害事象の発現状況の概要を Table 15 に示す。

有害事象は 100%（25/25 名）に発現し、治験薬との関連性が否定できない有害事象は 12.0%（3 名）に認められた。また、重篤な有害事象は 48.0%（12 名）、治験薬の投与中止に至った有害事象は 8.0%（2 名）に発現した。なお、本試験で死亡した患者はいなかった。

Table 15: 国内 302 試験での有害事象の発現状況の概要（安全性解析対象集団）

	アコラミジス N = 25 n (%)
有害事象	25 (100%)
重篤な有害事象	12 (48.0%)
死亡に至った有害事象	0
治験薬の投与中止に至った有害事象	2 (8.0%)
治験薬の投与中止に至った重篤な有害事象	0
治験薬との関連性が否定できない有害事象	3 (12.0%)
重症度別有害事象	
Grade 3	10 (40.0%)
Grade 4	1 (4.0%)
Grade 5	0
治験薬との関連性が否定できない重篤な有害事象	0

有害事象の重症度は米国国立がん研究所の CTCAE version 5.0 を用いて Grade 分類した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.1

2.1.1.3 海外 201 試験

海外 201 試験の安全性解析対象集団での有害事象の発現状況の概要を Table 16 に示す。

有害事象はアコラミジス 400 mg 群 62.5%、800 mg 群 68.8%、プラセボ群 88.2%に発現し、治験薬との関連性が否定できない有害事象はアコラミジス 400 mg 群 18.8%、800 mg 群 37.5%、プラセボ群 5.9%に認められた。また、重篤な有害事象はアコラミジス 400 mg 群 6.3%、プラセボ群 11.8%に発現した。なお、死亡に至った有害事象、及び治験薬の投与中止に至った有害事象は認められなかった。

Table 16: 海外 201 試験での有害事象の発現状況の概要（安全性解析対象集団）

	アコラミジス 400 mg 群 N = 16 n (%)	アコラミジス 800 mg 群 N = 16 n (%)	プラセボ群 N = 17 n (%)
有害事象	10 (62.5)	11 (68.8)	15 (88.2)
治験薬との関連性が否定できない有害事象	3 (18.8)	6 (37.5)	1 (5.9)
死亡に至った有害事象	0	0	0
重篤な有害事象	1 (6.3)	0	2 (11.8)
治験薬の投与中止に至った有害事象	0	0	0
治験中止に至った有害事象	0	0	0

Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.1.2

2.1.1.4 併合解析

2.1.1.4.1 アコラミジス治療集団

アコラミジス治療集団での有害事象の発現状況の概要を Table 17 に示す。

アコラミジス治療集団全体で、有害事象は 92.4%に発現し、治験薬との関連性が否定できない有害事象は 10.8%に認められた。また、死亡に至った有害事象は 14.9%、重篤な有害事象は 56.1%、治験薬の投与中止に至った有害事象は 9.1%に発現した。

Table 17: アコラミジス治療集団での有害事象の発現状況の概要

	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468	AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95		全体（アコラミジス治療集団） N = 563
		アコラミジス投与時 AG10-304 試験	プラセボ投与時 AG10-301 試験	
	n (%)	n (%)	n (%)	n (%)
有害事象	461 (98.5%)	59 (62.1%)	91 (95.8%)	520 (92.4%)
重篤な有害事象	286 (61.1%)	30 (31.6%)	54 (56.8%)	316 (56.1%)
重度の有害事象	206 (44.0%)	24 (25.3%)	31 (32.6%)	230 (40.9%)
治験薬との関連性が否定できない有害事象	56 (12.0%)	5 (5.3%)	4 (4.2%)	61 (10.8%)
治験薬の投与中止に至った有害事象	49 (10.5%)	2 (2.1%)	0	51 (9.1%)
死亡に至った有害事象	73 (15.6%)	11 (11.6%)	0	84 (14.9%)
治験薬との関連性が否定できない重篤な有害事象	3 (0.6%)	0	0	3 (0.5%)

Source: 5.3.5.3.1 項 ISS Table 2.1.3.1

2.1.1.4.1.1 曝露量で調整した有害事象の発現率

アコラミジス治療集団に対し、曝露量で調整した有害事象（患者数）の発現率（EAIR）を、有害事象が認められた患者数÷総曝露年/100 人年で算出した。曝露量で調整した有害事象の発現状況を、Table 18 に示す。

有害事象は 350.6/100 人年に認められた。また、死亡に至った有害事象は 7.2/100 人年、重篤な有害事象は 39.6/100 人年、治験薬の投与中止に至った有害事象は 4.4/100 人年に発現した。

Table 18: アコラミジス治療集団での曝露量で調整した有害事象の発現状況の概要

	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）
有害事象	130.5	461 (353.2)	17.8	59 (332.0)	40.7	91 (223.5)	148.3	520 (350.6)
重篤な有害事象	762.6	286 (37.5)	36.0	30 (83.3)	161.1	54 (33.5)	798.6	316 (39.6)
治験薬と関連性が否定できない有害事象	1028.4	56 (5.4)	42.8	5 (11.7)	228.8	4 (1.7)	1071.3	61 (5.7)
治験薬の投与中止に至った有害事象	1116.8	49 (4.4)	43.7	2 (4.6)	233.6	0	1160.6	51 (4.4)
死亡に至った有害事象	1122.8	73 (6.5)	42.8	11 (25.7)	233.6	0	1165.7	84 (7.2)
治験薬と関連性が否定できない重篤な有害事象	1124.7	3 (0.3)	43.8	0	233.6	0	1168.5	3 (0.3)

Source: 5.3.5.3.1 項 ISS Table 2.1.3.2、ISS Table 2.1.3.3、ISS Table 2.1.3.4、ISS Table 2.1.3.5、ISS Table 2.1.3.6、ISS Table 2.1.3.12

2.1.1.4.2 OLE 集団

OLE 集団での有害事象の概要を Table 19 に示す。

OLE 集団全体で、有害事象は 58.8%に発現し、治験薬との関連性が否定できない有害事象は 3.5%に認められた。また、死亡に至った有害事象は 6.9%、重篤な有害事象は 31.4%、治験薬の投与中止に至った有害事象は 3.5%に発現した。

Table 19: OLE 集団での有害事象の発現状況の概要

	AG10-202 試験 N = 47 n（%）	AG10-304 試験 N = 300 n（%）	全体 N = 347 n（%）
有害事象	47 (100.0%)	157 (52.3%)	204 (58.8%)
重篤な有害事象	37 (78.7%)	72 (24.0%)	109 (31.4%)
重度の有害事象	30 (63.8%)	56 (18.7%)	86 (24.8%)
治験薬との関連性が否定できない有害事象	5 (10.6%)	7 (2.3%)	12 (3.5%)
治験薬の投与中止に至った有害事象	9 (19.1%)	3 (1.0%)	12 (3.5%)
死亡に至った有害事象	11 (23.4%)	13 (4.3%)	24 (6.9%)
治験薬との関連性が否定できない重篤な有害事象	1 (2.1%)	0	1 (0.3%)

Source: 5.3.5.3.1 項 ISS Table 1.1.3.1

2.1.2 比較的よくみられる有害事象

2.1.2.1 海外 301 試験

海外 301 試験の安全性解析対象集団で比較的よくみられた有害事象（いずれかの群で MedDRA の基本語［PT］の発現割合 10%以上）を Table 20 に示し、すべての有害事象を M2.7.6-9 に示す。

MedDRA の器官別大分類（SOC）別の主な有害事象（発現割合 50%以上）は、アコラミジス群で「感染症および寄生虫症」（58.4%）、「心臓障害」（54.6%）、「胃腸障害」（52.5%）であり、プラセボ群で「心臓障害」（68.2%）、「感染症および寄生虫症」（55.0%）であった。

PT 別の主な有害事象（発現割合 20%以上）は、アコラミジス群で「心不全」（24.0%）、「COVID-19」（21.1%）であり、プラセボ群で「心不全」（39.3%）、「心房細動」（21.8%）であった。また、プラセボ群と比較してアコラミジス群での発現割合が 5%以上高かった PT 別の有害事象は「COVID-19」（アコラミジス群 21.1%、プラセボ群 14.2%）のみであり、MedDRA の標準検索式（広義）での新型コロナウイルス感染症（COVID-19）（定義の詳細は 5.3.5.1.2 項 AG10-301 CSR 16.1.9 解析計画書 12.3 項参照）の発現割合は、アコラミジス群 24.9%、プラセボ群：19.9%であった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.18）。

Table 20: **海外 301 試験で比較的よくみられた有害事象（いずれかの群で基本語の発現割合 10%以上）（安全性解析対象集団）**

器官別大分類 **基本語**	**アコラミジス群** **N=421** **n (%)**	**プラセボ群** **N=211** **n (%)**
有害事象発現患者数	413 (98.1%)	206 (97.6%)
心臓障害	230 (54.6%)	144 (68.2%)
心不全	101 (24.0%)	83 (39.3%)
心房細動	70 (16.6%)	46 (21.8%)
感染症および寄生虫症	246 (58.4%)	116 (55.0%)
COVID-19	89 (21.1%)	30 (14.2%)
尿路感染	51 (12.1%)	28 (13.3%)
胃腸障害	221 (52.5%)	98 (46.4%)
便秘	52 (12.4%)	32 (15.2%)
下痢	49 (11.6%)	16 (7.6%)
筋骨格系および結合組織障害	184 (43.7%)	83 (39.3%)
関節痛	48 (11.4%)	23 (10.9%)
神経系障害	182 (43.2%)	77 (36.5%)
浮動性めまい	46 (10.9%)	23 (10.9%)
代謝および栄養障害	149 (35.4%)	85 (40.3%)
痛風	47 (11.2%)	17 (8.1%)
呼吸器、胸郭および縦隔障害	146 (34.7%)	86 (40.8%)
呼吸困難	52 (12.4%)	40 (19.0%)
一般・全身障害および投与部位の状態	144 (34.2%)	79 (37.4%)
疲労	42 (10.0%)	26 (12.3%)
末梢性浮腫	33 (7.8%)	25 (11.8%)
傷害、中毒および処置合併症	137 (32.5%)	81 (38.4%)
転倒	67 (15.9%)	39 (18.5%)
腎および尿路障害	142 (33.7%)	64 (30.3%)
急性腎障害	52 (12.4%)	22 (10.4%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.2

2.1.2.2 国内 302 試験

国内 302 試験の安全性解析対象集団で比較的よくみられた有害事象（PT の発現割合 10%以上）を Table 21 に示し、すべての有害事象を M2.7.6-10 に示す。

SOC 別の主な有害事象（発現割合 50%以上）は、「胃腸障害」（56.0%）、「感染症および寄生虫症」（52.0%）であった。

PT 別の主な有害事象（発現割合 20%以上）は、「便秘」（28.0%）、「上咽頭炎」（24.0%）、「発熱」（20.0%）、「背部痛」（20.0%）であった。

Table 21: 国内 302 試験で比較的よくみられた有害事象（基本語の発現割合 10%以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス N = 25 n (%)
有害事象発現患者数	25 (100%)
心臓障害	10 (40.0%)
心不全	3 (12.0%)
胃腸障害	14 (56.0%)
便秘	7 (28.0%)
嘔吐	3 (12.0%)
一般・全身障害および投与部位の状態	8 (32.0%)
発熱	5 (20.0%)
感染症および寄生虫症	13 (52.0%)
COVID-19	4 (16.0%)
上咽頭炎	6 (24.0%)
筋骨格系および結合組織障害	9 (36.0%)
関節痛	3 (12.0%)
背部痛	5 (20.0%)
腎および尿路障害	6 (24.0%)
血尿	4 (16.0%)
腎機能障害	4 (16.0%)
皮膚および皮下組織障害	7 (28.0%)
発疹	3 (12.0%)

有害事象名は MedDRA/J version 26.1 を用いて表示した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.2.1

2.1.2.3 海外 201 試験

海外 201 試験の安全性解析対象集団で比較的よくみられた有害事象（いずれかの群で PT の発現患者数 2 名以上）を Table 22 に示し、すべての有害事象を M2.7.6-8 に示す。

PT 別の主な有害事象（発現患者数 3 名以上）は、アコラミジス 800 mg 群で「便秘」（3 名、18.8%）、「下痢」（3 名、18.8%）、プラセボ群で「動悸」（3 名、17.6%）であり、アコラミジス 400 mg 群ではいずれの有害事象も 2 名以下であった。

Table 22: 海外 201 試験で比較的よくみられた PT 別の有害事象（いずれかの群で基本語の発現患者数 2 名以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス 400 mg 群 N = 16 n (%)	アコラミジス 800 mg 群 N = 16 n (%)	プラセボ群 N = 17 n (%)
有害事象発現患者数	10 (62.5)	11 (68.8)	15 (88.2)
胃腸障害	3 (18.8)	7 (43.8)	2 (11.8)
便秘	1 (6.3)	3 (18.8)	2 (11.8)
下痢	2 (12.5)	3 (18.8)	0
筋骨格系および結合組織障害	2 (12.5)	4 (25.0)	3 (17.6)
筋痙縮	1 (6.3)	1 (6.3)	2 (11.8)
四肢痛	0	2 (12.5)	1 (5.9)
臨床検査	5 (31.5)	0	3 (17.6)
頚静脈圧上昇	2 (12.5)	0	0
代謝および栄養障害	0	2 (12.5)	5 (29.4)
体液貯留	0	1 (6.3)	2 (11.8)
心臓障害	1 (6.3)	2 (12.5)	3 (17.6)
心房細動	1 (6.3)	2 (12.5)	1 (5.9)
動悸	0	0	3 (17.6)
一般・全身障害および投与部位の状態	2 (12.5)	1 (6.3)	3 (17.6)
疲労	0	1 (6.3)	2 (11.8)
末梢性浮腫	2 (12.5)	0	0
神経系障害	1 (6.3)	3 (18.8)	2 (11.8)
頭痛	0	1 (6.3)	2 (11.8)
浮動性めまい	0	2 (12.5)	0
傷害、中毒および処置合併症	1 (6.3)	0	4 (23.5)
挫傷	0	0	2 (11.8)
転倒	0	0	2 (11.8)
呼吸器、胸郭および縦隔障害	1 (6.3)	1 (6.3)	3 (17.6)
呼吸困難	1 (6.3)	0	2 (11.8)
咳嗽	0	0	2 (11.8)
腎および尿路障害	0	1 (6.3)	2 (11.8)
頻尿	0	0	2 (11.8)

有害事象名は MedDRA/J version 21.0 を用いて表示した。
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.2

2.1.2.4 併合解析

2.1.2.4.1 アコラミジス治療集団

アコラミジス治療集団での併合解析では、有害事象の発現率として EAIR を算出し評価した。

アコラミジス治療集団で比較的よくみられた有害事象（全体で PT の EAIR が 5/100 人年以上）を Table 23 に示し、すべての有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.2 に示す。

アコラミジス治療集団全体での PT 別の主な有害事象（EAIR が 10/100 人年以上）は「心不全」（11.3/100 人年）及び「COVID-19」（10.2/100 人年）であった。

Table 23: アコラミジス治療集団で比較的よくみられた有害事象（全体で基本語の EAIR が 5/100 人年以上）

器官別大分類 基本語	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）
有害事象発現患者数	130.5	461 (353.2)	17.8	59 (332.0)	40.7	91 (223.5)	148.3	520 (350.6)
感染症および寄生虫症	670.0	297 (44.3)	35.9	25 (69.5)	154.4	62 (40.2)	706.0	322 (45.6)
COVID-19	1039.1	105 (10.1)	43.1	5 (11.6)	220.9	17 (7.7)	1082.2	110 (10.2)
尿路感染	1047.1	56 (5.3)	42.5	4 (9.4)	223.1	11 (4.9)	1089.6	60 (5.5)
心臓障害	733.7	268 (36.5)	33.4	25 (75.0)	142.4	59 (41.4)	767.1	293 (38.2)
心不全	1008.5	109 (10.8)	39.5	9 (22.8)	186.4	32 (17.2)	1048.1	118 (11.3)
心房細動	997.4	87 (8.7)	39.9	7 (17.5)	211.3	18 (8.5)	1037.3	94 (9.1)
胃腸障害	700.2	256 (36.6)	37.6	17 (45.2)	168.5	48 (28.5)	737.8	273 (37.0)
便秘	1032.7	64 (6.2)	43.5	1 (2.3)	218.8	11 (5.0)	1076.2	65 (6.0)
下痢	1043.2	57 (5.5)	42.6	4 (9.4)	224.7	9 (4.0)	1085.9	61 (5.6)
筋骨格系および結合組織障害	738.0	223 (30.2)	39.6	9 (22.7)	169.6	43 (25.3)	777.6	232 (29.8)
関節痛	1040.2	59 (5.7)	42.5	3 (7.1)	213.2	13 (6.1)	1082.7	62 (5.7)
神経系障害	779.5	213 (27.3)	40.4	8 (19.8)	184.6	34 (18.4)	819.9	221 (27.0)
浮動性めまい	1028.7	53 (5.2)	42.7	2 (4.7)	218.6	11 (5.0)	1071.4	55 (5.1)
代謝および栄養障害	841.3	184 (21.9)	40.9	14 (34.2)	186.5	39 (20.9)	882.3	198 (22.4)
痛風	1029.2	54 (5.2)	42.9	3 (7.0)	224.1	8 (3.6)	1072.2	57 (5.3)
呼吸器、胸郭および縦隔障害	813.4	181 (22.3)	39.8	9 (22.6)	169.6	39 (23.0)	853.2	190 (22.3)
呼吸困難	1025.7	64 (6.2)	43.5	2 (4.6)	205.7	18 (8.7)	1069.2	66 (6.2)
傷害、中毒および処置合併症	880.5	175 (19.9)	38.2	16 (41.9)	185.6	37 (19.9)	918.6	191 (20.8)
転倒	1002.5	93 (9.3)	41.5	4 (9.6)	222.3	13 (5.8)	1044.1	97 (9.3)
一般・全身障害および投与部位の状態	843.2	177 (21.0)	40.9	7 (17.1)	179.7	39 (21.7)	884.1	184 (20.8)
疲労	1024.8	57 (5.6)	43.0	1 (2.3)	213.3	13 (6.1)	1067.8	58 (5.4)
腎および尿路障害	880.6	170 (19.3)	39.6	14 (35.4)	202.3	24 (11.9)	920.2	184 (20.0)
急性腎障害	1060.8	65 (6.1)	43.1	4 (9.3)	220.6	9 (4.1)	1103.9	69 (6.3)

略語：EAIR = 曝露量で調整した有害事象の発現率
有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 2.1.3.2

2.1.2.4.2 OLE 集団

OLE 集団で比較的よくみられた有害事象（全体で PT の発現割合 5%以上）を Table 24 に示し、すべての有害事象を 5.3.5.3.1 項 ISS Table 1.1.3.2 に示す。

OLE 集団全体での PT 別の主な有害事象（発現割合 10%以上）は「転倒」（10.1%）であった。

Table 24: OLE 集団で比較的よくみられた有害事象（全体で基本語の発現割合 5%以上）

器官別大分類 基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
有害事象発現患者数	47 (100.0%)	157 (52.3%)	204 (58.8%)
感染症および寄生虫症	34 (72.3%)	70 (23.3%)	104 (30.0%)
COVID-19	3 (6.4%)	19 (6.3%)	22 (6.3%)
心臓障害	32 (68.1%)	48 (16.0%)	80 (23.1%)
心房細動	11 (23.4%)	14 (4.7%)	25 (7.2%)
心不全	6 (12.8%)	14 (4.7%)	20 (5.8%)
急性心不全	12 (25.5%)	7 (2.3%)	19 (5.5%)
傷害、中毒および処置合併症	26 (55.3%)	35 (11.7%)	61 (17.6%)
転倒	22 (46.8%)	13 (4.3%)	35 (10.1%)
腎および尿路障害	23 (48.9%)	28 (9.3%)	51 (14.7%)
急性腎障害	13 (27.7%)	5 (1.7%)	18 (5.2%)

有害事象名は MedDRA/J Version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.2

2.1.3 治験薬との関連性が否定できない有害事象

2.1.3.1 海外 301 試験

海外 301 試験の安全性解析対象集団での治験薬との関連性が否定できない主な有害事象（いずれかの群で PT の発現割合 1%以上）を Table 25 に示し、治験薬との関連性が否定できないすべての有害事象を M2.7.6-9 に示す。

PT 別の治験薬との関連性が否定できない有害事象の発現割合はいずれも 2%未満であり、アコラミジス群で最も発現割合の高かった治験薬との関連性が否定できない有害事象は「悪心」(1.4%)であった。

Table 25: 海外 301 試験での治験薬との関連性が否定できない有害事象（いずれかの群で基本語の発現割合 1%以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
治験薬との関連性が否定できない有害事象発現患者数	50 (11.9%)	11 (5.2%)
胃腸障害	20 (4.8%)	1 (0.5%)
悪心	6 (1.4%)	1 (0.5%)
下痢	4 (1.0%)	0
皮膚および皮下組織障害	7 (1.7%)	2 (0.9%)
発疹	4 (1.0%)	1 (0.5%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.5

2.1.3.2 国内 302 試験

国内 302 試験の安全性解析対象集団での治験薬との関連性が否定できないすべての有害事象を Table 26 に示す。

PT 別の治験薬との関連性が否定できない有害事象は 3 事象のみであり、その発現患者数は 2 名（8.0%）又は 1 名（4.0%）であった。

Table 26: 国内 302 試験での治験薬との関連性が否定できない有害事象（安全性解析対象集団）

器官別大分類 基本語	アコラミジス N = 25 n (%)
治験薬との関連性が否定できない有害事象発現患者数	3 (12.0%)
胃腸障害	1 (4.0%)
便秘	1 (4.0%)
腎および尿路障害	2 (8.0%)
腎機能障害	2 (8.0%)
皮膚および皮下組織障害	1 (4.0%)
薬疹	1 (4.0%)

有害事象名は MedDRA/J version 26.1 を用いて表示した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.3.2

2.1.3.3 海外 201 試験

海外 201 試験の安全性解析対象集団での治験薬との関連性が否定できない主な有害事象（いずれかの群で PT の発現患者数 2 名以上）を Table 27 に示し、治験薬との関連性が否定できないすべての有害事象を M2.7.6-8 に示す。

PT 別で発現割合が 2 名以上であった治験薬との関連性が否定できない有害事象は、アコラミジス 800 mg 群で「便秘」（3 名、18.8%）及び「下痢」（2 名、12.5%）であった。

Table 27: 海外 201 試験での治験薬との関連性が否定できない有害事象（いずれかの群で基本語の発現患者数 2 名以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス 400 mg 群 N = 16 n (%)	アコラミジス 800 mg 群 N = 16 n (%)	プラセボ群 N = 17 n (%)
治験薬との関連性が否定できない有害事象発現患者数	3 (18.8)	6 (37.5)	1 (5.9)
胃腸障害	1 (6.3)	6 (37.5)	1 (5.9)
便秘	0	3 (18.8)	1 (5.9)
下痢	1 (6.3)	2 (12.5)	0

有害事象名は MedDRA/J version 21.0 を用いて表示した。
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.4.2

2.1.3.4 併合解析

2.1.3.4.1 アコラミジス治療集団

アコラミジス治療集団での治験薬との関連性が否定できない主な有害事象（全体で PT の EAIR が 0.3/100 人年以上）を Table 28 に示し、治験薬との関連性が否定できないすべての有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.3 に示す。

PT 別で発現率の高かった治験薬との関連性が否定できない有害事象（全体で PT の EAIR が 0.5/100 人年以上）は「悪心」（0.6/100 人年）、「下痢」（0.5/100 人年）及び「発疹」（0.5/100 人年）であった。

Table 28: アコラミジス治療集団での治験薬との関連性が否定できない有害事象（全体で基本語の EAIR が 0.3/100 人年以上）

器官別大分類 基本語	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）
治験薬との関連性が否定できない有害事象発現患者数	1028.4	56 (5.4)	42.8	5 (11.7)	228.8	4 (1.7)	1071.3	61 (5.7)
胃腸障害	1085.2	23 (2.1)	43.2	2 (4.6)	233.6	1 (0.4)	1128.4	25 (2.2)
悪心	1116.0	7 (0.6)	43.8	0	233.6	0	1159.8	7 (0.6)
下痢	1117.4	5 (0.4)	43.6	1 (2.3)	233.6	1 (0.4)	1161.0	6 (0.5)
腹部不快感	1122.6	3 (0.3)	43.8	0	233.6	0	1166.4	3 (0.3)
上腹部痛	1121.1	3 (0.3)	43.8	0	233.6	0	1164.9	3 (0.3)
消化不良	1127.2	3 (0.3)	43.8	0	233.6	0	1171.0	3 (0.3)
臨床検査	1102.9	12 (1.1)	43.7	1 (2.3)	233.6	0	1146.6	13 (1.1)
血中クレアチニン増加	1122.3	3 (0.3)	43.8	0	233.6	0	1166.1	3 (0.3)
皮膚および皮下組織障害	1112.2	8 (0.7)	43.7	1 (2.3)	233.6	0	1155.9	9 (0.8)
発疹	1116.4	5 (0.4)	43.7	1 (2.3)	233.6	0	1160.1	6 (0.5)
一般・全身障害および投与部位の状態	1120.4	5 (0.4)	43.7	1 (2.3)	232.2	1 (0.4)	1164.1	6 (0.5)
疲労	1121.3	3 (0.3)	43.8	0	232.2	1 (0.4)	1165.1	3 (0.3)

略語：EAIR = 曝露量で調整した有害事象の発現率
有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 2.1.3.3

2.1.3.4.2 OLE 集団

OLE 集団での治験薬との関連性が否定できないすべての有害事象を Table 29 に示す。

PT 別で発現割合の高かった治験薬との関連性が否定できない有害事象（全体の発現患者数 2 名以上）は「下痢」（3 名、0.9%）及び発疹（2 名、0.6%）であった。

Table 29: OLE 集団での治験薬との関連性が否定できない有害事象

器官別大分類 基本語	AG10-202 試験 N = 47 n（%）	AG10-304 試験 N = 300 n（%）	全体 N = 347 n（%）
治験薬との関連性が否定できない有害事象発現患者数	5 (10.6%)	7 (2.3%)	12 (3.5%)
胃腸障害	3 (6.4%)	3 (1.0%)	6 (1.7%)
下痢	1 (2.1%)	2 (0.7%)	3 (0.9%)
顕微鏡的大腸炎	1 (2.1%)	0	1 (0.3%)
嚥下障害	0	1 (0.3%)	1 (0.3%)
悪心	1 (2.1%)	0	1 (0.3%)
臨床検査	1 (2.1%)	2 (0.7%)	3 (0.9%)
抗凝固薬濃度治療量以上	1 (2.1%)	0	1 (0.3%)
甲状腺機能検査異常	0	1 (0.3%)	1 (0.3%)
体重減少	0	1 (0.3%)	1 (0.3%)

器官別大分類 基本語	AG10-202 試験 N = 47 n（%）	AG10-304 試験 N = 300 n（%）	全体 N = 347 n（%）
皮膚および皮下組織障害	1 (2.1%)	1 (0.3%)	2 (0.6%)
発疹	1 (2.1%)	1 (0.3%)	2 (0.6%)
紫斑	1 (2.1%)	0	1 (0.3%)
内分泌障害	0	1 (0.3%)	1 (0.3%)
バセドウ病	0	1 (0.3%)	1 (0.3%)
一般・全身障害および投与部位の状態	0	1 (0.3%)	1 (0.3%)
無力症	0	1 (0.3%)	1 (0.3%)
筋骨格系および結合組織障害	1 (2.1%)	0	1 (0.3%)
関節痛	1 (2.1%)	0	1 (0.3%)
神経系障害	1 (2.1%)	0	1 (0.3%)
健忘	1 (2.1%)	0	1 (0.3%)
頭痛	1 (2.1%)	0	1 (0.3%)
精神障害	1 (2.1%)	0	1 (0.3%)
不眠症	1 (2.1%)	0	1 (0.3%)
腎および尿路障害	1 (2.1%)	0	1 (0.3%)
急性腎障害	1 (2.1%)	0	1 (0.3%)
呼吸器、胸郭および縦隔障害	0	1 (0.3%)	1 (0.3%)
呼吸困難	0	1 (0.3%)	1 (0.3%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.5

2.1.4 重症度別の有害事象

2.1.4.1 海外 301 試験

海外 301 試験の安全性解析対象集団での主な重度の有害事象（いずれかの群で PT の発現割合 2%以上）を Table 30 に示す。

重度の有害事象の発現割合は、アコラミジス群 37.3%、プラセボ群 45.5%であった。PT 別で発現割合の高かった重度の有害事象（発現割合 5%以上）は、アコラミジス群で「心不全」（7.6%）、プラセボ群で「心不全」（12.8%）であった。

Table 30: 海外 301 試験での重度の有害事象（いずれかの群で基本語の発現割合 2%以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス群 N=421 n (%)	プラセボ群 N=211 n (%)
重度の有害事象発現患者数	157 (37.3%)	96 (45.5%)
心臓障害	72 (17.1%)	57 (27.0%)
心不全	32 (7.6%)	27 (12.8%)
心房細動	8 (1.9%)	7 (3.3%)
急性心不全	11 (2.6)	4 (1.9)
感染症および寄生虫症	31 (7.4%)	22 (10.4%)
COVID-19肺炎	1 (0.2%)	5 (2.4%)
腎および尿路障害	17 (4.0%)	7 (3.3%)
急性腎障害	11 (2.6%)	5 (2.4%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.3

2.1.4.2 国内 302 試験

国内 302 試験の安全性解析対象集団での Grade 3 以上の有害事象を重症度別に Table 31 に示す。

PT 別の Grade 3 及び Grade 4 の有害事象の発現患者数はいずれも 1 名（4.0%）であった。また、Grade 5 の有害事象は認められなかった。

Table 31: 国内 302 試験での Grade 3 以上の有害事象（安全性解析対象集団）

器官別大分類 基本語	アコラミジス N = 25 n (%)	
	Grade 3	Grade 4
Grade 3 又は Grade 4 の有害事象発現患者数	10 (40.0%)	1 (4.0%)
心臓障害	3 (12.0%)	1 (4.0%)
心房粗動	1 (4.0%)	0
慢性心不全	1 (4.0%)	0
洞停止	0	1 (4.0%)
洞結節機能不全	1 (4.0%)	0
胃腸障害	2 (8.0%)	0
出血性腸憩室	1 (4.0%)	0
鼠径ヘルニア	1 (4.0%)	0
感染症および寄生虫症	3 (12.0%)	0
穿孔性虫垂炎	1 (4.0%)	0
細菌性前立腺炎	1 (4.0%)	0
肺炎球菌性肺炎	1 (4.0%)	0
臨床検査	1 (4.0%)	0
血中クレアチンホスホキナーゼ MB 増加	1 (4.0%)	0
代謝および栄養障害	2 (8.0%)	0
脱水	1 (4.0%)	0
高カリウム血症	1 (4.0%)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (4.0%)	0
前立腺癌	1 (4.0%)	0
神経系障害	1 (4.0%)	0
手根管症候群	1 (4.0%)	0
製品の問題	1 (4.0%)	0
医療機器位置異常	1 (4.0%)	0
腎および尿路障害	1 (4.0%)	0
血尿	1 (4.0%)	0
呼吸器、胸郭および縦隔障害	1 (4.0%)	0
間質性肺疾患	1 (4.0%)	0
皮膚および皮下組織障害	1 (4.0%)	0
薬疹	1 (4.0%)	0

有害事象の重症度は米国国立がん研究所の CTCAE version 5.0 を用いて Grade 分類した。有害事象名は MedDRA/J version 26.1 を用いて表示した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.4.2

2.1.4.3 海外 201 試験

海外 201 試験の安全性解析対象集団でのすべての重度の有害事象を Table 32 に示す。

重度の有害事象の発現割合はアコラミジス 400 mg 群 0%、800 mg 群 6.3%、プラセボ群 5.9%であり、アコラミジス 800 mg 群で「急性腎障害」及び「感音性難聴」（同一の患者 1 名、6.3%）が、プラセボ群で「蜂巣炎」（1 名、5.9%）が発現した。

Table 32: 海外 201 試験での重度の有害事象（安全性解析対象集団）

器官別大分類 基本語	アコラミジス 400 mg 群 N = 16 n (%)	アコラミジス 800 mg 群 N = 16 n (%)	プラセボ群 N = 17 n (%)
重度の有害事象発現患者数	0	1 (6.3)	1 (5.9)
感染症および寄生虫症	0	0	1 (5.9)
蜂巣炎	0	0	1 (5.9)
腎および尿路障害	0	1 (6.3)	0
急性腎障害	0	1 (6.3)	0
耳および迷路障害	0	1 (6.3)	0
感音性難聴	0	1 (6.3)	0

有害事象名は MedDRA/J version 21.0 を用いて表示した。
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.3.1

2.1.4.4 併合解析

2.1.4.4.1 アコラミジス治療集団

アコラミジス治療集団での併合解析では重症度別の有害事象の評価は実施しなかった。

2.1.4.4.2 OLE 集団

OLE 集団での主な重度の有害事象（全体で PT の発現患者数 3 名以上）を Table 33 に示し、重症度別のすべての有害事象を 5.3.5.3.1 項 ISS Table 1.1.3.4 に示す。

OLE 集団全体での重度の有害事象の発現割合は 24.8%であり、PT 別で発現割合の高かった重度の有害事象（発現患者数 10 名以上）は「心不全」（12 名、3.5%）及び「急性心不全」（11 名、3.2%）であった。

Table 33: OLE 集団での重度の有害事象（全体で基本語の発現患者数 3 名以上）

基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
重度の有害事象発現患者数	30 (63.8%)	56 (18.7%)	86 (24.8%)
心不全	2 (4.3%)	10 (3.3%)	12 (3.5%)
急性心不全	8 (17.0%)	3 (1.0%)	11 (3.2%)
急性腎障害	5 (10.6%)	3 (1.0%)	8 (2.3%)
心房細動	3 (6.4%)	4 (1.3%)	7 (2.0%)
うっ血性心不全	5 (10.6%)	0	5 (1.4%)
心原性ショック	4 (8.5%)	1 (0.3%)	5 (1.4%)
貧血	3 (6.4%)	1 (0.3%)	4 (1.2%)
転倒	4 (8.5%)	0	4 (1.2%)
急性呼吸不全	1 (2.1%)	2 (0.7%)	3 (0.9%)
COVID-19	0	3 (1.0%)	3 (0.9%)
末期腎疾患	1 (2.1%)	2 (0.7%)	3 (0.9%)
低血圧	2 (4.3%)	1 (0.3%)	3 (0.9%)
腎機能障害	1 (2.1%)	2 (0.7%)	3 (0.9%)

有害事象名は MedDRA/J Version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.4

2.1.5 死亡

2.1.5.1 海外 301 試験

海外 301 試験の安全性解析対象集団での主な死亡に至った有害事象（いずれかの群で PT の発現患者数 2 名以上）を Table 34 に示し、すべての死亡に至った有害事象を M2.7.6-9 に示す。

死亡に至った有害事象の発現割合はアコラミジス群 14.3%、プラセボ群 17.1%であった。

SOC 別で最も発現割合の高かった死亡に至った有害事象は、いずれの群でも「心臓障害」（アコラミジス群 8.6%、プラセボ群 10.9%）であった。

また、PT 別で発現した死亡に至った有害事象は、心筋症の進行又は本患者集団で予測される併存疾患と一致しており、治験責任医師等によって治験薬と関連ありと判断された事象はなかった。PT 別で最も発現割合が高かった死亡に至った有害事象はいずれの群でも「心不全」（アコラミジス群：4.3%、プラセボ群：3.8%）であった。

Table 34: 海外 301 試験での死亡に至った有害事象（いずれかの群で基本語の発現患者数 2 名以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
死亡に至った有害事象発現患者数	60 (14.3)	36 (17.1)
心臓障害	36 (8.6%)	23 (10.9%)
心不全	18 (4.3%)	8 (3.8%)
慢性心不全	5 (1.2%)	2 (0.9%)
心停止	2 (0.5%)	3 (1.4%)
心アミロイドーシス	2 (0.5%)	2 (0.9%)
うっ血性心不全	2 (0.5%)	1 (0.5%)
心腎症候群	0	3 (1.4%)
右室不全	1 (0.2%)	2 (0.9%)
急性心不全	2 (0.5%)	0
感染症および寄生虫症	8 (1.9%)	3 (1.4%)
敗血症性ショック	3 (0.7%)	0
COVID-19	2 (0.5%)	0
COVID-19 肺炎	0	2 (0.9%)
ブドウ球菌性菌血症	2 (0.5%)	0
一般・全身障害および投与部位の状態	5 (1.2%)	3 (1.4%)
死亡	3 (0.7%)	1 (0.5%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.17

2.1.5.2 国内 302 試験

国内 302 試験で死亡に至った有害事象は認められなかった。

2.1.5.3 海外 201 試験

海外 201 試験で死亡に至った有害事象は認められなかった。

2.1.5.4 併合解析

2.1.5.4.1 アコラミジス治療集団

アコラミジス治療集団での主な死亡に至った有害事象（全体で PT の EAIR が 0.3/100 人年以上）

を Table 35 に示し、すべての死亡に至った有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.4 に示す。

SOC 別で最も発現率が高かった死亡に至った有害事象は「心臓障害」(4.3/100 人年) であった。

また、PT 別で発現した死亡に至った有害事象は、心筋症の進行又は本患者集団で予測される併存疾患と一致しており、治験責任医師等によって治験薬と関連ありと判断された事象はなかった。PT 別で最も発現率が高かった死亡に至った有害事象は「心不全」(2.1/100 人年) であった。

Table 35: アコラミジス治療集団での死亡に至った有害事象（全体で基本語の EAIR が 0.3/100 人年以上）

器官別大分類 基本語	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）
死亡に至った有害事象発現患者数	1122.8	73 (6.5)	42.8	11 (25.7)	233.6	0	1165.7	84 (7.2)
心臓障害	1124.5	44 (3.9)	43.0	6 (14.0)	233.6	0	1167.5	50 (4.3)
心不全	1125.3	20 (1.8)	43.0	4 (9.3)	233.6	0	1168.3	24 (2.1)
慢性心不全	1128.0	5 (0.4)	43.8	1 (2.3)	233.6	0	1171.7	6 (0.5)
心アミロイドーシス	1127.8	4 (0.4)	43.8	0	233.6	0	1171.6	4 (0.3)
心停止	1128.1	3 (0.3)	43.8	0	233.6	0	1171.9	3 (0.3)
急性心不全	1128.0	3 (0.3)	43.8	0	233.6	0	1171.8	3 (0.3)
うっ血性心不全	1127.9	3 (0.3)	43.8	0	233.6	0	1171.6	3 (0.3)
感染症および寄生虫症	1127.9	9 (0.8)	43.7	2 (4.6)	233.6	0	1171.6	11 (0.9)
敗血症性ショック	1128.0	3 (0.3)	43.8	0	233.6	0	1171.8	3 (0.3)
ブドウ球菌性菌血症	1128.1	2 (0.2)	43.8	1 (2.3)	233.6	0	1171.8	3 (0.3)
一般・全身障害および投与部位の状態	1128.0	6 (0.5)	43.8	0	233.6	0	1171.8	6 (0.5)
死亡	1128.1	3 (0.3)	43.8	0	233.6	0	1171.9	3 (0.3)

略語：EAIR = 曝露量で調整した有害事象の発現率
有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 2.1.3.4

2.1.5.4.2 OLE 集団

OLE 集団での主な死亡に至った有害事象（全体で基本語の発現患者数 2 名以上）を Table 36 に示し、すべての死亡に至った有害事象を 5.3.5.3.1 項 ISS Table 1.1.3.6 に示す。

PT 別で発現割合の高かった死亡に至った有害事象（発現患者数 3 名以上）は「心不全」(6 名、1.7%)（AG10-202 試験で 1 名、AG10-304 試験で 5 名）のみであった。

Table 36: OLE 集団での死亡に至った有害事象（全体で基本語の発現患者数 2 名以上）

器官別大分類 基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
死亡に至った有害事象発現患者数	11 (23.4%)	13 (4.3%)	24 (6.9%)
心臓障害	7 (14.9%)	7 (2.3%)	14 (4.0%)
心不全	1 (2.1%)	5 (1.7%)	6 (1.7%)
心アミロイドーシス	2 (4.3%)	0	2 (0.6%)

有害事象名は MedDRA/J Version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.6

2.1.6 その他の重篤な有害事象

2.1.6.1 海外 301 試験

海外 301 試験の安全性解析対象集団での主な重篤な有害事象（いずれかの群で PT の発現割合 2%以上）を Table 37 に示し、すべての重篤な有害事象を M2.7.6-9 に示す。

重篤な有害事象の発現割合はアコラミジス群：54.6%、プラセボ群：64.9%であった。

PT 別で発現割合の高かった重篤な有害事象（発現割合 5%以上）は、アコラミジス群で「心不全」（10.7%）、「急性心不全」（5.0%）、「急性腎障害」（5.0%）であり、プラセボ群で「心不全」（18.5%）、「心房細動」（7.1%）、「急性心不全」（6.6%）であった。

「急性腎障害」に関連して、腎機能に関する総合評価を 5.3.5.1.2 項 AG10-301 CSR Section 12.3.4 に示した。臨床的に問題となる安全性シグナルは認められなかった。

重篤な「転倒」の発現割合はアコラミジス群：3.1%、プラセボ群：0.9%であり、アコラミジス群の方が高かったが、いずれも治験薬との関連性はないと判断された。

Table 37: 海外 301 試験での重篤な有害事象（いずれかの群で基本語の発現割合 2%以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
重篤な有害事象発現患者数	230 (54.6%)	137 (64.9%)
心臓障害	117 (27.8%)	83 (39.3%)
心不全	45 (10.7%)	39 (18.5%)
急性心不全	21 (5.0%)	14 (6.6%)
心房細動	19 (4.5%)	15 (7.1%)
徐脈	11 (2.6%)	2 (0.9%)
心室性頻脈	6 (1.4%)	5 (2.4%)
感染症および寄生虫症	62 (14.7%)	37 (17.5%)
肺炎	12 (2.9%)	6 (2.8%)
COVID-19	9 (2.1%)	4 (1.9%)
COVID-19 肺炎	2 (0.5%)	8 (3.8%)
傷害、中毒および処置合併症	41 (9.7%)	16 (7.6%)
転倒	13 (3.1%)	2 (0.9%)
腎および尿路障害	30 (7.1%)	11 (5.2%)
急性腎障害	21 (5.0%)	8 (3.8%)
代謝および栄養障害	11 (2.6%)	8 (3.8%)
血液量増加症	3 (0.7%)	5 (2.4%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.9

2.1.6.2 国内 302 試験

国内 302 試験の安全性解析対象集団でのすべての重篤な有害事象を Table 38 に示す。

PT 別の重篤な有害事象として、「大腸ポリープ」が 2 名（8.0%）に認められたのを除き、いずれの事象も各 1 名（4.0%）のみの発現であった。

Table 38: 国内 302 試験での重篤な有害事象（安全性解析対象集団）

器官別大分類 基本語	アコラミジス N = 25 n (%)
重篤な有害事象発現患者数	12 (48.0%)
心臓障害	5 (20.0%)
心房細動	1 (4.0%)
完全房室ブロック	1 (4.0%)
心不快感	1 (4.0%)
心不全	1 (4.0%)
慢性心不全	1 (4.0%)
洞停止	1 (4.0%)
洞結節機能不全	1 (4.0%)
胃腸障害	3 (12.0%)
出血性腸憩室	1 (4.0%)
鼠径ヘルニア	1 (4.0%)
大腸ポリープ	2 (8.0%)
感染症および寄生虫症	3 (12.0%)
穿孔性虫垂炎	1 (4.0%)
細菌性前立腺炎	1 (4.0%)
肺炎球菌性肺炎	1 (4.0%)
臨床検査	1 (4.0%)
血中クレアチンホスホキナーゼ MB 増加	1 (4.0%)
代謝および栄養障害	1 (4.0%)
脱水	1 (4.0%)
筋骨格系および結合組織障害	1 (4.0%)
軟部組織腫瘤	1 (4.0%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (8.0%)
膀胱癌	1 (4.0%)
前立腺癌	1 (4.0%)
製品の問題	1 (4.0%)
医療機器位置異常	1 (4.0%)
呼吸器、胸郭および縦隔障害	1 (4.0%)
間質性肺疾患	1 (4.0%)

有害事象名は MedDRA/J version 26.1 を用いて表示した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.5.1

2.1.6.3 海外 201 試験

海外 201 試験の安全性解析対象集団でのすべての重篤な有害事象を Table 39 に示す。

PT 別の重篤な有害事象として、アコラミジス 400 mg 群で「呼吸困難」（1 名、6.3%）が発現し、プラセボ群で「心房細動」、「うっ血性心不全」及び「蜂巣炎」（各 1 名、5.9%）が発現した。

Table 39: 海外 201 試験での重篤な有害事象（安全性解析対象集団）

器官別大分類 基本語	アコラミジス 400 mg 群 N = 16 n (%)	アコラミジス 800 mg 群 N = 16 n (%)	プラセボ群 N = 17 n (%)
重篤な有害事象発現患者数	1 (6.3)	0	2 (11.8)
心臓障害	0	0	1 (5.9)
心房細動	0	0	1 (5.9)
うっ血性心不全	0	0	1 (5.9)
感染症および寄生虫症	0	0	1 (5.9)
蜂巣炎	0	0	1 (5.9)
呼吸器、胸郭および縦隔障害	1 (6.3)	0	0
呼吸困難	1 (6.3)	0	0

有害事象名は MedDRA/J version 21.0 を用いて表示した。
Source: 5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.7

2.1.6.4 併合解析

2.1.6.4.1 アコラミジス治療集団

アコラミジス治療集団での主な重篤な有害事象（全体で PT の EAIR が 1.0/100 人年以上）を Table 40 に示し、すべての重篤な有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.5 に示す。

PT 別で発現率の高かった重篤な有害事象（EAIR が 3.0/100 人年以上）は「心不全」（5.3/100 人年）及び「急性心不全」（3.4/100 人年）であった。

Table 40: アコラミジス治療集団での重篤な有害事象（全体で基本語の EAIR が 1.0/100 人年以上）

器官別大分類 基本語	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）	総リスク人年	n（n/100 人年）
重篤な有害事象発現患者数	762.6	286 (37.5)	36.0	30 (83.3)	161.1	54 (33.5)	798.6	316 (39.6)
心臓障害	962.7	147 (15.3)	38.2	16 (41.9)	204.1	27 (13.2)	1000.9	163 (16.3)
心不全	1088.8	53 (4.9)	41.7	7 (16.8)	221.3	11 (5.0)	1130.5	60 (5.3)
急性心不全	1098.5	34 (3.1)	41.8	5 (12.0)	231.4	3 (1.3)	1140.3	39 (3.4)
心房細動	1092.6	25 (2.3)	42.6	3 (7.0)	224.3	9 (4.0)	1135.2	28 (2.5)
うっ血性心不全	1120.8	11 (1.0)	43.4	1 (2.3)	233.5	1 (0.4)	1164.2	12 (1.0)
徐脈	1112.1	11 (1.0)	43.8	0	232.4	1 (0.4)	1155.9	11 (1.0)
感染症および寄生虫症	1064.4	80 (7.5)	43.3	5 (11.6)	212.4	16 (7.5)	1107.6	85 (7.7)
肺炎	1119.7	15 (1.3)	43.7	1 (2.3)	229.7	3 (1.3)	1163.3	16 (1.4)
傷害、中毒および処置合併症	1080.7	54 (5.0)	43.0	5 (11.6)	229.5	5 (2.2)	1123.7	59 (5.3)
転倒	1117.9	19 (1.7)	43.8	0	233.6	0	1161.7	19 (1.6)
腎および尿路障害	1086.1	42 (3.9)	43.0	5 (11.6)	224.5	5 (2.2)	1129.1	47 (4.2)
急性腎障害	1102.3	29 (2.6)	43.4	3 (6.9)	226.2	4 (1.8)	1145.7	32 (2.8)

略語：EAIR = 曝露量で調整した有害事象の発現率
有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 2.1.3.5

2.1.6.4.2 OLE 集団

OLE 集団での主な重篤な有害事象（全体で PT の発現割合 1%以上）を Table 41 に示し、すべての重篤な有害事象を 5.3.5.3.1 項 ISS Table 1.1.3.7 に示す。

PT 別で発現割合の高かった重篤な有害事象（全体の発現割合 3%以上）は、「急性心不全」（5.2%）、「心不全」（4.9%）及び「急性腎障害」（3.5%）であった。

Table 41: OLE 集団での重篤な有害事象（全体で基本語の発現割合 1%以上）

器官別大分類 基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
重篤な有害事象発現患者数	37 (78.7%)	72 (24.0%)	109 (31.4%)
心臓障害	25 (53.2%)	28 (9.3%)	53 (15.3%)
急性心不全	12 (25.5%)	6 (2.0%)	18 (5.2%)
心不全	5 (10.6%)	12 (4.0%)	17 (4.9%)
心房細動	4 (8.5%)	5 (1.7%)	9 (2.6%)
うっ血性心不全	5 (10.6%)	2 (0.7%)	7 (2.0%)
心房粗動	5 (10.6%)	0	5 (1.4%)
心原性ショック	4 (8.5%)	1 (0.3%)	5 (1.4%)
心腎症候群	5 (10.6%)	0	5 (1.4%)
感染症および寄生虫症	9 (19.1%)	17 (5.7%)	26 (7.5%)
肺炎	3 (6.4%)	1 (0.3%)	4 (1.2%)
腎および尿路障害	10 (21.3%)	9 (3.0%)	19 (5.5%)
急性腎障害	8 (17.0%)	4 (1.3%)	12 (3.5%)
血尿	1 (2.1%)	3 (1.0%)	4 (1.2%)
傷害、中毒および処置合併症	8 (17.0%)	10 (3.3%)	18 (5.2%)
転倒	6 (12.8%)	0	6 (1.7%)
血液及びリンパ系障害	3 (6.4%)	2 (0.7%)	5 (1.4%)
貧血	2 (4.3%)	2 (0.7%)	4 (1.2%)

有害事象名は MedDRA/J Version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.7

2.1.7 治験薬の投与中止に至った有害事象

2.1.7.1 海外 301 試験

海外 301 試験の安全性解析対象集団での治験薬の投与中止に至った主な有害事象（いずれかの群で PT の発現患者数 2 名以上）を Table 42 に示し、治験薬の投与中止に至ったすべての有害事象を M2.7.6-9 に示す。

治験薬の投与中止に至った有害事象の発現割合は、アコラミジス群 9.3%、プラセボ群 8.5%であった。

PT 別の治験薬の投与中止に至った有害事象は、アコラミジス群の「心不全」（5 名、1.2%）を除き、いずれも 2 名以下であった。

Table 42: 海外 301 試験での治験薬の投与中止に至った有害事象（いずれかの群で基本語の発現患者数 2 名以上）（安全性解析対象集団）

器官別大分類 基本語	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
治験薬の投与中止に至った有害事象発現患者数	39 (9.3%)	18 (8.5%)
心臓障害	11 (2.6%)	7 (3.3%)
心不全	5 (1.2%)	2 (0.9%)
急性心不全	2 (0.5%)	0
心腎症候群	0	2 (0.9%)
胃腸障害	9 (2.1%)	0
下痢	2 (0.5%)	0
消化不良	2 (0.5%)	0
悪心	2 (0.5%)	0
神経系障害	5 (1.2%)	2 (0.9%)
認知症	2 (0.5%)	0
代謝および栄養障害	3 (0.7%)	1 (0.5%)
食欲減退	2 (0.5%)	1 (0.5%)
腎および尿路障害	4 (1.0%)	0
急性腎障害	2 (0.5%)	0

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.16

2.1.7.2 国内 302 試験

国内 302 試験の安全性解析対象集団での治験薬の投与中止に至った有害事象は 2 名（8.0%）にのみ認められ、その内容は「腎機能障害」、「薬疹」（各 1 名、4.0%）であった（5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.8）。

2.1.7.3 海外 201 試験

海外 201 試験では治験薬の投与中止に至った有害事象は認められなかった。

2.1.7.4 併合解析

2.1.7.4.1 アコラミジス治療集団

アコラミジス治療集団での治験薬の投与中止に至った主な有害事象（全体で PT の EAIR が 0.2/100 人年以上）を Table 43 に示し、治験薬の投与中止に至ったすべての有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.6 に示す。

PT 別で発現率の高かった治験薬の投与中止に至った有害事象（EAIR が 0.3/100 人年以上）は、「心不全」（0.6/100 人年）、「下痢」、「消化不良」、「悪心」及び「急性腎障害」（各 0.3/100 人年）であった。

Table 43: アコラミジス治療集団での治験薬の投与中止に至った有害事象（全体で基本語の EAIR が 0.2/100 人年以上）

器官別大分類 基本語	AG10-202 試験参加患者及び AG10-301 試験アコラミジス投与患者 N = 468		AG10-301 試験でプラセボが投与された AG10-304 試験参加患者 N = 95				全体（アコラミジス治療集団） N = 563	
			アコラミジス投与時 AG10-304 試験		プラセボ投与時 AG10-301 試験			
	総リスク人年	n（n/100人年）	総リスク人年	n（n/100人年）	総リスク人年	n（n/100人年）	総リスク人年	n（n/100人年）
治験薬の投与中止に至った有害事象発現患者数	1116.8	49 (4.4)	43.7	2 (4.6)	233.6	0	1160.6	51 (4.4)
心臓障害	1124.9	14 (1.2)	43.8	0	233.6	0	1168.6	14 (1.2)
心不全	1125.6	7 (0.6)	43.8	0	233.6	0	1169.4	7 (0.6)
急性心不全	1128.1	2 (0.2)	43.8	0	233.6	0	1171.8	2 (0.2)
胃腸障害	1124.8	13 (1.2)	43.8	0	233.6	0	1168.6	13 (1.1)
下痢	1127.7	3 (0.3)	43.8	0	233.6	0	1171.5	3 (0.3)
消化不良	1127.6	3 (0.3)	43.8	0	233.6	0	1171.4	3 (0.3)
悪心	1127.7	3 (0.3)	43.8	0	233.6	0	1171.5	3 (0.3)
神経系障害	1125.0	8 (0.7)	43.8	0	233.6	0	1168.8	8 (0.7)
認知症	1127.7	2 (0.2)	43.8	0	233.6	0	1171.4	2 (0.2)
腎および尿路障害	1127.7	5 (0.4)	43.7	1 (2.3)	233.6	0	1171.5	6 (0.5)
急性腎障害	1127.9	3 (0.3)	43.8	0	233.6	0	1171.6	3 (0.3)
末期腎疾患	1128.1	1 (0.1)	43.7	1 (2.3)	233.6	0	1171.8	2 (0.2)
代謝および栄養障害	1127.8	3 (0.3)	43.8	0	233.6	0	1171.6	3 (0.3)
食欲減退	1127.9	2 (0.2)	43.8	0	233.6	0	1171.7	2 (0.2)

略語：EAIR = 曝露量で調整した有害事象の発現率
有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 2.1.3.6

2.1.7.4.2 OLE 集団

OLE 集団での治験薬の投与中止に至ったすべての有害事象を Table 44 に示す。

OLE 集団全体での PT 別の治験薬の投与中止に至った有害事象として、「心不全」が 2 名（0.6%）に発現したことを除き、その他の事象はすべて各 1 名（0.3%）のみの発現であった。

Table 44: OLE 集団での治験薬の投与中止に至った有害事象

器官別大分類 基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
治験薬の投与中止に至った有害事象発現患者数	9 (19.1%)	3 (1.0%)	12 (3.5%)
胃腸障害	3 (6.4%)	1 (0.3%)	4 (1.2%)
下痢	0	1 (0.3%)	1 (0.3%)
消化不良	1 (2.1%)	0	1 (0.3%)
嚥下障害	1 (2.1%)	0	1 (0.3%)
悪心	1 (2.1%)	0	1 (0.3%)
心臓障害	3 (6.4%)	0	3 (0.9%)
心不全	2 (4.3%)	0	2 (0.6%)
心原性ショック	1 (2.1%)	0	1 (0.3%)
神経系障害	3 (6.4%)	0	3 (0.9%)
健忘	1 (2.1%)	0	1 (0.3%)
脳血管発作	1 (2.1%)	0	1 (0.3%)
頭痛	1 (2.1%)	0	1 (0.3%)

器官別大分類 基本語	AG10-202 試験 N = 47 n (%)	AG10-304 試験 N = 300 n (%)	全体 N = 347 n (%)
パーキンソン病	1 (2.1%)	0	1 (0.3%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (4.3%)	0	2 (0.6%)
子宮頚部癌	1 (2.1%)	0	1 (0.3%)
多形性神経膠芽細胞腫	1 (2.1%)	0	1 (0.3%)
腎および尿路障害	1 (2.1%)	1 (0.3%)	2 (0.6%)
急性腎障害	1 (2.1%)	0	1 (0.3%)
末期腎疾患	0	1 (0.3%)	1 (0.3%)
感染症および寄生虫症	0	1 (0.3%)	1 (0.3%)
ブドウ球菌性菌血症	0	1 (0.3%)	1 (0.3%)
筋骨格系および結合組織障害	1 (2.1%)	0	1 (0.3%)
関節痛	1 (2.1%)	0	1 (0.3%)
精神障害	1 (2.1%)	0	1 (0.3%)
不眠症	1 (2.1%)	0	1 (0.3%)
皮膚および皮下組織障害	1 (2.1%)	0	1 (0.3%)
紫斑	1 (2.1%)	0	1 (0.3%)
発疹	1 (2.1%)	0	1 (0.3%)

有害事象名は MedDRA/J Version 24.1 を用いて表示した。
Source: 5.3.5.3.1 項 ISS Table 1.1.3.9

2.1.8 器官別又は症候群別有害事象の解析

器官別又は症候群別の有害事象として、SOC 別の有害事象を評価した。

2.1.8.1 海外 301 試験

海外 301 試験の安全性解析対象集団での SOC 別の有害事象を Table 45 に示す。

SOC 別の主な有害事象（発現割合 50%以上）は、アコラミジス群で「感染症および寄生虫症」（58.4%）、「心臓障害」（54.6%）、「胃腸障害」（52.5%）であり、プラセボ群では「心臓障害」（68.2%）、「感染症および寄生虫症」（55.0%）であった。

Table 45: 海外 301 試験での SOC 別の有害事象（安全性解析対象集団）

器官別大分類	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
有害事象発現患者数	413 (98.1%)	206 (97.6%)
心臓障害	230 (54.6%)	144 (68.2%)
感染症および寄生虫症	246 (58.4%)	116 (55.0%)
胃腸障害	221 (52.5%)	98 (46.4%)
筋骨格系および結合組織障害	184 (43.7%)	83 (39.3%)
神経系障害	182 (43.2%)	77 (36.5%)
代謝および栄養障害	149 (35.4%)	85 (40.3%)
呼吸器、胸郭および縦隔障害	146 (34.7%)	86 (40.8%)
一般・全身障害および投与部位の状態	144 (34.2%)	79 (37.4%)
傷害、中毒および処置合併症	137 (32.5%)	81 (38.4%)
腎および尿路障害	142 (33.7%)	64 (30.3%)
臨床検査	127 (30.2%)	68 (32.2%)
皮膚および皮下組織障害	108 (25.7%)	53 (25.1%)
血管障害	88 (20.9%)	49 (23.2%)
精神障害	57 (13.5%)	39 (18.5%)

器官別大分類	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)
血液およびリンパ系障害	61 (14.5%)	29 (13.7%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	54 (12.8%)	36 (17.1%)
眼障害	46 (10.9%)	26 (12.3%)
生殖系および乳房障害	28 (6.7%)	23 (10.9%)
耳および迷路障害	22 (5.2%)	10 (4.7%)
内分泌障害	22 (5.2%)	9 (4.3%)
肝胆道系障害	11 (2.6%)	10 (4.7%)
免疫系障害	5 (1.2%)	4 (1.9%)
先天性、家族性および遺伝性障害	4 (1.0%)	1 (0.5%)
製品の問題	3 (0.7%)	2 (0.9%)
外科および内科処置	1 (0.2%)	1 (0.5%)

有害事象名は MedDRA/J version 24.1 を用いて表示した。
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.2.1

2.1.8.2 国内 302 試験

国内 302 試験の安全性解析対象集団での SOC 別の有害事象を Table 46 に示す。

SOC 別の主な有害事象（発現割合 50%以上）は、「胃腸障害」（56.0%）、「感染症および寄生虫症」（52.0%）であった。

Table 46: 国内 302 試験での SOC 別の有害事象（安全性解析対象集団）

器官別大分類	アコラミジス N = 25 n (%)
有害事象発現患者数	25 (100%)
胃腸障害	14 (56.0%)
感染症および寄生虫症	13 (52.0%)
代謝および栄養障害	11 (44.0%)
心臓障害	10 (40.0%)
筋骨格系および結合組織障害	9 (36.0%)
一般・全身障害および投与部位の状態	8 (32.0%)
神経系障害	8 (32.0%)
皮膚および皮下組織障害	7 (28.0%)
傷害、中毒および処置合併症	6 (24.0%)
腎および尿路障害	6 (24.0%)
臨床検査	5 (20.0%)
呼吸器、胸郭および縦隔障害	5 (20.0%)
眼障害	4 (16.0%)
生殖系および乳房障害	4 (16.0%)
血液およびリンパ系障害	2 (8.0%)
耳および迷路障害	2 (8.0%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (8.0%)
血管障害	2 (8.0%)
内分泌障害	1 (4.0%)
肝胆道系障害	1 (4.0%)
免疫系障害	1 (4.0%)
製品の問題	1 (4.0%)
精神障害	1 (4.0%)

有害事象名は MedDRA/J version 26.1 を用いて表示した。
Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.2.1

2.1.8.3 海外 201 試験

海外 201 試験の安全性解析対象集団での SOC 別の主な有害事象（発現割合 20%以上）は、アコラミジス 400 mg 群で「臨床検査」（31.3%）、800 mg 群で「胃腸障害」（43.8%）、「筋骨格系および結合組織障害」（25.0%）、「感染症および寄生虫症」（25.0%）、プラセボ群で「代謝および栄養障害」（29.4%）、「傷害、中毒および処置合併症」（23.5%）であった（5.3.5.1.1 項 AG10-201 CSR Table 14.3.2.2）。

2.1.8.4 併合解析

2.1.8.4.1 アコラミジス治療集団

アコラミジス治療集団でみられた SOC 別の有害事象を 5.3.5.3.1 項 ISS Table 2.1.3.2 に示す。

アコラミジス治療集団全体での SOC 別の主な有害事象（EAIR が 30/100 人年以上）は、「感染症および寄生虫症」（45.6/100 人年）、「心臓障害」（38.2/100 人年）及び「胃腸障害」（37.0/100 人年）であった。

2.1.8.4.2 OLE 集団

OLE 集団でみられた SOC 別の有害事象を 5.3.5.3.1 項 ISS Table 1.1.3.2 に示す。

OLE 集団全体での SOC 別の主な有害事象（発現割合 20%以上）は「感染症および寄生虫症」（30.0%）、「心臓障害」（23.1%）であった。

2.2 個別有害事象の文章による説明

死亡及びその他の重篤な有害事象並びに治験薬の投与中止に至った有害事象を発現した患者の詳細を Table 47 に示す。

Table 47: 個別有害事象の文章による説明の参照先

試験番号	参照先
AG10-001	該当なし
AG10-003	該当なし
AG10-004	該当なし
AG10-005	該当なし
AG10-007	該当なし
AG10-008	M2.7.6-6
ALXN2060-HV-101	該当なし
AG10-201	M2.7.6-8
AG10-202	5.3.5.3.1 項 ISS Section 9.1
AG10-301	M2.7.6-9
AG10-304	5.3.5.3.1 項 ISS Section 9.2
ALXN2060-TAC-302	M2.7.6-10

3　臨床検査値の評価

3.1　海外 301 試験

3.1.1　血液学的検査

血液学的検査パラメータの平均値は投与期間をとおして安定していた（5.3.5.1.2 項 AG10-301 CSR Table 14.3.4.1.1～Table 14.3.4.1.10）。

個々の患者での変動では、ベースライン値が正常であった患者の多く（70%超）は、ベースライン後の最終時点でも正常であり、両群間で意味のある差は認められなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.4.1.1b～Table 14.3.4.1.10b、Table 14.3.4.1.1e～Table 14.3.4.1.10e）。

3.1.2　血液生化学的検査

ほとんどの血液生化学的検査パラメータの平均値は、投与期間をとおして安定していた（5.3.5.1.2 項 AG10-301 CSR Table 14.3.5.1.1～Table 14.3.5.1.6、Table 14.3.5.1.9～Table 14.3.5.1.26）。血清レチノール結合タンパクの平均値は、ベースラインでは両群で同程度であったが、投与期間中にアコラミジス群では低下した。また、アラニンアミノトランスフェラーゼ（ALT）若しくはアスパラギン酸アミノトランスフェラーゼ（AST）が治験薬投与期間中に正常範囲上限（ULN）の 3 倍以上及び総ビリルビンが ULN の 2 倍超又は ALT 若しくは AST の変化が ULN の 10 倍超となった患者はいなかった。

個々の患者での変動でも、全体としてベースライン値が正常であった患者の多く（60%超）が、ベースライン後の最終時点でも正常であった。血清ビリルビン、直接ビリルビン、血清クロール、血清グルコースではベースライン後に異常値へシフトした患者の割合はプラセボ群の方が高かった。血清中遊離チロキシン及び血清中クレアチンキナーゼでベースライン後に異常値へシフトした患者の割合はアコラミジス群の方が高かったが、これらの変化は本試験の対象疾患及び本患者集団で予想される併存疾患と一致しており、臨床的に問題となる安全性シグナルは認められなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.5.1.1b～Table 14.3.5.1.5b、Table 14.3.5.1.9b～Table 14.3.5.1.26b、Table 14.3.5.1.1e～Table 14.3.5.1.5e、Table 14.3.5.1.9e～Table 14.3.5.1.26e ）。

3.1.3　尿検査

尿検査（タンパク尿、尿中アルブミン、尿中クレアチニン、尿中グルコース）での治験薬投与期間中の変動はアコラミジス群とプラセボ群との間で同様であり、臨床的に問題となる安全性シグナルは認められなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.6.1.1～Table 14.3.6.1.7）。

3.1.4　腎機能に関する総合評価

海外 301 試験での腎機能に関する総合評価を 5.3.5.1.2 項 AG10-301 CSR Section 12.3.4 に示した。臨床的に問題となる安全性シグナルは認められなかった。また、腎機能障害別の安全性の評価は、5.1.3 に示した。

3.2　国内 302 試験

国内 302 試験全体で、血液学的検査、血液生化学的検査及び尿検査にベースラインからの顕著な変化は認められなかった（5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.4.1.1～Table 14.3.4.4.3）。また、国内 302 試験での腎機能に関する総合評価を 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Section 5.3.3.4 に示した。臨床的に問題となる安全性シグナルは認められなかった。

3.3 海外 201 試験

海外 201 試験での血液学的検査及び血液生化学的検査の平均値のベースラインからの変化にアコラミジス 400 mg 群、800 mg 群、プラセボ群の間で意味のある差は認められず、臨床的に意味のある傾向は認められなかった（5.3.5.1.1 項 AG10-201 CSR Table 14.3.3.1.1、Table 14.3.3.2.1）。

3.4 併合解析

3.4.1 アコラミジス治療集団

アコラミジス治療集団での併合解析では臨床検査値の評価は実施しなかった。

3.4.2 OLE 集団

3.4.2.1 血液学的検査

血液学的検査パラメータでは、全体として臨床的に意味のあるベースラインからの変化は認められなかった（5.3.5.3.1 項 ISS Table 1.1.4.1 及び Table 1.1.4.4）。

3.4.2.2 血液生化学的検査

血液生化学的検査パラメータでは、全体として臨床的に意味のあるベースラインからの変化は認められなかった（5.3.5.3.1 項 ISS Table 1.1.4.2.1 及び Table 1.1.4.5.1）。また、治験薬投与期間中に ALT 又は AST が ULN の 3 倍以上かつ総ビリルビンが ULN の 2 倍超となった患者もいなかった（5.3.5.3.1 項 ISS Table 1.1.4.7）。

3.4.2.3 尿検査

尿検査パラメータでは、全体として臨床的に意味のあるベースラインからの変化は認められなかった（5.3.5.3.1 項 ISS Table 1.1.4.3 及び Table 1.1.4.6）。

4　バイタルサイン、身体的所見及び安全性に関連する他の観察項目

4.1　バイタルサイン

4.1.1　海外 301 試験

バイタルサインの所見は患者集団で一貫しており、収縮期血圧、拡張期血圧及び心拍数のベースラインからの変化は両群で同様であった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.7.1～Table 14.3.7.6）。

4.1.2　国内 302 試験

バイタルサイン（血圧、脈拍数、呼吸数）にベースラインからの顕著な変化は認められなかった（5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.5.1）。

4.1.3　海外 201 試験

バイタルサインに対する臨床的に重要な影響は認められなかった（5.3.5.1.1 項 AG10-201 CSR Section 12.5.1）。

4.1.4　併合解析

4.1.4.1　アコラミジス治療集団

アコラミジス治療集団での併合解析ではバイタルサインの評価は実施しなかった。

4.1.4.2　OLE 集団

バイタルサインに対する臨床的に重要な影響は認められなかった（5.3.5.3.1 項 ISS Table 1.1.6.1）。

4.2　心電図の結果

4.2.1　海外 301 試験

心電図の結果を 5.3.5.1.2 項 AG10-301 CSR Section 12.4.2 に示す。

心電図所見はベースライン時にはほとんどの患者（97.3%）で異常所見が認められたが、その後は試験期間をとおして顕著な変化は認められず、臨床的に意味のあるベースラインからの変化は認められなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.9.3、Table 14.3.10.1）。

有害事象（PT）として「心電図 QT 延長」がアコラミジス群の 1.2%（5 名）及びプラセボ群の 0.9%（2 名）に発現したが、「トルサード ド ポアント」はみられなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.2.2）。

また、ベースライン後の Fridericia 式を用いた補正 QT 間隔（QTcF）が 450 ms 超、480 ms 超及び 500 ms 超であった患者の割合又は QTcF のベースラインからの変化量に群間で臨床的に意味のある差は認められず、QTcF の閾値に対する解析でもプラセボと比較してアコラミジスの投与によって補正 QC 間隔（QTc）延長の頻度が増加するような傾向はみられなかった（Table 48）。

Table 48: 海外 301 試験の QTcF の閾値ごとの中央測定機関による心電図間隔（安全性解析対象集団）

	QTcF > 500 ms		QTcF のベースラインからの変化 > 60 ms	
	アコラミジス群	プラセボ群	アコラミジス群	プラセボ群
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Month 6	19/269 (7.1%)	7/134 (5.2%)	1/267 (0.4%)	2/133 (1.5%)
Month 12	17/264 (6.4%)	9/130 (6.9%)	2/262 (0.8%)	2/128 (1.6%)
Month 18	11/236 (4.7%)	9/124 (7.3%)	6/236 (2.5%)	6/120 (5.0%)
Month 24	14/225 (6.2%)	3/106 (2.8%)	6/224 (2.7%)	2/104 (1.9%)
Month 30	16/205 (7.8%)	8/93 (8.6%)	8/203 (3.9%)	4/91 (4.4%)

略語：QTcF = Fridericia 式を用いた補正 QT 間隔
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.9.1

4.2.2 国内 302 試験

心電図間隔及び所見に、ベースラインからの顕著な変化は認められなかった（5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.6.1.1、Table 14.3.6.1.2 及び 14.3.6.1.6）。

4.2.3 海外 201 試験

心電図所見及び心エコー所見に関して、試験期間をとおして臨床的に重要な変化は認められなかった（5.3.5.1.1 項 AG10-201 CSR Section 12.5.3）。

4.2.4 第 1 相試験

健康被験者を対象とした第 1 相試験では、全試験をとおして安全性に関する心電図パラメータ（心拍数、PR、QRS、QT 及び QTcF 間隔）の各評価時点の平均値はいずれも正常範囲内であり、試験期間をとおして臨床的に重要な変化は認められなかった

AG10-005 試験では、4 名（アコラミジス 1200 mg コホートの 1 名、アコラミジス 2000 mg コホートの 1 名、プラセボコホートの 2 名）で 450 msec 超、ベースライン値から 30 msec 超の QTcF 間隔延長が認められたが（5.3.3.1.2 項 AG10-005 CSR Appendix 16.2.8.3.2）、これらの変化は軽度であり、臨床でみられる正常な変動の範囲内であると考えられた。

いずれの試験でも心臓関連の有害事象は認められず、治験責任医師等によって個々の心電図の結果はいずれも臨床的に重要ではないと判断された。

4.2.5 併合解析

4.2.5.1 アコラミジス治療集団

アコラミジス治療集団での併合解析では心電図の評価は実施しなかった。

4.2.5.2 OLE 集団

OLE 集団での QTcF の閾値に対する解析の結果、アコラミジスの長期投与時に ATTR-CM 患者で QTc 延長の頻度が増加するような傾向はみられなかった（Table 49）。

有害事象（PT）として「心電図 QT 延長」が AG10-304 試験の 1 名（0.3%）で報告されたが、「トルサード ド ポアント」は認められなかった（5.3.5.3.1 項 ISS Table 1.1.3.2）。

Table 49: OLE 集団の QTcF 閾値ごとの中央測定機関による心電図間隔

	QTcF > 500 ms		QTcF のベースラインからの変化 > 60 ms	
	AG10-202	AG10-304	AG10-202	AG10-304
	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Month 3	3/30 (10.0%)	1/17 (5.9%)	1/30 (3.3%)	1/17 (5.9%)
Month 6	2/28 (7.1%)	8/99 (8.1%)	0/28	2/99 (2.0%)
Month 12	2/23 (8.7%)	1/15 (6.7%)	0/23	1/15 (6.7%)
Month 24	3/10 (30.0%)	0	1/10 (10.0%)	0
Month 36	1/12 (8.3%)	0	1/12 (8.3%)	0
Month 48	3/10 (30.0%)	0	2/10 (20.0%)	0

略語：QTcF = Fridericia 式を用いた補正 QT 間隔
Source: 5.3.5.3.1 項 ISS Table 1.1.7.2

4.2.5.3 心電図評価

健康被験者を対象とした 2 つの第 1 相 AG10-001 試験及び AG10-005 試験で心電図評価を実施した。アコラミジスの濃度-QTc 関係は両試験の併合データを用いて評価した。結果の詳細は AG10-001 Cardiac Safety Report 及び AG10-005 Cardiac Safety Report に示し、その要約を M2.7.2-2.6 項に示す。

AG10-001 試験では、連続 12 誘導 24 時間ホルター心電図をベースライン時（投与前）並びに単回投与パートでは投与日、反復投与パートでは投与初日及び最終日の投与後 24 時間まで連続して抽出した。データは、アコラミジスの各用量群の 6 名（単回投与パートでは 50、150、300 及び 800 mg、反復投与パートでは 100、300 及び 800 mg）、並びに単回投与及び反復投与パートの併合プラセボ群のそれぞれ 8 名及び 6 名から得られた。その結果、検討したアコラミジスの用量及び濃度はいずれの心電図パラメータに対しても臨床的に重要な影響を及ぼさず、観察されたアコラミジス及びその代謝物アコラミジスアシルグルクロニド（アコラミジス-AG）の血漿中濃度の範囲内では 10 msec を超える QTc 間隔への影響は非常に少ないと考えられた。

AG10-005 試験では、ベースライン時から投与後 24 時間まで、連続 12 誘導心電図記録（ホルター）を実施した。ベースライン時に、各用量群（アコラミジス 1200、1600 又は 2000 mg の空腹時単回投与）の 6 名及び全用量を併合したプラセボ群の 9 名からデータが得られた。その結果、検討した用量のアコラミジスは心電図パラメータに臨床的に重要な影響を及ぼさなかった。

AG10-001 試験及び AG10-005 試験の併合データを用いた濃度-QTc 解析の結果も各試験での結果と同様であり、アコラミジス及びアコラミジス-AG の血漿中濃度とプラセボで補正した QTcF のベースラインからの変化量との間に負の相関が認められた。観察されたアコラミジスの血漿中濃度（～27500 ng/mL）及びアコラミジス-AG の血漿中濃度（～17500 ng/mL）の範囲内では、QTcF の影響は非常に少ないと考えられた。

4.3 身体所見

4.3.1 海外 301 試験

いずれの群でも、ベースライン時の身体所見は正常であり、Month 30 までに臨床的に重要な異常にシフトした患者の割合は低かった。身体所見では、両群間に意味のある差は認められなかった（5.3.5.1.2 項 AG10-301 CSR Table 14.3.6.2）。

4.3.2 国内 302 試験

臨床的に重要な身体所見は認められなかった（5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.6.2）。

4.3.3 海外 201 試験

認められた身体所見は、患者の基礎疾患を反映したものであった（5.3.5.1.1 項 AG10-201 CSR Section 12.5.2）。

4.3.4 併合解析

4.3.4.1 アコラミジス治療集団

アコラミジス治療集団での併合解析では身体所見の評価は実施しなかった。

4.3.4.2 OLE 集団

認められた身体所見は、患者の基礎疾患を反映したものであった（5.3.5.3.1 項 ISS Table 1.1.5.1）。

5　特別な患者集団及び状況下における安全性

5.1　内因性要因

5.1.1　年齢及び性別

年齢及び性別による安全性は国内 302 試験で評価した。

国内 302 試験では、すべての患者に有害事象が認められており、年齢及び性別による発現割合の差は認められなかった。また、年齢及び性別による重篤な有害事象の発現割合を検討した結果を Table 50 に示す。78 歳未満及び 78 歳以上、並びに男性及び女性の間に、重篤な有害事象の発現割合の顕著な差は認められなかった。

Table 50:　国内 302 試験での年齢、性別の重篤な有害事象の発現割合（安全性解析対象集団）

サブグループ	カテゴリー	アコラミジス N = 25 n (%)
年齢	78 歳未満	7/15 (46.7%)
	78 歳以上	5/10 (50.0%)
性別	男性	11/22 (50.0%)
	女性	1/3 (33.3%)

Source: 5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.5.2、Table 14.3.1.3.5.3

5.1.2　人種

人種によるアコラミジスの安全性は、海外 301 試験、国内 302 試験及び AG10-004 試験を用いて評価した。

海外 301 試験では患者のほとんどが白人（87.8%、632 名中 555 名）で、国内 302 試験ではすべての患者が日本人であった。海外 301 試験及び国内 302 試験での有害事象の発現状況を Table 51 に示す。両試験の有害事象の発現状況はおおむね同様であり、人種による大きな違いや日本人特有の問題は認められなかった。

また、AG10-004 試験では日本人及び外国人の健康成人にアコラミジスを単回投与した。その結果、いずれの人種でも忍容性はおおむね良好であり、安全性上の懸念は認められず、日本人と外国人でアコラミジスの安全性プロファイルに臨床的に意味のある差は認められなかった（M2.7.6-5）。

Table 51:　海外 301 試験及び国内 302 試験での有害事象の発現状況（安全性解析対象集団）

	海外 301 試験		国内 302 試験
	アコラミジス群 N = 421 n (%)	プラセボ群 N = 211 n (%)	アコラミジス N = 25 n (%)
有害事象	413 (98.1%)	206 (97.6%)	25 (100%)
死亡に至った有害事象	60 (14.3%)	36 (17.1%)	0
治験薬の投与中止に至った有害事象	39 (9.3%)	18 (8.5%)	2 (8.0%)
重篤な有害事象	230 (54.6%)	137 (64.9%)	12 (48.0%)
治験薬との関連性が否定できない有害事象	50 (11.9%)	11 (5.2%)	3 (12.0%)

Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.1、5.3.5.2.1 項 ALXN2060-TAC-302 CSR Table 14.3.1.3.1

5.1.3 腎機能障害

腎機能障害別のアコラミジスの安全性は海外 301 試験を用いて評価した。海外 301 試験の安全性解析対象集団での腎機能障害別（スクリーニング時に 30 mL/min/1.73 m^2 以上又は 30 mL/min/1.73 m^2 未満）の有害事象の発現状況の概要を Table 52 に示す。

スクリーニング時の eGFR が 30 mL/1.73 m^2 以上の集団での有害事象はアコラミジス群 98.3%、プラセボ群 97.5%、死亡に至った有害事象はアコラミジス群 13.7%、プラセボ群 17.3%、重篤な有害事象はアコラミジス群 54.0%、プラセボ群 63.9%に発現し、両群間で差は認められなかった。

また、スクリーニング時の eGFR が 30 mL/1.73 m^2 未満の集団での有害事象はアコラミジス群 91.7%、プラセボ群 100%に認められ、死亡に至った有害事象はアコラミジス群 33.3%、プラセボ群 11.1%に、重篤な有害事象はアコラミジス群 75.0%、プラセボ群 88.9%に発現した。当該集団のアコラミジス群での死亡に至った有害事象は 4 名に認められ、「心不全」、「脳梗塞」、「敗血症性ショック」及び「ブドウ球菌性菌血症」であったが、いずれの事象も治験責任医師等によって治験薬と関連なしと判定された。

eGFR が 30 mL/1.73 m^2 以上の集団、30 mL/1.73 m^2 未満の集団のいずれでも、臨床的に懸念される安全性シグナルは特定されなかった。

Table 52: **海外 301 試験での腎機能障害別の有害事象発現状況の概要（安全性解析対象集団）**

	eGFR ≥ 30 mL/min/1.73 m^2		**eGFR < 30 mL/min/1.73 m^2**	
	アコラミジス群 N = 409 n (%)	**プラセボ群 N = 202 n (%)**	**アコラミジス群 N = 12 n (%)**	**プラセボ群 N = 9 n (%)**
有害事象	402 (98.3%)	197 (97.5%)	11 (91.7%)	9 (100.0%)
死亡に至った有害事象	56 (13.7%)	35 (17.3%)	4 (33.3%)	1 (11.1%)
入院に至った有害事象	204 (49.9%)	120 (59.4%)	8 (66.7%)	8 (88.9%)
治験薬の投与中止に至った有害事象	36 (8.8%)	16 (7.9%)	3 (25.0%)	2 (22.2%)
治験薬の減量に至った有害事象	4 (1.0%)	0	0	0
重篤な有害事象	221 (54.0%)	129 (63.9%)	9 (75.0%)	8 (88.9%)
治験薬の投与中止に至った重篤な有害事象	20 (4.9%)	14 (6.9%)	1 (8.3%)	1 (11.1%)
治験薬の減量に至った重篤な有害事象	2 (0.5%)	0	0	0
治験薬との関連性が否定できない有害事象	45 (11.0%)	10 (5.0%)	5 (41.7%)	1 (11.1%)
治験薬との関連性が否定できない重篤な有害事象	2 (0.5%)	0	0	0
重度の有害事象	149 (36.4%)	93 (46.0%)	8 (66.7%)	3 (33.3%)

略語：eGFR＝推算糸球体濾過量
Source: 5.3.5.1.2 項 AG10-301 CSR Table 14.3.1.1a

5.1.4 肝機能障害

肝機能障害を有する患者を対象としたアコラミジスの試験は実施していない。

ATTR-CM の患者を対象としたアコラミジスの臨床試験では、スクリーニング時に ALT 及び AST が ULN の 3 倍以下かつ総ビリルビンが ULN の 3 倍以下（海外 201 試験では ULN の 2 倍以下）であることを要件とし、正常な肝機能又は軽度の肝機能障害を有する患者のみを組み入れた。

5.2 外因性要因

アコラミジスの安全性に対する喫煙や飲酒などの外因性要因の影響は評価していない。

5.3 薬物相互作用

5.3.1 食事の影響

食事の影響は健康成人を対象とした AG10-001 試験及び ALXN2060-HV-101 試験で評価した。食事の影響に関する検討結果の詳細は M2.7.1-3.2 項に示す。

AG10-001 試験の Part A（単回投与）及び ALXN2060-HV-101 試験での安全性はいずれも良好であり、食事の有無による安全性の違いは認められなかった（5.3.3.1.1 項 AG10-001 CSR Section 12、5.3.3.4.2 項 ALXN2060-HV-101 CSR Section 5.1）。

5.3.2 薬物間の相互作用

薬物相互作用は健康成人を対象とした AG10-008 試験で評価した。薬物相互作用に関する検討結果の詳細を M2.7.2-2.4.1 項に示す。

AG10-008 試験では、健康成人を対象に有機アニオントランスポーター（OAT）1/OAT3 の基質であるアデホビル及びオセルタミビルカルボン酸とアコラミジスとの薬物相互作用を評価した。その結果、アデホビル又はオセルタミビルの単回投与と併用したアコラミジスの反復経口投与の忍容性はおおむね良好であった（5.3.3.4.1 項 AG10-008 CSR Section 12）。

5.4 妊娠及び授乳時の使用

妊婦でのアコラミジスの使用に関するデータはない。また、ヒト又は動物の乳汁中のアコラミジスの存在、並びに授乳中の乳児又は母乳産生に対するアコラミジスの影響に関するデータは得られていない。アコラミジスの臨床試験では、妊婦及び授乳婦は対象から除外し、妊娠可能な女性患者は効果の高い避妊法をランダム化から開始し、治験実施計画書に記載されているアコラミジスの最終投与後 30 日間、継続して使用することを義務付けた。

AG10-001 試験では、健康成人被験者 1 名で試験期間中の妊娠が判明したが、追跡不能であった（5.3.3.1.1 項 AG10-001 CSR Section 12.4.4）。

5.5 過量投与

これまでの臨床試験で健康成人被験者に投与されたアコラミジスの最高用量はアコラミジス 2000 mg の単回投与であったが、この用量では治験薬と関連のある有害事象は報告されなかった（5.3.3.1.2 項 AG10-005 CSR Table 14.3.1.3）。

また、ATTR-CM 患者に投与されたアコラミジスの最高用量は 800 mg 1 日 2 回投与であり、その安全性は良好であったが、当該用量を超える過量投与での安全性は明らかでない。

5.6 薬物乱用

アコラミジスに依存性の可能性を示唆するエビデンスはない。これまでにアコラミジスの薬物乱用は認められておらず、薬理作用及び受容体結合の観点からも予測されない。

5.7 離脱症状及び反跳現象

アコラミジスの離脱症状及び反跳現象は認められていない。

5.8 自動車運転及び機械操作に対する影響又は精神機能の障害

自動車の運転や機械の操作に対するアコラミジスの影響を検討する試験は実施されていない。また、自動車運転及び機械操作能力に影響を及ぼすと予想されるリスクは特定されていない。

5.9 その他の臨床試験でのアコラミジスの安全性

5.9.1 第 1 相試験での安全性

本申請で安全性評価のための臨床データパッケージに含めて提出した 7 つの第 1 相試験の安全性の結果を示す。AG10-001 試験、AG10-003 試験、AG10-005 試験、AG10-007 試験、AG10-008 試験、ALXN2060-HV-101 試験では外国人健康成人、AG10-004 試験では日本人及び外国人健康成人が対象であった。各試験の概要（試験デザイン、投与レジメン等）は Table 1 に示す。

5.9.1.1 人口統計学的特性

第 1 相試験（7 試験）の健康成人の人口統計学的特性を試験別に Table 53 に示す。

年齢の範囲は 18～55 歳（中央値：34.0～46.0 歳）であった。ほとんどの試験で男性が多く、大半が白人であった。

Table 53: 第 1 相試験での人口統計学的特性及びベースライン特性

	AG10-001				AG10-003	AG10-004		AG10-005		AG10-007	AG10-008		ALXN2060-HV-101
	単回投与		反復投与								Part 1	Part 2	
	A N= 24	P N=8	A N=18	P N=6	A N=24	日本 N = 9	外国 N = 10	A N=18	P N=9	A N=6	A N=14	A N=18	A N=18
年齢（歳）													
平均値（標準偏差）	37.2 (9.29)	38.5 (11.61)	40.8 (8.97)	46.7 (5.01)	39.2 (7.25)	42.0 (9.41)	42.3 (8.72)	42.4 (7.94)	35.4 (5.77)	34.0 (10.24)	38.6 (10.70)	38.3 (8.92)	39.2 (8.45)
中央値	37.5	38.5	42.0	46.0	38.0	44.0	41.5	42.5	35.0	34.0	39.0	38.0	40.0
範囲	18, 55	23, 53	25, 55	41, 53	26, 53	26, 54	30, 55	23, 54	28, 45	21, 49	21, 54	26, 54	28, 54
性別 n（%）													
男性	17 (71)	6 (75)	13 (72)	5 (83)	12 (50)	6 (67)	6 (60)	9 (50)	5 (56)	6 (100)	13 (93)	15 (83)	13 (72)
女性	7 (29)	2 (25)	5 (28)	1 (17)	12 (50)	3 (33)	4 (40)	9 (50)	4 (44)	0	1 (7)	3 (17)	5 (28)
人種 n（%）													
アメリカ／アラスカ先住民	0	1 (13)	0	0	0	0	NR	0	0	0	0	0	0
アジア系	0	0	0	0	0	9 (100)	NR	0	0	0	0	1 (6)	2 (11)
黒人	3 (13)	1 (13)	3 (17)	1 (17)	0	0	NR	1 (6)	0	2 (33)	4 (29)	8 (44)	6 (33)
ハワイ先住民／太平洋諸島民	0	0	0	0	0	0	NR	0	1 (11)	0	1 (7)	0	0
白人	20 (83)	6 (75)	15 (83)	5 (83)	24 (100)	0	NR	17 (94)	8 (89)	4 (67)	9 (64)	9 (50)	10 (56)
白人又は黒人	1 (4)	0	0	0	0	0	NR	0	0	0	0	0	0

	AG10-001				AG10-003	AG10-004		AG10-005		AG10-007	AG10-008		ALXN2060-HV-101
	単回投与		反復投与								Part 1	Part 2	
	A N= 24	P N=8	A N=18	P N=6	A N=24	日本 N = 9	外国 N = 10	A N=18	P N=9	A N=6	A N=14	A N=18	A N=18
民族 n（%）													
ヒスパニック／ラテン系	17 (71)	4 (50)	14 (78)	5 (83)	21 (87.5)	0	4 (40)	15 (83)	7 (78)	1 (17)	2 (14)	1 (6)	0
ヒスパニック／ラテン系以外	7 (29)	4 (50)	4 (22)	1 (17)	3 (12.5)	9 (100)	6 (60)	3 (17)	2 (22)	4 (67)	12 (86)	17 (94)	18 (100)
報告なし	0	0	0	0	0	0	0	0	0	1 (17)	0	0	0
BMI（kg/m^2）													
平均値（標準偏差）	27.08 (3.295)	27.43 (3.417)	27.78 (2.831)	29.72 (0.962)	27.42 (2.387)	23.19 (1.92)	26.61 (3.16)	28.28 (2.274)	27.79 (2.524)	28.19 (3.335)	27.74 (2.902)	26.84 (3.070)	25.89 (3.261)
中央値	27.35	28.13	27.84	29.82	27.70	23.46	27.70	28.14	28.26	28.77	28.90	26.75	25.85
範囲	21.53, 31.69	20.34, 31.78	23.16, 31.18	27.92, 30.79	23.66, 31.72	20.61, 25.74	20.44, 30.67	24.40, 31.63	23.64, 31.08	23.13, 31.44	21.95, 31.17	21.70, 31.31	21.50, 30.91

略語：A＝アコラミジス；BMI＝体格指数；P＝プラセボ；日本＝日本人；外国＝外国人；NR＝報告なし
Source: AG10-001 CSR Section 11.2、AG10-003 CSR Section 11.2、AG10-004 CSR Section 11.2、AG10-005 CSR Section 11.2、AG10-007 CSR Section 11.2、AG10-008 CSR Section 11.2、ALXN2060-HV-101 CSR Section 4.4

5.9.1.2 安全性の結果

第 1 相試験の健康成人被験者での有害事象の発現状況の概要を試験別に Table 54 に示す。これらの試験全体で、アコラミジスが投与された被験者での有害事象の発現割合は 8%～44%、プラセボが投与された被験者での有害事象の発現割合は 25%～56%の範囲であった。死亡に至った有害事象、重篤な有害事象及び重度の有害事象はいずれの試験でも発現しなかった。

第 1 相試験での PT 別の主な有害事象（発現被験者数 2 名以上）は、AG10-001 試験の「頭痛」（8%、単回投与時）及び「上気道感染」（11%、反復投与時）、AG10-005 試験の「浮動性めまい」（17%、アコラミジス群）、「咽頭炎」（11%、アコラミジス群）、「頭痛」（22%、プラセボ群）、AG10-008 試験の「COVID-19」（14%、Part 1）及び「頭痛」（11%、Part 2）、ALXN2060-HV-101 試験の「悪心」、「頭痛」及び「背部痛」（各 11%）であった。

また、治験薬の投与中止に至った有害事象が AG10-004 試験の 1 名及び AG10-008 試験の Part 1 の 3 名に認められ、その内訳は AG10-004 試験で「肉離れ」、AG10-008 試験で「COVID-19」が 2 名、「上腹部痛」が 1 名であった。

Table 54: 第 1 相試験での有害事象の発現状況の概要

	AG10-001				AG10-003	AG10-004	AG10-005		AG10-007	AG10-008		ALXN2060-HV-101
	単回投与		反復投与							Part 1	Part 2	
	A N= 24	P N=8	A N=18	P N=6	A N=24	A N=19	A N=18	P N=9	A N=6	A N=14	A N=18	A N=18
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象	7 (29)	2 (25)	8 (44)	3 (50)	2 (8)	4 (21)	7 (39)	5 (56)	1 (17)	5 (36)	7 (39)	6 (33)
重篤な有害事象	0	0	0	0	0	0	0	0	0	0	0	0
重度の有害事象	0	0	0	0	0	0	0	0	0	0	0	0
治験薬との関連性が否定できない有害事象	5 (21)	2 (25)	3 (17)	1 (17)	1 (4)	0	3 (17)	3 (33)	0	2 (14)	3 (17)	1 (6)
治験薬の投与中止に至った有害事象	0	0	0	0	0	1 (5)[a]	0	0	0	3 (21)	0	0
死亡に至った有害事象	0	0	0	0	0	0	0	0	0	0	0	0

[a] 投与期 1 の投与後に治験薬と関連のない有害事象を発現し、投与期 2 の投与を受けることなく中止した。
略語：A＝アコラミジス；P＝プラセボ
Source: AG10-001 CSR Section 12.1.1 and Appendix 16.2.7.1.2、AG10-003 CSR Section 12.2、AG10-004 CSR Section 12.2.1、AG10-005 CSR Section 12.2.1 and Appendix 16.2.7.1.2、AG10-007 CSR Section 12.2.1、AG10-008 CSR Section 12.2.1、ALXN2060-HV-101 CSR Section 5.1.1.1

6　市販後データ

アコラミジスは世界のいずれの国でも販売されていないため、市販後データは得られていない。

7　付録

7.1　死亡に至った有害事象の一覧表

7.2　重篤な有害事象の一覧表

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
004	[redacted] / M / 7[redacted]	Acoramidis	N	心臓障害 / 心不全 / PROGRESSIVE HEART FAILURE	Blinded Treatment	20[redacted] / 500 Days	20[redacted] / 34 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
007	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / ブドウ球菌性菌血症 / BACTEREMIA DUE TO STAPHYLOCOCCUS	Blinded Treatment	20[redacted] / 540 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心室細動 / CARDIAC ARREST DUE TO VENTRICULAR FIBRILLATION	Blinded Treatment	20[redacted] / 422 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
011	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HF EXACERBATION	Blinded Treatment	20[redacted] / 670 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
011	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 335 Days	20[redacted] / 89 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
013	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 505 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Fatal	Not Related / Y
021	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 289 Days	20[redacted] / 20 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
022	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 397 Days	20[redacted] / 39 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 420 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
033	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性左室不全 / CHRONIC DIASTOLIC HEART FAILURE (CARDIAC DEATH)	Blinded Treatment	20[redacted] / 344 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
034	[redacted] / M / 8[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 再発膀胱癌 / RECURRENCE OF BLADDER CANCER	Blinded Treatment	20[redacted] / 170 Days	20[redacted] / 94 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
103	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 頭蓋脳損傷 / TRAUMATIC BRAIN INJURY	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
103	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 転倒 / ACCIDENTAL FALL	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
				傷害、中毒および処置合併症 / 硬膜下出血 / SUBDURAL HEMORRHAGE	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
				神経系障害 / くも膜下出血 / SUBARACHNOID HEMORRHAGE	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
200	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 呼吸不全 / RESPIRATORY INSUFFICIENCY	Blinded Treatment	20[redacted] / 686 Days	20[redacted] / 24 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
200	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART INSUFFICIENCY	Blinded Treatment	20[redacted] / 702 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
201	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心アミロイドーシス / EXACERBATED CARDIAC ATTR AMYLOIDOSIS	Blinded Treatment	20[redacted] / 113 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED CARDIAC FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 13 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 脳血管発作 / LEFT TOTAL ANTERIOR CIRCULATION STROKE	Blinded Treatment	20[redacted] / 777 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 腸管虚血 / ISCHAEMIC BOWEL	Blinded Treatment	20[redacted] / 198 Days		Drug Interrupted	Severe / Fatal	Not Related / Y
202	[redacted] / M / 7[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 息詰まり / EXITUS DUE TO CHOKE	Blinded Treatment	20[redacted] / 421 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 397 Days	20[redacted] / 22 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
203	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 外傷性頭蓋内出血 / POSTRAUMATIC BRAIN HEMORRHAGE	Blinded Treatment	20[redacted] / 736 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 腸閉塞 / INTESTINAL BLOCKAGE	Blinded Treatment	20[redacted] / 109 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DEATH FOR HEART FAILURE	Blinded Treatment	20[redacted] / 607 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH IN SLEEP (NO FURTHER INFORMATION)	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
212	[redacted] / M / 8[redacted]	Acoramidis	Y	代謝および栄養障害 / 悪液質 / ORGANIC CACHEXIA	Blinded Treatment	20[redacted] / -	20[redacted] / 56 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	N	感染症および寄生虫症 / ブドウ球菌性菌血症 / BACTEREMIA: STAPHYLOCOCCUS AUREUS INFECTION	Blinded Treatment	20[redacted] / 773 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 754 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 236 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 448 Days	20[redacted] / 17 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 324 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
216	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 831 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
228	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / CARDIAC FAILURE DUE TO ATTR AMYLOIDOSIS	Blinded Treatment	20[redacted] / 442 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
229	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE (NOT CONFIRMED)	Blinded Treatment	*27MONTH / -	20[redacted] / 45 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / -	20[redacted] / 723 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / -	20[redacted] / 16 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / HEART FAILURE (CHRONIC) RESULTING IN SUBJECT DEATH	Blinded Treatment	20[redacted] / 158 Days	20[redacted] / 1 Days	Unknown	Severe / Fatal	Not Related / Y
230	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心停止 / SUDDEN CARDIAC ARREST	Blinded Treatment	20[redacted] / 623 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
230	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う肺癌 / METASTATIC LUNG CANCER	Blinded Treatment	20[redacted] / 504 Days	20[redacted] / 79 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 完全房室ブロック / THIRD DEGREE AV-BLOCK	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				臨床検査 / 心拍出量低下 / LOW CARDIAC OUTPUT	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
231	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 全身健康状態悪化 / GENERAL PHYSICAL HEALTH DETERIORATION	Blinded Treatment	20[redacted] / 433 Days	20[redacted] / 1 Days	Unknown	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
231	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID INFECTOIN	Blinded Treatment	20[redacted] / 393 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Fatal	Not Related / Y
233	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 844 Days	20[redacted] / 1 Days	Not Applicable	Severe / Fatal	Not Related / Y
235	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 慢性腎臓病 / WORSENING CHRONIC KIDNEY DISEASE	Blinded Treatment	20[redacted] / 377 Days	20[redacted] / 125 Days	Drug Withdrawn	Moderate / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 6 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
235	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症性ショック / SEPCTIC SHOCK	Blinded Treatment	20[redacted] / 277 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
307	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症性ショック / SEPTIC SHOCK	Blinded Treatment	20[redacted] / 177 Days	20[redacted] / 30 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
310	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 598 Days	20[redacted] / 23 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
401	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENED CARDIAC FAILURE	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 5 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
401	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 右室不全 / SEVERE RIGHT HEART FAILURE	Blinded Treatment	20[redacted] / 393 Days	20[redacted] / 13 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
402	[redacted] / F / 6[redacted]	Acoramidis	Y	心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 176 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症 / SEPSIS [SECONDARY TO SPINAL OSTEOMYELITIS]	Blinded Treatment	20[redacted] / 287 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 293 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 7[redacted]	Acoramidis	N	神経系障害 / 脳梗塞 / ACUTE RIGHT MIDDLE CEREBRAL ARTERY INFARCTION	Blinded Treatment	20[redacted] / 835 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 末期腎疾患 / ENDSTAGE RENAL FAILURE	Blinded Treatment	20[redacted] / 734 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
405	[redacted] / M / 7[redacted]	Acoramidis	N	感染症および寄生虫症 / 敗血症性ショック / SEPTIC SHOCK FROM ESCHERICHIA COLI	Blinded Treatment	20[redacted] / 537 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
406	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心アミロイドーシス / WORSENING OF FAMILIAL CARDIAC AMYLOIDOSIS CARDIOMYOPATHY	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 659 Days	20[redacted] / 20 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 突然死 / SUDDEN DEATH OF UNKNOWN CAUSE	Blinded Treatment	20[redacted] / 125 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / CARDIAL DECOMPESATION BASED ON ATTR CM	Blinded Treatment	20[redacted] / 163 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
702	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID 19 INFECTION	Blinded Treatment	20[redacted] / 117 Days	20[redacted] / 5 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
737	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH OF UNKNOWN REASON	Blinded Treatment	20[redacted] / 621 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH [NO FURTHER INFORMATION]	Blinded Treatment	20[redacted] / 440 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
025	[redacted] / M / 7[redacted]	Placebo	Y	免疫系障害 / アミロイドーシス / END STAGE AMYLOIDOSIS	Blinded Treatment	20[redacted] / 722 Days	20[redacted] / 13 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心アミロイドーシス / END STAGE CARDIAC AMYLOIDOSIS	Blinded Treatment	20[redacted] / 291 Days	20[redacted] / 9 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 211 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	N	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う消化器癌 / METASTATIC GI CANCER WITH UNKNOWN PRIMARY	Blinded Treatment	20[redacted] / 881 Days	20[redacted] / 11 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
030	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心アミロイドーシス / WORSENED CARDIAC AMYLOIDOSIS	Blinded Treatment	20[redacted] / 121 Days	20[redacted] / 4 Days	Not Applicable	Severe / Fatal	Not Related / Y
036	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 多臓器機能不全症候群 / MULTI ORGAN FAILURE	Blinded Treatment	20[redacted] / 750 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
043	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 537 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
052	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH-NO FURTHER INFORMATION)	Blinded Treatment	20[redacted] / 607 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
200	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / CARDIAC INSUFFICIENCY	Blinded Treatment	20[redacted] / 691 Days	20[redacted] / 45 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
201	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 7[redacted]	Placebo	Y	血管障害 / 血栓症 / EXTENSIVE SYSTEMIC THROMBUS	Blinded Treatment	20[redacted] / 820 Days	20[redacted] / 25 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
202	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 469 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
203	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / REFRACTORY HEART FAILURE	Blinded Treatment	20[redacted] / 638 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 811 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
204	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 右室不全 / RIGHT HEART FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 32 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				臨床検査 / 心拍出量低下 / LOW CARDIAC OUTPUT	Blinded Treatment	20[redacted] / 671 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
211	[redacted] / F / 7[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / PNEUMONIA COVID 19	Blinded Treatment	20[redacted] / 342 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	肝胆道系障害 / 肝不全 / LIVER FAILURE	Blinded Treatment	20[redacted] / 669 Days	20[redacted] / 10 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
213	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心肺停止 / CARDIAC AND RESPIRATORY ARREST	Blinded Treatment	20[redacted] / 80 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
215	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 慢性心不全 / WORSENING OF END STAGE HEARTFAILURE	Blinded Treatment	20[redacted] / 578 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 611 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
222	[redacted] / M / 8[redacted]	Placebo	Y	外科および内科処置 / 安楽死 / EUTHANASIA	Blinded Treatment	20[redacted] / 277 Days	20[redacted] / 1 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
222	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 疾患進行 / DECEASED AFTER PALLIATIVE CARE FOR DISEASE PROGRESSION	Blinded Treatment	20[redacted] / 666 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
229	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 836 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / -	20[redacted] / 52 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 339 Days	20[redacted] / 1 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 273 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心筋梗塞 / MYOCARDIAL INFARCTION	Blinded Treatment	20[redacted] / 739 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
230	[redacted] / F / 9[redacted]	Placebo	Y	感染症および寄生虫症 / 腹部敗血症 / ABDOMINAL SEPSIS	Blinded Treatment	20[redacted] / 579 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
235	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENINF HEART FAILURE	Blinded Treatment	20[redacted] / 147 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
235	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心腎症候群 / CARDIORENAL	Blinded Treatment	20[redacted] / 222 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / PNEUMONIA DUE TO COVID-19	Blinded Treatment	20[redacted] / 162 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
402	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / パーキンソン病 / WORSENING PARKINSON'S DISEASE	Blinded Treatment	20[redacted] / 587 Days	20[redacted] / 20 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
403	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 706 Days	20[redacted] / 79 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.5
Treatment Emergent Adverse Events[1] Leading to Fatal Outcome
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 6[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う扁桃癌 / METASTATIC LUNG LESION FROM THE TONSILLAR PRIMARY TUMOR	Blinded Treatment	20[redacted] / 730 Days	20[redacted] / 110 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
409	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 右室不全 / WORSENING RIGHT SIDED HEART FAILURE	Blinded Treatment	20[redacted] / 672 Days	20[redacted] / 1 Days	Not Applicable	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 303 Days	20[redacted] / 54 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
				腎および尿路障害 / 末期腎疾患 / END STAGE RENAL FAILURE	Blinded Treatment	20[redacted] / 348 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. We only include TEAEs that lead to a fatal outcome.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
002	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / WORSENING PAROXYSMAL ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 84 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 肋骨骨折 / BROKEN RIBS	Blinded Treatment	20[redacted] / 171 Days	20[redacted] / 187 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 418 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 425 Days	20[redacted] / 10 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
002	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 475 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房頻脈 / ATRIAL TACHYCARDIA	Blinded Treatment	20[redacted] / 671 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / CELLULITIS OF LEFT ANTERIOR LOWER LEG	Blinded Treatment	20[redacted] / 804 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
003	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 足関節部骨折 / FRACTURED ANKLE	Blinded Treatment	20[redacted] / 62 Days	20[redacted] / 61 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
003	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 蜂巣炎 / CELLULITIS	Blinded Treatment	20[redacted] / 68 Days	20[redacted] / 20 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
004	[redacted] / M / 7[redacted]	Acoramidis	N	心臓障害 / 心不全 / PROGRESSIVE HEART FAILURE	Blinded Treatment	20[redacted] / 500 Days	20[redacted] / 34 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
006	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 619 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 633 Days	20[redacted] / 17 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
006	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / びまん性大細胞型B細胞性リンパ腫 / HHV8-POSITIVE LARGE CELL LYMPHOMA	Blinded Treatment	20[redacted] / 635 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸膜炎 / PLEURISY DUE TO PLEURAL DISEASE (NO FURTHER INFORMATION)	Blinded Treatment	20[redacted] / 675 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				臨床検査 / 酸素飽和度低下 / LOW BLOOD OXYGEN SATURATION	Blinded Treatment	20[redacted] / 733 Days		Dose Not Changed	Severe / Unknown	Not Related / Y
007	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 洞結節機能不全 / SINUS NODE DYSFUNCTION	Blinded Treatment	20[redacted] / 359 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 胸痛 / CHEST PAIN, UNSPECIFIED	Blinded Treatment	20[redacted] / 202 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / BRADYCARDIA (INFRA-HISIAN CONDUCTION DISEASE) SYMPTOMATIC	Blinded Treatment	20[redacted] / 49 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 脚ブロック / ALTERNATING BUNDLE BRANCH BLOCK	Blinded Treatment	20[redacted] / 49 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 関節炎 / WORSENING ARTHRITIS HIP	Blinded Treatment	20[redacted] / 188 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / ブドウ球菌性菌血症 / BACTEREMIA DUE TO STAPHYLOCOCCUS	Blinded Treatment	20[redacted] / 540 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / CHRONIC MIXED SYSTOLIC/DIASTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 272 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 硬膜下血腫 / ACUTE PARAFALCINE SUBDURAL HEMATOMA	Blinded Treatment	20[redacted] / 546 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 誤嚥性肺炎 / ACUTE ASPIRATION PNEUMONIA	Blinded Treatment	20[redacted] / 556 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 蜂巣炎 / CELLULITIS OF RIGHT LOWER EXTREMITY	Blinded Treatment	20[redacted] / 819 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 大動脈弁狭窄 / STENOSIS AORTIC VALVE ACQUIRED	Blinded Treatment	20[redacted] / 322 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室細動 / CARDIAC ARREST DUE TO VENTRICULAR FIBRILLATION	Blinded Treatment	20[redacted] / 422 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
008	[redacted] / M / 6[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC RENAL INSUFFICIENCY	Blinded Treatment	20[redacted] / 274 Days	20[redacted] / 185 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
009	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 胃腸出血 / GI BLEED	Blinded Treatment	20[redacted] / 35 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 胃腸出血 / GI BLEED	Blinded Treatment	20[redacted] / 50 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
011	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE DECOMPENSATION	Blinded Treatment	20[redacted] / 665 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
				心臓障害 / 心不全 / HF EXACERBATION	Blinded Treatment	20[redacted] / 670 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
011	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 335 Days	20[redacted] / 89 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
013	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 349 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 肝機能異常 / LIVER DYSFUNCTION	Blinded Treatment	20[redacted] / 505 Days		Drug Interrupted	Moderate / Not Recovered/Not Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 横紋筋融解症 / RHABDOMYOLYSIS	Blinded Treatment	20[redacted] / 505 Days		Drug Interrupted	Moderate / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
013	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 505 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 胃腸出血 / GASTROINTESTINAL HEMORRHAGE	Blinded Treatment	20[redacted] / 821 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
016	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / NEW ONSET ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 449 Days	20[redacted] / 45 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	代謝および栄養障害 / 脱水 / DEHYDRATION	Blinded Treatment	20[redacted] / 656 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
016	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / WORSENING BRADYCARDIA	Blinded Treatment	20[redacted] / 827 Days	20[redacted] / 28 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
018	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 517 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 587 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE DECOMPENSATED HEART SYSTOLIC FAILURE	Blinded Treatment	20[redacted] / 602 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
019	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 硬膜下血腫 / BILATERAL SUBDURAL HEMATOMA DUE TO CLOSED HEAD INJURY	Blinded Treatment	20[redacted] / 63 Days	20[redacted] / 163 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 746 Days	20[redacted] / 4 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	血管障害 / 末梢血管障害 / PERIPHERAL VASCULAR DISEASE	Blinded Treatment	20[redacted] / 484 Days	20[redacted] / 17 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / CELLULITIS OF LEFT FOOT	Blinded Treatment	20[redacted] / 487 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
019	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / WORSENING ACUTE CONGESTIVE HEART FAILURE UNSPECIFIED HEART FAILURE TYPE	Blinded Treatment	20[redacted] / 910 Days	20[redacted] / 7 Days	Not Applicable	Mild / Recovered/Resolved	Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 滑液嚢腫 / LEFT LEG EDEMA DUE TO BAKER'S CYST	Blinded Treatment	20[redacted] / 29 Days	20[redacted] / 55 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				血管障害 / 低血圧 / HYPOTENSION	Blinded Treatment	20[redacted] / 280 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
021	[redacted] / M / 6[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / RIGHT INGUINAL HERNIA	Blinded Treatment	20[redacted] / 428 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
021	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 631 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 781 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 146 Days	20[redacted] / 21 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
021	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / ASYMPTOMATIC COVID19	Blinded Treatment	20[redacted] / 154 Days	20[redacted] / 10 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				内分泌障害 / 甲状腺機能低下症 / HYPOTHYROIDISM	Blinded Treatment	20[redacted] / 180 Days	20[redacted] / 125 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 皮膚裂傷 / LEFT FOOT LACERATION	Blinded Treatment	20[redacted] / 201 Days	20[redacted] / 3 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 259 Days	20[redacted] / 22 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
021	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 289 Days	20[redacted] / 20 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
022	[redacted] / M / 8[redacted]	Acoramidis	Y	皮膚および皮下組織障害 / 皮脂欠乏性湿疹 / XEROTIC ECZEMA	Blinded Treatment	20[redacted] / 220 Days	20[redacted] / 81 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				皮膚および皮下組織障害 / 老人性紫斑 / SENILE PURPURA	Blinded Treatment	20[redacted] / 220 Days	20[redacted] / 81 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / TYPE II NSTEMI	Blinded Treatment	20[redacted] / 241 Days	20[redacted] / 14 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 多臓器機能不全症候群 / MULTI-ORGAN FAILURE	Blinded Treatment	20[redacted] / 241 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 菌血症 / HIGH GRADE GPC BACTEREMIA	Blinded Treatment	20[redacted] / 241 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 細菌性敗血症 / SEVERE SEPSIS (SECONDARY BACTEREMIA)	Blinded Treatment	20[redacted] / 241 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / NSTEMI	Blinded Treatment	20[redacted] / 327 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE CONGESTIVE HEART FAILURE EXACERBATION REQUIRING HOSPITALIZATION	Blinded Treatment	20[redacted] / 327 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 骨挫傷 / RIGHT-SIDED RIB CONTUSION	Blinded Treatment	20[redacted] / 327 Days	20[redacted] / 45 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 血腫感染 / RIGHT UPPER EXTREMITY INFECTED HEMATOMA	Blinded Treatment	20[redacted] / 397 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
				傷害、中毒および処置合併症 / 焼痂 / RIGHT UPPER EXTREMITY ESCHAR	Blinded Treatment	20[redacted] / 397 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 397 Days	20[redacted] / 39 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / SYMPTOMATIC BRADYCARDIA	Blinded Treatment	20[redacted] / 560 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE DIASTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 560 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心筋梗塞 / NSTEMI	Blinded Treatment	20[redacted] / 756 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / RAPID ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 756 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE REQUIRING HOSPITALIZATION	Blinded Treatment	20[redacted] / 153 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸水 / CHRONIC LEFT PLEURAL EFFUSION	Blinded Treatment	20[redacted] / 153 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / うっ血性心不全 / CONGESTIVE CARDIAC FAILURE	Blinded Treatment	20[redacted] / 409 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 420 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
024	[redacted] / M / 6[redacted]	Acoramidis	Y	血管障害 / 大動脈狭窄 / WORSENING AORTIC STENOSIS	Blinded Treatment	20[redacted] / 30 Days	20[redacted] / 29 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 66 Days	20[redacted] / 412 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				製品の問題 / 医療機器不具合 / PRIOR LEFT KNEE ARTHROPLASTY FAILURE	Blinded Treatment	*21MONTH / -	*3MONTH / -	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
025	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY [SECONDARY TO OVERDIURESIS]	Blinded Treatment	20[redacted] / 14 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
028	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 上室性頻脈 / SUPRAVENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 331 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / SYMPTOMATIC ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 492 Days		Drug Interrupted	Moderate / Recovering/Resolving	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心室性頻脈 / INTERMITTENT NONSUSTAINED VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 337 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 医療機器関連合併症 / MECHANICAL COMPLICATION OF CARDIAC ELECTRODE	Blinded Treatment	20[redacted] / 490 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 570 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 腰部脊柱管狭窄症 / WORSENING LUMBAR SPINAL STENOSIS	Blinded Treatment	20[redacted] / 25 Days	20[redacted] / 100 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 動悸 / PALPITATIONS	Blinded Treatment	20[redacted] / 515 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 616 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
032	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 大腸炎 / ACUTE COLITIS	Blinded Treatment	20[redacted] / 154 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE ON CHRONIC DIASTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 713 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
033	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性左室不全 / CHRONIC DIASTOLIC HEART FAILURE (CARDIAC DEATH)	Blinded Treatment	20[redacted] / 344 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
034	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 慢性腎臓病 / WORSENING CHRONIC RENAL DISEASE	Blinded Treatment	20[redacted] / 29 Days	20[redacted] / 116 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 房室ブロック / AV BLOCK	Blinded Treatment	20[redacted] / 51 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 房室ブロック / AV BLOCK	Blinded Treatment	20[redacted] / 64 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 再発膀胱癌 / RECURRENCE OF BLADDER CANCER	Blinded Treatment	20[redacted] / 170 Days	20[redacted] / 94 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
034	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 腹痛 / ACUTE ABDOMINAL PAIN	Blinded Treatment	20[redacted] / 193 Days		Dose Not Changed	Moderate / Unknown	Not Related / Y
				胃腸障害 / 下痢 / DIARRHEA	Blinded Treatment	20[redacted] / 197 Days		Drug Withdrawn	Moderate / Not Recovered/Not Resolved	Not Related / Y
048	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 757 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / COVID-19	Blinded Treatment	20[redacted] / 757 Days	20[redacted] / 9 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
049	[redacted] / M / 9[redacted]	Acoramidis	N	傷害、中毒および処置合併症 / 転倒 / MECHANICAL FALL	Blinded Treatment	20[redacted] / 27 Days	20[redacted] / 1 Days	Not Applicable	Severe / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神寸前の状態 / NEAR SYNCOPE	Blinded Treatment	20[redacted] / 27 Days	20[redacted] / 1 Days	Not Applicable	Severe / Recovered/Resolved	Not Related / Y
100	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 膀胱癌 / URINARY BLADDER CARCINOMA	Blinded Treatment	20[redacted] / 767 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 裂孔ヘルニア / WORSENED HIATUS HERNIA	Blinded Treatment	20[redacted] / 424 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
100	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 無力症 / WORSENED GENERALIZED WEAKNESS	Blinded Treatment	20[redacted] / 424 Days	20[redacted] / 110 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 疲労 / WORSENED FATIQUE	Blinded Treatment	20[redacted] / 424 Days	20[redacted] / 110 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 虚血性脳卒中 / ISCHEMIC STROKE	Blinded Treatment	20[redacted] / 115 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 完全房室ブロック / COMPLETE HEART BLOCK	Blinded Treatment	20[redacted] / 499 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
101	[redacted] / M / 9[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 27 Days	20[redacted] / 7 Days	Drug Withdrawn	Severe / Recovered/Resolved	Not Related / Y
102	[redacted] / F / 7[redacted]	Acoramidis	N	腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC KIDNEY DISEASE	Blinded Treatment	20[redacted] / 4 Days	20[redacted] / 47 Days	Drug Withdrawn	Severe / Recovered/Resolved	Not Related / Y
103	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 嚥下障害 / DYSPHAGIA OF UNKNOWN ETIOLOGY	Blinded Treatment	20[redacted] / 368 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				神経系障害 / 構語障害 / WORSENING OF DYSARTHRIA	Blinded Treatment	20[redacted] / 368 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
103	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 完全房室ブロック / THIRD-DEGREE ATRIOVENTRICULAR BLOCK	Blinded Treatment	20[redacted] / 642 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症 / SEPSIS	Blinded Treatment	20[redacted] / 123 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				臨床検査 / トロポニンT増加 / POSSIBLE TYPE 2 NSTEMI (INCREASE IN TROPONIN T HS)	Blinded Treatment	20[redacted] / 123 Days	20[redacted] / 5 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / CELLULITIS	Blinded Treatment	20[redacted] / 123 Days	20[redacted] / 19 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
103	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / WORSENING OF ANEMIA	Blinded Treatment	20[redacted] / 201 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 創傷出血 / LOWER LEFT LEG WOUND BLEEDING	Blinded Treatment	20[redacted] / 201 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 頭蓋脳損傷 / TRAUMATIC BRAIN INJURY	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / ACCIDENTAL FALL	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
103	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 硬膜下出血 / SUBDURAL HEMORRHAGE	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
				神経系障害 / くも膜下出血 / SUBARACHNOID HEMORRHAGE	Blinded Treatment	20[redacted] / 398 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
106	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 扁桃癌 / RIGHT TONSIL CANCER	Blinded Treatment	20[redacted] / 456 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
107	[redacted] / M / 6[redacted]	Acoramidis	Y	胃腸障害 / 歯肉出血 / BLEEDING GUM	Blinded Treatment	20[redacted] / 642 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
107	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / ATRIAL FIBRILLATION WITH FAST VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 643 Days	20[redacted] / 17 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 29 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
108	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 交通事故 / CAR ACCIDENT	Blinded Treatment	20[redacted] / 779 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR ARRHYTHMIA (TACHYCARDIA)	Blinded Treatment	20[redacted] / 779 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
111	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 659 Days	20[redacted] / 7 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
200	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / EXACERBATION OF HEART FAILURE	Blinded Treatment	20[redacted] / 482 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	神経系障害 / 脳血管発作 / STROKE	Blinded Treatment	20[redacted] / 683 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 呼吸不全 / RESPIRATORY INSUFFICIENCY	Blinded Treatment	20[redacted] / 512 Days	20[redacted] / 29 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
200	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / ANEMIA	Blinded Treatment	20[redacted] / 670 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				傷害、中毒および処置合併症 / 放射線性膀胱炎 / CYSTITIS RADIATION	Blinded Treatment	20[redacted] / 670 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 呼吸不全 / RESPIRATORY INSUFFICIENCY	Blinded Treatment	20[redacted] / 686 Days	20[redacted] / 24 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				心臓障害 / 心不全 / HEART INSUFFICIENCY	Blinded Treatment	20[redacted] / 702 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 再発膀胱癌 / RECURRENCE OF BLADDER CANCER	Blinded Treatment	20[redacted] / 734 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 小腸腺癌 / DUODENAL INTRAMUCOSAL ADENOCARCINOMA	Blinded Treatment	20[redacted] / 792 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 房室ブロック / 2:1 HEART BLOCK REQUIRING PACEMAKER INSERTION	Blinded Treatment	20[redacted] / 169 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	肝胆道系障害 / 胆嚢炎 / CHOLECYSTITIS	Blinded Treatment	20[redacted] / 24 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 胃食道逆流性疾患 / GASTROESOPHAGEAL REFLUX DISEASE	Blinded Treatment	20[redacted] / 195 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神寸前の状態 / VASOVAGAL EPISODE	Blinded Treatment	20[redacted] / 195 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心アミロイドーシス / EXACERBATED CARDIAC ATTR AMYLOIDOSIS	Blinded Treatment	20[redacted] / 113 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 311 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 361 Days	20[redacted] / 15 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心腎症候群 / ACUTE DECOMPENSATED CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 361 Days	20[redacted] / 51 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 581 Days		Drug Interrupted	Moderate / Recovering/Resolving	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED CARDIAC FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 13 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 脳血管発作 / LEFT TOTAL ANTERIOR CIRCULATION STROKE	Blinded Treatment	20[redacted] / 777 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 完全房室ブロック / COMPLETE HEART BLOCK	Blinded Treatment	20[redacted] / 237 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 前立腺癌 / PROSTATE CANCER	Blinded Treatment	20[redacted] / 366 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	感染症および寄生虫症 / 処置後感染 / HOSPITAL ACQUIRED INFECTION	Blinded Treatment	20[redacted] / 669 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 8[redacted]	Acoramidis	Y	神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 668 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	感染症および寄生虫症 / 胃腸炎 / GASTROENTERITIS	Blinded Treatment	20[redacted] / 122 Days	20[redacted] / 16 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房頻脈 / ATRIAL TACHYCARDIA	Blinded Treatment	20[redacted] / 136 Days	20[redacted] / 2 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 136 Days	20[redacted] / 28 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 590 Days	20[redacted] / 39 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	感染症および寄生虫症 / 医療機器関連感染 / PACEMAKER INFECTION	Blinded Treatment	20[redacted] / 629 Days	20[redacted] / 18 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 術後尿閉 / POST-OPERATIVE URINARY RETENTION	Blinded Treatment	20[redacted] / 391 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 5[redacted]	Acoramidis	Y	感染症および寄生虫症 / 精巣炎 / EPIDIDYMO-ORCHITIS	Blinded Treatment	20[redacted] / 849 Days	20[redacted] / 20 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 55 Days	20[redacted] / 13 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 偶発的過量投与 / SPIRONOLACTONE OVERDOSE (PATIENT DRUG ERROR)	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 16 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 高カリウム血症 / HYPERKALEMIA	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 19 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				神経系障害 / 頭痛 / HEADACHE	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 19 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 腸管虚血 / ISCHAEMIC BOWEL	Blinded Treatment	20[redacted] / 198 Days		Drug Interrupted	Severe / Fatal	Not Related / Y
202	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 226 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 301 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 息詰まり / EXITUS DUE TO CHOKE	Blinded Treatment	20[redacted] / 421 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / LEFT INGUINOSCROTAL HERNIA	Blinded Treatment	20[redacted] / 341 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 鉄欠乏性貧血 / ACUTE EPISODE OF CHRONIC IRON DEFICIENCY ANEMIA	Blinded Treatment	20[redacted] / 176 Days	20[redacted] / 23 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 176 Days	20[redacted] / 23 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 処置後血尿 / POST PROCEDURAL HAEMATURIA	Blinded Treatment	20[redacted] / 181 Days	20[redacted] / 18 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症性ショック / URINARY SEPTIC SHOCK	Blinded Treatment	20[redacted] / 183 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				皮膚および皮下組織障害 / 毛細血管拡張症 / HEMORRHAGIC TELANGIECTASIAS	Blinded Treatment	20[redacted] / 203 Days	20[redacted] / 18 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 細菌性尿路感染 / URINARY TRACT INFECTION (E.COLI BACTEREMIA)	Blinded Treatment	20[redacted] / 255 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 外傷性血尿 / HEMATURIA DUE TO ACCIDENTAL SELFREMOVE OF URINARY CATHETER	Blinded Treatment	20[redacted] / 255 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / SEVERE ACUTE ANEMIA	Blinded Treatment	20[redacted] / 399 Days	20[redacted] / 16 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 下部消化管出血 / LOWER GASTROINTESTINAL BLEEDING	Blinded Treatment	20[redacted] / 399 Days	20[redacted] / 16 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 慢性閉塞性肺疾患 / WORSENING OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	Blinded Treatment	20[redacted] / 485 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 9 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY INFECTION	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 9 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 急性呼吸不全 / ACUTE RESPIRATORY FAILURE	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 9 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 596 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 急性肺水腫 / ACUTE PULMONARY EDEMA	Blinded Treatment	20[redacted] / 596 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 呼吸不全 / RESPIRATORY FAILURE	Blinded Treatment	20[redacted] / 596 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / SARS-COV-2 INFECTION	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 狭心症 / ANGINA PECTORIS	Blinded Treatment	20[redacted] / 655 Days	20[redacted] / 11 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / SEVERE ACUTE ANEMIA	Blinded Treatment	20[redacted] / 664 Days	20[redacted] / 11 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 直腸出血 / RECTAL BLEEDING	Blinded Treatment	20[redacted] / 664 Days	20[redacted] / 149 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 全身健康状態悪化 / MULTIFACTORIAL DETERIORATION OF GENERAL CONDITION	Blinded Treatment	20[redacted] / 181 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 397 Days	20[redacted] / 22 Days	Drug Interrupted	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 尿路感染 / URINARY INFECTION	Blinded Treatment	20[redacted] / 411 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY FAILURE	Blinded Treatment	20[redacted] / 411 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
203	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 転倒 / FALL	Blinded Treatment	20[redacted] / 804 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Acoramidis	Y	胃腸障害 / 胃炎 / GASTRITIS (PREVIOUSLY REPORTED AS ABDOMINAL PAIN)	Blinded Treatment	20[redacted] / 59 Days	20[redacted] / 11 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
203	[redacted] / F / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / SARS-COV2 INFECTION WITHOUT PNEUMONIA	Blinded Treatment	20[redacted] / 64 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / シュードモナス性尿路感染 / URINARY TRACT INFECTION SECONDARY TO PSEUDOMONA AERUGINOSA	Blinded Treatment	20[redacted] / 296 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				胃腸障害 / 絞扼性鼠径ヘルニア / STRANGLED INGUINAL HERNIA	Blinded Treatment	20[redacted] / 454 Days	20[redacted] / 5 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19肺炎 / BILATERAL PNEUMONIA DUE TO SARS-COV2	Blinded Treatment	20[redacted] / 1 Days	20[redacted] / 12 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
203	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 94 Days	20[redacted] / 8 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 大腿骨骨折 / FEMUR FRACTURE	Blinded Treatment	20[redacted] / 608 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 外傷性頭蓋内出血 / POSTRAUMATIC BRAIN HEMORRHAGE	Blinded Treatment	20[redacted] / 736 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
204	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心腎症候群 / WORSENING CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 54 Days	20[redacted] / 31 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
204	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE HOSPITALIZATION	Blinded Treatment	20[redacted] / 231 Days	20[redacted] / 13 Days	Drug Withdrawn	Severe / Recovered/Resolved With Sequelae	Not Related / Y
205	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 373 Days	20[redacted] / 23 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 502 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 572 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
205	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 失神寸前の状態 / PRE SYNCOPE	Blinded Treatment	*26MONTH / -	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
208	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 狭心症 / EFFORT ANGINA	Blinded Treatment	20[redacted] / 57 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
210	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 移行上皮癌 / RIGHT UROTHELIAL CARCINOMA	Blinded Treatment	20[redacted] / 489 Days	20[redacted] / 120 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 貧血 / SEVERE ANEMIA	Blinded Treatment	20[redacted] / 552 Days	20[redacted] / 20 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 一過性脳虚血発作 / TRANSITOR ISCHEMI ATTACK	Blinded Treatment	20[redacted] / 432 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 216 Days	20[redacted] / 25 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 320 Days	20[redacted] / 8 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 頭部損傷 / HEAD INGIURY	Blinded Treatment	20[redacted] / 330 Days	20[redacted] / 9 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 345 Days	20[redacted] / 36 Days	Dose Reduced	Mild / Recovered/Resolved	Not Related / Y
				胃腸障害 / 直腸出血 / RECTORRHAGIA	Blinded Treatment	20[redacted] / 428 Days	20[redacted] / 28 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / クロストリジウム・ディフィシレ感染 / CLOSTRIDIUM DIFFICILE INFECTION	Blinded Treatment	20[redacted] / 428 Days	20[redacted] / 68 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 尿路感染 / URINARY INFECTION	Blinded Treatment	20[redacted] / 520 Days	20[redacted] / 14 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / WORSENING HIGH FREQUENCY ARTIAL FIBRILLATION	Blinded Treatment	20[redacted] / 87 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 胃腸炎 / ACUTE GASTROENTERITIS	Blinded Treatment	20[redacted] / 778 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / LEFT INGUINAL HERNIA	Blinded Treatment	20[redacted] / 43 Days	20[redacted] / 1 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				胃腸障害 / 腸閉塞 / INTESTINAL BLOCKAGE	Blinded Treatment	20[redacted] / 109 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DEATH FOR HEART FAILURE	Blinded Treatment	20[redacted] / 607 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	*7MONTH / -	20[redacted] / 137 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE	Blinded Treatment	20[redacted] / 288 Days	20[redacted] / 23 Days	Dose Reduced	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / ATRIAL FIBRILATION AND FLUTTER HIGH-FREQUENCY	Blinded Treatment	20[redacted] / 433 Days	20[redacted] / 2 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / レンサ球菌性化膿性関節炎 / STREPTOCOCCUS GALLOLYTICUS SEPTIC ARTHRITIS	Blinded Treatment	20[redacted] / 501 Days		Dose Not Changed	Mild / Recovering/Resolving	Not Related / Y
				傷害、中毒および処置合併症 / 仙骨骨折 / DISPLACED SACRAL FRACTURE	Blinded Treatment	20[redacted] / 587 Days		Dose Not Changed	Mild / Recovering/Resolving	Not Related / Y
				傷害、中毒および処置合併症 / 腰椎骨折 / THE TRASVERSE PROCESS L5 FRACTURE	Blinded Treatment	20[redacted] / 587 Days		Dose Not Changed	Mild / Recovering/Resolving	Not Related / Y
				傷害、中毒および処置合併症 / 大腿骨骨折 / LEFT FEMURE FRACTURE	Blinded Treatment	20[redacted] / 665 Days	20[redacted] / 10 Days	Dose Not Changed	Mild / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH IN SLEEP (NO FURTHER INFORMATION)	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
212	[redacted] / M / 7[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 急性呼吸不全 / HYPOXEMIC HYPERCAPNIC ACUTE RESPIRATORY FAILURE	Blinded Treatment	20[redacted] / 109 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 833 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 864 Days	20[redacted] / 13 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
212	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 908 Days	20[redacted] / 14 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	代謝および栄養障害 / 悪液質 / ORGANIC CACHEXIA	Blinded Treatment	*5MONTH / -	20[redacted] / 56 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
				胃腸障害 / 胃腸出血 / ACUTE GASTROINTESTINAL BLEEDING	Blinded Treatment	20[redacted] / 193 Days	20[redacted] / 8 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
213	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 104 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
213	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 心房血栓症 / TROMBUS IN LEFT ATRIUM	Blinded Treatment	20[redacted] / 558 Days		Dose Not Changed	Severe / Unknown	Not Related / Y
				臨床検査 / 国際標準比増加 / INR ELEVATION	Blinded Treatment	20[redacted] / 568 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	胃腸障害 / 腸閉塞 / BOWEL OBSTRUCTION	Blinded Treatment	20[redacted] / 31 Days		Drug Withdrawn	Severe / Not Recovered/Not Resolved	Not Related / Y
214	[redacted] / M / 6[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 変形性関節症 / WORSENING OSTEOARTHRITIS	Blinded Treatment	20[redacted] / 538 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
214	[redacted] / M / 6[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 脊柱管狭窄症 / WORSENING SPINAL STENOSIS	Blinded Treatment	*24MONTH / -	20[redacted] / 42 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心房粗動 / UNRESOLVED ATRIAL AFLUTTER	Blinded Treatment	20[redacted] / 408 Days	20[redacted] / 28 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
215	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE WORSENING	Blinded Treatment	20[redacted] / 684 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神 / LIPOTYMI, CAUSE UNKNOWN	Blinded Treatment	20[redacted] / 824 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	精神障害 / 双極性障害 / BIPOLAR DISORDER	Blinded Treatment	20[redacted] / 826 Days	20[redacted] / 33 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	N	感染症および寄生虫症 / 細菌性肺炎 / BILATERAL BACTERIAL PNEUMONIA	Blinded Treatment	20[redacted] / 476 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 椎間板炎 / SPONDYLODISCITIS	Blinded Treatment	20[redacted] / 568 Days	20[redacted] / 40 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				皮膚および皮下組織障害 / 皮膚潰瘍 / ULCERATION RIGHT FOOT	Blinded Treatment	20[redacted] / 710 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	N	感染症および寄生虫症 / ブドウ球菌性菌血症 / BACTEREMIA: STAPHYLOCOCCUS AUREUS INFECTION	Blinded Treatment	20[redacted] / 773 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	代謝および栄養障害 / 脱水 / DEHYDRATION	Blinded Treatment	20[redacted] / 28 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 便秘 / CONSTIPATION	Blinded Treatment	20[redacted] / 310 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 丹毒 / ERYSIPELAS	Blinded Treatment	20[redacted] / 574 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
				INTERMITTANT ACUTE OUTBREAKS						

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 体位性めまい / ORTHOSTATIC DIZZINESS	Blinded Treatment	20[redacted] / 630 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 658 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 埋込み部位感染 / INFECTION PACEMAKER POCKET SITE	Blinded Treatment	20[redacted] / 678 Days	20[redacted] / 25 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 754 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE WORSENING	Blinded Treatment	20[redacted] / 136 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART FAILURE WORSENING	Blinded Treatment	20[redacted] / 151 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART FAILURE WORSENING	Blinded Treatment	20[redacted] / 182 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 低カリウム血症 / HYPOKALEMIA	Blinded Treatment	20[redacted] / 226 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 236 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 754 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 尿路性敗血症 / UROSEPSIS	Blinded Treatment	20[redacted] / 74 Days	20[redacted] / 5 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / NON STEMI	Blinded Treatment	20[redacted] / 418 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心筋梗塞 / STEMI	Blinded Treatment	20[redacted] / 428 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 大動脈狭窄 / AORTASTENOSIS	Blinded Treatment	20[redacted] / 537 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 気道感染 / RESPIRATORY INFECTION	Blinded Treatment	20[redacted] / 208 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / PAROXYSMAL ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 237 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 肺水腫 / PULMONARY OEDEMA	Blinded Treatment	20[redacted] / 257 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 肺水腫 / PULMONARY OEDEMA	Blinded Treatment	20[redacted] / 267 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 肺水腫 / PULMONARY OEDEMA	Blinded Treatment	20[redacted] / 412 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING OF HEARTFAILURE	Blinded Treatment	20[redacted] / 873 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 58 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 脱水 / DEHYDRATION	Blinded Treatment	20[redacted] / 78 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸水 / WORSENING OF DYSPNOE DUE TO PLEURAL EFFUSION RIGHT LUNG.	Blinded Treatment	20[redacted] / 350 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / ACCIDENTAL FALL	Blinded Treatment	20[redacted] / 380 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 448 Days	20[redacted] / 17 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 218 Days	20[redacted] / 13 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / EXACERBATION OF ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 225 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 膀胱炎 / CYSTITIS	Blinded Treatment	20[redacted] / 249 Days	20[redacted] / 11 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE WORSENING	Blinded Treatment	20[redacted] / 611 Days	20[redacted] / 32 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 腰部脊柱管狭窄症 / WORSENING LUMBAL STENOSIS	Blinded Treatment	20[redacted] / 470 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 大腿骨頚部骨折 / FRACTURE COLLUM FEMORIS RIGHT SIDE	Blinded Treatment	20[redacted] / 87 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEARTFAILURE	Blinded Treatment	20[redacted] / 295 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 324 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 脳振盪 / CONCUSSION	Blinded Treatment	20[redacted] / 286 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	N	胃腸障害 / 便秘 / WORSENING OF OBSTIPATION	Blinded Treatment	20[redacted] / 455 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 肺うっ血 / PULMONARY CONGESTION	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

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216	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE PRERENAL FAILURE	Blinded Treatment	20[redacted] / 796 Days	20[redacted] / 15 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 急性心不全 / CHF EXACERBATION	Blinded Treatment	20[redacted] / 929 Days		Not Applicable	Moderate / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / WORSENING OF CONGESTIVE HEART FAILURE.	Blinded Treatment	20[redacted] / 49 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / FALL	Blinded Treatment	20[redacted] / 729 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

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Treatment Emergent Serious Adverse Events[1]
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Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
216	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 831 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / WORSENING OF ANEMIA	Blinded Treatment	20[redacted] / 279 Days	20[redacted] / 45 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE	Blinded Treatment	20[redacted] / 543 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 呼吸困難 / DYSPNEA	Blinded Treatment	20[redacted] / 573 Days	20[redacted] / 9 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
216	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 労作性呼吸困難 / EXERTIONAL DYSPNEA	Blinded Treatment	20[redacted] / 834 Days	20[redacted] / 70 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 労作性呼吸困難 / EXERTIONAL DYSPNEA	Blinded Treatment	20[redacted] / 597 Days	20[redacted] / 43 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 徐脈 / EXCESSIVE BRADYCARDIA	Blinded Treatment	20[redacted] / 652 Days	20[redacted] / 38 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				製品の問題 / リードの位置ずれ / DISLODGMENT OF RV ELECTRODE	Blinded Treatment	20[redacted] / 716 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
216	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / BRADYCARDIA	Blinded Treatment	20[redacted] / 383 Days	20[redacted] / 18 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
218	[redacted] / M / 8[redacted]	Acoramidis	Y	呼吸器、胸郭および縦隔障害 / 労作性呼吸困難 / DYSPNOE D'EFFORT	Blinded Treatment	20[redacted] / 128 Days	20[redacted] / 24 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 上気道感染 / UPPER RESPIRATORY TRACT INFECTION	Blinded Treatment	20[redacted] / 859 Days	20[redacted] / 21 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 基底細胞癌 / BASOCELLULAR SKIN CARCINOMA	Blinded Treatment	20[redacted] / 52 Days	20[redacted] / 237 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE CORDECOMPENSATION	Blinded Treatment	20[redacted] / 165 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / BRADYCARDIA	Blinded Treatment	20[redacted] / 90 Days	20[redacted] / 60 Days	Drug Withdrawn	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / CARDIAC CORDECOMPENSATION	Blinded Treatment	20[redacted] / 499 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸膜炎 / PLEURITIS	Blinded Treatment	20[redacted] / 499 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / F / 8[redacted]	Acoramidis	Y	神経系障害 / 失神寸前の状態 / PRE-SYNCOPE	Blinded Treatment	20[redacted] / 520 Days	20[redacted] / 12 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 気道感染 / RESPIRATORY INFECTION	Blinded Treatment	20[redacted] / 576 Days	20[redacted] / 13 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 795 Days	20[redacted] / 17 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
220	[redacted] / M / 6[redacted]	Acoramidis	Y	腎および尿路障害 / 膀胱結石 / LARGE BLADDER STONE (URINARY)	Blinded Treatment	20[redacted] / 79 Days	20[redacted] / 39 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
220	[redacted] / M / 6[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 処置後出血 / POST PROCEDURAL HEMORRHAGE	Blinded Treatment	20[redacted] / 575 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE EPISODE	Blinded Treatment	20[redacted] / 578 Days	20[redacted] / 35 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
221	[redacted] / M / 8[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 腎細胞癌 / LEFT CELL CARCINOMA - KIDNEY	Blinded Treatment	20[redacted] / 50 Days		Drug Withdrawn	Moderate / Recovering/Resolving	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / FALL WITHOUT LOSS OF CONSCIOUSNESS AND WAS HOSPITALISED.	Blinded Treatment	20[redacted] / 50 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
222	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 機械的イレウス / MECHANICAL ILEUS, DUE TO ADHESIONS	Blinded Treatment	20[redacted] / 12 Days	20[redacted] / 23 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
226	[redacted] / M / 8[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 椎間板突出 / RECURRENT HERNIATED DISC L4-5	Blinded Treatment	20[redacted] / 15 Days	20[redacted] / 225 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				製品の問題 / 医療機器のゆるみ / LOOSENING OF CUP RIGHT TOTAL HIP PROSTHESIS	Blinded Treatment	20[redacted] / 43 Days	20[redacted] / 197 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
228	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / CARDIAC FAILURE DUE TO ATTR AMYLOIDOSIS	Blinded Treatment	20[redacted] / 442 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 結腸直腸癌 / COLORECTAL CANCER	Blinded Treatment	20[redacted] / 336 Days	*2MONTH / -	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 尿路性敗血症 / UROSEPSIS	Blinded Treatment	20[redacted] / 440 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				胃腸障害 / イレウス / SMALL BOWEL ILEUS	Blinded Treatment	20[redacted] / 445 Days	20[redacted] / 9 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 小腸閉塞 / SMALL BOWEL OBSTRUCTION	Blinded Treatment	20[redacted] / 664 Days	20[redacted] / 10 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 上部消化管出血 / UPPER GASTROINTESTINAL BLEED	Blinded Treatment	20[redacted] / 782 Days	20[redacted] / 93 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 腸管穿孔 / INTESTINAL PERFORATION	Blinded Treatment	20[redacted] / 783 Days	20[redacted] / 35 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症 / SEPSIS	Blinded Treatment	20[redacted] / 639 Days		Not Applicable	Moderate / Recovering/Resolving	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	血液およびリンパ系障害 / 貧血 / ANAEMIA	Blinded Treatment	20[redacted] / 176 Days	*同月 / -	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 筋骨格系胸痛 / MUSCULOSKELETAL CHEST PAIN	Blinded Treatment	20[redacted] / 643 Days	20[redacted] / 3 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				胃腸障害 / 小腸閉塞 / SMALL BOWEL OBSTRUCTION	Blinded Treatment	20[redacted] / 787 Days	20[redacted] / 24 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 塞栓症 / CARDIAC EMBOLUS	Blinded Treatment	20[redacted] / 787 Days	20[redacted] / 24 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 完全房室ブロック / COMPLETE HEART BLOCK	Blinded Treatment	20[redacted] / 838 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 甲状腺髄様癌 / MEDULLARY THYROID CARCINOMA	Blinded Treatment	20[redacted] / -		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 脳梗塞 / RIGHT MCA TERRITORY INFRACT	Blinded Treatment	20[redacted] / 231 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				神経系障害 / 脳血管発作 / CEREBROVASCULAR ACCIDENT	Blinded Treatment	20[redacted] / 373 Days	20[redacted] / 11 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				傷害、中毒および処置合併症 / 大腿骨頚部骨折 / RIGHT NECK OF FEMUR FRACTURE	Blinded Treatment	20[redacted] / 750 Days	20[redacted] / 34 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Acoramidis	Y	血管障害 / 起立性低血圧 / POSTURAL HYPOTENSION	Blinded Treatment	20[redacted] / 36 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	神経系障害 / 舞踏病 / UNDIAGNOSED CHORELFORM DISORDER (WORSENING OF)	Blinded Treatment	*2MONTH / -		Drug Withdrawn	Moderate / Recovering/Resolving	Not Related / Y
				神経系障害 / 舞踏病 / UNDIAGNOSED CHOREIFORM DISORDER (WORSENING OF)	Blinded Treatment	*2MONTH / -	20[redacted] / 65 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 鼻出血 / EPISTAXIS	Blinded Treatment	20[redacted] / 692 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	*23MONTH / -	20[redacted] / 69 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / FALL	Blinded Treatment	20[redacted] / 821 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE (NOT CONFIRMED)	Blinded Treatment	*27MONTH / -	20[redacted] / 45 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	*5MONTH / -	20[redacted] / 723 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / BRADYCARDIA	Blinded Treatment	20[redacted] / 804 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 腎結石症 / RENAL CALCULI	Blinded Treatment	20[redacted] / 748 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 三束ブロック / TRIFASCICULAR BLOCK	Blinded Treatment	20[redacted] / 225 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				神経系障害 / 浮動性めまい / DIZZINESS	Blinded Treatment	20[redacted] / 238 Days	20[redacted] / 5 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / -	20[redacted] / 27 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う前立腺癌 / METASTATIC PROSTATE CANCER	Blinded Treatment	20[redacted] / 645 Days	20[redacted] / 378 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	神経系障害 / 脳梗塞 / LEFT MCA INFARCT	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	*29MONTH / -	20[redacted] / 16 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 企図的過量投与 / DELIBERATE DRUG OVERDOSE	Blinded Treatment	20[redacted] / 908 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	眼障害 / 黄斑円孔 / MACULAR HOLE	Blinded Treatment	20[redacted] / -	20[redacted] / 126 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	神経系障害 / 神経系障害 / NERVOUS SYSTEM DISORDER	Blinded Treatment	*5MONTH / -		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
				神経系障害 / 神経系障害 / NERVOUS SYSTEM DISORDER	Blinded Treatment	*5MONTH / -	20[redacted] / 75 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 6[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 247 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 非心臓性胸痛 / CHEST PAIN (NON CARDIAC)	Blinded Treatment	20[redacted] / 279 Days	20[redacted] / 368 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 大腿骨頚部骨折 / FRACTURED NECK OF FEMUR- RIGHT	Blinded Treatment	20[redacted] / 166 Days	20[redacted] / 33 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 79 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 慢性心不全 / HEART FAILURE (CHRONIC) RESULTING IN SUBJECT DEATH	Blinded Treatment	20[redacted] / 158 Days	20[redacted] / 1 Days	Unknown	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 三束ブロック / TRISFASCICULAR BLOCK	Blinded Treatment	20[redacted] / -	20[redacted] / 24 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺膿瘍 / LEFT LUNG ABSCESS	Blinded Treatment	20[redacted] / -	20[redacted] / 141 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 転倒 / FALL	Blinded Treatment	20[redacted] / 507 Days	20[redacted] / 19 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	*同月 / -	20[redacted] / 35 Days	Drug Interrupted	Mild / Recovered/Resolved With Sequelae	Not Related / Y
				血液およびリンパ系障害 / 免疫性血小板減少症 / IMMUNE THROMBOCYTOPENIC PURPURA	Blinded Treatment	20[redacted] / 701 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
230	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / BRADYCARDIA	Blinded Treatment	20[redacted] / 165 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 起立性低血圧 / SYNCOPE DUE TO ORTHOSTATIC HYPOTENSION	Blinded Treatment	20[redacted] / 165 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
230	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID19-INFECTION	Blinded Treatment	20[redacted] / 590 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心停止 / SUDDEN CARDIAC ARREST	Blinded Treatment	20[redacted] / 623 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う肺癌 / METASTATIC LUNG CANCER	Blinded Treatment	20[redacted] / 504 Days	20[redacted] / 79 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 丹毒 / ERYSIPELAS LEFT LOWER LEG	Blinded Treatment	20[redacted] / 229 Days	20[redacted] / 20 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
230	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 丹毒 / ERYSIPELAS LOWER LEGS	Blinded Treatment	20[redacted] / 282 Days	20[redacted] / 28 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / ブドウ球菌性肺炎 / STAPHYLOCOCCAL PNEUMONIA	Blinded Treatment	20[redacted] / 406 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE EPISODE HEART FAILURE	Blinded Treatment	20[redacted] / 406 Days	20[redacted] / 23 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 気胸 / PNEUMOTHORAX RIGHT LUNG	Blinded Treatment	20[redacted] / 417 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
230	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 完全房室ブロック / THIRD DEGREE AV-BLOCK	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				臨床検査 / 心拍出量低下 / LOW CARDIAC OUTPUT	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 396 Days	20[redacted] / 27 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE EPISODE OF HEART FAILUE	Blinded Treatment	20[redacted] / 399 Days	20[redacted] / 24 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
231	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 腹痛 / ABDOMINAL PAIN	Blinded Treatment	20[redacted] / 337 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 全身健康状態悪化 / GENERAL PHYSICAL HEALTH DETERIORATION	Blinded Treatment	20[redacted] / 433 Days	20[redacted] / 1 Days	Unknown	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心筋梗塞 / SUBACUTE NON STEMI	Blinded Treatment	20[redacted] / 326 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING OF DECOMPENSATIO CORDIS	Blinded Treatment	20[redacted] / 382 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
231	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID INFECTOIN	Blinded Treatment	20[redacted] / 393 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Fatal	Not Related / Y
233	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 徐脈 / SYMPTOMATIC BRADYCARDIA	Blinded Treatment	*1MONTH / -	20[redacted] / 116 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / PAUCISINTOMATIC INFECTION WITH SARS COV 2	Blinded Treatment	20[redacted] / 771 Days	20[redacted] / 11 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 49 Days	20[redacted] / 17 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
233	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 772 Days	20[redacted] / 9 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 慢性閉塞性肺疾患 / COPD EXACERBATION	Blinded Treatment	20[redacted] / 772 Days	20[redacted] / 9 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 844 Days	20[redacted] / 1 Days	Not Applicable	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE DECOMPENSATION	Blinded Treatment	*13MONTH / -	20[redacted] / 48 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
233	[redacted] / F / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 575 Days		Drug Interrupted	Moderate / Recovering/Resolving	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE ON CHRONIC	Blinded Treatment	20[redacted] / 575 Days	20[redacted] / 10 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 呼吸困難 / WORSENING DYSPNOEA	Blinded Treatment	20[redacted] / 622 Days	20[redacted] / 4 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	神経系障害 / 失神寸前の状態 / PRE-SYNCOPE	Blinded Treatment	20[redacted] / 713 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
233	[redacted] / F / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE	Blinded Treatment	20[redacted] / 713 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / BRADIFREQUENT ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 888 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 肝転移 / LIVER METASTASIS DUE TO COLON CANCER	Blinded Treatment	20[redacted] / -		Drug Interrupted	Moderate / Recovering/Resolving	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	血管障害 / 大動脈狭窄 / LOW - FLOW, LOW GRADIENT SEVERE AORTIC STENOSIS	Blinded Treatment	20[redacted] / 762 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
234	[redacted] / M / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 変形性関節症 / COXARTHROSIS	Blinded Treatment	20[redacted] / 842 Days	20[redacted] / 19 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	肝胆道系障害 / 胆管炎 / WORSENING OF CHOLANGITIS	Blinded Treatment	20[redacted] / 170 Days	20[redacted] / 7 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 胆管炎 / WORSENING OF CHOLANGITIS	Blinded Treatment	20[redacted] / 190 Days	20[redacted] / 37 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 胆管炎 / WORSENING OF CHOLANGITIS	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 8 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
234	[redacted] / M / 8[redacted]	Acoramidis	Y	肝胆道系障害 / 胆管炎 / WORSENING OF CHOLANGITIS	Blinded Treatment	20[redacted] / 682 Days	20[redacted] / 28 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / NOCOSOMIAL PNEUMONIA	Blinded Treatment	20[redacted] / 698 Days	20[redacted] / 42 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 胆管炎 / RECURRENT CHOLANGITIS	Blinded Treatment	20[redacted] / 730 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心房粗動 / ATRIAL FLUTTER	Blinded Treatment	20[redacted] / 41 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
234	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / INGUINAL HERNIA	Blinded Treatment	20[redacted] / 396 Days	20[redacted] / 10 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 840 Days	20[redacted] / 7 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心粗動 / FLUTTER ABLATION	Blinded Treatment	20[redacted] / 227 Days	20[redacted] / 2 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				生殖系および乳房障害 / 前立腺炎 / PROSTATITIS	Blinded Treatment	20[redacted] / 637 Days	20[redacted] / 4 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
235	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 慢性腎臓病 / WORSENING CHRONIC KIDNEY DISEASE	Blinded Treatment	20[redacted] / 377 Days	20[redacted] / 125 Days	Drug Withdrawn	Moderate / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19肺炎 / COVID-19 PNEUMONIA	Blinded Treatment	20[redacted] / 173 Days	20[redacted] / 22 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				神経系障害 / 脳神経麻痺 / INCOMPLETE PARALYSIS OF THE RIGHT THIRD CRANIAL NERVE	Blinded Treatment	20[redacted] / 541 Days	20[redacted] / 16 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / RIGHT PNEUMONIA	Blinded Treatment	20[redacted] / 552 Days	20[redacted] / 49 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
235	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 6 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 人工関節周囲骨折 / LEFT PERIPROSTHETIC FRACTURE TYPE A VANCOUVER	Blinded Treatment	20[redacted] / 891 Days		Drug Interrupted	Severe / Recovering/Resolving	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / 敗血症性ショック / SEPCTIC SHOCK	Blinded Treatment	20[redacted] / 277 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
304	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 212 Days	20[redacted] / 7 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
307	[redacted] / M / 8[redacted]	Acoramidis	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 移行上皮癌 / UROTHELIAL CARCINOMA	Blinded Treatment	20[redacted] / 76 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 177 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y
				感染症および寄生虫症 / 敗血症性ショック / SEPTIC SHOCK	Blinded Treatment	20[redacted] / 177 Days	20[redacted] / 30 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
310	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 439 Days	20[redacted] / 23 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
310	[redacted] / F / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 493 Days	20[redacted] / 11 Days	Unknown	Severe / Recovered/Resolved	Not Related / Y
				臨床検査 / 心電図QT延長 / WORSENING QTC INTERVAL WIDENING	Blinded Treatment	20[redacted] / 573 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 598 Days	20[redacted] / 23 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
312	[redacted] / M / 8[redacted]	Acoramidis	N	感染症および寄生虫症 / ウイルス性上気道感染 / UPPER AIRWAY INFECTION OF VIRAL ETIOLOGY	Blinded Treatment	20[redacted] / 234 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
312	[redacted] / M / 8[redacted]	Acoramidis	N	心臓障害 / 心不全 / HEART DISEASE DECOMPENSATION	Blinded Treatment	20[redacted] / 239 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 腎機能障害 / WORSENING RENAL FUNCTION	Blinded Treatment	20[redacted] / 239 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 555 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART DISEASE DECOMPENSATION	Blinded Treatment	20[redacted] / 661 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
312	[redacted] / M / 8[redacted]	Acoramidis	N	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 661 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 上気道感染 / UPPER AIRWAY INFECTION	Blinded Treatment	20[redacted] / 756 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
401	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 274 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA WORSENING	Blinded Treatment	20[redacted] / 410 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
401	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 肋骨骨折 / FRACTURED RIBS RIGHT 4-6	Blinded Treatment	20[redacted] / 461 Days	20[redacted] / 12 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 発熱 / FEBRILE ILLNESS	Blinded Treatment	20[redacted] / 137 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	肝胆道系障害 / 胆管結石 / CHOLEDOCHOLITHIASIS	Blinded Treatment	20[redacted] / 48 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 胆管炎 / CHOLANGITIS	Blinded Treatment	20[redacted] / 293 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
401	[redacted] / M / 6[redacted]	Acoramidis	Y	代謝および栄養障害 / 脱水 / DEHYDRATION (FORMERLY ACUTE KIDNEY INJURY)	Blinded Treatment	20[redacted] / 651 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENED CARDIAC FAILURE	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 5 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	臨床検査 / 血中クレアチニン増加 / ELEVATED CREATININE WORSENED DUE TO ENALOPRIL	Blinded Treatment	20[redacted] / 29 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 大腿骨頚部骨折 / FRACTURED NECK OF FEMUR LEFT	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 14 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
401	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 222 Days	20[redacted] / 27 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 230 Days	20[redacted] / 16 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 右室不全 / SEVERE RIGHT HEART FAILURE	Blinded Treatment	20[redacted] / 393 Days	20[redacted] / 13 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 変形性関節症 / OSTEOARTHRITIS OF LEFT SHOULDER (PREVIOUSLY WORSENING OF LEFT SHOULDER PAIN)	Blinded Treatment	20[redacted] / 480 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / F / 6[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC KIDNEY DISEASE	Blinded Treatment	20[redacted] / 88 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 骨盤骨折 / LEFT PUBIC BONE FRACTURE	Blinded Treatment	20[redacted] / 117 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 152 Days	20[redacted] / 14 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 167 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / F / 6[redacted]	Acoramidis	Y	心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 176 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 中毒性腎症 / NSAIDS INDUCED ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 337 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心停止 / VENTRICULAR STANDSTILL	Blinded Treatment	20[redacted] / 320 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	血管障害 / 低血圧 / HYPOTENSION	Blinded Treatment	20[redacted] / 251 Days	20[redacted] / 7 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 8[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 背部痛 / LUMBAR BACK PAIN	Blinded Treatment	20[redacted] / 278 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				感染症および寄生虫症 / 敗血症 / SEPSIS [SECONDARY TO SPINAL OSTEOMYELITIS]	Blinded Treatment	20[redacted] / 287 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 290 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 293 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 7[redacted]	Acoramidis	N	心臓障害 / 完全房室ブロック / COMPLETE HEART BLOCK	Blinded Treatment	20[redacted] / 119 Days	20[redacted] / 25 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 675 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				神経系障害 / 脳梗塞 / ACUTE RIGHT MIDDLE CEREBRAL ARTERY INFARCTION	Blinded Treatment	20[redacted] / 835 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
				感染症および寄生虫症 / 誤嚥性肺炎 / ASPIRATION PNEUMONIA	Blinded Treatment	20[redacted] / 836 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 6[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 肋骨骨折 / MULTIPLE FRACTURED RIBS	Blinded Treatment	20[redacted] / 512 Days	20[redacted] / 59 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 足関節部骨折 / FRACTURED RIGHT ANKLE	Blinded Treatment	20[redacted] / 749 Days	20[redacted] / 18 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 皮膚裂傷 / NUMEROUS LACERATIONS TO RIGHT FOOT	Blinded Treatment	20[redacted] / 749 Days	20[redacted] / 18 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	代謝および栄養障害 / 血液量増加症 / FLUID OVERLOADED	Blinded Treatment	20[redacted] / 500 Days	20[redacted] / 17 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 513 Days	20[redacted] / 6 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / MECHANICAL FALL	Blinded Treatment	20[redacted] / 514 Days	20[redacted] / 1 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 腸上皮化生 / GASTRIC INTESTINAL METAPLASIA	Blinded Treatment	20[redacted] / 722 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / WORSENING CELLULITIS LEFT LEG	Blinded Treatment	20[redacted] / 722 Days		Drug Interrupted	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 末期腎疾患 / ENDSTAGE RENAL FAILURE	Blinded Treatment	20[redacted] / 734 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 14 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY (SECONDARY TO HYPOTENSION)	Blinded Treatment	20[redacted] / 14 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 起立性低血圧 / POSTURAL HYPOTENSION	Blinded Treatment	20[redacted] / 23 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
404	[redacted] / M / 7[redacted]	Acoramidis	Y	皮膚および皮下組織障害 / 血管浮腫 / ANGIOEDEMA-ACE INHIBITOR INDUCED	Blinded Treatment	20[redacted] / 66 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / MECHANICAL FALL FROM ROOF	Blinded Treatment	20[redacted] / 828 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 尾骨骨折 / MULTI TRAUMA - FRACTURED COCCYX	Blinded Treatment	20[redacted] / 828 Days	20[redacted] / 70 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 肋骨骨折 / MULTI TRAUMA - FRACTURED RIBS	Blinded Treatment	20[redacted] / 828 Days	20[redacted] / 70 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
404	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 脳出血 / MULTI TRAUMA - SMALL BRAIN BLEED	Blinded Treatment	20[redacted] / 828 Days	20[redacted] / 70 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 徐脈 / POSSIBLE WORSENING OF BRADYCARDIA	Blinded Treatment	20[redacted] / 831 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC KIDNEY DISEASE	Blinded Treatment	20[redacted] / 834 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / WORSENING RIGHT INGUINAL HERNIA	Blinded Treatment	20[redacted] / 285 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
404	[redacted] / M / 8[redacted]	Acoramidis	Y	血管障害 / 低血圧 / HYPOTENSION	Blinded Treatment	20[redacted] / 17 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Related / Y
				神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 34 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Related / Y
				心臓障害 / 徐脈 / BRADYCARDIA DUE TO SOTOLOL	Blinded Treatment	20[redacted] / 126 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 発熱 / FEVER OF UNKNOWN ORIGIN	Blinded Treatment	20[redacted] / 347 Days	20[redacted] / 4 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
404	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心房細動 / EXACERBATION OF AF	Blinded Treatment	20[redacted] / 527 Days	20[redacted] / 74 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 四肢損傷 / L SHOULDER INJURY	Blinded Treatment	20[redacted] / 167 Days	20[redacted] / 130 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 深部静脈血栓症 / SMALL VASUCLAR CLOT IN R LOWER LEG	Blinded Treatment	20[redacted] / 324 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
405	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 末梢腫脹 / BILATERAL HAND SWELLING	Blinded Treatment	20[redacted] / 642 Days	20[redacted] / 264 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 末梢性ニューロパチー / WORSENING PERIPHERAL NEUROPATHY	Blinded Treatment	20[redacted] / 676 Days	20[redacted] / 131 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID-19 INFECTION	Blinded Treatment	20[redacted] / 821 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	N	神経系障害 / くも膜下出血 / SUB ARAHCNOID HAEMORRHAGE	Blinded Treatment	20[redacted] / 433 Days	20[redacted] / 19 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 血尿 / HAEMATURIA	Blinded Treatment	20[redacted] / 531 Days		Drug Interrupted	Moderate / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / M / 7[redacted]	Acoramidis	N	感染症および寄生虫症 / 敗血症性ショック / SEPTIC SHOCK FROM ESCHERICHIA COLI	Blinded Treatment	20[redacted] / 537 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Acoramidis	Y	感染症および寄生虫症 / 副鼻腔炎 / SINUSITIS	Blinded Treatment	20[redacted] / 515 Days	20[redacted] / 92 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 二束ブロック / BIFASICULAR BLOCK	Blinded Treatment	20[redacted] / 542 Days	20[redacted] / 64 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 585 Days	20[redacted] / 146 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 上部消化管出血 / UPPER GASTOINTESTINAL BLEEDING	Blinded Treatment	20[redacted] / 628 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 関節痛 / ACUTE LEFT HIP PAIN	Blinded Treatment	20[redacted] / 752 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 転倒 / MECHANICAL FALL	Blinded Treatment	20[redacted] / 58 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 頭部損傷 / HEADSTRIKE	Blinded Treatment	20[redacted] / 58 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / F / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 肋骨骨折 / RIGHT FRACTURED RIB	Blinded Treatment	20[redacted] / 58 Days	20[redacted] / 43 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				胃腸障害 / 上腹部痛 / EPIGASTRIC PAIN	Blinded Treatment	20[redacted] / 72 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 転倒 / FALL	Blinded Treatment	20[redacted] / 216 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 足関節部骨折 / RIGHT TRIMALLEOLAR FRACTURE	Blinded Treatment	20[redacted] / 361 Days	20[redacted] / 277 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / F / 8[redacted]	Acoramidis	Y	心臓障害 / 心筋虚血 / RATE RELATED, ATRIAL FIBRILLATION, ISCHAEMIA WITH TROPONIN RISE	Blinded Treatment	20[redacted] / 369 Days	20[redacted] / 8 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 低カルシウム血症 / HYPOCALCAEMIA-1.80L[2.10-2.60MMOL/L	Blinded Treatment	20[redacted] / 379 Days	20[redacted] / 5 Days	Drug Withdrawn	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 7 Days	20[redacted] / 22 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 喘息 / INFECTIVE EXACERBATION OF ASTHMA	Blinded Treatment	20[redacted] / 284 Days	20[redacted] / 41 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 頚髄神経根障害 / ACUTE C5 RADICULOPATHY	Blinded Treatment	20[redacted] / 319 Days	20[redacted] / 67 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 四肢膿瘍 / ABSCESS OF DORSUM OF MID RIGHT HAND	Blinded Treatment	20[redacted] / 806 Days	20[redacted] / 17 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
406	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 気管支炎 / BRONCHIAL INFECTION	Blinded Treatment	20[redacted] / 230 Days	20[redacted] / 45 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / HOSPITALIZATION NEW ONSET ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 232 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY TRACT INFECTION	Blinded Treatment	20[redacted] / 244 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY TRACT INFECTION	Blinded Treatment	20[redacted] / 269 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神 / HYPOTENSIVE SYNCOPE	Blinded Treatment	20[redacted] / 329 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY POSSIBLE ETIOLOGY OVER DIURESIS	Blinded Treatment	20[redacted] / 330 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Acoramidis	Y	傷害、中毒および処置合併症 / 靱帯捻挫 / SPRAIN LEFT HIP	Blinded Treatment	20[redacted] / 381 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / FALL - MULTIFACTORIAL ETIOLOGY	Blinded Treatment	20[redacted] / 489 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房粗動 / SLOW ATRIAL FLUTTER	Blinded Treatment	20[redacted] / 489 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 洞結節機能不全 / TACHY-BRADY SYNDROME	Blinded Treatment	20[redacted] / 497 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 感染による気管支拡張症の増悪 / INFECTIVE EXACERBATION OF BRONCHIECTISIS	Blinded Treatment	20[redacted] / 525 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / NON ST-ELEVATION MYOCARDIAL INFARCTION	Blinded Treatment	20[redacted] / 527 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / EXACERBATION OF CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 656 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / BILATERAL BRONCHOPNEUMONIA	Blinded Treatment	20[redacted] / 697 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY TRACT INFECTION	Blinded Treatment	20[redacted] / 820 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / COMMUNITY ACQUIRED PNEUMONIA	Blinded Treatment	20[redacted] / 852 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY INFECTION	Blinded Treatment	20[redacted] / 875 Days	20[redacted] / 19 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 876 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

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Treatment Emergent Serious Adverse Events[1]
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Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 便秘 / CONSTIPATION CAUSING HOSPITALIZATION	Blinded Treatment	20[redacted] / 925 Days	20[redacted] / 6 Days	Not Applicable	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	胃腸障害 / 十二指腸炎 / ACUTE DUODENITIS	Blinded Treatment	20[redacted] / 153 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心停止 / VENTRICULAR TACHYCARDIC ARREST	Blinded Treatment	20[redacted] / 166 Days	20[redacted] / 1 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 非心臓性胸痛 / NON CARDIAC CHEST PAIN	Blinded Treatment	20[redacted] / 764 Days	20[redacted] / 17 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

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Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 6[redacted]	Acoramidis	Y	心臓障害 / 心アミロイドーシス / WORSENING OF FAMILIAL CARDIAC AMYLOIDOSIS CARDIOMYOPATHY	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 完全房室ブロック / COMPLETE HEART BLOCK	Blinded Treatment	20[redacted] / 876 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	臨床検査 / 血中クレアチニン増加 / WORSENING SERUM CREATININE RISE SECONDARY TO ATORVASTATIN	Blinded Treatment	20[redacted] / 92 Days	20[redacted] / 92 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 背部痛 / SEVERE BACK PAIN	Blinded Treatment	20[redacted] / 197 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

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Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
407	[redacted] / M / 8[redacted]	Acoramidis	Y	神経系障害 / 失神 / SYNCOPE CAUSE TO HAVE BEEN CARDIOGENIC	Blinded Treatment	20[redacted] / 585 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 鼠径ヘルニア / WORSENING INGUINAL HERNIA	Blinded Treatment	20[redacted] / 53 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 虚血性脳卒中 / RIGHT OCCIPIAL ISCHAEMIC STROKE	Blinded Treatment	20[redacted] / 798 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
409	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 血尿 / HAEMATURIA	Blinded Treatment	20[redacted] / 713 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 8[redacted]	Acoramidis	Y	腎および尿路障害 / 血尿 / EXACERBATION OF HAEMATURIA	Blinded Treatment	20[redacted] / 56 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 血尿 / WORSENING HAEMATURIA	Blinded Treatment	20[redacted] / 64 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 尿閉 / URINARY RETENTION	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 貧血 / SEVERE ANAEMIA	Blinded Treatment	20[redacted] / 436 Days	20[redacted] / 26 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 8[redacted]	Acoramidis	Y	胃腸障害 / 胃腸出血 / GASTROINTESTINAL HAEMORRHAGE	Blinded Treatment	20[redacted] / 645 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 腎前性腎不全 / ACUTE PRERENAL INSUFFICIENCY FAILURE	Blinded Treatment	20[redacted] / 648 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 血尿 / EXACERBATION OF HAEMATURIA	Blinded Treatment	20[redacted] / 713 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 完全房室ブロック / COMPLETE ATRIOVENTRICULAR BLOCK	Blinded Treatment	20[redacted] / 719 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / WORSENING OF CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 738 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / CELLULITIS OF LEFT LOWER LEG	Blinded Treatment	20[redacted] / 738 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 痛風 / ACUTE GOUT	Blinded Treatment	20[redacted] / 738 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 腎機能障害 / WORSENING RENAL IMPAIRMENT	Blinded Treatment	20[redacted] / 738 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 8[redacted]	Acoramidis	Y	皮膚および皮下組織障害 / 薬疹 / ALLERGIC DRUG RASH-BUMETANIDE AND INDAPAMIDE	Blinded Treatment	20[redacted] / 758 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 772 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 貧血 / WORSENING ANAEMIA	Blinded Treatment	20[redacted] / 780 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 下気道感染 / LOWER RESPIRATORY TRACT INFECTION	Blinded Treatment	20[redacted] / 871 Days	20[redacted] / 21 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 8[redacted]	Acoramidis	Y	血管障害 / リンパ浮腫 / RIGHT LEG LYMPHOEDEMA	Blinded Treatment	20[redacted] / 874 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 927 Days	20[redacted] / 14 Days	Not Applicable	Severe / Recovered/Resolved	Not Related / Y
420	[redacted] / M / 7[redacted]	Acoramidis	Y	筋骨格系および結合組織障害 / 変形性脊椎症 / SPONDYLOSIS LUMBOSACRAL REGION	Blinded Treatment	20[redacted] / 127 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
700	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 洞結節機能不全 / SICK SINUS SYNDROME	Blinded Treatment	20[redacted] / 571 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 659 Days	20[redacted] / 20 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	N	心臓障害 / 心不全 / CARDIAL DECOMPENSATION AT CHRONIC HEART FAILURE BASED ON ATTR-CM	Blinded Treatment	20[redacted] / 264 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Acoramidis	Y	血管障害 / 大腿動脈塞栓症 / EMBOLIZATION OF THE FEMORAL ARTERY COMMUNIS IN THE LEFT LOWER LIMB	Blinded Treatment	20[redacted] / 539 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 突然死 / SUDDEN DEATH OF UNKNOWN CAUSE	Blinded Treatment	20[redacted] / 125 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 7[redacted]	Acoramidis	Y	感染症および寄生虫症 / 感染性胆嚢炎 / GANGRENOUS CHOLECYSTITIS	Blinded Treatment	20[redacted] / 327 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 敗血症 / SEPSIS (OF ALREADY REPORTED CHOLECYSTITIS ORIGIN)	Blinded Treatment	20[redacted] / 329 Days	20[redacted] / 12 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心不全 / CARDIAL DECOMPENSATION MOSTLY RIGHT SIDED BASED ON ATTR-CM	Blinded Treatment	20[redacted] / 105 Days	20[redacted] / 79 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / CARDIAL DECOMPESATION BASED ON ATTR CM	Blinded Treatment	20[redacted] / 163 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 7[redacted]	Acoramidis	Y	神経系障害 / 塞栓性脳卒中 / ISCHAEMIC STROKE OF CARDIOEMBOLIC ORIGIN (PREVIOUSLY REPORTED AS DIZZINESS)	Blinded Treatment	20[redacted] / 308 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 気管支炎 / ACUTE BRONCHITIS (PREVIOUSLY REPORTED AS BRONCHITIS)	Blinded Treatment	20[redacted] / 862 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE OF PRERENAL DEHYDRATION (PREVIOUSLY REPORTED WORSENING OF RENAL FAILURE)	Blinded Treatment	20[redacted] / 410 Days	20[redacted] / 7 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 腸炎 / ACUTE ENTEROCOLITIS SYNDROME	Blinded Treatment	20[redacted] / 473 Days	20[redacted] / 13 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 7[redacted]	Acoramidis	Y	腎および尿路障害 / 腎機能障害 / ACUTE RENAL IMPAIRMENT OF PRERENAL ETIOLOGY	Blinded Treatment	20[redacted] / 473 Days	20[redacted] / 13 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 正色素性正球性貧血 / WORSENING OF NORMOCHROMIC NORMOCYTIC ANAEMIA	Blinded Treatment	20[redacted] / 806 Days	20[redacted] / 31 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
701	[redacted] / M / 7[redacted]	Acoramidis	Y	心臓障害 / 心室性頻脈 / WORSENING OF NON SUSTAINED VENTRICULAR TACHYCARDIAICD IMPLANTATION	Blinded Treatment	20[redacted] / 317 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
702	[redacted] / M / 8[redacted]	Acoramidis	Y	神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 100 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
702	[redacted] / M / 8[redacted]	Acoramidis	Y	感染症および寄生虫症 / COVID-19 / COVID 19 INFECTION	Blinded Treatment	20[redacted] / 117 Days	20[redacted] / 5 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
737	[redacted] / M / 8[redacted]	Acoramidis	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH OF UNKNOWN REASON	Blinded Treatment	20[redacted] / 621 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Acoramidis	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 344 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 死亡 / DEATH [NO FURTHER INFORMATION]	Blinded Treatment	20[redacted] / 440 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 慢性左室不全 / CHRONIC DIASTOLIC HEART FAILURE, NYHA CLASS 3	Blinded Treatment	20[redacted] / 104 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心膜炎 / PROBABLE PERICARDITIS (SYMPTOM: CHEST PAIN)	Blinded Treatment	20[redacted] / 112 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 胸痛 / CHEST PAIN UNSPECIFIED TYPE	Blinded Treatment	20[redacted] / 115 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				胃腸障害 / 上部消化管出血 / UPPER GI BLEED	Blinded Treatment	20[redacted] / 268 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 急性左室不全 / ACUTE DIASTOLIC CONGESTIVE HEART FAILURE NYHA CLASS 3	Blinded Treatment	20[redacted] / 290 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / ATRIAL FIBRILLATION WITH RAPID VENTICULAR RESPONSE	Blinded Treatment	20[redacted] / 884 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE ON CHRONIC CONGESTIVE HEART FAILURE, WORSENING	Blinded Treatment	20[redacted] / 358 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC RENAL FAILURE(CAUSALITY INTRAVASCULAR VOLUME DEPLETION)	Blinded Treatment	20[redacted] / 31 Days	20[redacted] / 66 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
007	[redacted] / M / 7[redacted]	Placebo	Y	胃腸障害 / 小腸閉塞 / SMALL BOWEL OBSTRUCTION	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / F / 9[redacted]	Placebo	N	心臓障害 / 完全房室ブロック / BLOCK ATRIOVENTRICULAR COMPLETE	Blinded Treatment	20[redacted] / 521 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 腱鞘炎 / TENOSYNOVITIS FINGER FLEXOR RIGHT	Blinded Treatment	20[redacted] / 824 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
010	[redacted] / M / 8[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 膵腺癌 / PANCREATIC HEAD ADENOCARCINOMA	Blinded Treatment	20[redacted] / 781 Days	20[redacted] / 28 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
010	[redacted] / M / 8[redacted]	Placebo	Y	血管障害 / 起立性低血圧 / ORTHOSTATIC HYPOTENSION	Blinded Treatment	20[redacted] / 788 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 感染性腱鞘炎 / INFECTIOUS TENOSYNOVITIS	Blinded Treatment	20[redacted] / 101 Days	20[redacted] / 11 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 徐脈 / BRADYCARDIA	Blinded Treatment	20[redacted] / 471 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 呼吸困難 / DYSPNEA	Blinded Treatment	20[redacted] / 471 Days	20[redacted] / 13 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
010	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE CONGESTIVE HEART FAILURE EPISODE	Blinded Treatment	20[redacted] / 705 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				胃腸障害 / 胃腸出血 / GASTROINTESTINAL HEMORRHAGE	Blinded Treatment	20[redacted] / 794 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
013	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 頚椎骨折 / NONDISPLACED DENS FRACTURE	Blinded Treatment	20[redacted] / 860 Days	20[redacted] / 92 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	N	腎および尿路障害 / 中毒性腎症 / ACUTE KIDNEY INJURY SECONDARY TO NAPROXEN	Blinded Treatment	20[redacted] / 255 Days	20[redacted] / 55 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
015	[redacted] / M / 5[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE ON CHRONIC CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 106 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
021	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / インフルエンザ / INFLUENZA	Blinded Treatment	20[redacted] / 107 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
022	[redacted] / F / 7[redacted]	Placebo	Y	胃腸障害 / 腹痛 / ABDOMINAL PAIN	Blinded Treatment	20[redacted] / 384 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 473 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / F / 7[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 非心臓性胸痛 / CHEST PAIN; NON-CARDIAC	Blinded Treatment	20[redacted] / 473 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE ON CHRONIC SYSTOLIC AND DIASTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 526 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 胸痛 / ATYPICAL CHEST PAIN	Blinded Treatment	20[redacted] / 526 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE ON CHRONIC COMBINED DIASTOLIC/SYSTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 566 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / F / 7[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 胸痛 / ATYPICAL CHEST PAIN	Blinded Treatment	20[redacted] / 566 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性左室不全 / ACUTE ON CHRONIC SYSTOLIC HEART FAILURE	Blinded Treatment	20[redacted] / 625 Days	20[redacted] / 14 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				胃腸障害 / 腹痛 / ABDOMINAL PAIN	Blinded Treatment	20[redacted] / 625 Days	20[redacted] / 14 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				胃腸障害 / 胃食道逆流性疾患 / EXACERBATION OF GERD	Blinded Treatment	20[redacted] / 625 Days	20[redacted] / 14 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 急性心筋梗塞 / NSTEMI TYPE II	Blinded Treatment	20[redacted] / 656 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE ON CHRONIC HEART FAILURE WITH REDUCED EJECTION FRACTION	Blinded Treatment	20[redacted] / 656 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 656 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / AKI	Blinded Treatment	20[redacted] / 673 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 6[redacted]	Placebo	Y	呼吸器、胸郭および縦隔障害 / 呼吸困難 / SHORTNESS OF BREATH REQUIRING HOSPITALIZATION	Blinded Treatment	20[redacted] / 48 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / WORSENING OF RAPID ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 447 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
				心臓障害 / 心房細動 / WORSENING OF RAPID ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 487 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 虚血性肝炎 / ISCHEMIC HEPATITIS	Blinded Treatment	20[redacted] / 490 Days	20[redacted] / 24 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
022	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 572 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 非心臓性胸痛 / CHEST PAIN; NON CARDIAC	Blinded Treatment	20[redacted] / 572 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 筋骨格系胸痛 / MUSCULOSKELETAL CHEST PAIN	Blinded Treatment	20[redacted] / 102 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				製品の問題 / 医療機器機能不良 / CARDIAC PACEMAKER LEAD MALFUNCTION	Blinded Treatment	20[redacted] / 106 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
025	[redacted] / M / 7[redacted]	Placebo	Y	呼吸器、胸郭および縦隔障害 / 胸水 / WORSENING PLEURAL EFFUSION	Blinded Treatment	20[redacted] / 682 Days		Drug Interrupted	Severe / Recovering/Resolving	Not Related / Y
				免疫系障害 / アミロイドーシス / END STAGE AMYLOIDOSIS	Blinded Treatment	20[redacted] / 722 Days	20[redacted] / 13 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / PAROXYSMAL ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 203 Days	20[redacted] / 21 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE ON CHRONIC KIDNEY DISEASE SECONDARY TO OVERDIURESIS	Blinded Treatment	20[redacted] / 224 Days	20[redacted] / 45 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
025	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 狭心症 / ANGINA PECTORIS	Blinded Treatment	20[redacted] / 165 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE CONGESTIVE HEART FAILURE EXACERBATION	Blinded Treatment	20[redacted] / 236 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE CONGESTIVE HEART FAILURE EXACERBATION	Blinded Treatment	20[redacted] / 244 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心アミロイドーシス / END STAGE CARDIAC AMYLOIDOSIS	Blinded Treatment	20[redacted] / 291 Days	20[redacted] / 9 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 急性心不全 / CONGESTIVE HEART FAILURE EXACERBATION	Blinded Treatment	20[redacted] / 196 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 211 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / NEW ONSET ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 380 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	N	感染症および寄生虫症 / 肺炎 / COMMUNITY ACQUIRED PNEUMONIA	Blinded Treatment	20[redacted] / 546 Days	20[redacted] / 13 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / M / 7[redacted]	Placebo	N	筋骨格系および結合組織障害 / 変形性関節症 / WORSENING OSTEOARTHRITIS OF RIGHT HIP JOINT	Blinded Treatment	20[redacted] / 749 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 878 Days		Drug Withdrawn	Severe / Not Recovered/Not Resolved	Not Related / Y
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う消化器癌 / METASTATIC GI CANCER WITH UNKNOWN PRIMARY	Blinded Treatment	20[redacted] / 881 Days	20[redacted] / 11 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / EXACERBATION OF ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Blinded Treatment	20[redacted] / 128 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
028	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 128 Days	20[redacted] / 4 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / パスツレラ菌性敗血症 / INFECTION AND SEPSIS DUE TO PASTEURELLA MULTOCIDA	Blinded Treatment	20[redacted] / 493 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 医療機器関連感染 / RIGHT SHOULDER PERIPROSTHETIC JOINT INFECTION	Blinded Treatment	20[redacted] / 785 Days	20[redacted] / 130 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
030	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 急性心不全 / CONGESTIVE HEART FAILURE EXACERBATION	Blinded Treatment	20[redacted] / 642 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
030	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房粗動 / RECURRENT ATRIAL FLUTTER	Blinded Treatment	20[redacted] / 724 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 50 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神 / SYNCOPE (ONCE DUE TO DEHYDRATION, SEPARATELY REPORTED)	Blinded Treatment	20[redacted] / 113 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心アミロイドーシス / WORSENED CARDIAC AMYLOIDOSIS	Blinded Treatment	20[redacted] / 121 Days	20[redacted] / 4 Days	Not Applicable	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
031	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 145 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
033	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 258 Days	20[redacted] / 5 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / ATRIAL FIBRILLATION WITH RVR	Blinded Treatment	20[redacted] / 347 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE ON CHRONIC RIGHT HEART FAILURE	Blinded Treatment	20[redacted] / 404 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
033	[redacted] / M / 6[redacted]	Placebo	Y	神経系障害 / 肝性脳症 / HEPATIC ENCEPHALOPATHY	Blinded Treatment	20[redacted] / 542 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 尿路性敗血症 / UROSEPSIS	Blinded Treatment	20[redacted] / 793 Days	20[redacted] / 33 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
036	[redacted] / M / 6[redacted]	Placebo	Y	肝胆道系障害 / 胆道仙痛 / GALLBLADDER COLIC	Blinded Treatment	20[redacted] / 121 Days	20[redacted] / 9 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				傷害、中毒および処置合併症 / 投薬過誤 / MEDICATION ERROR (METOLAZONE)	Blinded Treatment	20[redacted] / 547 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
036	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 64 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				血管障害 / 起立性低血圧 / ORTHOSTATIC HYPOTENSION	Blinded Treatment	20[redacted] / 260 Days	20[redacted] / 14 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 呼吸困難 / SHORTNESS OF BREATH	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 2 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / MECHANICAL FALL	Blinded Treatment	20[redacted] / 492 Days	20[redacted] / 1 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
036	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 多臓器機能不全症候群 / MULTI ORGAN FAILURE	Blinded Treatment	20[redacted] / 750 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
037	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILLATION REQUIRING CARDIOVERSION	Blinded Treatment	20[redacted] / 845 Days	20[redacted] / 4 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 845 Days	20[redacted] / 4 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
039	[redacted] / M / 6[redacted]	Placebo	Y	臨床検査 / トロポニン増加 / ELEVATED TROPONINE. FLAT CURVE WITHOUT CHEST PAIN	Blinded Treatment	20[redacted] / 87 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
039	[redacted] / M / 6[redacted]	Placebo	Y	眼障害 / 結膜出血 / BILATERAL SUBCONJUNCTIVAL HEMORRHAGE	Blinded Treatment	20[redacted] / 87 Days	20[redacted] / 11 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 414 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 低カリウム血症 / WORSENING HYPOKALEMIA	Blinded Treatment	20[redacted] / 453 Days	20[redacted] / 2 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
043	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 537 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
052	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 死亡 / DEATH-NO FURTHER INFORMATION)	Blinded Treatment	20[redacted] / 607 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
100	[redacted] / M / 7[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 慢性リンパ性白血病 / CHRONIC LYMPHOCYTIC LEUKEMIA	Blinded Treatment	20[redacted] / 765 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE RENAL FAILURE	Blinded Treatment	20[redacted] / 765 Days	20[redacted] / 48 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	N	血液およびリンパ系障害 / 貧血 / WORSENED ANEMIA	Blinded Treatment	20[redacted] / 119 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
100	[redacted] / F / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 敗血症 / SEPSIS	Blinded Treatment	20[redacted] / 916 Days	20[redacted] / 23 Days	Not Applicable	Severe / Recovered/Resolved	Not Related / Y
101	[redacted] / M / 8[redacted]	Placebo	Y	胃腸障害 / 血便排泄 / BLOOD IN STOOL	Blinded Treatment	20[redacted] / 57 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 114 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 肺塞栓症 / SEGMENTAL PULMONARY EMBOLISM WHILE ON DIRECT ORAL ANTICOAGULANT	Blinded Treatment	20[redacted] / 135 Days	20[redacted] / 78 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
103	[redacted] / M / 8[redacted]	Placebo	Y	血管障害 / 末梢動脈閉塞性疾患 / RIGHT LOWER LIMB ACUTE ARTERIAL OCCLUSION	Blinded Treatment	20[redacted] / 407 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
105	[redacted] / M / 5[redacted]	Placebo	Y	神経系障害 / 不全片麻痺 / TRANSIENT RIGHT SIDED HEMIPARESIS	Blinded Treatment	20[redacted] / 32 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
110	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 半月板損傷 / TORN MENISCUS LEFT KNEE	Blinded Treatment	20[redacted] / 487 Days	20[redacted] / 68 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
200	[redacted] / F / 8[redacted]	Placebo	Y	神経系障害 / 脳血管発作 / ICTUS	Blinded Treatment	20[redacted] / 105 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
200	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 182 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DESCOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 419 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DESCOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 453 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DESCOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 495 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
200	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / CARDIAC INSUFFICIENCY	Blinded Treatment	20[redacted] / 691 Days	20[redacted] / 45 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
201	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 33 Days	20[redacted] / 8 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 616 Days	20[redacted] / 11 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 744 Days	20[redacted] / 6 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 6[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 筋骨格系胸痛 / MUSCULOSKELETAL CHEST PAIN	Blinded Treatment	20[redacted] / 96 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				肝胆道系障害 / 胆石症 / CHOLELITHIASIS	Blinded Treatment	20[redacted] / 205 Days	20[redacted] / 12 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 732 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 747 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
201	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 慢性心不全 / END STAGE HEART FAILURE	Blinded Treatment	20[redacted] / 567 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / COVID-19 PNEUMONIA	Blinded Treatment	20[redacted] / 734 Days	20[redacted] / 36 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 血栓症 / EXTENSIVE SYSTEMIC THROMBUS	Blinded Treatment	20[redacted] / 820 Days	20[redacted] / 25 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
202	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 469 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
202	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 四肢膿瘍 / LEFT GLUTEAL ABSCESS	Blinded Treatment	20[redacted] / 518 Days	20[redacted] / 31 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / COVID19 INFECTION	Blinded Treatment	20[redacted] / 532 Days	20[redacted] / 17 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 539 Days	20[redacted] / 93 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
203	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / BILATERIAL PNEUMONIA COVID 19	Blinded Treatment	20[redacted] / 308 Days	20[redacted] / 16 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
203	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 完全房室ブロック / COMPLETE ATRIOVENTRICULAR BLOCK	Blinded Treatment	20[redacted] / 455 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATION HEART FAILURE	Blinded Treatment	20[redacted] / 571 Days		Dose Not Changed	Mild / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 238 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART FAILURE DECOMPENSATION	Blinded Treatment	20[redacted] / 475 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
203	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 565 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				胃腸障害 / メレナ / MALAENA	Blinded Treatment	20[redacted] / 571 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19肺炎 / COVID-19 PNEUMONIA	Blinded Treatment	20[redacted] / 598 Days	20[redacted] / 21 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / REFRACTORY HEART FAILURE	Blinded Treatment	20[redacted] / 638 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
203	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 722 Days	20[redacted] / 8 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 811 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
204	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / HF DECOMPENSATION	Blinded Treatment	20[redacted] / 183 Days	20[redacted] / 29 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 起立性低血圧 / ORTHOSTATIC HYPOTENSION	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
204	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 右室不全 / RIGHT HEART FAILURE	Blinded Treatment	20[redacted] / 660 Days	20[redacted] / 32 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
				臨床検査 / 心拍出量低下 / LOW CARDIAC OUTPUT	Blinded Treatment	20[redacted] / 671 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
208	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 86 Days	20[redacted] / 12 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				臨床検査 / SARS-CoV-2検査陽性 / POSITIVE COVID-19	Blinded Treatment	20[redacted] / 93 Days	20[redacted] / 41 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
210	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 544 Days	20[redacted] / 33 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / ブドウ球菌性敗血症 / S. AREUS SEPSIS	Blinded Treatment	20[redacted] / 549 Days	20[redacted] / 25 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				精神障害 / 錯乱状態 / CONFUSIONAL STATE	Blinded Treatment	20[redacted] / 617 Days	20[redacted] / 2 Days	Drug Withdrawn	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	N	心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 154 Days	20[redacted] / 11 Days	Not Applicable	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
210	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 549 Days	20[redacted] / 28 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 618 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 完全房室ブロック / TOTAL ATRIOVENTRICULAR BLOCK	Blinded Treatment	20[redacted] / 619 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 15 Days	Drug Interrupted	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 369 Days	20[redacted] / 12 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 敗血症 / SEPTIC EPISODE	Blinded Treatment	20[redacted] / 540 Days	20[redacted] / 11 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 695 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 801 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 8[redacted]	Placebo	Y	代謝および栄養障害 / 脱水 / MUCOCUTANEOS DEHYDRATION	Blinded Treatment	20[redacted] / 732 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 房室ブロック / SYNPTOMATIC ATRIAL VENTRICULAR BLOCK	Blinded Treatment	20[redacted] / 169 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19肺炎 / PNEUMONIA COVID 19	Blinded Treatment	20[redacted] / 342 Days	20[redacted] / 11 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING OF HEART FAILURE IN AMYLOID-INDUCE CARDIOMIOPATHY	Blinded Treatment	20[redacted] / 184 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 201 Days	20[redacted] / 17 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	生殖系および乳房障害 / 良性前立腺肥大症 / WORSENING PROSTATIC HYPERTROPHY	Blinded Treatment	20[redacted] / 467 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 528 Days	20[redacted] / 13 Days	Dose Not Changed	Mild / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 540 Days	20[redacted] / 139 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
211	[redacted] / M / 7[redacted]	Placebo	Y	肝胆道系障害 / 肝不全 / LIVER FAILURE	Blinded Treatment	20[redacted] / 669 Days	20[redacted] / 10 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 546 Days	20[redacted] / 85 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / SUSTAINED VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 827 Days	20[redacted] / 13 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 変形性関節症 / PRIMARY GONARTHROSIS LEFT KNEE	Blinded Treatment	20[redacted] / 166 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
212	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心室性頻脈 / NON SUSTAINED VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 609 Days	20[redacted] / 3 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19肺炎 / COVID-19 INFECTION/SARS-COV2 INFECTION/COVID-19 PNEUMONIA	Blinded Treatment	20[redacted] / 720 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 775 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 816 Days	20[redacted] / 10 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
212	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 887 Days	20[redacted] / 22 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / ブドウ球菌感染 / S.AUREUS INFECTION	Blinded Treatment	20[redacted] / 890 Days	20[redacted] / 15 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
213	[redacted] / M / 7[redacted]	Placebo	Y	代謝および栄養障害 / 低ナトリウム血症 / HYPONATREMIA	Blinded Treatment	20[redacted] / 16 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸水 / PLEURAL EFFUSION	Blinded Treatment	20[redacted] / 16 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
213	[redacted] / M / 7[redacted]	Placebo	Y	呼吸器、胸郭および縦隔障害 / 喀血 / HEMOPTYSIS	Blinded Treatment	20[redacted] / 496 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 急性心筋梗塞 / ACUTE ST ELEVATION INFERIOR MI	Blinded Treatment	20[redacted] / 146 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 僧帽弁閉鎖不全症 / MITRAL REGURGITATION EXACERBATION	Blinded Treatment	20[redacted] / 435 Days	20[redacted] / 69 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心肺停止 / CARDIAC AND RESPIRATORY ARREST	Blinded Treatment	20[redacted] / 80 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
214	[redacted] / M / 8[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 横紋筋融解症 / RHABDOMYOLYSIS	Blinded Treatment	20[redacted] / 500 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / うっ血性心不全 / HOSPITAL ADMISSION FOR CONGESTIVE CARDIAC FAILURE	Blinded Treatment	20[redacted] / 211 Days	20[redacted] / 10 Days	Dose Not Changed	Mild / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 徐脈 / SYMPTOMATIC BRADYCARDIA	Blinded Treatment	20[redacted] / 347 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 479 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
214	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / 失神寸前の状態 / PRESYNCOPE	Blinded Treatment	20[redacted] / 503 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 630 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / COVID 19 INFECTION	Blinded Treatment	20[redacted] / 644 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 大腸菌性菌血症 / BLOOD BORNE E-COLI INFECTION	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
214	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 尿路感染 / URINARY TRACT INFECTION	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 16 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 653 Days	20[redacted] / 16 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 657 Days	20[redacted] / 12 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 転倒 / FELL DOWN STAIRS	Blinded Treatment	20[redacted] / 712 Days	20[redacted] / 23 Days	Drug Withdrawn	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 肺炎 / INFECTION PNEUMONIA	Blinded Treatment	20[redacted] / 253 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 処置後感染 / INFECTION RIGHT TOE POST SURGERY	Blinded Treatment	20[redacted] / 529 Days	20[redacted] / 18 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING OF HEARTFAILURE	Blinded Treatment	20[redacted] / 751 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 関節炎 / HIP ARTHRITIS RIGHT SIDE	Blinded Treatment	20[redacted] / 819 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Placebo	N	一般・全身障害および投与部位の状態 / 全身健康状態悪化 / GENERAL PHYSICAL HEALTH DETERIORATION	Blinded Treatment	20[redacted] / -	20[redacted] / 87 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 慢性心不全 / HEART FAILURE END STAGE	Blinded Treatment	20[redacted] / 141 Days	20[redacted] / 129 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 251 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 523 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Placebo	Y	代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 538 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 慢性心不全 / WORSENING OF END STAGE HEARTFAILURE	Blinded Treatment	20[redacted] / 578 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	呼吸器、胸郭および縦隔障害 / 胸水 / PLEURAL EXUDATE	Blinded Treatment	20[redacted] / 274 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 312 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 493 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICILAR TACHYCARDIA	Blinded Treatment	20[redacted] / 499 Days	20[redacted] / 14 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / RAPID ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 542 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心停止 / CARDIAC ARREST	Blinded Treatment	20[redacted] / 611 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 後腹膜膿瘍 / RECURRENT RETROPERITONEAL ABSCESS	Blinded Treatment	20[redacted] / 230 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / CARDIAC FLUID OVERLOAD	Blinded Treatment	20[redacted] / 693 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	胃腸障害 / 腹水 / ASCITIS	Blinded Treatment	20[redacted] / 259 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 中毒性腎症 / KIDNEY FUNCTION IMPAIRED, DRUG INDUCED	Blinded Treatment	20[redacted] / 298 Days	20[redacted] / 147 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 315 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 大腿骨骨折 / PERTROCHANTERIC FRACTURE	Blinded Treatment	20[redacted] / 381 Days	20[redacted] / 273 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 処置による疼痛 / INCREASED PAIN DUE TO HIP SURGERY IN FEB.2021	Blinded Treatment	20[redacted] / 478 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 529 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
215	[redacted] / M / 7[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 変形性関節症 / SEVERE HIP ARTHROSIS RIGHT HIP	Blinded Treatment	20[redacted] / 620 Days	20[redacted] / 34 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 丹毒 / ERYSIPELAS	Blinded Treatment	20[redacted] / 816 Days	20[redacted] / 20 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血管障害 / 起立性低血圧 / ORTOSTATIC HYPOTENSION	Blinded Treatment	20[redacted] / 885 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 再発肺腺癌 / RECURRENCE ADENOCARCINOMA LUNG DXT	Blinded Treatment	20[redacted] / 243 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / M / 7[redacted]	Placebo	Y	胃腸障害 / マロリー・ワイス症候群 / MALLORY WEISS LESION	Blinded Treatment	20[redacted] / 892 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / CARDIAC DECOMPENSATION	Blinded Treatment	20[redacted] / 754 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / CORDECOMPENSATION	Blinded Treatment	*18MONTH / -	20[redacted] / 102 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 鉄欠乏性貧血 / WORSENING OF FERRIPRIVE ANEMIA	Blinded Treatment	20[redacted] / 625 Days	20[redacted] / 92 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / F / 8[redacted]	Placebo	Y	血液およびリンパ系障害 / 鉄欠乏性貧血 / WORSENING OF FERRIPRIVE ANEMIA	Blinded Treatment	20[redacted] / 750 Days	20[redacted] / 4 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / CORDECOMPENSATION	Blinded Treatment	20[redacted] / 750 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 胸水 / WORSENING PLEURAL EFFUSION LEFT	Blinded Treatment	20[redacted] / 816 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 852 Days	20[redacted] / 13 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / F / 8[redacted]	Placebo	Y	血液およびリンパ系障害 / 鉄欠乏性貧血 / WORSENING OF FERRIPRIVE ANEMIA	Blinded Treatment	20[redacted] / 856 Days	20[redacted] / 9 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 骨髄異形成症候群 / MYELODYSPLASTIC SYNDROME	Blinded Treatment	20[redacted] / 858 Days		Dose Not Changed	Moderate / Recovering/Resolving	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 883 Days		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房粗動 / ATRIAL FLUTTER	Blinded Treatment	20[redacted] / 717 Days	20[redacted] / 50 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
218	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 房室ブロック / AV CONDUCTION BLOCK	Blinded Treatment	20[redacted] / 765 Days	20[redacted] / 38 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 慢性リンパ性白血病 / CHRONIC LYMPHATIC LEUKEMIA	Blinded Treatment	20[redacted] / 373 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
219	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / ブドウ球菌性敗血症 / STAPHYLOCOCCUS AUREUS SEPSIS	Blinded Treatment	20[redacted] / 52 Days	20[redacted] / 21 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 医療機器関連敗血症 / CATHETER SEPSIS WITH ACINETOBACTER	Blinded Treatment	20[redacted] / 71 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
219	[redacted] / M / 7[redacted]	Placebo	Y	胃腸障害 / 鼠径ヘルニア / INGUINAL HERNIA	Blinded Treatment	20[redacted] / 581 Days	20[redacted] / 36 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
222	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 頭部損傷 / TRAUMA CAPITIS	Blinded Treatment	20[redacted] / 206 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				外科および内科処置 / 安楽死 / EUTHANASIA	Blinded Treatment	20[redacted] / 277 Days	20[redacted] / 1 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Placebo	N	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 283 Days	20[redacted] / 6 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
222	[redacted] / F / 8[redacted]	Placebo	N	心臓障害 / 心不全 / WORSENING HEARTFAILURE	Blinded Treatment	20[redacted] / 314 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	血液およびリンパ系障害 / 貧血 / WORSENING ANEMIA	Blinded Treatment	20[redacted] / 83 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 貧血 / WORSENING ANEMIA	Blinded Treatment	20[redacted] / 160 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				血液およびリンパ系障害 / 貧血 / WORSENING ANEMIA	Blinded Treatment	20[redacted] / 687 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
222	[redacted] / M / 7[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う前立腺癌 / METASTASIZED PROSTATE CARCINOMA	Blinded Treatment	20[redacted] / 637 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 疾患進行 / DECEASED AFTER PALLIATIVE CARE FOR DISEASE PROGRESSION	Blinded Treatment	20[redacted] / 666 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
223	[redacted] / F / 8[redacted]	Placebo	Y	一般・全身障害および投与部位の状態 / 全身健康状態悪化 / OVERALL DECLINE	Blinded Treatment	20[redacted] / 517 Days	20[redacted] / 4 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 肺炎 / PNEUMONIA	Blinded Treatment	20[redacted] / 783 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
223	[redacted] / F / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 大腿骨骨折 / PETROCHANTARY FEMURFRACTURE RIGHT	Blinded Treatment	20[redacted] / 863 Days	20[redacted] / 43 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
226	[redacted] / M / 7[redacted]	Placebo	Y	腎および尿路障害 / 急性腎障害 / ACUTE PRERENAL FAILURE	Blinded Treatment	20[redacted] / 94 Days	20[redacted] / 12 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / WORSENING OF COVID INFECTION	Blinded Treatment	20[redacted] / 94 Days	20[redacted] / 42 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / PERMANENT ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 582 Days	20[redacted] / 2 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
228	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILLATION GR3.(TTR AMYLOIDOSIS RELATED)	Blinded Treatment	20[redacted] / 90 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	神経系障害 / 脳血管発作 / STROKE	Blinded Treatment	20[redacted] / 365 Days	20[redacted] / 17 Days	Drug Withdrawn	Severe / Recovered/Resolved With Sequelae	Not Related / Y
229	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 233 Days		Not Applicable	Severe / Recovering/Resolving	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 233 Days		Not Applicable	Severe / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 三束ブロック / TRIFASCICULAR BLOCK	Blinded Treatment	20[redacted] / 649 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	*23MONTH / -	20[redacted] / 20 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 741 Days	20[redacted] / 54 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 836 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 72 Days	20[redacted] / 2 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 348 Days	20[redacted] / 41 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	*27MONTH / -	20[redacted] / 52 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 241 Days	20[redacted] / 24 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 273 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 299 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / うっ血性心不全 / CONGESTIVE HEART FAILURE	Blinded Treatment	20[redacted] / 339 Days	20[redacted] / 1 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 252 Days	20[redacted] / 8 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心腎症候群 / CARDIORENAL SYNDROME	Blinded Treatment	20[redacted] / 273 Days	20[redacted] / 10 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 蜂巣炎 / CELLULITIS	Blinded Treatment	20[redacted] / 69 Days	20[redacted] / 11 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 109 Days	*同月 / -	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 889 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 人工関節周囲骨折 / LEFT SIDED PERI-PROSTHETIC HIP FRACTURE	Blinded Treatment	20[redacted] / 816 Days	*3MONTH / -	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	*30MONTH / -	20[redacted] / 74 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 5[redacted]	Placebo	Y	心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 325 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 387 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 5[redacted]	Placebo	Y	心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 408 Days	20[redacted] / 14 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心室性頻脈 / VENTRICULAR TACHYCARDIA	Blinded Treatment	20[redacted] / 808 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心筋梗塞 / MYOCARDIAL INFARCTION	Blinded Treatment	20[redacted] / 739 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 147 Days	20[redacted] / 3 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / 失神 / SYNCOPE	Blinded Treatment	20[redacted] / 166 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 207 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 354 Days	20[redacted] / 11 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / RIGHT ARM CELLULITIS	Blinded Treatment	20[redacted] / 469 Days	20[redacted] / 42 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
229	[redacted] / M / 7[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 滑液包炎 / OLECRANON BURSITIS	Blinded Treatment	20[redacted] / 469 Days	20[redacted] / 42 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
230	[redacted] / F / 9[redacted]	Placebo	Y	感染症および寄生虫症 / 腹部敗血症 / ABDOMINAL SEPSIS	Blinded Treatment	20[redacted] / 579 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Fatal	Not Related / Y
233	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 背部損傷 / LUMBAR TRAUMA	Blinded Treatment	20[redacted] / 93 Days	20[redacted] / 11 Days	Drug Interrupted	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				胃腸障害 / 上部消化管出血 / UPPER GASTROINTESTINAL BLEEDING	Blinded Treatment	20[redacted] / 224 Days	20[redacted] / 25 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
233	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING OFHEART FAILURE	Blinded Treatment	20[redacted] / 268 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心不全 / ACUTE HEART FAILURE	Blinded Treatment	20[redacted] / 292 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / WORSENING OF HEART FAILURE	Blinded Treatment	20[redacted] / 379 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / F / 7[redacted]	Placebo	N	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 悪性黒色腫 / MALIGNANT MELANOMA	Blinded Treatment	20[redacted] / 639 Days	20[redacted] / 82 Days	Unknown	Mild / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
233	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 冠動脈疾患 / CORONARY ARTERY DISEASE	Blinded Treatment	20[redacted] / 107 Days	20[redacted] / 74 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
234	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 細菌性肺炎 / BACTERIAL PENUMONIA	Blinded Treatment	20[redacted] / 187 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / HEART FAILURE DECOMPENSATION	Blinded Treatment	20[redacted] / 43 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19肺炎 / COVID-19 PNEUMONIA	Blinded Treatment	20[redacted] / 351 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
234	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心房細動 / WORSENING ATRIAL FIBRILATION	Blinded Treatment	20[redacted] / 548 Days	20[redacted] / 10 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 563 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / CARDIAC INSUFICIENCY	Blinded Treatment	20[redacted] / 612 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / HEART FAILURE	Blinded Treatment	20[redacted] / 758 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
234	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / HEART FAILURE DESCOMPENSATION	Blinded Treatment	20[redacted] / 828 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
235	[redacted] / M / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENINF HEART FAILURE	Blinded Treatment	20[redacted] / 147 Days	20[redacted] / 4 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / PNEUMONIA DUE TO COVID 19 INFECTION	Blinded Treatment	20[redacted] / 90 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心腎症候群 / CARDIORENAL	Blinded Treatment	20[redacted] / 222 Days	20[redacted] / 4 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
235	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / COVID-19肺炎 / PNEUMONIA DUE TO COVID-19	Blinded Treatment	20[redacted] / 162 Days	20[redacted] / 8 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
307	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 肺炎 / BRONCHOPNEUMONIA	Blinded Treatment	20[redacted] / 664 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				眼障害 / 網膜動脈閉塞 / CENTRAL RETINAL ARTERY OCCLUSION	Blinded Treatment	20[redacted] / 810 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
312	[redacted] / F / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 頭蓋脳損傷 / TRAUMATIC CRANIOENCEPHALIC	Blinded Treatment	20[redacted] / 877 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
312	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 徐脈性不整脈 / SYNCOPE DUE TO BRADYARRHYTHMIA	Blinded Treatment	20[redacted] / 877 Days	20[redacted] / 45 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 硬膜下血腫 / SUBDURAL HEMATOMA	Blinded Treatment	20[redacted] / 886 Days		Dose Not Changed	Severe / Recovering/Resolving	Not Related / Y
402	[redacted] / M / 7[redacted]	Placebo	Y	生殖系および乳房障害 / 良性前立腺肥大症 / WORSENING OF BENIGN PROSTATIC HYPERPLASIA	Blinded Treatment	20[redacted] / 213 Days	20[redacted] / 9 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / 下肢静止不能症候群 / WORSENING OF RESTLESS LEG SYNDROME	Blinded Treatment	20[redacted] / 155 Days	20[redacted] / 5 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / パーキンソン病 / WORSENING OF PARKINSONS DISEASE WITH INCREASING BRADYKINESIA	Blinded Treatment	20[redacted] / 165 Days	20[redacted] / 28 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				胃腸障害 / 便秘 / CONSTIPATION (MILD FAECAL LOADING)	Blinded Treatment	20[redacted] / 313 Days	20[redacted] / 16 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 370 Days	20[redacted] / 6 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				神経系障害 / 下肢静止不能症候群 / WORSENING OF RESTLESS LEG SYNDROME	Blinded Treatment	20[redacted] / 454 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / パーキンソン病 / WORSENING PARKINSON'S DISEASE	Blinded Treatment	20[redacted] / 587 Days	20[redacted] / 20 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	胃腸障害 / 絞扼性鼠径ヘルニア / R) STRANGULATED INGUINAL HERNIA	Blinded Treatment	20[redacted] / 343 Days	20[redacted] / 3 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / RAPID AF WITH RAPID VENTRICULAR RESPONSE(PREVIOUSLY CALLED CHEST PAIN)	Blinded Treatment	20[redacted] / 434 Days	20[redacted] / 18 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 440 Days	20[redacted] / 12 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 457 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 476 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 531 Days	20[redacted] / 10 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 531 Days	20[redacted] / 63 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心タンポナーデ / PERICARDIAL EFFUSION WITH TAMPONADE	Blinded Treatment	20[redacted] / 532 Days	20[redacted] / 2 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 外傷性血胸 / LEFT HAEMOHYDROPNEUMOTHORAX	Blinded Treatment	20[redacted] / 532 Days	20[redacted] / 7 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOAD	Blinded Treatment	20[redacted] / 589 Days	20[redacted] / 5 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房粗動 / ATRIAL FLUTTER - SYMPTOMATIC	Blinded Treatment	20[redacted] / 749 Days	20[redacted] / 7 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
402	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心原性ショック / CARDIOGENIC SHOCK	Blinded Treatment	20[redacted] / 751 Days	20[redacted] / 1 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 筋骨格系胸痛 / MUSCULOSKELETAL CHEST PAIN	Blinded Treatment	20[redacted] / 288 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / ANTERIOR STEMI	Blinded Treatment	20[redacted] / 701 Days	20[redacted] / 26 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心停止 / VENTRICULAR FIBRILLATION ARREST	Blinded Treatment	20[redacted] / 703 Days	20[redacted] / 24 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 428 Days	20[redacted] / 26 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 529 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 706 Days	20[redacted] / 79 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	神経系障害 / 塞栓性脳卒中 / EMBOLIC STROKE	Blinded Treatment	20[redacted] / 737 Days	20[redacted] / 9 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 人工関節周囲骨折 / PERIPROSTHETIC HIP FRACTURE	Blinded Treatment	20[redacted] / 737 Days	20[redacted] / 14 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				製品の問題 / 医療機器位置異常 / RECURRENT LEFT HIP DISLOCATION	Blinded Treatment	20[redacted] / 766 Days	20[redacted] / 80 Days	Not Applicable	Moderate / Recovered/Resolved With Sequelae	Not Related / Y
				呼吸器、胸郭および縦隔障害 / 肺塞栓症 / PULMONARY EMBOLUS	Blinded Treatment	20[redacted] / 788 Days	*同月 / -	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	感染症および寄生虫症 / 皮膚感染 / MULTIPLE INFECTED SKIN LESIONS BILATERAL LOWER LEGS	Blinded Treatment	20[redacted] / 638 Days	20[redacted] / 21 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 7[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 基底細胞癌 / ULCERATED NODULAR BASAL CELL CARCINOMA	Blinded Treatment	20[redacted] / 644 Days	20[redacted] / 15 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 植皮感染 / INFECTED SKIN GRAFT	Blinded Treatment	20[redacted] / 678 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 無力症 / PHYSICAL FRAILTY	Blinded Treatment	20[redacted] / 724 Days	20[redacted] / 19 Days	Drug Interrupted	Severe / Recovered/Resolved With Sequelae	Not Related / Y
				代謝および栄養障害 / 血液量増加症 / FLUID OVERLOADED	Blinded Treatment	20[redacted] / 735 Days	20[redacted] / 8 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
403	[redacted] / M / 7[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 交通事故 / LOW SPEED MOTOR VEHICLE ACCIDENT	Blinded Treatment	20[redacted] / 822 Days	20[redacted] / 1 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				腎および尿路障害 / 急性腎障害 / ACUTE KIDNEY INJURY	Blinded Treatment	20[redacted] / 890 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
405	[redacted] / F / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 501 Days	20[redacted] / 18 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 519 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / F / 6[redacted]	Placebo	Y	心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 552 Days	20[redacted] / 95 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 646 Days	20[redacted] / 1 Days	Drug Withdrawn	Severe / Recovered/Resolved	Not Related / Y
	[redacted] / M / 8[redacted]	Placebo	Y	胃腸障害 / 便秘 / CONSTIPATION	Blinded Treatment	20[redacted] / 62 Days	20[redacted] / 10 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				心臓障害 / 急性心筋梗塞 / NON ST ELEVATION MI	Blinded Treatment	20[redacted] / 290 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
405	[redacted] / M / 8[redacted]	Placebo	Y	傷害、中毒および処置合併症 / 四肢損傷 / INJURED RIGHT SHOULDER	Blinded Treatment	20[redacted] / 499 Days	20[redacted] / 79 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心不全 / DECOMPENSATED HEART FAILURE	Blinded Treatment	20[redacted] / 806 Days	20[redacted] / 5 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				感染症および寄生虫症 / 蜂巣炎 / CELLULITIS LEFT LOWER LEG	Blinded Treatment	20[redacted] / 806 Days	20[redacted] / 128 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				胃腸障害 / 直腸出血 / BLEEDING PER RECTUM	Blinded Treatment	20[redacted] / 815 Days	20[redacted] / 3 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 7[redacted]	Placebo	Y	血管障害 / 大動脈狭窄 / WORSENING AORTIC STENOSIS	Blinded Treatment	20[redacted] / 719 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	神経系障害 / 認知症 / EARLY DEMENTIA	Blinded Treatment	*14MONTH / -		Dose Not Changed	Moderate / Not Recovered/Not Resolved	Not Related / Y
				感染症および寄生虫症 / COVID-19 / COVID-19 INFECTION REQUIRING HOSPITALISATION	Blinded Treatment	20[redacted] / 727 Days	20[redacted] / 8 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 6[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 扁桃癌 / SQUARMOUS CELL CARCINOMA OF LEFT TONSIL	Blinded Treatment	20[redacted] / 37 Days	20[redacted] / 121 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

＊新薬承認情報提供時に置き換え

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 6[redacted]	Placebo	Y	感染症および寄生虫症 / 肺炎 / RIGHT LOWER LOBE PNEUMONIA REQUIRING HOSPITALISATION	Blinded Treatment	20[redacted] / 41 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 粘膜の炎症 / MUCOCITIS THROAT PAIN	Blinded Treatment	20[redacted] / 212 Days	20[redacted] / 7 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				神経系障害 / 浮動性めまい / DIZZINESS CAUSING HOSPITALISATION	Blinded Treatment	20[redacted] / 420 Days	20[redacted] / 2 Days	Dose Not Changed	Mild / Recovered/Resolved With Sequelae	Not Related / Y
				精神障害 / 不眠症 / WORSENING INSOMNIA	Blinded Treatment	20[redacted] / 550 Days	20[redacted] / 6 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
406	[redacted] / M / 6[redacted]	Placebo	Y	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 悪性胸水 / PLEURAL EFFUSION SECONDARY TO CANCER	Blinded Treatment	20[redacted] / 725 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う扁桃癌 / METASTATIC LUNG LESION FROM THE TONSILLAR PRIMARY TUMOR	Blinded Treatment	20[redacted] / 730 Days	20[redacted] / 110 Days	Drug Withdrawn	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
				良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） / 遠隔転移を伴う扁桃癌 / HOSPITALIZATION FOR PROGRESSIVE METASTATIC TONSILLAR SQUAMOUS CELL CANCER WITH LUNG METASTASES	Blinded Treatment	20[redacted] / 757 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				精神障害 / 譫妄 / DELIRIUM CAUSING HOSPITALISATION	Blinded Treatment	20[redacted] / 787 Days		Dose Not Changed	Severe / Not Recovered/Not Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
407	[redacted] / M / 6[redacted]	Placebo	Y	心臓障害 / 心房細動 / RAPID ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 407 Days	20[redacted] / 3 Days	Unknown	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / RAPID ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 826 Days	20[redacted] / 4 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
409	[redacted] / M / 6[redacted]	Placebo	Y	胃腸障害 / 鼠径ヘルニア / WORSENING OF RIGHT INGUINAL HERNIA.	Blinded Treatment	20[redacted] / 20 Days	20[redacted] / 10 Days	Drug Interrupted	Severe / Recovered/Resolved	Not Related / Y
				傷害、中毒および処置合併症 / 処置後血腫 / POST PROCEDURAL HAEMATOMA RIGHT GROIN	Blinded Treatment	20[redacted] / 23 Days	20[redacted] / 71 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
409	[redacted] / M / 6[redacted]	Placebo	Y	血管障害 / 静脈瘤破裂 / RUPTURED VARICOSE VEIN L) LEG	Blinded Treatment	20[redacted] / 431 Days	20[redacted] / 1 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				心臓障害 / 右室不全 / WORSENING RIGHT SIDED HEART FAILURE	Blinded Treatment	20[redacted] / 672 Days	20[redacted] / 1 Days	Not Applicable	Severe / Fatal	Not Related / Y
	[redacted] / F / 8[redacted]	Placebo	Y	心臓障害 / 心不全 / WORSENING HEART FAILURE	Blinded Treatment	20[redacted] / 303 Days	20[redacted] / 54 Days	Drug Interrupted	Severe / Fatal	Not Related / Y
				腎および尿路障害 / 末期腎疾患 / END STAGE RENAL FAILURE	Blinded Treatment	20[redacted] / 348 Days	20[redacted] / 9 Days	Dose Not Changed	Severe / Fatal	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
700	[redacted] / M / 8[redacted]	Placebo	Y	筋骨格系および結合組織障害 / 変形性関節症 / WORSENING OF ARTHROSIS OF THE RIGHT SHOULDER	Blinded Treatment	20[redacted] / -	20[redacted] / 169 Days	Drug Interrupted	Moderate / Recovered/Resolved	Not Related / Y
701	[redacted] / M / 8[redacted]	Placebo	Y	感染症および寄生虫症 / 肺炎 / BRONCHOPNEUMONIA	Blinded Treatment	20[redacted] / 358 Days	20[redacted] / 15 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
				筋骨格系および結合組織障害 / 関節痛 / JOINT PAINT - REHABILITATION	Blinded Treatment	20[redacted] / 480 Days	20[redacted] / 19 Days	Dose Not Changed	Mild / Recovered/Resolved	Not Related / Y
				一般・全身障害および投与部位の状態 / 嚢胞 / CYST LOCATED ON THE LEFT SHOULDER	Blinded Treatment	20[redacted] / 559 Days	20[redacted] / 162 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.6
Treatment Emergent Serious Adverse Events[1]
Safety Population

Site	Subject Number / Sex / Age	Treatment Received	mITT[2]	SOC / Preferred Term / Verbatim[3]	Phase	Onset Date / Day of Treatment[4]	Stop Date / Duration	Action Taken with Study Treatment	Severity / Outcome	Related / SAE
701	[redacted] / M / 8[redacted]	Placebo	Y	胃腸障害 / 出血性腸憩室 / DIVERTICULUM INTESTINAL HAEMORRHAGIC	Blinded Treatment	20[redacted] / 663 Days	20[redacted] / 12 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
702	[redacted] / F / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILATION	Blinded Treatment	20[redacted] / 791 Days	20[redacted] / 23 Days	Dose Not Changed	Moderate / Recovered/Resolved	Not Related / Y
	[redacted] / M / 7[redacted]	Placebo	Y	心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 406 Days	20[redacted] / 4 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y
				心臓障害 / 心房細動 / WORSENING OF ATRIAL FIBRILLATION	Blinded Treatment	20[redacted] / 491 Days	20[redacted] / 2 Days	Dose Not Changed	Severe / Recovered/Resolved	Not Related / Y

1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE.
2: The mITT population includes subjects who meet the definition of ITT and have a baseline eGFR >= 30 mL/min/1.73 m^2.
3: System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1.
4: Day of treatment. Day of first dose of study drug is day 1.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/8[redacted]y/Asian/Not Hispanic or Latino/16[redacted].3cm/6[redacted].3kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
感染症および寄生虫症/ 肺炎球菌性肺炎/ Pneumococcal pneumonia	20[redacted]/ 20[redacted]/ 19	285/ 303	Grade 3	NR/ INT/ REC	MEDICATION	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular

Relationship: NR = Not Related; REL = Related.

Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.

Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.

Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/16[redacted].7cm/5[redacted].5kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
胃腸障害/ 出血性腸憩室/ colonic diverticular bleeding	20[redacted]/ 20[redacted]/ 15	542/ 556	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y
胃腸障害/ 出血性腸憩室/ colonic diverticular bleeding	20[redacted]/ 20[redacted]/ 13	562/ 574	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y
胃腸障害/ 出血性腸憩室/ colonic diverticular bleeding	20[redacted]/ 20[redacted]/ 7	855/ 861	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y
胃腸障害/ 出血性腸憩室/ colonic diverticular bleeding	20[redacted]/ 20[redacted]/ 5	867/ 871	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y
胃腸障害/ 大腸ポリープ/ Large intestine polyp	20[redacted]/ 20[redacted]/ 44	856/ 899	Grade 2	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/16[redacted].7cm/5[redacted].5kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
感染症および寄生虫症/ 細菌性前立腺炎/ Acute bacterial prostatitis	20[redacted]/ 20[redacted]/ 12	33/ 44	Grade 3	NR/ NC/ REC	MEDICATION	HOS	N	N	Y
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 前立腺癌/ Prostate cancer	20[redacted]/ Ongoing	90/	Grade 3	NR/ NC/ NORC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	OTH		N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Female/7[redacted]y/Asian/Not Hispanic or Latino/15[redacted].0cm/4[redacted].9kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
心臓障害/ 慢性心不全/ Worsening of chronic heart failure	20[redacted]T15:45/ 20[redacted]T14:00/ 11	709/ 719	Grade 3	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y
代謝および栄養障害/ 脱水/ Dehydration	20[redacted]T09:00/ 20[redacted]T10:00/ 10	678/ 687	Grade 3	NR/ NC/ REC	MEDICATION	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/8[redacted]y/Asian/Not Hispanic or Latino/15[redacted].1cm/5[redacted].7kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
呼吸器、胸郭および縦隔障害/ 間質性肺疾患/ Interstitial pneumonia	20[redacted]/ 20[redacted]/ 19	242/ 260	Grade 3	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/16[redacted].7cm/7[redacted].3kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
感染症および寄生虫症/ 穿孔性虫垂炎/ Appendicitis purulent perforated	20[redacted]/ 20[redacted]/ 23	432/ 454	Grade 3	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y
感染症および寄生虫症/ 穿孔性虫垂炎/ Appendicitis purulent perforated	20[redacted]/ 20[redacted]/ 16	469/ 484	Grade 3	NR/ NC/ REC	MEDICATION	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/5[redacted]y/Asian/Not Hispanic or Latino/17[redacted].6cm/7[redacted].7kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
心臓障害/ 心房細動/ Atrial fibrillation	20[redacted]T11:00/ 20[redacted]T10:00/ 4	124/ 127	Grade 2	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/6[redacted]y/Asian/Not Hispanic or Latino/13[redacted].7cm/4[redacted].8kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
筋骨格系および結合組織障害/ 軟部組織腫瘤/ Soft tissue formation around the thoracic lumbar spine	20[redacted]/ 20[redacted]/ 6	100/ 105	Grade 2	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/16[redacted].5cm/6[redacted].7kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
心臓障害/ 洞結節機能不全/ sick sinus syndrome	20[redacted]/ 20[redacted]/ 8	532/ 539	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y
製品の問題/ 医療機器位置異常/ both intracular lens subluxation	20[redacted]/ 20[redacted]/ 12	578/ 589	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/8[redacted]y/Asian/Not Hispanic or Latino/15[redacted].5cm/5[redacted].0kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
胃腸障害/ 鼠径ヘルニア/ Worsened right inguinal hernia	20[redacted]/ 20[redacted]/ 4	676/ 679	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/8[redacted]y/Asian/Not Hispanic or Latino/15[redacted].2cm/5[redacted].0kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
心臓障害/ 完全房室ブロック/ AF bradycardia with complete AV block	20[redacted]T17:00/ 20[redacted]/ 17	873/ 889	Grade 2	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y
心臓障害/ 心不快感/ cardiac chest discomfort	20[redacted]T00:30/ 20[redacted]/ 7	772/ 778	Grade 2	NR/ NC/ REC	NONE	HOS	Y	N	Y
心臓障害/ 心不全/ exacerbation of heart failure	20[redacted]/ 20[redacted]/ 14	843/ 856	Grade 2	NR/ NC/ REC	MEDICATION/ NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）/ 膀胱癌/ bladder cancer	20[redacted]/ 20[redacted]/ 19	818/ 836	Grade 2	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/17[redacted].6cm/8[redacted].5kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
胃腸障害/ 大腸ポリープ/ Colorectal polyps	20[redacted]/ 20[redacted]/ 2	325/ 326	Grade 1	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	N	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular

Relationship: NR = Not Related; REL = Related.

Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.

Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.

Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1.3
Serious Adverse Events
Parts A and B
Safety Set

Participant: [redacted] (ALXN2060/Male/7[redacted]y/Asian/Not Hispanic or Latino/17[redacted].1cm/6[redacted].6kg, First Dose: 20[redacted], Last Dose in Intervention Period: 20[redacted])

System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date Time/ AE End Date Time/ Duration (Days)	Start Day/ End Day	Toxicity	Relationship/ Action Taken/ Outcome	Other Action Taken	Seriousness Criteria	CV-Related Hospitalization	Event of Interest (Per CRF)	Treatment-Emergent
心臓障害/ 洞停止/ sinus arrest	20[redacted]/ 20[redacted]/ 15	470/ 484	Grade 4	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS; THRT	Y	N	Y
臨床検査/ 血中クレアチンホスホキナーゼMB増加/ CK-MB elevation	20[redacted]/ 20[redacted]/ 2	658/ 659	Grade 3	NR/ NC/ REC	NON-PHARMACOLOGIC THERAPY/PROCEDURE	HOS	Y	N	Y

System organ classes and preferred terms were coded using MedDRA version 26.1. Toxicity is an assessment of AE intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017. Abbreviation: CV=Cardiovascular
Relationship: NR = Not Related; REL = Related.
Action Taken with Study Treatment: NC=Dose Not Changed; INC=Dose Increased; RED=Dose Reduced; INT=Drug Interrupted; WTHD=Drug Withdrawn; NA=Not Applicable; UNK=Unknown.
Outcome: NORC=Not Recovered/Not Resolved; RC = Recovering/Resolving; RCSQ=Recovered/Resolved with Sequelae; RCNG=Recovering/Resolving; REC=Recovered/Resolved; FATL=Fatal; UNK=Unknown.
Seriousness Criteria: ANOM=Congenital Anomaly or Birth Defect; INCP=Persistent or Significant Disability/Incapacity; DTH=Results in Death; HOS=Requires or Prolongs Hospitalization; THRT=Is Life Threatening; OTH=Other Medically Important Serious Event.

Listing 16.2.7.1 Treatment-Emergent Adverse Events
(Safety Set)

Actual Treatment: AG10 400 mg

Subject ID/ Age/Race/Sex	MedDRA SOC/ Preferred Term/ Verbatim Term	Start Date (Day)/ Stop Date (Day)	SAE Rsn(s)[a]	Sev-erity[b]	Out-come[c]	Related[d]	Action[e]	Led to Study DC	CM ID[f]
[redacted]/ 7[redacted]/B/F	呼吸器、胸郭および縦隔障害/ 呼吸困難/ SHORTNESS OF BREATH	20[redacted] (14) 20[redacted] (14)	4	1	3	2	1	N	

W = white; B = black or African American; P = native Hawaiian or other Pacific Islander; A = Asian; I = American Indian or Alaska native; O = Other; M = male; F = female.
AE = adverse event; CRF = case report form; DC = discontinuation; Rsn = reason; SAE = serious adverse event; SOC = system organ class.

a Reason(s) for SAE: 1 = Congenital abnormality/birth defect; 2 = Results in persistent or significant disability/incapacity; 3 = Results in death; 4 = Requires or prolongs hospitalization; 5 = Life threatening; 6 = Other medically important event.
b Severity: 1 = mild; 2 = moderate; 3 = severe.
c Outcome: 1 = Fatal; 2 = Not recovered/not resolved; 3 = Recovered/resolved; 4 = Recovered/resolved with sequelae; 5 = Recovering/resolving; 6 = Unknown.
d Relationship to study drug: 1 = Not related; 2 = Unlikely related; 3 = Possibly related; 4 = Related.
e Action Taken with Study Treatment: 1 = Dose not changed; 2 = Drug interrupted; 3 = Drug withdrawn; 4 = Not applicable; 5 = Unknown.
f CM ID is the concomitant medication sequence number on the CRF and provides a cross reference on Listing 16.2.4.3 to any medications that were prescribed for this adverse event.
Note: Adverse events were coded using MedDRA version 21.0. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Listing 16.2.7.1 Treatment-Emergent Adverse Events
(Safety Set)

Actual Treatment: Placebo

Subject ID/ Age/Race/Sex	MedDRA SOC/ Preferred Term/ Verbatim Term	Start Date (Day)/ Stop Date (Day)	SAE Rsn(s)[a]	Sev-erity[b]	Out-come[c]	Related[d]	Action[e]	Led to Study DC	CM ID[f]
[redacted]/ 7[redacted]/B/M	心臓障害/ 心房細動/ WORSENING A-FIB	20[redacted] (39) 20[redacted] (42)	4	2	3	1	4	N	020,021,022,028,029,031

W = white; B = black or African American; P = native Hawaiian or other Pacific Islander; A = Asian; I = American Indian or Alaska native; O = Other; M = male; F = female.
AE = adverse event; CRF = case report form; DC = discontinuation; Rsn = reason; SAE = serious adverse event; SOC = system organ class.

a Reason(s) for SAE: 1 = Congenital abnormality/birth defect; 2 = Results in persistent or significant disability/incapacity; 3 = Results in death; 4 = Requires or prolongs hospitalization; 5 = Life threatening; 6 = Other medically important event.
b Severity: 1 = mild; 2 = moderate; 3 = severe.
c Outcome: 1 = Fatal; 2 = Not recovered/not resolved; 3 = Recovered/resolved; 4 = Recovered/resolved with sequelae; 5 = Recovering/resolving; 6 = Unknown.
d Relationship to study drug: 1 = Not related; 2 = Unlikely related; 3 = Possibly related; 4 = Related.
e Action Taken with Study Treatment: 1 = Dose not changed; 2 = Drug interrupted; 3 = Drug withdrawn; 4 = Not applicable; 5 = Unknown.
f CM ID is the concomitant medication sequence number on the CRF and provides a cross reference on Listing 16.2.4.3 to any medications that were prescribed for this adverse event.
Note: Adverse events were coded using MedDRA version 21.0. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Listing 16.2.7.1 Treatment-Emergent Adverse Events
(Safety Set)

Actual Treatment: Placebo

Subject ID/ Age/Race/Sex	MedDRA SOC/ Preferred Term/ Verbatim Term	Start Date (Day)/ Stop Date (Day)	SAE Rsn(s)[a]	Sev-erity[b]	Out-come[c]	Related[d]	Action[e]	Led to Study DC	CM ID[f]
[redacted]/ 7[redacted]/B/M	心臓障害/ うっ血性心不全/ CONGESTIVE HEART FAILURE EXACERBATION	20[redacted] (39) 20[redacted] (42)	4	2	3	1	4	N	027,030

W = white; B = black or African American; P = native Hawaiian or other Pacific Islander; A = Asian; I = American Indian or Alaska native; O = Other; M = male; F = female.
AE = adverse event; CRF = case report form; DC = discontinuation; Rsn = reason; SAE = serious adverse event; SOC = system organ class.

a Reason(s) for SAE: 1 = Congenital abnormality/birth defect; 2 = Results in persistent or significant disability/incapacity; 3 = Results in death; 4 = Requires or prolongs hospitalization; 5 = Life threatening; 6 = Other medically important event.
b Severity: 1 = mild; 2 = moderate; 3 = severe.
c Outcome: 1 = Fatal; 2 = Not recovered/not resolved; 3 = Recovered/resolved; 4 = Recovered/resolved with sequelae; 5 = Recovering/resolving; 6 = Unknown.
d Relationship to study drug: 1 = Not related; 2 = Unlikely related; 3 = Possibly related; 4 = Related.
e Action Taken with Study Treatment: 1 = Dose not changed; 2 = Drug interrupted; 3 = Drug withdrawn; 4 = Not applicable; 5 = Unknown.
f CM ID is the concomitant medication sequence number on the CRF and provides a cross reference on Listing 16.2.4.3 to any medications that were prescribed for this adverse event.
Note: Adverse events were coded using MedDRA version 21.0. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Listing 16.2.7.1 Treatment-Emergent Adverse Events
(Safety Set)

Actual Treatment: Placebo

Subject ID/ Age/Race/Sex	MedDRA SOC/ Preferred Term/ Verbatim Term	Start Date (Day)/ Stop Date (Day)	SAE Rsn(s)[a]	Sev-erity[b]	Out-come[c]	Related[d]	Action[e]	Led to Study DC	CM ID[f]
[redacted]/ 7[redacted]/W/M	感染症および寄生虫症/ 蜂巣炎/ LEFT LEG CELLULITIS	20[redacted] (52) 20[redacted] (59)	4	3	3	1	4	N	017,018,019,023,033

W = white; B = black or African American; P = native Hawaiian or other Pacific Islander; A = Asian; I = American Indian or Alaska native; O = Other; M = male; F = female.
AE = adverse event; CRF = case report form; DC = discontinuation; Rsn = reason; SAE = serious adverse event; SOC = system organ class.

a Reason(s) for SAE: 1 = Congenital abnormality/birth defect; 2 = Results in persistent or significant disability/incapacity; 3 = Results in death; 4 = Requires or prolongs hospitalization; 5 = Life threatening; 6 = Other medically important event.
b Severity: 1 = mild; 2 = moderate; 3 = severe.
c Outcome: 1 = Fatal; 2 = Not recovered/not resolved; 3 = Recovered/resolved; 4 = Recovered/resolved with sequelae; 5 = Recovering/resolving; 6 = Unknown.
d Relationship to study drug: 1 = Not related; 2 = Unlikely related; 3 = Possibly related; 4 = Related.
e Action Taken with Study Treatment: 1 = Dose not changed; 2 = Drug interrupted; 3 = Drug withdrawn; 4 = Not applicable; 5 = Unknown.
f CM ID is the concomitant medication sequence number on the CRF and provides a cross reference on Listing 16.2.4.3 to any medications that were prescribed for this adverse event.
Note: Adverse events were coded using MedDRA version 21.0. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

AG10-001 試験、AG10-003 試験、AG10-004 試験、AG10-005 試験、AG10-007 試験、AG10-008 試験及び ALXN2060-HV-101 試験では、重篤な有害事象は報告されなかった。

2.7.5　参考文献

1　2.7.1 生物薬剤学及び関連する分析法の概要で引用した参考文献

該当なし

2　2.7.2 臨床薬理試験で引用した参考文献

M2.7.2-5 項参照

3　2.7.3 臨床的有効性で引用した参考文献

M2.7.3-6 項参照

4　2.7.4 臨床的安全性で引用した文献

該当なし

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3 第 1 相試験【AG10-005】（海外）［評価資料］ 38
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1　第 1 相試験【AG10-003】（海外）［評価資料］

1.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-003】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-003】

治験の標題：健康成人被験者を対象に 2 種類の AG10 錠剤の空腹時投与での生物学的同等性を検討する第 1 相、オープンラベル、2 期クロスオーバー、単回投与試験	
治験実施計画書番号：AG10-003	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の完了日：20[redacted] 年 [redacted] 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： 健康成人被験者を対象に、「高含量」のアコラミジス塩酸塩 400 mg 錠 × 1 と、アコラミジス塩酸塩 200 mg 錠 × 2 の生物学的同等性を評価する。 副次目的： 健康成人被験者でのアコラミジス塩酸塩の安全性及び忍容性を評価する。 探索的目的： 蛍光プローブ排除（FPE）及びウエスタンブロット法を含む確立された ex vivo アッセイ及び循環血中プレアルブミン濃度の測定を用いて、アコラミジス結合及びトランスサイレチン（TTR）安定化によって評価されるアコラミジスの薬力学的作用（PD）の特性を評価する。	
方法： 本試験は、絶食条件下での生物学的同等性を検討するオープンラベル、ランダム化、2 投与順、2 期クロスオーバー試験であった。健康な成人男性及び女性（妊娠可能な女性は除く）の被験者 24 名を登録した。被験者のスクリーニングは治験薬の初回投与前 28 日以内に実施した。第 1 期の Day 1 に、被験者を 2 つの投与順序のいずれかにランダム割付けした。各投与期の Day 1 にアコラミジス塩酸塩の「高含量」製剤（400 mg × 1）又は標準製剤（200 mg × 2）を単回投与し、投与後 120 時間にわたり薬物動態（PK）用の検体を採取した。被験者は、各投与期の Day -1 から、24 時間の採血及び／又は試験手順が終了するまで治験実施施設に入院し、試験の評価スケジュールに従って試験手順のために来院した。治験責任医師等の判断により、被験者は更に長期間治験実施施設に滞在できることとした。各投与期の投与前から投与後 120 時間まで、PD マーカー用の血液検体も採取した。各投与間には 10 日間以上のウォッシュアウト期間を設けた。治験薬が 1 回以上投与されたすべての被験者（治験を早期に中止した被験者を含む）に対し、追跡調査として治験薬の最終投与から約 14 日後に連絡を取り、最終来院以降の有害事象発現の有無を確認した。安全性は、臨床評価及び臨床検査を繰り返し実施し、試験期間をとおしてモニタリングした。	
被験者数（計画時及び解析時）： 計画時：24 名 解析時：本試験には 24 名が組み入れられ、すべての被験者が試験を完了した。全 24 名が PK 解	

析対象集団、PD 解析対象集団及び安全性解析対象集団に含まれた。

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす被験者を本試験の組入れ対象とした。

1. スクリーニング時に 18 歳以上 55 歳以下の健康な成人男性又は女性(妊娠可能な女性を除く)。
2. 被験者の自己報告に基づき、治験薬の初回投与前少なくとも 6 ヵ月間ニコチン含有製品を使用していない、また、試験期間をとおして使用しない、継続的な非喫煙者。
3. スクリーニング時点の体格指数が 18.0 kg/m^2 以上 32.0 kg/m^2 以下の者。
4. 医学的に健康であり、臨床的に重要な病歴、身体検査所見、臨床検査プロファイル、バイタルサイン又は心電図所見がないと治験責任医師等が判断した者。
5. 女性の場合、治験薬の初回投与 6 ヵ月以上前に以下のいずれかの避妊法を受けている者。
   - 子宮鏡下避妊術
   - 両側卵管結紮術又は両側卵管切除術
   - 子宮摘出
   - 両側卵巣摘出術

   又は、治験薬の初回投与前 1 年以上無月経で、スクリーニング時の卵胞刺激ホルモン血清中濃度が閉経後の状態と一致している、閉経後の女性。
6. 男性で精管切除術を受けていない場合、試験期間中から治験薬の最終投与後 90 日まで殺精子剤付きコンドームを使用するか、性交渉を控えることに同意する者（治験薬の初回投与 4 ヵ月以上前に精管切除術を受けた男性は、この制限を設けない。精管切除術後、治験薬の初回投与までが 4 ヵ月未満の男性は、精管切除術を受けていない男性と同様の制限を設ける)。
7. 男性の場合、治験薬の初回投与から最終投与後 90 日まで精子を提供しないことに同意する者。
8. 同意説明文書の試験手順を理解し、治験実施計画書を遵守する意思及び能力がある者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. スクリーニング来院時に精神的又は法的な能力がない、若しくは重大な感情的問題を有する、又は試験実施中にそのような状態が予測される者。
2. 治験責任医師等の判断で、臨床的に意味のある医学的若しくは精神的状態又は疾患の既往歴若しくは現病歴を有する者。
3. 治験責任医師等の判断で、試験結果に影響を及ぼす可能性がある、又は試験参加により被験者にさらなるリスクをもたらす可能性がある疾患の既往歴を有する者。
4. 治験薬の初回投与前 2 年以内にアルコール依存症又は薬物乱用の既往歴又は現病歴を有する者。
5. 治験薬又は関連化合物に対する過敏症又は特異体質反応の既往歴又は現病歴を有する者。
6. スクリーニング時の心電図で第二度若しくは第三度房室ブロックを示す臨床的に重要な異常が認められた者、又は以下の 1 項目以上に該当する者 : QRS が 110 msec 超、Fridericia 式を用いた補正 QT 間隔（QTcF）が 450 msec 超（男性及び女性）、PR 間隔が 220 msec 超。また、軽度の非特異的 T 波変化（平坦 T 波を含む）以外に、QT 解析を妨げる又は臨床的に重要であ

ると治験責任医師が判断した重大な形態学的変化が認められた者。
7. 心筋梗塞、急性冠動脈症候群、脳血管発作、一過性脳虚血発作、心室性頻脈、心房細動の既往歴、先天性 QT 延長症候群の既往歴若しくは既知の家族歴、又は原因不明の突然死、ペースメーカー若しくは植込み型除細動器、心臓又は脳へのステント留置若しくは血管形成術、又は臨床的に重要な心臓弁膜症の既知の家族歴を有する者。
8. 以下のいずれかの臨床検査値異常が認められる者：肝機能検査値（アラニンアミノトランスフェラーゼ、アスパラギン酸アミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限（ULN）超、トロポニンが ULN 超、甲状腺刺激ホルモンが ULN 超、クレアチニンクリアランスが基準値下限未満、スクリーニング時に臨床的に重要な低カリウム血症、低マグネシウム血症又は低カルシウム血症を有する者。
9. 妊娠可能な女性。
10. 妊娠検査陽性又は授乳中の女性。
11. スクリーニング時又は初回入院時の尿中薬物又はアルコール検査結果が陽性の者。
12. スクリーニング時にヒト免疫不全ウイルス、B 型肝炎表面抗原又は C 型肝炎ウイルスの検査結果が陽性の者。
13. スクリーニング時の座位血圧が 90/40 mmHg 未満又は 140/90 mmHg 超の者。
14. スクリーニング時の座位心拍数が 40 bpm 未満又は 99 bpm 超の者。
15. 治験薬の初回投与前 4 週間以内に、ホルモン補充療法を含む処方薬を使用した者。
16. Day -1 前の 7 日間又は半減期の 5 倍（いずれか長い方）以内に、ハーブ又は定期的にビタミン、ミネラル、又はその他のサプリメントを含む市販薬を使用した者、又は試験参加中に処方薬又は市販薬の継続的な使用を必要とする者。ランダム化後、治験責任医師等の判断でアセトアミノフェン（24 時間あたり 2 g まで）は投与可能とする。
17. 胆嚢摘出術の既往歴を有する者。
18. 治験責任医師等の判断で、治験薬の初回投与前 30 日以内に試験期間中の食事内容と一致しない食事を摂取した、又は試験期間中に摂取予定の者。
19. 治験薬の初回投与前 56 日以内の献血又は重大な失血をした者。
20. 治験薬の初回投与前 7 日以内に血漿を提供した者。
21. 治験薬の初回投与前 30 日以内に他の臨床試験に参加した者。30 日間の許容期間は、前の試験の最終採血日又は投与日のいずれか遅い方から本試験の第 1 期 Day 1 までとする。

治験薬、用法・用量：

試験製剤：一晩絶食後にアコラミジス塩酸塩 400 mg 錠 × 1（ロット番号：[redacted]）を約 240 mL の水とともに経口投与した。

標準製剤：一晩絶食後にアコラミジス塩酸塩 200 mg 錠 × 2（ロット番号：[redacted]）を約 240 mL の水とともに経口投与した。

治療期間：

各被験者のスクリーニング期を含む総試験期間は約 66 日間であった（スクリーニング期：28 日、投与期：約 7 日間 × 2 期、各投与間のウォッシュアウト期間：10 日間、追跡調査：最終投与約 14 日後）。

評価項目：

薬物動態

PK の評価項目として、アコラミジス塩酸塩 400 mg 用量の 2 製剤（400 mg × 1 vs 200 mg × 2）の自然対数変換した時間 0 から血漿中濃度測定可能最終時点(t)までの時間濃度曲線下面積(AUC$_t$)、時間 0 から無限時間までの濃度時間曲線下面積（AUC$_{0-\infty}$)、最高血漿中濃度（C$_{max}$）の解析から得られた最小二乗平均（LSM）の比の 90%信頼区間を評価した。

安全性

安全性の評価項目として、12 誘導心電図、バイタルサイン、臨床検査及び有害事象を評価した。

薬力学的作用

PD の評価項目として、2 つの in vitro 実験系（FPE アッセイ及びウエスタンブロット分析）を用いて TTR へのアコラミジス結合及び TTR 安定化を評価した。プレアルブミン濃度測定用に採血を行った。

統計手法：

薬物動態：

アコラミジスの PK 濃度及び PK パラメータの記述統計量はすべて SAS® Version 9.3 を用いて作成した。

自然対数変換した PK パラメータ（AUC$_t$、AUC$_{0-\infty}$及び C$_{max}$）を比較し、SAS®の PROC MIXED を用いた分散分析（ANOVA）モデルにより、アコラミジス塩酸塩 400 mg 錠 × 1（試験製剤）と 200 mg 錠 × 2（標準製剤）の相対的生物学的同等性を評価した。ANOVA モデルには、投与順序、投与及び投与期を固定効果、投与順序内でネストした被験者を変量効果として含めた。推測結果（LSM、LSM 間の差、差の 90%信頼区間）を元の尺度に累乗した。幾何 LSM、幾何平均比（GMR）及び 90%信頼区間を示した。

標準製剤に対する試験製剤の AUC$_t$、AUC$_{0-\infty}$及び C$_{max}$ の LSM の比の 90%信頼区間がいずれも 80.00%～125.00%以内に含まれた場合に、生物学的に同等であると判定することとした。投与順序内でネストした被験者を誤差項として、有意水準 10%で投与順序を検定した。有意であれば、追加の by-sequence 解析を実施できることとした。

薬力学的作用：

TTR へのアコラミジス結合、TTR 安定化及びプレアルブミン値の測定に関するすべての結果は、SAS® Version 9.3 を用いて作成した。

TTR へのアコラミジス結合に関する個々のデータを示す表には、プレプローブ蛍光、動態学的データ蛍光、及びベースライン補正値を記載し、生体試料分析機関から受領した値と同レベルの精度で示した。動態学的データ蛍光とベースライン補正値は重複して示した。さらに、6 時間 FPE 試験での各血液検体のベースライン補正値の平均値及び標準偏差（SD）を 15 分間隔で同じ表に示した。TTR へのアコラミジス結合に関する個々の図を、各被験者の 6 時間 FPE 試験での投与前及び投与後 0.5、1、2、4、12、24、48 時間の時点の SD を用いて線形スケールで示した。

TTR 安定化に関する個々のデータの表には、TTR 及び免疫グロブリン G（IgG）の生のデンシトメトリー値を生体試料分析機関から受領した値と同レベルの精度で示した。投与前及び投与後

0.5、1、2 時間の時点の TTR 安定化に関するデータを示した。TTR 及び IgG の生のデンシトメトリー値は重複して示した。各採血時点（0 時間又は 72 時間）の酸性化時間も示した。TTR の IgG デンシトメトリー値への正規化も示した。各採血時点の生データ及び酸性化に関する平均値及び SD を示した。酸性化に関して、各採血時点の IgG 値への正規化 TTR の平均値及び SD を示した。TTR 安定化の個別の棒グラフは、各被験者の正規化データ及び生データの SD とともに示した。プレアルブミン濃度のベースライン値、投与後値、ベースラインからの変化量を、記述統計量を用いて表に示した。

安全性：

推測統計は実施しなかった。

結果の要約：

薬物動態：

血漿中アコラミジスの PK パラメータの要約を以下に示す。

アコラミジス塩酸塩 400 mg 錠 × 1 を単回経口投与したときとアコラミジス塩酸塩 200 mg 錠 × 2 を単回経口投与したときの血漿中アコラミジスの PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	400 mg (1 x 400 mg) AG10 (Test)	400 mg (2 x 200 mg) AG10 (Reference)
AUC_t (ng*hr/mL)	60700 (26.7) [n=24]	60200 (27.6) [n=24]
$AUC_{0-\infty}$(ng*hr/mL)	62000 (28.3) [n=24]	62400 (27.7) [n=23]
$AUC_{\%extrap}$	2.13 ± 2.19 [n=24]	1.72 ± 1.52 [n=23]
C_{max} (ng/mL)	4190 (28.0) [n=24]	5330 (30.9) [n=24]
t_{max} (hr)	0.748 (0.499, 3.00) [n=24]	0.759 (0.500, 2.00) [n=24]
λ_z (1/hr)	0.0356 ± 0.00968 [n=24]	0.0362 ± 0.00852 [n=23]
$t_{1/2}$ (hr)	21.1 ± 6.63 [n=24]	20.2 ± 4.72 [n=23]

400 mg (1 x 400 mg) AG10 (Test): 400 mg AG10 (1 x 400 mg AG10 HCl tablet) at Hour 0 on Day 1
400 mg (2 x 200 mg) AG10 (Reference): 400 mg AG10 (2 x 200 mg AG10 HCl tablets) at Hour 0 on Day 1
AUCs and C_{max} are presented as geometric mean and geometric CV%
t_{max} are presented as Median (Minimum, Maximum)
Other parameters are presented as arithmetic mean ± SD
Source: 5.3.1.2.1 項 AG10-003 CSR Tables 14.2.1.1.3 and 14.2.1.1.4

本試験では血漿中アコラミジスの PK プロファイルの特徴が明らかにされ、両投与後の外挿した $AUC_{0-\infty}$に対する割合（$AUC\%_{extrap}$）の算術平均は 2.5%未満であった。アコラミジスへの総曝露量（AUC_t 及び $AUC_{0-\infty}$）は両投与後で同程度であったが、C_{max} は、アコラミジス塩酸塩 200 mg × 2 単回経口投与後と比較してアコラミジス塩酸塩 400 mg × 1 単回経口投与後の方が低かった。終末相消失半減期（$t_{1/2}$）の算術平均値及び最高血漿中濃度到達時間（t_{max}）の中央値は、両投与後で同程度であった。

血漿中アコラミジスの PK パラメータの統計学的比較を以下に示す。

アコラミジス塩酸塩 400 mg 錠 × 1 を単回経口投与したときとアコラミジス塩酸塩 200 mg 錠 × 2 を単回経口投与したときの血漿中アコラミジスの PK パラメータの統計学的比較の要約（PK 評価可能集団）

	400 mg (1 x 400 mg) AG10 (Test)		400 mg (2 x 200 mg) AG10 (Reference)				
Parameter	Geometric LSM	n	Geometric LSM	n	GMR (%)	90% Confidence Interval	Intra-subject CV%
AUC_t (ng*hr/mL)	60700	24	60200	24	100.77	96.43 - 105.30	8.89
$AUC_{0-\infty}$ (ng*hr/mL)	62000	24	61400	23	100.95	95.81 - 106.36	10.32
C_{max} (ng/mL)	4190	24	5330	24	78.72	71.51 - 86.66	19.57

400 mg (1 x 400 mg) AG10 (Test): 400 mg AG10 (1 x 400 mg AG10 HCl tablet) at Hour 0 on Day 1
400 mg (2 x 200 mg) AG10 (Reference): 400 mg AG10 (2 x 200 mg AG10 HCl tablets) at Hour 0 on Day 1
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from the ANOVA.
Geometric Mean Ratio (GMR) = 100*(test/reference)
Intra-subject CV% was calculated as 100 x square root(exp[residual variance]-1).
Source: 5.3.1.2.1 項 AG10-003 CSR Table 14.2.1.1.7

アコラミジス塩酸塩 400 mg 錠 × 1 単回経口投与後とアコラミジス塩酸塩 200 mg 錠 × 2 単回経口投与後で、アコラミジスの自然対数変換した PK パラメータ（AUC_t、$AUC_{0-\infty}$、C_{max}）を比較した解析から得られた LSM の比の 90%信頼区間は、AUC_t 及び $AUC_{0-\infty}$は完全に 80.00%～125.00%の生物学的同等性範囲内であったが、C_{max} は範囲外であった。AUC_t 及び $AUC_{0-\infty}$（全身曝露量）の 90%信頼区間が 80.00%～125.00%の範囲内であったことから、両製剤のバイオアベイラビリティは同程度であると考えられる。

薬力学的作用：

アコラミジス塩酸塩 400 mg 単回経口投与後のプレアルブミン濃度のベースライン値、名目上の値及びベースラインからの変化量の要約を以下に示す。

アコラミジス塩酸塩 400 mg 錠×1 を単回経口投与したときとアコラミジス塩酸塩 200 mg 錠×2 を単回経口投与したときのプレアルブミン濃度のベースライン値及びベースラインからの変化量の要約（PD 評価可能集団）

Treatment	Baseline (mg/dL)	Postdose (mg/dL)	Change from Baseline (mg/dL)
400 mg (1 x 400 mg) AG10 (Test)	23.7 (19.4) [n=24]	26.3 (17.3) [n=24]	2.45 (51.9) [n=24]
400 mg (2 x 200 mg) AG10 (Reference)	23.6 (16.9) [n=24]	26.3 (15.1) [n=24]	2.21 (84.3) [n=24]

400 mg (1 x 400 mg) AG10 (Test): 400 mg AG10 (1 x 400 mg AG10 HCl tablet) at Hour 0 on Day 1
400 mg (2 x 200 mg) AG10 (Reference): 400 mg AG10 (2 x 200 mg AG10 HCl tablets) at Hour 0 on Day 1
Baseline, postdose and change from baseline values are presented as geometric mean and geometric CV%.
Baseline is -0.5 hours.
Source: 5.3.1.2.1 項 AG10-003 CSR Tables 14.2.2.1.1 and 14.2.2.1.2

アコラミジス塩酸塩 400 mg 錠 × 1 単回経口投与後とアコラミジス塩酸塩 200 mg 錠 × 2 単回経口投与後を比較したとき、循環血中プレアルブミン濃度のベースラインからの変化量の幾何平均はそれぞれ 2.45 mg/dL 及び 2.21 mg/dL であった（24 時間後に約 11%の増加）。

安全性：

本試験では、死亡、重篤な有害事象及び中止に至った有害事象は認められなかった。全体で、アコラミジス塩酸塩 400 mg 錠 × 1 単回経口投与後に 2 名（8%）で有害事象が発現した。有害事象の大部分は軽度であり、1 件は中等度であった。その他に本試験の臨床検査、バイタルサイン、心電図又は身体所見の安全性評価で臨床的に重要な所見は認められなかった。

結論：

- アコラミジス塩酸塩 400 mg 錠 × 1 単回経口投与後とアコラミジス塩酸塩 200 mg 錠 × 2 単回経口投与後でアコラミジスの AUC_t、$AUC_{0-\infty}$、C_{max} を比較した解析では、AUC_t 及び $AUC_{0-\infty}$ は 90%信頼区間が完全に 80.00%～125.00%の生物学的同等性範囲内であったが、C_{max} は範囲外であった。AUC_t 及び $AUC_{0-\infty}$の 90%信頼区間が 80.00%～125.00%の範囲内であったことから、両製剤のバイオアベイラビリティは同程度であると考えられる。
- 24 時間間隔で測定した結果、アコラミジス塩酸塩 400 mg（400 mg 錠 × 1 及び 200 mg 錠 × 2）の投与後に循環血中プレアルブミン濃度が約 11%増加した。

- FPE による標的結合率及びウエスタンブロット法による TTR 安定化に基づき、ex vivo 有効性評価として PD 活性に差は認められなかった。
- first-in-human 単回投与漸増試験及び反復投与漸増試験では、TTR のほぼ完全な安定化の程度が定常状態のトラフ濃度と関連することが既に示されており、本試験の 2 種類の製剤は PD プロファイルと関連する同様の PK プロファイルを示している。
- アコラミジス塩酸塩の経口投与後は速やかに t_{max} に到達するため、被験者ごとに C_{max} を正確に把握することは困難である。一部の C_{max} 値は真の t_{max} に対応していない可能性があることから、報告された C_{max} の解釈には限界がある。AUC_t 及び $AUC_{0-\infty}$ の生物学的同等性（GMR = 101%）並びに両製剤間でほぼ完全な TTR 占有率及び安定化が認められることを考慮すると、本試験で C_{max} に生物学的同等性の基準を適用することの重要性は低いと考えられる。
- 本試験では、健康成人被験者にアコラミジス塩酸塩を「高含量」の 400 mg 錠 × 1 又は 200 mg 錠 × 2 で単回経口投与したときの安全性に問題はなく、忍容性はおおむね良好であった。

報告書作成日：20[redacted] 年 [redacted] 月 [redacted] 日

1.2 有害事象

すべての有害事象を以下に示す。本試験で重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Table 14.3.1.1
治験薬との関連性が否定できない有害事象	Table 14.3.1.3
重篤な有害事象	Table 14.3.2.1（該当なし）
治験薬の投与中止に至った有害事象	該当なし

1.3 個別被験者の詳細

本試験で死亡又は重篤な有害事象は発現していないため、該当なし。

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting the Event (% of Subjects Dosed) (Safety Population)

Adverse Event*	Treatment A	Treatment B	Overall
Number of Subjects Dosed	24 (100%)	24 (100%)	24 (100%)
Number of Subjects With TEAEs	2 (8%)	0 (0%)	2 (8%)
Number of Subjects Without TEAEs	22 (92%)	24 (100%)	22 (92%)
胃腸障害	1 (4%)	0 (0%)	1 (4%)
下腹部痛	1 (4%)	0 (0%)	1 (4%)
上腹部痛	1 (4%)	0 (0%)	1 (4%)
便秘	1 (4%)	0 (0%)	1 (4%)
消化器痛	1 (4%)	0 (0%)	1 (4%)
一般・全身障害および投与部位の状態	2 (8%)	0 (0%)	2 (8%)
胸痛	1 (4%)	0 (0%)	1 (4%)
悪寒	1 (4%)	0 (0%)	1 (4%)

Note: * Adverse events (AEs) are classified according to MedDRA Version 21.0.
TEAE = Treatment-Emergent Adverse Event
Treatment A: 400 mg AG10 (1 x 400 mg AG10 HCl tablet) at Hour 0 on Day 1
Treatment B: 400 mg AG10 (2 x 200 mg AG10 HCl tablets) at Hour 0 on Day 1

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug - Number of Adverse Events (Safety Population)

			Severity#			Relationship to Study Drug	
Adverse Event*	Treatment	Number of AEs	Mild	Moderate	Severe	Yes	No
下腹部痛	A	1	1	0	0	1	0
上腹部痛	A	1	0	1	0	1	0
胸痛	A	1	1	0	0	0	1
悪寒	A	1	1	0	0	1	0
便秘	A	1	1	0	0	1	0
消化器痛	A	1	1	0	0	1	0
	A	6	5	1	0	5	1
	B	0	0	0	0	0	0
	Overall	6	5	1	0	5	1

Note: * Adverse events (AEs) are classified according to MedDRA Version 21.0.
No subject experienced a potentially life-threatening or fatal adverse event.
Treatment A: 400 mg AG10 (1 x 400 mg AG10 HCl tablet) at Hour 0 on Day 1
Treatment B: 400 mg AG10 (2 x 200 mg AG10 HCl tablets) at Hour 0 on Day 1

Table 14.3.2.1 Serious Adverse Events (Safety Population)

No serious adverse event was reported.

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2　第 1 相試験【AG10-001】（海外）［評価資料］

2.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-001】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-001】

治験の標題：健康成人被験者を対象に AG10 の安全性、忍容性、薬物動態及び薬力学的作用を評価する第 1 相ランダム化プラセボ対照単回及び反復投与用量漸増試験	
治験実施計画書番号：AG10-001	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：2017 年 8 月 [redacted] 日 最後の被験者の完了日：2018 年 2 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的 • 健康成人被験者にアコラミジス塩酸塩を単回及び反復投与したときの安全性及び忍容性を評価する。 副次目的 • 健康成人被験者でのアコラミジスの薬物動態（PK）の特性を明らかにする。 • トランスサイレチン（TTR）安定化の確立されたアッセイを用いてアコラミジスの薬力学的作用（PD）の特性を明らかにし、健康成人被験者でのアコラミジスの PK-PD 関係を明らかにする。 • アコラミジスの PK に対する食事の影響を評価する。	
方法： 本試験は、健康成人被験者を対象としたアコラミジス塩酸塩の単一施設、前向き、ランダム化、プラセボ対照試験であった。本試験は Part A 及び Part B で構成された。 <u>Part A</u> Part A は単回用量漸増デザインであり、各コホート健康成人 8 名とし、最大 6 つのコホート全体で 3 : 1 の比となるように、センチネル投与では 1 : 1、その後の投与では 5 : 1 の比で、アコラミジス又はプラセボにランダム割付けした。アコラミジス塩酸塩の開始用量は 50 mg とし、さらに 150、300、600、1200 及び 2000 mg の用量レベルを想定したが、先行コホートの安全性及び PK データのレビューに基づいて増量した結果、実際は 50、150、300、800 mg が投与された。なお、Part A のコホート 3 では、2 群 2 期クロスオーバー法に基づき、各被験者にアコラミジス塩酸塩を 2 回（第 1 期は空腹時、第 2 期は食後）投与し、各期の間には 14 日間のウォッシュアウトを設けた。 <u>Part B</u> Part B は反復用量漸増デザインであり、各コホート健康成人 8 名とし、最大 6 つのコホートでアコラミジス又はプラセボに 3 : 1 の比でランダム割付けした。Part B の開始用量は Part A で得られた安全性データに基づいて決定することとし、その結果、Part B の用法・用量は 100、300 及び	

800 mg を 1 日 2 回とした。Part B の投与は空腹時に行い、朝は投与 1 時間後に朝食を摂取し、朝の投与の 12 時間後、空腹時に夜の投与を行うこととした。

被験者数（計画時及び解析時）：

計画時：Part A　最大 48 名、Part B　最大 48 名

登録時：Part A　32 名（アコラミジス塩酸塩 24 名、プラセボ 8 名）、全 32 名が試験を完了

Part B　24 名（アコラミジス塩酸塩 18 名、プラセボ 6 名）、全 24 名が試験を完了

解析時：安全性解析対象集団 56 名、PK 評価可能集団 42 名、PD 評価可能集団 56 名

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす被験者を試験の組入れ対象とした。

1. 18 歳以上 55 歳以下の成人の男女。
2. スクリーニング時の体重が 50 kg 超 110 kg 以下の者。
3. スクリーニング時の体格指数が 18 kg/m^2 以上 32 kg/m^2 以下の者。
4. 女性の場合、以下のいずれかにより定義される妊娠の可能性がない者：
   a. 避妊手術を受けている（すなわち、治験薬の初回投与 6 ヵ月以上前に両側卵管結紮術、両側卵巣又は子宮の摘出、子宮頸管不妊手術［Essure］、又は卵管切除術を受けている）、又は
   b. 初回投与前に 12 ヵ月以上連続して閉経しており（自然閉経）、スクリーニング時の卵胞刺激ホルモン値が治験責任医師等の判断で閉経基準と一致。
5. 女性の場合、スクリーニング時及び各期の入院時（Day -1）の血清妊娠検査が陰性の者。
6. 男性の場合、精管切除、コンドーム+殺精子剤又は禁欲により定義される男性避妊法を使用することに同意できる者。
7. 男性の場合、治験薬の最終投与後最低 90 日間は精子を提供しないことに同意できる者。
8. 既往歴、身体所見、12 誘導心電図及び甲状腺刺激ホルモン（TSH）を含む標準的な臨床検査から健康と判断される者。
9. スクリーニング時及び入院時に薬物乱用及びアルコール検査で陰性の者。
10. 非喫煙者又はスクリーニング前 6 ヵ月以内に他のタバコ若しくはニコチン含有製品を使用していない者（例：紙巻きタバコ、葉巻、噛みタバコ、嗅ぎタバコ、電子タバコ、ニコチンガム／パッチ等）。
11. 治験実施施設等の治験審査委員会が承認した同意説明文書を読み、同意書に署名できる者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. 治験薬の初回投与前 4 週間以内にホルモン補充療法を含む処方薬を使用した者。
2. 過去に胆嚢摘出術を受けた者。
3. Day -1 前の 7 日間又は半減期の 5 倍の期間（いずれか長い方）以内に、ハーブ、定期的にビタミン若しくはミネラル、その他のサプリメントを含む市販薬を使用した者、又は試験参加中に処方薬又は市販薬の継続使用を必要とする者。
4. 呼吸器系、胃腸系、腎臓系、肝臓系、血液系、リンパ系、神経系、心血管系、精神系、筋骨格系、泌尿生殖器系、免疫系、皮膚系又は結合組織系の疾患若しくは障害の臨床的に重要な既往歴又は現病歴のある者。

5. スクリーニング時の心電図で第二度若しくは第三度房室ブロックを示す臨床的に重要な異常が認められた者、又は以下の 1 項目以上に該当する者：QRS が 110 msec 超、Fridericia 式で補正した QT 間隔が 450 msec 超（男女）、又は PR 間隔が 220 msec 超。また、軽度の非特異的 T 波の変化以外に、平坦 T 波を含む重大な形態学的変化が認められ、治験責任医師等により QT 解析の妨げとなる、又は臨床的に重要であると判断された者。
6. 心筋梗塞、急性冠症候群、脳血管発作、一過性脳虚血発作、心室頻拍、心房細動の既往歴、先天性 QT 延長症候群の既往歴若しくは既知の家族歴、又は原因不明の突然死の既知の家族歴、ペースメーカー若しくは植込み型除細動器、心臓若しくは脳のステント留置若しくは血管形成、又は臨床的に重要な心臓弁膜症の既往歴を有する者。
7. スクリーニング前 2 年以内にアルコール中毒を含む薬物乱用の既往がある者、又はスクリーニング時若しくは入院時に薬物乱用若しくはアルコールのスクリーニング検査で陽性の者。
8. 各試験期間の治験実施施設入院の 48 時間前から最終 PK 検体採取完了まで、カフェイン又はキサンチン含有製品（例：紅茶、コーヒー、チョコレート、コーラ等）の摂取を控える意思がない者。
9. 第 1 期 Day -1 の治験実施施設入院の 48 時間前から最終 PK 検体採取までアルコールの摂取を控える意思がない者。
10. 第 1 期 Day -1 の治験実施施設入院前 14 日以内にグレープフルーツ、セビリアオレンジ又はそれらに由来する製品を摂取し、試験終了までこれらの摂取を控える意思のない者。
11. 各試験期間の治験実施施設入院の 24 時間前から各試験期間の最終 PK 検体採取までに激しい身体運動（ウエイトトレーニング、エアロビクス等）を控える意思がない者。
12. 入院前の 30 日以内又は半減期の 10 倍のいずれか長い方の期間内に、他の臨床試験で何らかの治験薬を使用した者。
13. 以下のいずれかの臨床検査値異常が認められた者：肝機能検査値（アスパラギン酸アミノトランスフェラーゼ、アラニンアミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限（ULN）超；トロポニンが ULN 超；TSH が ULN 超；推算糸球体濾過量が基準値下限（LLN）未満；臨床的に重要な低カリウム血症、低マグネシウム血症又は低カルシウム血症。
14. スクリーニング時のバイタルサインが以下の範囲を超える者：収縮期血圧が 90 mmHg 以上、140 mmHg 以下；拡張期血圧が 40 mmHg 以上、90 mmHg 以下；心拍数 40 bpm 以上、99 bpm 以下。
15. スクリーニング前 56 日以内に献血及び／又は 7 日以内に血漿を提供した者。
16. 本試験の食後投与群に参加する場合は、乳糖不耐症の者。

治験薬、用法・用量：

- アコラミジス：アコラミジス塩酸塩 50 mg 錠又は 200 mg 錠として、Part A では 50、150、300、800 mg（コホート 1～4）を単回、Part B では 100、300、800 mg（コホート 1～3）を 1 日 2 回 12 日間、いずれも水 240 mL とともに経口投与した（ロット番号：[redacted]、[redacted]）。
- プラセボ：アコラミジス塩酸塩に対応するプラセボ錠を水 240 mL とともに経口投与した（ロット番号：[redacted]）。

治療期間：

Part A：最大 49 日（スクリーニング 30 日間、入院 5 日間、外来追跡 14 日間）。

ただし、コホート 3 では最大 70 日（スクリーニング 30 日間、第 1 期の入院 5 日間、ウォッシュアウト 9～16 日間、第 2 期の入院 5 日間、外来追跡 14 日間）

Part B：最大 76 日間（スクリーニング 30 日間、入院 16 日間、外来追跡 30 日間）

評価項目：

主要評価項目：

安全性及び忍容性の評価項目として、バイタルサイン（血圧、心拍数）、身体所見、臨床検査（血液学的検査、血液生化学的検査、尿検査［顕微鏡検査を含む］）、心電図、有害事象及び 24 時間連続 12 誘導心電図（ホルター心電図を抽出）を評価する。

副次評価項目：

- Part A（単回漸増投与）の PK 評価項目として、アコラミジス及びその代謝物アコラミジスアシルグルクロニド（アコラミジス-AG）の分布相の消失半減期（$t_{1/2,d}$）及び終末相の消失半減期（$t_{1/2,t}$）、最高血漿中濃度到達時間（t_{max}）、最高血漿中濃度（C_{max}）、定常状態での平均血漿中濃度（C_{ave}）、時間 0 から投与 24 時間後までの濃度時間曲線下面積（AUC_{0-24}）、時間 0 から血漿中濃度測定可能最終時点までの濃度時間曲線下面積（AUC_{0-t}）、時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0-\infty}$）、みかけの全身クリアランス（CL/F）、終末相のみかけの分布容積（V_z/F）を評価する。

  Part B（反復漸増投与）の PK 評価項目として、アコラミジス及びその代謝物アコラミジス-AG の $t_{1/2,d}$ 及び $t_{1/2,t}$、t_{max}、C_{max}、最小血漿中濃度（C_{min}）、C_{ave}、C_{max} の累積係数（$R_{A,Cmax}$）、C_{ave} の累積係数（$R_{A,Cave}$）、AUC_{0-24}、AUC_{0-t}、$AUC_{0-\infty}$、CL/F、定常状態でのみかけの分布容積（$V_{z,ss}$/F）を評価する。

  また、用量補正した（DN）AUC_{0-24} 及び DN C_{max} を算出する。

  Part A 及び Part B の尿中データから PK パラメータとして腎クリアランス（CLr）及び投与後 72 時間（単回漸増投与）／24 時間（反復漸増投与）までの未変化体の尿中総排泄量（Ae）を算出する。
- アコラミジスの TTR への結合及び TTR の安定化を、2 つの in vitro 実験系（蛍光プローブ排除［FPE］アッセイ及びウェスタンブロット分析）を用いて評価する。プレアルブミンの測定及び追加の探索的な PD アッセイのために追加の採血を行う。TTR 安定化の評価を一覧にし、適切な要約統計量を用いてパート別、投与群別及び時点別に要約する。
- Part A のコホート 3 で、同一被験者にアコラミジス塩酸塩を 2 群 2 期クロスオーバー法（食後及び空腹時）で 2 回投与したときの、食後投与時の PK パラメータ（Part A の空腹時投与と同じパラメータ）を算出する。

統計手法：

安全性：

安全性の評価は安全性解析対象集団を対象に解析し、その定義は「治験薬が 1 回以上投与されたすべての被験者」とした。Part A と Part B の結果は別々に示した。

すべての安全性データは被験者別及び評価時点別に時系列に一覧表に示した。連続変数は、投与群別及び実薬合計の要約統計量（n、平均値、標準偏差［SD］、中央値、最小値及び最大値）を算出した。カテゴリカルデータは必要に応じて頻度数を示した。収集したすべての有害事象に対し、報告された用語、ICH 国際医薬用語集（MedDRA）の器官別大分類（SOC）及び基本語（PT）、

投与、重症度、治験薬との因果関係及び処置などの被験者別のデータ一覧表に示したが、要約表には治験薬投与後に発現した有害事象のみを含めた。要約表には、有害事象発現者数及び発現割合を用量別及び実薬合計で示した。臨床検査値は評価時点及び投与群別に要約統計量（n、平均値、中央値、SD、最小値、最大値）を示した。バイタルサインの評価時点別の値及びベースラインからの変化量の要約統計量を投与群別に示した。心電図パラメータも同様に要約した。

薬物動態：

PK 解析対象集団は「治験薬が 1 回以上投与され、測定可能な血漿中濃度を示す血液検体を 1 つ以上有する被験者」と定義した。PK 評価可能集団は「実薬が投与され、評価可能な PK 測定値を有し、治験実施計画書からの重大な逸脱のない被験者」と定義した。

アコラミジス及びアコラミジス-AG のすべての血漿中濃度及び PK パラメータの要約統計量は SAS® version 9.3 以上を用いて要約した。

データの要約

PK 解析対象集団の全被験者のアコラミジス及びアコラミジス-AG の血漿中及び尿中回収率を一覧表に示し、コホート別及び時点別に要約した。全ての名目上の濃度測定時点で、PK 評価可能集団に対して被験者数（n）、算術平均値、標準偏差（SD）、変動係数（CV%）、平均値の標準誤差（SEM）、最小値、中央値及び最大値を含む要約統計量を算出した。濃度一覧表では、定量下限値未満（BLQ）の値はすべて「BLQ」と表記した。

PK 解析対象集団の全被験者の血漿中及び尿中アコラミジス及びアコラミジス-AG の PK パラメータを一覧表に示し、コホート別、投与別及び試験パート別に要約した。PK 評価可能集団に対して、血漿中及び尿中アコラミジス及びアコラミジス-AG の PK パラメータの要約統計量（n、算術平均値、SD、CV%、SEM、最小値、中央値、最大値、幾何平均値及び幾何 CV%）を算出した。

PK パラメータの統計解析

SAS®の PROC MIXED を用いた分散分析（ANOVA）モデルを実施して自然対数（ln）変換した PK パラメータ（C_{max}、AUC_{0-t} 及び $AUC_{0-\infty}$）を比較し、食事の影響コホートでの食後投与と空腹時投与での相対的バイオアベイラビリティを評価した。ANOVA モデルには、投与を固定効果、被験者を変量効果として含めた。推測結果（最小二乗［LS］平均値、LS 平均値の差及び差の 90%信頼区間）を元の尺度に指数変換した。幾何 LS 平均値、幾何平均比（GMR）及び 90%信頼区間を示した。

用量比例性解析（Part A 及び Part B）

アコラミジス塩酸塩を空腹時に単回漸増投与及び反復漸増投与したときのアコラミジス及びアコラミジス-AG の ln 変換した C_{max}、AUC_{0-t} 及び $AUC_{0-\infty}$の用量比例性を評価した。ln 変換した PK パラメータと ln 変換した用量の間の線形関係は、以下の線形回帰モデルを用いて当てはめた。

$$\ln(Y) = \ln b0 + b \ln \text{用量} + e$$

ここで、Y は C_{max}、AUC_{0-t} 及び $AUC_{0-\infty}$の PK パラメータ、e は誤差項を表す。この方法は通常、パワーモデルと呼ばれ、これは指数変換後の次の理由による。

$$Y = b0\ (\text{用量})^{b}$$

用量比例性を示すためには $b = 1$ である必要がある。したがって、これらの用量依存性パラメータの 95%信頼区間に 1 が含まれていれば、用量比例性が確認されることとした。すべての用量で用量比例性が結論づけられなかった場合は、最高（又は最低）用量のデータを除外した後に再度検定を行った。この目的は、曝露量が用量に比例する用量範囲を決定することであった。

Step 1 として、モデルに（ln 用量）2 項及び（ln 用量）3 項（それぞれ二次及び三次効果に相当）を含め、ln 変換した PK パラメータと ln 変換した用量の間の線形関係を検証した。二次及び三次効果の検定には有意水準 5%を用いた（第 I 種の過誤）。二次及び三次項が統計学的に有意でない場合、線形性が結論づけられた。Step 1 で線形性が成立した後、Step 2 を実施した。Step 2 では、線形モデルを用いて、上記の ln 変換した PK パラメータの傾きの 95%信頼区間を算出した。直線の傾き、標準誤差、傾きの 95%信頼区間及び p 値を示した。
また、ln 変換した PK パラメータ値と ln 変換した用量との関係を図示した。
定常状態解析（Part B）
定常状態解析の詳細は、Part A（単回漸増投与）が完了した時点で決定した。Day 10～12 の投与前のトラフ濃度（C_{trough}）（ln 変換値）に対し、Helmert 対比を用いて定常状態解析を実施した。ANOVA は、Day を固定効果として投与群別に行った。定常状態の解析に用いる Day は、本試験の Part A（単回漸増投与）での所見に基づき変更される可能性があった。
各時点をその後の時点の平均値と比較できるように Helmert 対比を構築した。統計学的な差（$\alpha = 5\%$）が観察されなくなった時点で、定常状態と結論された。対比は以下のとおりであった。
比較 1：［Day 10、0 時間目の C_{trough}］対［Day 11、0 時間目及び Day 12、0 時間目の各 C_{trough} の平均値］
比較 2：［Day 11、0 時間目の C_{trough}］対［Day 12、0 時間目の C_{trough}］

薬力学的作用：
PD 評価可能集団は「安全性解析対象集団のうち、投与前及び 1 つ以上の投与後の定量可能な PD バイオマーカー値を有する被験者」と定義した。
アコラミジスの TTR への結合の個別データの表には、プローブ前蛍光強度、キネティクスデータ蛍光強度及びベースライン補正値を示した。キネティクスデータ蛍光強度及びベースライン補正値は 3 部提示した。さらに、同表を用いて 6 時間 FPE 試験中の各血液検体のベースライン補正値の平均値及び SD を示した（15 分間隔）。アコラミジスの TTR への結合の個々の数値は各被験者の 6 時間 FPE 試験中の全血液試料採取時点で SD を伴う線形スケールを用いて示した。
TTR の安定化に関する個別データの表には、TTR 及び IgG の生デンシトメトリー値を記載した。TTR 及び IgG の生デンシトメトリー値は 2 部提示した。各血液検体の採取時点別に酸性化時間（0 時間又は 72 時間のいずれか）も示した。IgG デンシトメトリー値に対する TTR の正常化も示した。各血液検体の採取時点別の生データ及び酸性化の平均値及び SD を示した。酸性化に関する各血液検体の採取時点別の標準化 TTR-IgG 値の平均値及び SD を示した。TTR 安定化の個別の棒グラフを、各被験者の標準化及び生データの SD とともに示した。
ベースライン値、投与後値及びベースラインからの変化量は、要約統計量を示した。ベースラインからの変化量は、各被験者の投与後の値から投与前の値を差し引いて算出した。ベースラインからの変化量が負の値であった場合は、この値を要約統計量の算出に使用した。

結果の要約：

薬物動態：
Part A（単回漸増投与）：アコラミジスの薬物動態
アコラミジス塩酸塩 50～800 mg を空腹時に単回経口投与したときの血漿中及び尿中 PK パラメータの要約を以下に示す。

空腹時にアコラミジス塩酸塩を単回経口投与したときの血漿中及び尿中アコラミジスの薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	50 mg AG10 (fasted)	150 mg AG10 (fasted)	300 mg AG10 (fasted)	800 mg AG10 (fasted)
AUC_{0-24} (ng*hr/mL)	17200 (6.87) [n=6]	27200 (17.1) [n=6]	29200 (9.23) [n=6]	51400 (16.2) [n=6]
AUC_{0-t} (ng*hr/mL)	27800 (12.6) [n=6]	48400 (25.6) [n=6]	54600 (36.5) [n=6]	120000 (19.5) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	28400 (12.7) [n=6]	49200 (25.8) [n=6]	50700 (31.2) [n=5]	121000 (20.5) [n=6]
C_{max} (ng/mL)	2100 (10.5) [n=6]	3320 (42.1) [n=6]	4420 (22.2) [n=6]	11000 (33.3) [n=6]
C_{ave} (ng/mL)	717 (6.87) [n=6]	1130 (17.1) [n=6]	1220 (9.23) [n=6]	2140 (16.2) [n=6]
T_{max} (hr)	0.8 (0.5, 2.0) [n=6]	0.8 (0.5, 3.0) [n=6]	0.8 (0.5, 1.1) [n=6]	1.0 (0.5, 1.0) [n=6]
$t_{1/2,d}$ (hr)	3.5 ± 1.1 [n=6]	3.4 ± 3.0 [n=6]	4.9 ± 5.8 [n=6]	2.2 ± 1.1 [n=6]
$t_{1/2,t}$ (hr)	25.2 ± 2.9 [n=6]	27.6 ± 7.8 [n=6]	21.5 ± 5.9 [n=5]	27.5 ± 9.2 [n=6]
CL/F (L/hr)	1.58 ± 0.203 [n=6]	2.79 ± 0.646 [n=6]	5.44 ± 1.40 [n=5]	5.98 ± 1.18 [n=6]
V_z/F (L)	57.2 ± 9.69 [n=6]	106 ± 18.9 [n=6]	161 ± 30.7 [n=5]	226 ± 32.5 [n=6]
Ae (mg)	2.30 ± 0.396 [n=6]	6.54 ± 2.27 [n=6]	18.7 ± 10.9 [n=6]	68.1 ± 26.5 [n=6]
CLr (mL/hr)	91.4 ± 19.9 [n=6]	154 ± 41.7 [n=6]	382 ± 179 [n=6]	697 ± 240 [n=6]
DN_AUC_{0-24} (ng*hr/mL/mg)	387 (6.87) [n=6]	203 (17.1) [n=6]	109 (9.23) [n=6]	72.2 (16.2) [n=6]
DN_C_{max} (ng/mL/mg)	47.3 (10.5) [n=6]	24.8 (42.1) [n=6]	16.5 (22.2) [n=6]	15.5 (33.3) [n=6]

50 mg AG10 (fasted): Administration of a Single Oral Dose of 50 mg AG10 Under Fasted Conditions (SAD Cohort 1)
150 mg AG10 (fasted): Administration of a Single Oral Dose of 150 mg AG10 Under Fasted Conditions (SAD Cohort 2)
300 mg AG10 (fasted): Administration of a Single Oral Dose of 300 mg AG10 Under Fasted Conditions (SAD Cohort 3)
800 mg AG10 (fasted): Administration of a Single Oral Dose of 800 mg AG10 Under Fasted Conditions (SAD Cohort 4)
AUCs, C_{ave}, and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1項AG10-001 CSR Tables 14.2.1.1.2.1 ~ 14.2.1.1.2.4, Tables 14.2.1.1.4.1 ~ 14.2.1.1.4.4

アコラミジス塩酸塩 50～800 mg を空腹時に単回経口投与後、AUC_{0-24}、AUC_{0-t} 及び $AUC_{0-\infty}$の幾何平均値により測定したアコラミジスの総曝露量は、50 mg と 150 mg の間で約 1.6～1.7 倍、150 mg と 300 mg の間で約 1.0～1.1 倍、300 mg と 800 mg の間で約 1.8～2.4 倍増加した。C_{ave} の平均値も同様な増加を示した。C_{max} の幾何平均値は、50 mg と 150 mg の間で 1.6 倍、150 mg と 300 mg の間で 1.3 倍、300 mg と 800 mg の間で 2.5 倍増加した。用量補正した血漿中アコラミジスの AUC_{0-24} 及び C_{max} 値は、300 mg と 800 mg の用量間での DN_C_{max}（比 0.94）を除き、異なる用量間で同等ではなかった（比 0.5～0.7）。

血漿中アコラミジスの t_{max} の中央値は、各用量で 0.8～1.0 時間であった。アコラミジス塩酸塩単回経口投与後のクリアランスの算術平均は、50、150、300 及び 800 mg の用量でそれぞれ 1.6、2.8、5.4 及び 6.0 L/hr であった。$t_{1/2,\ d}$ はアコラミジス塩酸塩のすべての用量間で同程度であり、約 2.2～4.9 時間の範囲であった。$t_{1/2,\ t}$ はすべての用量で同程度であり、21.5～27.6 時間の範囲であった。

アコラミジス塩酸塩を単回経口投与したとき、投与後 72 時間に尿中に排泄されたアコラミジス未変化体の平均累積量は約 2.3～68.1 mg の範囲であり、アコラミジス塩酸塩の用量増加に伴って増加した。アコラミジス未変化体の平均累積排泄量は、すべての用量で投与した用量の約 10%未満と比較的低く、最大で用量の 9.6%であった。

空腹時にアコラミジス塩酸塩を 50～800 mg の用量（コホート 1～4）で単回投与したときの、血漿中アコラミジスの PK パラメータの用量比例性解析の結果を以下に示す。

空腹時にアコラミジス塩酸塩を単回漸増経口投与したときの血漿中アコラミジスの用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	0.5042	0.0528	(0.3946, 0.6137)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * Dose b which was equivalent to ln (Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Dose proportionality is rejected for $AUC_{0-\infty}$ and C_{max} due to non-linear relationship (p-value of cubic term = 0.0269 for

$AUC_{0-\infty}$ and p-value of quadratic term = 0.0346 for C_{max}).
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.1.2.7

また、空腹時にアコラミジス塩酸塩を 50～800 mg の用量で単回投与したとき、血漿中アコラミジスの AUC_{0-t} は用量との統計学的な線形関係が認められた。$AUC_{0-\infty}$及び C_{max} では非線形関係が認められたため、用量比例性は棄却された。AUC_{0-t} では、傾きの 95%信頼区間に 1 の値は含まれなかった。したがって、アコラミジス塩酸塩 50～800 mg を単回経口投与したときの血漿中アコラミジスの PK パラメータのいずれでも、用量比例性を結論付けることはできなかった。

Part A（単回漸増投与）：アコラミジス-AG の薬物動態

アコラミジス塩酸塩 50～800 mg を空腹時に単回経口投与したときの血漿中及び尿中アコラミジス-AG の PK パラメータの要約を以下に示す。

空腹時にアコラミジス塩酸塩を単回経口投与したときの血漿中及び尿中アコラミジス-AG の薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	50 mg AG10 (fasted)	150 mg AG10 (fasted)	300 mg AG10 (fasted)	800 mg AG10 (fasted)
AUC_{0-24} (ng*hr/mL)	1070 (12.8) [n=6]	2740 (37.0) [n=6]	5760 (35.1) [n=6]	15600 (17.4) [n=6]
AUC_{0-t} (ng*hr/mL)	1220 (13.3) [n=6]	3140 (38.9) [n=6]	6480 (37.0) [n=6]	17800 (14.1) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	1260 (12.9) [n=6]	3230 (38.5) [n=6]	6350 (41.1) [n=5]	17900 (14.0) [n=6]
C_{max} (ng/mL)	447 (41.3) [n=6]	1480 (59.1) [n=6]	2930 (28.0) [n=6]	7540 (26.6) [n=6]
C_{ave} (ng/mL)	44.5 (12.8) [n=6]	114 (37.0) [n=6]	240 (35.1) [n=6]	648 (17.4) [n=6]
T_{max} (hr)	1.0 (0.5, 3.0) [n=6]	1.0 (0.5, 3.0) [n=6]	1.1 (1.0, 1.1) [n=6]	1.0 (1.0, 1.0) [n=6]
$t_{1/2,d}$ (hr)	1.9 ± 1.1 [n=6]	2.3 ± 1.2 [n=6]	1.8 ± 1.3 [n=6]	1.3 ± 1.1 [n=6]
$t_{1/2,t}$ (hr)	16.9 ± 3.0 [n=6]	28.2 ± 15.8 [n=6]	18.8 ± 9.7 [n=5]	24.2 ± 7.3 [n=6]
Ae (mg)	21.3 ± 6.56 [n=6]	56.4 ± 11.3 [n=6]	93.9 ± 44.9 [n=6]	271 ± 80.9 [n=6]
CLr (mL/hr)	16900 ± 3630 [n=6]	18600 ± 5240 [n=6]	14200 ± 3890 [n=6]	16000 ± 5550 [n=6]
DN_AUC_{0-24} (ng*hr/mL/mg)	24.0 (12.8) [n=6]	20.5 (37.0) [n=6]	21.6 (35.1) [n=6]	21.8 (17.4) [n=6]
DN_C_{max} (ng/mL/mg)	10.1 (41.3) [n=6]	11.1 (59.1) [n=6]	11.0 (28.0) [n=6]	10.6 (26.6) [n=6]

50 mg AG10 (fasted): Administration of a Single Oral Dose of 50 mg AG10 Under Fasted Conditions (SAD Cohort 1)
150 mg AG10 (fasted): Administration of a Single Oral Dose of 150 mg AG10 Under Fasted Conditions (SAD Cohort 2)
300 mg AG10 (fasted): Administration of a Single Oral Dose of 300 mg AG10 Under Fasted Conditions (SAD Cohort 3)
800 mg AG10 (fasted): Administration of a Single Oral Dose of 800 mg AG10 Under Fasted Conditions (SAD Cohort 4)
AUCs, C_{ave}, and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1項AG10-001 CSR Tables 14.2.1.2.2.1 ~ 14.2.1.2.2.4, Tables 14.2.1.2.4.1 ~14.2.1.2.4.4

アコラミジス塩酸塩 50～800 mg を空腹時に単回経口投与したとき、AUC_{0-t}、AUC_{0-24} 及び $AUC_{0-\infty}$ の幾何平均値により測定したアコラミジス-AG の総曝露量は、50 mg と 150 mg の間で約 2.6 倍、150 mg と 300 mg の間で約 2.0～2.1 倍、300 mg と 800 mg の間で約 2.7～2.8 倍増加した。C_{ave} 平均値も同様に増加した。C_{max} の幾何平均値は、50 mg と 150 mg の間で約 3.3 倍、150 mg と 300 mg の間で約 2 倍、300 mg と 800 mg の間で約 2.6 倍増加した。用量補正した血漿中アコラミジス-AG の AUC_{0-24} 及び C_{max} は、すべての用量レベルで同程度であった。

血漿中アコラミジス-AG の t_{max} の中央値は、すべての用量レベルで 1 時間であった。$t_{1/2,d}$ は、50、150、300 及び 800 mg の用量でそれぞれ 1.9、2.3、1.8 及び 1.3 時間であった。$t_{1/2,t}$ は、50、150、300 及び 800 mg の用量でそれぞれ 16.9、28.2、18.8 及び 24.2 時間であった。これらのパラメータの被験者間変動は概して大きかった。

アコラミジス塩酸塩を単回経口投与したとき、投与後 72 時間に尿中に排泄されたアコラミジス-AG の平均累積量は約 21.3～271 mg の範囲であり、アコラミジス塩酸塩の用量増加に伴って増加

した。アコラミジス塩酸塩 50～800 mg の単回投与後のアコラミジス-AG の平均累積排泄量は、投与したアコラミジス塩酸塩の約 22.0%～29.8%に相当した。CLr の算術平均値は約 14.2～18.6 L/hr であった。

また、空腹時にアコラミジス塩酸塩を単回経口投与したとき（コホート 1～4）の血漿中アコラミジス-AG の PK パラメータの用量比例性解析の結果を以下に示す。

空腹時にアコラミジス塩酸塩を単回漸増経口投与したときの血漿中アコラミジス-AG の用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	0.9701	0.0542	(0.8577, 1.0826)
$AUC_{0-\infty}$ (ng*hr/mL)	0.9558	0.0551	(0.8411, 1.0705)
C_{max} (ng/mL)	1.0178	0.0750	(0.8623, 1.1732)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * Dose b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.2.2.7

空腹時にアコラミジス塩酸塩を単回経口投与したとき、血漿中アコラミジス-AG の PK パラメータのすべてで、用量との統計学的線形関係が確立された。すべての PK パラメータで、傾きの 95%信頼区間には 1 が含まれた。したがって、アコラミジス塩酸塩を 50～800 mg の範囲で単回経口投与したときの血漿中アコラミジス-AG の C_{max}、AUC_{0-t} 及び $AUC_{0-\infty}$は用量比例性を示すと結論付けられた。

Part A（単回漸増投与）：食事の影響（アコラミジス）

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中及び尿中アコラミジスの PK パラメータを以下に示す。

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中及び尿中アコラミジスの薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	300 mg AG (fasted)	300 mg AG (fed)
AUC_{0-24} (ng*hr/mL)	29200 (9.23) [n=6]	32500 (11.8) [n=6]
AUC_{0-t} (ng*hr/mL)	54600 (36.5) [n=6]	66100 (30.1) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	50700 (31.2) [n=5]	62800 (28.8) [n=5]
C_{max} (ng/mL)	4420 (22.2) [n=6]	2980 (20.0) [n=6]
C_{ave} (ng/mL)	1220 (9.23) [n=6]	1350 (11.8) [n=6]
T_{max} (hr)	0.8 (0.5, 1.1) [n=6]	1.5 (1.0, 4.0) [n=6]
$t_{1/2,d}$ (hr)	4.9 ± 5.8 [n=6]	5.4 ± 1.6 [n=6]
$t_{1/2,t}$ (hr)	21.5 ± 5.9 [n=5]	21.6 ± 6.4 [n=5]
CL/F (L/hr)	5.44 ± 1.40 [n=5]	4.37 ± 1.03 [n=5]
V_z/F (L)	161 ± 30.7 [n=5]	129 ± 8.73 [n=5]
Ae (mg)	18.7 ± 10.9 [n=6]	18.0 ± 5.88 [n=6]
CLr (mL/hr)	382 ± 179 [n=6]	326 ± 77.7 [n=6]
DN_AUC_{0-24} (ng*hr/mL/mg)	109 (9.23) [n=6]	122 (11.8) [n=6]
DN_C_{max} (ng/mL/mg)	16.5 (22.2) [n=6]	11.2 (20.0) [n=6]

300 mg AG10 (fasted): Administration of a Single Oral Dose of 300 mg AG10 Under Fasted Conditions (SAD Cohort 3)
300 mg AG10 (fed): Administration of a Single Oral Dose of 300 mg AG10 Under Fed Conditions (SAD Cohort 3)
AUCs, C_{ave}, and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.1.2.3, 14.2.1.1.2.8, 14.2.1.1.4.3, 14.2.1.1.4.5

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したとき、AUC_{0-t}、AUC_{0-24} 及び $AUC_{0-\infty}$の幾何平均値により測定したアコラミジスの総曝露量は、空腹時投与と比べて食後投与で

高かった。また、C_{ave} は食後投与の方が高かったが、C_{max} は食後投与の方が空腹時投与よりも低かった。アコラミジスの t_{max} は、空腹時投与と比較して食後投与で遅延した（t_{max} の中央値はそれぞれ 0.8 時間及び 1.5 時間）。食後投与及び空腹時投与のいずれでも、$t_{1/2,\ d}$ は約 5 時間、$t_{1/2,\ t}$ は約 21.5 時間であった。

アコラミジス塩酸塩 300 mg を単回経口投与したとき、投与後 72 時間までに尿中に排泄されたアコラミジス未変化体の平均累積量は、空腹時と食後で同程度であった。CLr の算術平均値は、空腹時に約 0.382 L/hr、食後で約 0.326 L/hr であった。

また、食後及び空腹時にアコラミジス塩酸塩 300 mg を単回投与したときの血漿中アコラミジスの PK パラメータの統計学的比較を以下に示す。

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中アコラミジスの薬物動態パラメータの統計学的比較（PK 評価可能集団）

	300 mg AG10 - Fed (Test)		300 mg AG10 -Fasted (Reference)				
Parameter	**Geometric LSMs**	**n**	**Geometric LSMs**	**n**	**GMR (%)**	**90% Confidence Interval**	**Intra-subject CV%**
$AUC_{0\text{-}t}$ (ng*hr/mL)	66130	6	54580	6	121.16	109.71 - 133.80	8.55
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	62800	5	50710	5	123.85	111.69 - 137.32	7.67
C_{max} (ng/mL)	2984	6	4417	6	67.55	57.20 - 79.79	14.38

300 mg (Fed): Administration of a single oral dose of 300 mg AG10 within 30 minutes of a high-fat breakfast in Period 2
300 mg (Fasted): Administration of a single oral dose of 300 mg AG10 following an 8 hour fast in Period 1 Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from the ANOVA.
Geometric Mean Ratio = 100*(test/reference)
Intra-subject CV (CV%) = 100 x (square root (exp[MSE]-1)), where MSE = Residual variance from ANOVA.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.1.2.9

LSM の GMR（%）に基づくと、血漿中アコラミジスの AUC 値は空腹時投与と比較して食後投与で約 21%～24%高く、C_{max} の GMR（%）は空腹時投与と比較して食後投与で約 32%低かった。

Part A（単回漸増投与）：食事の影響（アコラミジス-AG）

アコラミジス塩酸塩 300 mg を空腹時及び食後に単回経口投与したときの血漿中及び尿中アコラミジス-AG の PK パラメータの要約を以下に示す。

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中及び尿中アコラミジス-AG の薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	**300 mg AG10 (fasted)**	**300 mg AG10 (fed)**
$AUC_{0\text{-}24}$ (ng*hr/mL)	5760 (35.1) [n=6]	5520 (37.9) [n=6]
$AUC_{0\text{-}t}$ (ng*hr/mL)	6480 (37.0) [n=6]	6350 (39.3) [n=6]
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	6350 (41.1) [n=5]	5310 (27.8) [n=4]
C_{max} (ng/mL)	2930 (28.0) [n=6]	1460 (53.4) [n=6]
C_{ave} (ng/mL)	240 (35.1) [n=6]	230 (37.9) [n=6]
T_{max} (hr)	1.1 (1.0, 1.1) [n=6]	2.5 (1.0, 4.0) [n=6]
$t_{1/2,d}$ (hr)	1.8 ± 1.3 [n=6]	2.1 ± 1.3 [n=6]
$t_{1/2,t}$ (hr)	18.8 ± 9.7 [n=5]	14.9 ± 2.1 [n=4]
Ae (mg)	93.9 ± 44.9 [n=6]	99.8 ± 28.4 [n=6]
CLr (mL/hr)	14200 ± 3890 [n=6]	15700 ± 1320 [n=6]
DN_$AUC_{0\text{-}24}$ (ng*hr/mL/mg)	21.6 (35.1) [n=6]	20.7 (37.9) [n=6]
DN_C_{max} (ng/mL/mg)	11.0 (28.0) [n=6]	5.46 (53.4) [n=6]

300 mg AG10 (fasted): Administration of a Single Oral Dose of 300 mg AG10 Under Fasted Conditions (SAD Cohort 3)
300 mg AG10 (fed): Administration of a Single Oral Dose of 300 mg AG10 Under Fed Conditions (SAD Cohort 3)
AUCs, C_{ave}, and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.2.2.3, 14.2.1.2.2.8, 14.2.1.2.4.3, 14.2.1.2.4.5

アコラミジス塩酸塩 300 mg を空腹時及び食後に単回経口投与したとき、AUC_{0-t} 及び AUC_{0-24} の幾何平均値により測定したアコラミジス-AG の総曝露量は、食後及び空腹時におおむね同程度であったが、$AUC_{0-\infty}$は食後投与下でわずかに低かった。また、C_{ave} は食後投与と空腹時投与で比較的同程度であったが、C_{max} の幾何平均値は食後投与の方が空腹時投与よりも約 50%低かった。
アコラミジス-AG の t_{max} は、空腹時投与と比較して食後投与で遅延した（中央値は食後で 2.5 時間、空腹時で 1.1 時間）。$t_{1/2, d}$ は食後及び空腹時のいずれでも約 2 時間であり、$t_{1/2, t}$ も両条件下で比較的同程度であった（食後で約 14.9 時間、空腹時で約 18.8 時間）。
アコラミジス塩酸塩 300 mg を単回経口投与したとき、投与後 72 時間までに尿中に排泄されたアコラミジス-AG の平均累積量は、空腹時投与と比較して食後投与で約 6 mg 高かった。また、CLr の算術平均値は、空腹時で 14.2 L/hr、食後で 15.7 L/hr であった。
また、空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中アコラミジス-AG の PK パラメータの統計学的比較を以下に示す。

空腹時及び食後にアコラミジス塩酸塩 300 mg を単回経口投与したときの血漿中アコラミジス-AG の薬物動態パラメータの統計学的比較（PK 評価可能集団）

	300 mg AG10 - Fed (Test)		300 mg AG10 -Fasted (Reference)				
Parameter	**Geometric LSMs**	**n**	**Geometric LSMs**	**n**	**GMR (%)**	**90% Confidence Interval**	**Intra-subject CV%**
AUC_{0-t} (ng*hr/mL)	6348	6	6485	6	97.88	91.69 - 104.50	5.62
$AUC_{0-\infty}$ (ng*hr/mL)	6174	4	6346	5	97.28	87.05 - 108.72	6.70
C_{max} (ng/mL)	1457	6	2928	6	49.76	37.76 - 65.57	24.06

300 mg (Fed): Administration of a single oral dose of 300 mg AG10 within 30 minutes of a high-fat breakfast in Period 2
300 mg (Fasted): Administration of a single oral dose of 300 mg AG10 following an 8 hour fast in Period 1
Parameters were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from the ANOVA.
Geometric Mean Ratio = 100*(test/reference)
Intra-subject CV (CV%) = 100 x (square root (exp[MSE]-1)), where MSE = Residual variance from ANOVA.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.2.2.9

LSM の GMR（%）に基づくと、血漿中アコラミジス-AG の AUC は食後投与と空腹時投与で同程度であったが、C_{max} の GMR（%）は食後投与の方が空腹時投与よりも約 50%低かった。

Part B（反復漸増投与）：アコラミジスの薬物動態

アコラミジス塩酸塩を空腹時に反復漸増投与したときの Day 1（単回経口投与）及び Day 12 の血漿中アコラミジスの PK パラメータの要約をそれぞれ以下に示す。

空腹時にアコラミジス塩酸塩を単回経口投与したとき（Part B の Day 1）の血漿中アコラミジスの薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	**100 mg AG10 Fasted**	**300 mg AG10 Fasted**	**800 mg AG10 Fasted**
AUC_{0-12} (ng*hr/mL)	13600 (12.4) [n=6]	19100 (17.6) [n=6]	35200 (17.2) [n=6]
C_{ave} (ng/mL)	1130 (12.4) [n=6]	1590 (17.6) [n=6]	2930 (17.2) [n=6]
C_{max} (ng/mL)	2530 (29.9) [n=6]	4180 (45.6) [n=6]	9290 (53.3) [n=6]
T_{max} (hr)	0.8 (0.5, 2.0) [n=6]	0.8 (0.5, 1.0) [n=6]	1.1 (0.5, 1.1) [n=6]

100 mg AG10 Fasted: Administration of the First Oral Dose of 100 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 1)
300 mg AG10 Fasted: Administration of the First Oral Dose of 300 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 2)
800 mg AG10 Fasted: Administration of the First Oral Dose of 800 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 3)
AUC_{0-12}, C_{ave} and C_{max} are presented as geometric mean and geometric CV%.
T_{max} are presented as Median (Minimum, Maximum).
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.1.6.1 ~ 14.2.1.1.6.3

空腹時にアコラミジス塩酸塩を反復経口投与したとき（Day 12）の血漿中及び尿中アコラミジスの薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	100 mg AG10 (fasted)	300 mg AG10 (fasted)	800 mg AG10 (fasted)
AUC_{tau} (ng*hr/mL)	20500 (8.80) [n=6]	28600 (9.64) [n=6]	46400 (21.2) [n=6]
AUC_{0-t} (ng*hr/mL)	84600 (32.3) [n=6]	125000 (27.9) [n=6]	244000 (36.4) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	85300 (32.0) [n=6]	126000 (28.4) [n=6]	246000 (36.6) [n=6]
C_{max} (ng/mL)	3540 (18.8) [n=6]	6870 (56.8) [n=6]	12400 (54.3) [n=6]
C_{min} (ng/mL)	1140 (13.0) [n=6]	1720 (12.4) [n=6]	2450 (23.7) [n=6]
C_{ave} (ng/mL)	1710 (8.80) [n=6]	2390 (9.64) [n=6]	3860 (21.2) [n=6]
$R_{A,Cmax}$	1.40 (31.8) [n=6]	1.64 (52.9) [n=6]	1.34 (51.4) [n=6]
$R_{A,Cave}$	1.52 (6.12) [n=6]	1.50 (12.1) [n=6]	1.32 (15.8) [n=6]
T_{max} (hr)	0.5 (0.5, 1.0) [n=6]	0.5 (0.5, 1.0) [n=6]	1.0 (0.5, 1.0) [n=6]
$t_{1/2,d}$ (hr)	10.5 ± 4.8 [n=6]	17.5 ± 4.0 [n=6]	7.0 ± 3.7 [n=6]
$t_{1/2,t}$ (hr)	23.5 ± 2.6 [n=6]	29.8 ± 5.7 [n=6]	28.8 ± 5.8 [n=6]
CL/F (L/hr)	4.35 ± 0.382 [n=6]	9.36 ± 0.936 [n=6]	15.6 ± 3.16 [n=6]
V_z/F (L)	147 ± 20.9 [n=6]	398 ± 60.2 [n=6]	654 ± 182 [n=6]
Ae (mg)	8.75 ± 5.06 [n=6]	31.8 ± 14.2 [n=6]	139 ± 67.8 [n=6]
CLr (mL/hr)	239 ± 119 [n=6]	629 ± 272 [n=6]	1750 ± 608 [n=6]
DN_AUC_{tau} (ng*hr/mL/mg)	231 (8.80) [n=6]	107 (9.64) [n=6]	65.1 (21.2) [n=6]
DN_C_{max} (ng/mL/mg)	39.8 (18.8) [n=6]	25.7 (56.8) [n=6]	17.5 (54.3) [n=6]

100 mg AG10 (fasted): Administration of multiple oral Q12h doses of 100 mg AG10
300 mg AG10 (fasted): Administration of multiple oral Q12h doses of 300 mg AG10
800 mg AG10 (fasted): Administration of multiple oral Q12h doses of 800 mg AG10
AUCs, C_{ave}, C_{min} and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.1.6.5 ~ 14.2.1.1.6.7, Tables 14.2.1.1.8.1 ~ 14.2.1.1.8.3

アコラミジス塩酸塩 100～800 mg を空腹時に単回経口投与したとき（Day 1）、AUC、C_{ave} 及び C_{max} の幾何平均値によって測定した血漿中アコラミジスのピーク及び総曝露量は、100 mg と 300 mg の用量間でいずれも用量比を下回って増加した。血漿中アコラミジスの AUC_{0-12}、C_{ave} 及び C_{max} の幾何平均値は、300 mg と 800 mg の用量間でいずれも用量比を下回って増加した。Day 1 の血漿中アコラミジスの t_{max} の中央値は、100 及び 300 mg では 0.8 時間、800 mg では 1.1 時間であったが、最小値及び最大値はすべての用量で同程度であった。

アコラミジス塩酸塩 100～800 mg を空腹時に 1 日 2 回（q12h）12 日間反復経口投与したとき（Day 12）、AUC、C_{max}、C_{min} 及び C_{ave} の幾何平均値によって測定した血漿中アコラミジスのピーク及び総曝露量は、100 mg と 300 mg の用量間でいずれも用量比を下回って増加した。血漿中アコラミジスの AUC、C_{max}、C_{min} 及び C_{ave} の幾何平均値は、300 mg と 800 mg の用量間でいずれも用量比を下回って増加した。Day 12 の血漿中アコラミジスの t_{max} の中央値は、100 及び 300 mg で 0.5 時間、800 mg で 1.0 時間であったが、最小値及び最大値はすべての用量で同程度であった。

アコラミジス塩酸塩を反復経口投与したとき、投与後 24 時間に尿中に排泄された未変化体アコラミジスの平均累積量は約 8.7～139 mg の範囲であり、アコラミジス塩酸塩の用量増加に伴って増加した。

血漿中アコラミジスの C_{trough} 濃度の定常状態の解析結果を以下に示す。

空腹時にアコラミジス塩酸塩を反復経口投与したときの Helmert 対比を用いた血漿中アコラミジスの定常状態の解析（PK 評価可能集団）

Treatment	Days	Geometric LSM	p-value
Multiple oral doses of 100 mg AG10	Day 10	1444.2605	0.9370
	Day 11	1392.0749	0.5339
	Day 12	1359.6097	.
Multiple oral doses of 300 mg AG10	Day 10	1814.6924	0.3806
	Day 11	1836.9194	0.0344
	Day 12	1945.0272	.

Multiple oral doses of 800 mg AG10	Day 10	2765.4787	0.3858
	Day 11	2613.8011	0.0864
	Day 12	2599.7824	.

Concentrations were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) were obtained by taking exponential of the LSMs from the ANOVA.
P-value corresponds to the Helmert contrast, i.e., the comparison of that day versus the average of the remaining days.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.1.6.4

定常状態での血漿中アコラミジスの C_{trough} 濃度を用量別に解析した結果、100 及び 800 mg では Day 10 及び 11 の血漿中アコラミジスの C_{trough} 値は、他の日の値と統計学的な差は認められなかった。300 mg では、Day 10 の C_{trough} 値に他の日の値と統計学的な差は認められなかったが、Day 11 の C_{trough} 値は他の日の値と統計学的な差が認められた。300 mg 用量の Day 12 の C_{trough} を除き、Day 10～12 の血漿中アコラミジス濃度はおおむね一定に推移し、この傾向は早くて Day 4 以降からみられた。
アコラミジス塩酸塩を反復経口投与したときの血漿中アコラミジスの PK パラメータの用量比例性解析の結果を以下に示す。

空腹時にアコラミジス塩酸塩を反復経口投与したときの Day 12 の血漿中アコラミジスの用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	0.5054	0.0879	(0.3190, 0.6917)
$AUC_{0-\infty}$ (ng*hr/mL)	0.5053	0.0881	(0.3185, 0.6922)
C_{max} (ng/mL)	0.6040	0.1174	(0.3551, 0.8528)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * Dose b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.1.6.10

アコラミジス塩酸塩を 12 日間反復経口投与したとき、すべての血漿中アコラミジス PK パラメータで統計学的な用量線形性が確立された。しかし、すべての PK パラメータで、傾きの 95%信頼区間に 1 の値は含まれなかった。したがって、アコラミジス塩酸塩を 100～800 mg の用量範囲で反復経口投与したときの血漿中アコラミジスの全体及びピーク曝露量パラメータ AUC_{0-t}、$AUC_{0-\infty}$ 及び C_{max} の用量比例性を結論付けることはできなかった。

Part B（反復漸増投与）：アコラミジス-AG の薬物動態

アコラミジス塩酸塩を反復漸増投与したときの Day 1 及び Day 12 の血漿中アコラミジス-AG の PK パラメータの要約をそれぞれ以下に示す。

空腹時にアコラミジス塩酸塩を単回経口投与したとき（Part B の Day 1）の血漿中アコラミジス-AG の薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	100 mg AG10 Fasted	300 mg AG10 Fasted	800 mg AG10 Fasted
AUC_{0-12} (ng*hr/mL)	1570 (45.5) [n=6]	5640 (39.9) [n=6]	14900 (38.3) [n=6]
C_{ave} (ng/mL)	131 (45.5) [n=6]	470 (39.9) [n=6]	1240 (38.3) [n=6]
C_{max} (ng/mL)	936 (95.6) [n=6]	2890 (64.4) [n=6]	5990 (45.0) [n=6]
T_{max} (hr)	1.0 (0.5, 3.0) [n=6]	1.0 (0.5, 1.0) [n=6]	1.5 (1.0, 3.0) [n=6]

100 mg AG10 Fasted: Administration of the First Oral Dose of 100 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 1)
300 mg AG10 Fasted: Administration of the First Oral Dose of 300 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 2)
800 mg AG10 Fasted: Administration of the First Oral Dose of 800 mg AG10 Under Fasted Conditions on Day 1 (MAD Cohort 3)
AUC_{0-12}, C_{ave} and C_{max} are presented as geometric mean and geometric CV%.
T_{max} are presented as Median (Minimum, Maximum).
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.2.6.1 ~ 14.2.1.2.6.3

空腹時にアコラミジス塩酸塩を反復経口投与したとき（Day 12）の血漿中及び尿中アコラミジス-AG の薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	100 mg AG10 (fasted)	300 mg AG10 (fasted)	800 mg AG10 (fasted)
AUC_{tau} (ng*hr/mL)	2410 (26.7) [n=6]	10000 (33.7) [n=6]	30100 (25.7) [n=6]
AUC_{0-t} (ng*hr/mL)	4660 (9.72) [n=6]	17000 (23.7) [n=6]	63400 (29.9) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	4710 (9.68) [n=6]	17100 (23.6) [n=6]	63400 (29.9) [n=6]
C_{max} (ng/mL)	1160 (46.9) [n=6]	3800 (76.0) [n=6]	9510 (28.5) [n=6]
C_{min} (ng/mL)	45.2 (13.7) [n=6]	180 (36.9) [n=6]	736 (34.8) [n=6]
C_{ave} (ng/mL)	201 (26.7) [n=6]	837 (33.7) [n=6]	2510 (25.7) [n=6]
$R_{A,Cmax}$	1.24 (112) [n=6]	1.32 (50.7) [n=6]	1.59 (47.1) [n=6]
$R_{A,Cave}$	1.53 (34.4) [n=6]	1.78 (24.4) [n=6]	2.02 (16.3) [n=6]
T_{max} (hr)	0.8 (0.5, 1.0) [n=6]	1.0 (0.5, 4.0) [n=6]	1.0 (1.0, 2.0) [n=6]
$t_{1/2,d}$ (hr)	3.4 ± 1.2 [n=6]	4.5 ± 2.0 [n=6]	2.9 ± 0.9 [n=6]
$t_{1/2,t}$ (hr)	21.4 ± 3.9 [n=6]	23.6 ± 5.4 [n=6]	18.4 ± 3.5 [n=6]
Ae (mg)	70.8 ± 29.6 [n=6]	282 ± 86.5 [n=6]	967 ± 123 [n=6]
CLr (mL/hr)	23700 ± 10300 [n=6]	23700 ± 10600 [n=6]	24100 ± 5720 [n=6]
DN_AUC_{tau} (ng*hr/mL/mg)	27.1 (26.7) [n=6]	37.6 (33.7) [n=6]	42.3 (25.7) [n=6]
DN_C_{max} (ng/mL/mg)	13.1 (46.9) [n=6]	14.2 (76.0) [n=6]	13.4 (28.5) [n=6]

100 mg AG10 (fasted): Administration of multiple oral Q12h doses of 100 mg AG10
300 mg AG10 (fasted): Administration of multiple oral Q12h doses of 300 mg AG10
800 mg AG10 (fasted): Administration of multiple oral Q12h doses of 800 mg AG10
AUCs, C_{ave}, C_{min} and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.1.2.6.5 ~ 14.2.1.2.6.7, Tables 14.2.1.2.8.1 ~ 14.2.1.2.8.3

アコラミジス塩酸塩 100～800 mg を空腹時に単回経口投与したとき（Day 1）、C_{max}、C_{ave} 及び AUC_{0-12} の幾何平均値によって測定した血漿中アコラミジス-AG のピーク、平均及び総曝露量は、100 mg と 300 mg の間でいずれも用量比に応じて増加した。300 mg と 800 mg の間でもいずれも用量比に応じて増加した。Day 1 の血漿中アコラミジス-AG の t_{max} の中央値は、100 及び 300 mg で 1.0 時間、800 mg で 1.5 時間であった。

アコラミジス塩酸塩 100～800 mg を空腹時に 1 日 2 回 12 日間反復経口投与したとき（Day 12）、C_{max}、C_{ave}、C_{min} 及び AUC の幾何平均値によって測定した血漿中アコラミジス-AG のピーク、平均、最小値及び総曝露量は、100 mg と 300 mg の間でいずれも用量比を上回って増加した。また、300 mg と 800 mg の間では、C_{max} は用量比に応じて増加したが、その他のパラメータは用量比を上回って増加した。

血漿中アコラミジス-AG の t_{max} の中央値は、Day 12 の 100 mg で 0.8 時間、300 及び 800 mg では 1.0 時間であった。

アコラミジス塩酸塩の反復経口投与後、投与後 24 時間に尿中に排泄されたアコラミジス-AG の平均累積量は 70.8～967 mg の範囲であり、アコラミジス塩酸塩の用量増加に伴って増加した。CLr の算術平均値は 23.7～24.1 L/hr であった。

定常状態での血漿中アコラミジス-AG の C_{trough} 濃度の解析結果を以下に示す。

空腹時にアコラミジス塩酸塩を反復経口投与したときの Helmert 対比を用いた血漿中アコラミジス-AG の定常状態解析（PK 評価可能集団）

Treatment	Days	Geometric LSM	p-value
Multiple oral doses of 100 mg AG10	Day 10	64.5200	0.4521
	Day 11	60.7894	0.9834
	Day 12	60.9202	.
Multiple oral doses of 300 mg AG10	Day 10	193.4858	0.1799
	Day 11	201.3714	0.0813
	Day 12	233.7977	.
Multiple oral doses of 800 mg AG10	Day 10	948.2485	0.3766
	Day 11	873.1222	0.9683
	Day 12	876.7050	.

Concentrations were ln-transformed prior to analysis.
Geometric least-squares means (LSMs) were obtained by taking exponential of the LSMs from the ANOVA.
P-value corresponds to the Helmert contrast, i.e., the comparison of that day versus the average of the remaining days.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.2.6.4

定常状態での血漿中アコラミジス-AG の C_{trough} 濃度を用量別に解析した結果、Day 10 及び Day 11 の血漿中アコラミジス-AG の C_{trough} 値は、他の日の値と統計学的に差がないことが示された。100 及び 300 mg では、Day 10～12 の血漿中アコラミジス-AG のトラフ濃度はおおむね一定に推移し、この傾向は早くて Day 4 以降からみられた。800 mg では、アコラミジス-AG のトラフ濃度は全体的に変動が大きく、Day 10～12 にかけてわずかに減少した。全体として、3 用量すべてで Day 10 までに定常状態に達した。
アコラミジス塩酸塩を反復経口投与としたときの血漿中アコラミジス-AG の PK パラメータの用量比例性解析の結果を以下に示す。

空腹時にアコラミジス塩酸塩を反復経口投与したときの Day 12 の血漿中アコラミジス-AG の用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
$AUC_{0\text{-}t}$ (ng*hr/mL)	1.2535	0.0611	(1.1239, 1.3830)
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	1.2490	0.0611	(1.1195, 1.3784)
C_{max} (ng/mL)	1.0115	0.1331	(0.7293, 1.2938)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * Dose b which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.1 項 AG10-001 CSR Table 14.2.1.2.6.10

アコラミジス塩酸塩を 1 日 2 回（q12h）12 日間反復投与したとき、血漿中アコラミジス-AG のすべての PK パラメータに対して用量との統計学的な線形関係が認められた。しかし、傾きの 95%信頼区間に 1 が含まれたのは C_{max} のみであった。このため、アコラミジス塩酸塩を 100～800 mg の範囲で反復経口投与したときの血漿中アコラミジス-AG の C_{max} は用量比例性があると結論付けられたが、$AUC_{0\text{-}t}$ 及び $AUC_{0\text{-}\infty}$に対しては結論付けられなかった。

<u>薬力学的作用</u>

アコラミジス塩酸塩 50～800 mg を空腹時及び食後に単回経口投与したときのプレアルブミンのベースラインからの変化の要約を以下に示す。

空腹時及び食後にアコラミジス塩酸塩を単回経口投与したときのプレアルブミンのベースライン値及びベースラインからの変化の要約（PD 評価可能集団）

Treatment	Baseline (mg/dL)	Postdose (mg/dL)	Change from Baseline (mg/dL)
50 mg AG10 (fasted)	27.7 (4.58) [n=6]	26.9 (3.76) [n=6]	-0.783 (2.74) [n=6]
150 mg AG10 (fasted)	26.0 (4.17) [n=6]	29.1 (4.04) [n=6]	3.10 (1.34) [n=6]
300 mg AG10 (fasted)	22.0 (3.57) [n=6]	23.9 (2.85) [n=6]	1.87 (0.814) [n=6]
300 mg AG10 (fed)	21.2 (2.31) [n=6]	24.6 (1.98) [n=6]	3.33 (1.42) [n=6]
800 mg AG10 (fasted)	24.7 (4.11) [n=6]	27.3 (3.83) [n=6]	2.58 (0.882) [n=6]
Placebo (pooled fasted)	24.3 (6.27) [n=8]	24.8 (6.38) [n=8]	0.500 (1.82) [n=8]
Placebo (fed)	25.3 (4.38) [n=2]	26.9 (2.97) [n=2]	1.60 (1.41) [n=2]

Mean (SD)
50 mg AG10 (fasted): Administration of a single oral dose of 50 mg AG10 following an 8 hour fast
150 mg AG10 (fasted): Administration of a single oral dose of 150 mg AG10 following an 8 hour fast
300 mg AG10 (fasted): Administration of a single oral dose of 300 mg AG10 following an 8 hour fast
300 mg AG10 (fed): Administration of a single oral dose of 300 mg AG10 within 30 minutes of a high-fat breakfast
800 mg AG10 (fasted): Administration of a single oral dose of 800 mg AG10 following an 8 hour fast
Placebo (pooled fasted): Administration of placebo following an 8 hour fast
Placebo (fed): Administration of placebo following a high-fat breakfast
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.2.1.1.1 ~14.2.2.1.1.6

アコラミジス塩酸塩 50～800 mg を空腹時に単回経口投与したときのプレアルブミンのベースラインからの変化量の平均値は-0.783～3.10 mg/dL の範囲であった。食後にアコラミジス塩酸塩 300 mg を単回経口投与したときのプレアルブミンのベースラインからの変化量の平均値は 3.33 mg/dL であった。
また、アコラミジス塩酸塩 100～800 mg を空腹時に反復経口投与したときのプレアルブミンのベースラインから変化の要約を以下に示す。

空腹時にアコラミジス塩酸塩を反復経口投与したときのプレアルブミンのベースライン値及びベースラインからの変化の要約（PD 評価可能集団）

Treatment	Baseline (mg/dL)	Postdose (mg/dL)	Change from Baseline (mg/dL)
100 mg AG10 (fasted)	25.4 (4.22) [n=6]	28.2 (3.95) [n=6]	2.80 (1.11) [n=6]
300 mg AG10 (fasted)	22.2 (4.89) [n=6]	24.0 (3.97) [n=6]	1.73 (1.79) [n=6]
800 mg AG10 (fasted)	27.1 (4.26) [n=6]	29.2 (4.01) [n=6]	2.12 (1.83) [n=6]
Placebo (pooled fasted)	24.7 (3.24) [n=6]	23.7 (3.33) [n=6]	-1.03 (1.07) [n=6]

Mean (SD)
100 mg AG10 (fasted): Administration of multiple oral doses of 100 mg AG10 following an 8 hour fast
300 mg AG10 (fasted): Administration of multiple oral doses of 300 mg AG10 following an 8 hour fast
800 mg AG10 (fasted): Administration of multiple oral doses of 800 mg AG10 following an 8 hour fast
Placebo (pooled fasted): Administration of placebo following an 8 hour fast
Source: 5.3.3.1.1 項 AG10-001 CSR Tables 14.2.2.1.2.1 ~ 14.2.2.1.2.4

アコラミジス塩酸塩 100～800 mg を空腹時に反復経口投与したときのプレアルブミンのベースラインからの変化量の平均値は 1.73～2.80 mg/dL の範囲であった。

安全性：

本試験の Part A 及び Part B のいずれでも、死亡、重篤な有害事象又は投与中止に至った有害事象は認められなかった。
Part A の各用量レベルで 2 名以上に認められた PT 別の有害事象はなかった。治験薬との関連性が否定できない有害事象はアコラミジス群の 5 名に 8 件（このうち 1 名は中等度の尿路感染）、プラセボ群の 2 名に 3 件（このうち 1 名は軽度の好中球数減少）発現した。また、プラセボ群の 1 名で軽度のアラニンアミノトランスフェラーゼ増加、アスパラギン酸アミノトランスフェラーゼ増加、γ-グルタミルトランスフェラーゼ増加及び血中乳酸脱水素酵素増加も認められたが、いずれも治験薬との関連性は否定された。用量別又は空腹時／食後投与別で有害事象に特定の傾向は認められなかった。
Part B で 2 名以上に認められた治験薬との関連性が否定できない PT 別の有害事象はなかった。治験薬との関連性が否定できない有害事象は、アコラミジス群の 3 名に 5 件、プラセボ群の 1 名に 1 件発現した。アコラミジス群とプラセボ群との間で有害事象を発現した被験者数に顕著な差はなく、用量漸増に関連する傾向も認められなかった。
本試験全体の安全性に関して、Part A 及び B で、その他の有害事象、バイタルサイン、心電図、臨床検査又は身体所見に顕著な所見は認められなかった。

結論：

安全性

アコラミジス塩酸塩を 800 mg までの用量で単回及び反復経口投与したときの忍容性は良好であり、臨床的に懸念される安全性の問題は認められなかった。

薬物動態

- アコラミジス塩酸塩 50～800 mg の用量範囲で単回漸増経口投与及び 100～800 mg の用量範囲で反復漸増経口投与したときのアコラミジス及びその代謝物アコラミジス-AG の血漿中及び尿中 PK の特性はおおむね明らかとなった。
- 空腹時にアコラミジス塩酸塩を単回経口投与したとき、血漿中アコラミジスの曝露量パラメータ（AUC_{0-t}、$AUC_{0-\infty}$及び C_{max}）は用量比を下回って増加した。
- 空腹時にアコラミジス塩酸塩を単回経口投与したとき、血漿中アコラミジス-AG の曝露量パラメータ（AUC_{0-t}、$AUC_{0-\infty}$及び C_{max}）はおおむね用量比に応じて増加した。
- アコラミジス塩酸塩 300 mg を食後投与したとき、空腹時投与と比較してアコラミジスの平均ピーク濃度（C_{max}）は低くアコラミジス吸収速度（t_{max}）は遅延したが、吸収の全体の程度（AUC_{0-t}、$AUC_{0-\infty}$）は食事の影響を受けなかった。
- Day 10～12 の投与前トラフで実施した Helmert 対比の結果、アコラミジスは反復経口投与後、Day 10 までに定常状態に到達した。
- アコラミジス及びアコラミジス-AG の累積排泄量は、アコラミジス塩酸塩の単回及び反復漸増経口投与により増加した。尿中排泄はアコラミジス及びその代謝物アコラミジス-AG の血漿クリアランスに重要ではないと考えられた。

薬力学的作用

- FPE 及びウェスタンブロットによる PD 測定の結果、アコラミジス塩酸塩 800 mg（12 時間間隔）を投与した全被験者の反復投与後の ex vivo 評価で、それぞれ本質的に完全かつ持続的な標的結合及び TTR の安定化を達成した。
- TTR 安定化として、in vivo ではアコラミジス塩酸塩 100、300、又は 800 mg（12 時間間隔）の反復経口投与後にプレアルブミン濃度が増加した。24 時間間隔の測定では、循環プレアルブミン濃度の平均 8%の増加がみられた。プラセボ群では、プレアルブミン濃度の一貫した増加は認められなかった。プレアルブミンの血中半減期は 2～3 日のため、24 時間間隔の測定では、臨床的に意味のある定常状態でのプレアルブミン値の変化を予測することはできないと考えられる。

報告書作成日：20[redacted]年[redacted]月[redacted]日（Errata 20[redacted]年[redacted]月[redacted]日、20[redacted]年[redacted]月[redacted]日、20[redacted]年[redacted]月[redacted]日）

2.2 有害事象

すべての有害事象及び治験薬との関連性が否定できない有害事象を以下に示す。本試験で重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Part A（単回漸増投与）：Table 14.3.1.1 Part B（反復漸増投与）：Table 14.3.1.4
治験薬との関連性が否定できない有害事象	Part A（単回漸増投与）：Table 14.3.1.3 Part B（反復漸増投与）：Table 14.3.1.6
重篤な有害事象	Table 14.3.2（該当なし）
治験薬の投与中止に至った有害事象	該当なし

2.3 個別被験者の詳細

本試験で死亡又は重篤な有害事象は発現していないため、該当なし。

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting Events
(% of Subjects Dosed, SAD Cohorts 1-4)

		AG10 SAD Cohort					
Adverse Event*	Placebo	50 mg (1, Fasted)	150 mg (2, Fasted)	300 mg (3, Fasted)	300 mg (3, Fed)	800 mg (4, Fasted)	Total
Number of Subjects Dosed	8 (100%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	6 (100%)	24 (100%)
Number of Subjects With TEAEs	2 (25%)	3 (50%)	2 (33%)	0 (0%)	1 (17%)	1 (17%)	7 (29%)
Number of Subjects Without TEAEs	6 (75%)	3 (50%)	4 (67%)	6 (100%)	5 (83%)	5 (83%)	17 (71%)
胃腸障害	1 (13%)	1 (17%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	2 (8%)
腹部不快感	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
口内乾燥	1 (13%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (4%)
一般・全身障害および投与部位の状態	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
血管穿刺部位疼痛	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
感染症および寄生虫症	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (4%)
尿路感染	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (4%)
傷害、中毒および処置合併症	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
靱帯捻挫	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
臨床検査	2 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
アラニンアミノトランスフェラーゼ増加	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
アスパラギン酸アミノトランスフェラーゼ増加	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
血中乳酸脱水素酵素増加	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
γ－グルタミルトランスフェラーゼ増加	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
好中球数減少	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
神経系障害	0 (0%)	1 (17%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)
浮動性めまい	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
頭痛	0 (0%)	1 (17%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	2 (8%)
精神障害	1 (13%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
不安	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
不眠症	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
腎および尿路障害	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
夜間頻尿	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
呼吸器、胸郭および縦隔障害	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (4%)

Note: * Adverse events are classified according to MedDRA Version 20.0.
To assess each food effect, Cohort 3 was dosed in Period 1 under fasted conditions and Period 2 under fed conditions.
In each category (cell), a subjects if presents is counted only once. Placebo subjects of food effect cohort include both fasted and fed states.
TEAE = Treatment-Emergent Adverse Event

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting Events
(% of Subjects Dosed, SAD Cohorts 1-4)

		AG10 SAD Cohort					
Adverse Event*	Placebo	50 mg (1, Fasted)	150 mg (2, Fasted)	300 mg (3, Fasted)	300 mg (3, Fed)	800 mg (4, Fasted)	Total
口腔咽頭痛	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (4%)
鼻漏	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
皮膚および皮下組織障害	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
多汗症	0 (0%)	0 (0%)	1 (17%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)

Note: * Adverse events are classified according to MedDRA Version 20.0.
To assess each food effect, Cohort 3 was dosed in Period 1 under fasted conditions and Period 2 under fed conditions.
In each category (cell), a subjects if presents is counted only once. Placebo subjects of food effect cohort include both fasted and fed states.
TEAE = Treatment-Emergent Adverse Event

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity and Relationship to Study Drug - Number of Adverse Events (SAD Cohorts 1-4)

Adverse Event*	AG10 Cohort	Number of Adverse Events	Severity#			Relationship to Study Drug			
			Mild	Moderate	Severe	Probable	Possible	Unlikely	Unrelated
腹部不快感	1 (50 mg, fasted)	1	1	0	0	0	1	0	0
アラニンアミノトランスフェラーゼ増加	Placebo	1	1	0	0	0	0	0	1
不安	1 (50 mg, fasted)	1	1	0	0	0	1	0	0
アスパラギン酸アミノトランスフェラーゼ増加	Placebo	1	1	0	0	0	0	0	1
血中乳酸脱水素酵素増加	Placebo	1	1	0	0	0	0	0	1
浮動性めまい	2 (150 mg, fasted)	1	1	0	0	0	1	0	0
口内乾燥	3 (300 mg, fed)	1	1	0	0	0	1	0	0
	Placebo	1	1	0	0	0	0	0	1
γ－グルタミルトランスフェラーゼ増加	Placebo	1	1	0	0	0	0	0	1
頭痛	1 (50 mg, fasted)	1	0	1	0	0	1	0	0
	2 (150 mg, fasted)	1	1	0	0	0	1	0	0
多汗症	2 (150 mg, fasted)	1	1	0	0	0	1	0	0
不眠症	Placebo	1	1	0	0	0	1	0	0
靱帯捻挫	1 (50 mg, fasted)	1	0	1	0	0	0	0	1
好中球数減少	Placebo	1	1	0	0	0	1	0	0
夜間頻尿	Placebo	1	1	0	0	0	1	0	0
口腔咽頭痛	4 (800 mg, fasted)	1	1	0	0	0	0	1	0
鼻漏	Placebo	1	1	0	0	0	0	1	0
尿路感染	3 (300 mg, fed)	1	0	1	0	0	1	0	0
血管穿刺部位疼痛	2 (150 mg, fasted)	1	1	0	0	0	0	0	1
Placebo		9	9	0	0	0	3	1	5
1 (50 mg, fasted)		4	2	2	0	0	3	0	1
2 (150 mg, fasted)		4	4	0	0	0	3	0	1
3 (300 mg, fed)		2	1	1	0	0	2	0	0
4 (800 mg, fasted)		1	1	0	0	0	0	1	0
Total (AG10 Dose)		11	8	3	0	0	8	1	2

Note: * Adverse events are classified according to MedDRA Version 20.0.
No subject experienced a potentially life-threatening or fatal adverse event.
To assess food effect, Cohort 3 was dosed in Period 1 under fasted conditions and Period 2 under fed conditions.
Placebo subjects of food effect cohort include both fasted and fed states.

Table 14.3.1.4 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting Events
(% of Subjects Dosed, MAD Cohorts 1-3)

		AG10 MAD Cohort			
Adverse Event*	Placebo	100 mg (1, Fasted)	300 mg (2, Fasted)	800 mg (3, Fasted)	Total
Number of Subjects Dosed	6 (100%)	6 (100%)	6 (100%)	6 (100%)	18 (100%)
Number of Subjects With TEAEs	3 (50%)	2 (33%)	5 (83%)	1 (17%)	8 (44%)
Number of Subjects Without TEAEs	3 (50%)	4 (67%)	1 (17%)	5 (83%)	10 (56%)
胃腸障害	0 (0%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
口唇のひび割れ	0 (0%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
感染症および寄生虫症	0 (0%)	0 (0%)	2 (33%)	0 (0%)	2 (11%)
口腔ヘルペス	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
中耳炎	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
上気道感染	0 (0%)	0 (0%)	2 (33%)	0 (0%)	2 (11%)
筋骨格系および結合組織障害	2 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
背部痛	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
筋骨格硬直	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
神経系障害	0 (0%)	0 (0%)	1 (17%)	1 (17%)	2 (11%)
浮動性めまい	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
失神寸前の状態	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (6%)
呼吸器、胸郭および縦隔障害	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
鼻出血	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
鼻部不快感	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
皮膚および皮下組織障害	1 (17%)	1 (17%)	2 (33%)	0 (0%)	3 (17%)
脱毛症	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
皮膚乾燥	0 (0%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
多汗症	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
そう痒症	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
紅斑性皮疹	1 (17%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
丘疹性皮疹	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
皮膚亀裂	0 (0%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)

Note: * Adverse events are classified according to MedDRA Version 20.0.
In each category (cell), a subjects if presents is counted only once.
TEAE = Treatment-Emergent Adverse Event

Table 14.3.1.6 Treatment-Emergent Adverse Event Frequency by Treatment, Severity and Relationship to Study Drug - Number of Adverse Events (MAD Cohorts 1-3)

Adverse Event*	AG10 Cohort	Number of Adverse Events	Severity#			Relationship to Study Drug			
			Mild	Moderate	Severe	Probable	Possible	Unlikely	Unrelated
脱毛症	2 (300 mg, fasted)	1	1	0	0	0	1	0	0
背部痛	Placebo	1	0	1	0	0	1	0	0
口唇のひび割れ	1 (100 mg, fasted)	1	1	0	0	0	0	1	0
浮動性めまい	2 (300 mg, fasted)	1	1	0	0	0	0	1	0
皮膚乾燥	1 (100 mg, fasted)	1	1	0	0	0	0	1	0
鼻出血	2 (300 mg, fasted)	1	1	0	0	0	1	0	0
多汗症	2 (300 mg, fasted)	1	1	0	0	0	1	0	0
筋骨格硬直	Placebo	1	1	0	0	0	0	1	0
鼻部不快感	2 (300 mg, fasted)	1	1	0	0	0	1	0	0
口腔ヘルペス	2 (300 mg, fasted)	1	1	0	0	0	0	1	0
中耳炎	2 (300 mg, fasted)	1	1	0	0	0	0	0	1
失神寸前の状態	3 (800 mg, fasted)	1	1	0	0	0	0	0	1
そう痒症	Placebo	1	1	0	0	0	0	1	0
紅斑性皮疹	Placebo	1	1	0	0	0	0	1	0
丘疹性皮疹	2 (300 mg, fasted)	1	1	0	0	0	1	0	0
皮膚亀裂	1 (100 mg, fasted)	1	1	0	0	0	0	1	0
上気道感染	2 (300 mg, fasted)	2	1	1	0	0	0	0	2
Placebo		4	3	1	0	0	1	3	0
1 (100 mg, fasted)		3	3	0	0	0	0	3	0
2 (300 mg, fasted)		10	9	1	0	0	5	2	3
3 (800 mg, fasted)		1	1	0	0	0	0	0	1
Total (AG10 Dose)		14	13	1	0	0	5	5	4

Note: * Adverse events are classified according to MedDRA Version 20.0.
No subject experienced a potentially life-threatening or fatal adverse event.

Table 14.3.2 Serious Adverse Events

No serious adverse event was reported.

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3　第 1 相試験【AG10-005】（海外）［評価資料］

3.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-005】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-005】

治験の標題：健康被験者を対象に治療用量よりも高用量の AG10 の安全性、忍容性、薬物動態及び薬力学的作用を検討する第 1 相、ランダム化、プラセボ対照、単回漸増投与試験	
治験実施計画書番号：AG10-005	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の完了日：20[redacted] 年 [redacted] 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： 健康成人被験者を対象に治療用量よりも高用量でアコラミジス塩酸塩を単回経口投与したときの安全性及び忍容性を評価する。 副次目的： 1. 健康成人被験者に治療用量よりも高用量でアコラミジス塩酸塩を単回経口投与したときの薬物動態（PK）を明らかにする。 2. トランスサイレチン（TTR）安定化の確立されたアッセイを用いて治療用量よりも高用量でアコラミジス塩酸塩を単回経口投与したときの薬力学的作用（PD）の特性を明らかにする。 3. 健康成人被験者に治療用量よりも高用量でアコラミジス塩酸塩を単回経口投与したときの心臓伝導及び再分極並びに TTR 安定化の測定値と PK-PD の関係を明らかにする。	
方法： 本試験は、健康成人被験者を対象に治療用量よりも高用量のアコラミジス塩酸塩の単回経口投与を評価する単一施設、前向き、ランダム化、プラセボ対照試験であった。 本試験は単回漸増投与デザインであり、各 9 名からなる 3 つのコホートを設定した。各コホートでは全体でアコラミジス塩酸塩又はプラセボに 2：1 の比となるよう、Day 1 には 1：1 の比でセンチネル投与を行い、Day 2 に 5：2 の比で残りの被験者をランダム割付けした。アコラミジス塩酸塩 1200 mg を開始用量とし（コホート 1）、1600 mg（コホート 2）及び 2000 mg（コホート 3）へ用量漸増した。各用量漸増の前に、前の用量レベルでの投与 72 時間後までに得られたすべての安全性データを評価した。 同意説明文書に署名し、適格性が確認された被験者は Day -1 に治験実施施設に入院し、投与後約 72 時間（Day 4）まで入院した。12 誘導ホルター心電図による 24 時間連続モニタリングを Day 1 に開始し、投与 24 時間後まで継続した。 被験者は Day 1 の朝の空腹時（8 時間以上絶食）に治験薬を投与され、投与 4 時間後の PK 用採血時点まで絶食状態を維持した。Day 4 に治験実施施設を退院後、Day 6、8 及び 10 に有害事象の確認及び採血のために来院し、最終来院は Day 20（± 3 日）とした。	

PK 用血液検体の採取時間及び期間は、先行コホートの PK 結果に応じて最長 20 日間調整できることとしたが、評価回数は変更しないこととした。ただし、本試験では PK 用血液検体の採取時間の調整は行われなかった。

被験者数（計画時及び解析時）：

計画時：最大 27 名

解析時：27 名（アコラミジス塩酸塩 18 名、プラセボ 9 名）が登録され、全 27 名が試験を完了した。全 27 名が PD 評価可能集団及び安全性解析対象集団に含まれ、アコラミジス塩酸塩が投与された全 18 名が PK 解析対象集団に含まれた。

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす被験者を本試験の組入れ対象とした。

1. 18 歳以上 55 歳以下の男女。
2. スクリーニング時の体重が 50 kg 超、110 kg 以下の者。
3. スクリーニング時の体格指数が 18.0 kg/m^2 以上 32.0 kg/m^2 以下の者。
4. 女性の場合、以下のいずれかにより定義される妊娠の可能性がない者：
   a. 避妊手術を受けている（すなわち、治験薬の投与 6 ヵ月以上前に両側卵管結紮術若しくは両側卵巣及び/又は子宮の摘出、子宮頸管不妊術［Essure］又は卵管切除術を受けている）、又は
   b.初回投与前 12 ヵ月以上連続して閉経状態（自然閉経）であり、スクリーニング時の卵胞刺激ホルモン値が治験責任医師等の判断で閉経状態と一致している。
5. 女性の場合、スクリーニング時及び入院時（Day -1）の血清妊娠検査が陰性の者。
6. 男性で精管切除術を受けていない場合は、試験期間中及び治験薬投与 90 日後まで殺精子剤付きコンドームを使用するか、性交渉を控えることに同意する者。
7. 男性の場合、治験薬投与後少なくとも 90 日間、精子の提供を行わないことに同意する者。
8. 既往歴、身体所見、12 誘導心電図及び甲状腺刺激ホルモン（TSH）を含む標準的な臨床検査により健康と判断される者。
9. スクリーニング時及び入院時（Day -1）の薬物乱用及びアルコール検査が陰性の者。
10. 非喫煙者、又はスクリーニング前 6 ヵ月以上にわたって他のタバコ若しくはニコチン含有製品を使用していない者（例：紙タバコ、葉巻、噛みタバコ、嗅ぎタバコ、電子タバコ、ニコチンガム／パッチ等）。
11. 同意説明文書を読み、治験審査委員会が承認した同意説明文書に署名できる者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. ホルモン補充療法を含め、治験薬の投与前 4 週間以内に処方薬を使用した者、又は試験参加中に処方薬若しくは市販薬の継続的な使用が必要な者。
2. 胆嚢摘出術の既往がある者。
3. 治験薬の投与前 7 日以内又は半減期の 5 倍以内（いずれか長い方）に、ハーブ、定期的なビタミン、ミネラル、又はその他のサプリメントを含む市販薬を使用した者。
4. 呼吸器系、消化器系、腎臓系、肝臓系、血液系、リンパ系、神経系、心血管系、精神系、筋

骨格系、泌尿生殖器系、免疫系、皮膚系又は結合組織系の疾患又は障害の臨床的に重要な既往歴又は現病歴のある者。

5. スクリーニング時の心電図に臨床的に重要な異常が認められ、第二度又は第三度房室ブロックを示す、又は以下のうち一つ以上を示す者：QRS が 110 msec 超、Fridericia 式を用いて補正した QT 間隔が 450 msec 超（男性及び女性）、PR 間隔が 220 msec 超。また、軽度の非特異的 T 波変化以外に、QT 解析を妨げる又は臨床的に重要であると治験責任医師等が判断した重大な形態学的変化（平坦 T 波を含む）が認められた者。
6. 心筋梗塞、急性冠症候群、脳血管発作、一過性脳虚血発作、心室頻拍、心房細動、先天性 QT 延長症候群の既往歴若しくは既知の家族歴、又は原因不明の突然死の既知の家族歴、ペースメーカー若しくは植込み型除細動器、心臓若しくは脳のステント留置若しくは血管形成、又は臨床的に重要な心臓弁膜症の既往歴がある者。
7. スクリーニング前 2 年以内にアルコール中毒を含む薬物乱用の既往がある者、又はスクリーニング時若しくは入院時に薬物乱用若しくはアルコールのスクリーニング検査で陽性の者。
8. 治験実施施設入院 48 時間前から PK 検体の最終採取まで、カフェイン又はキサンチン含有製品（例：紅茶、コーヒー、チョコレート、コーラ等）の摂取を控える意思がない者。
9. Day -1 の治験実施施設入院 48 時間前から本試験の最終 PK 検体採取までアルコール摂取を控える意思がない者。
10. 治験実施施設入院 24 時間前から本試験の最終 PK 検体採取まで激しい身体運動（ウエイトトレーニング、エアロビクス等）を控える意思がない者。
11. 治験実施施設入院前 30 日以内又は半減期の 10 倍の期間内（いずれか長い方）に何らかの治験薬を使用した者。
12. 以下のいずれかの臨床検査値異常が認められる者：肝機能検査値（アスパラギン酸アミノトランスフェラーゼ、アラニンアミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限（ULN）超、トロポニンが ULN 超、TSH が ULN 超、推算糸球体濾過量が基準値下限未満、臨床的に重大な低カリウム血症、低マグネシウム血症又は低カルシウム血症。
13. スクリーニング時のバイタルサインが以下の範囲外の者：収縮期血圧が 90 mmHg 以上、140 mmHg 以下；拡張期血圧が 40 mmHg 以上、90 mmHg 以下；心拍数が 40 bpm 以上、99 bpm 以下。
14. スクリーニング前 56 日以内に献血又はスクリーニング前 7 日以内に血漿献血をした者。

治験薬、用法・用量：

被験薬：アコラミジス塩酸塩 200 mg フィルムコーティング錠（ロット番号：[redacted]、[redacted]）を水 240 mL とともに監視下で投与し、投与後 4 時間以上絶食した。

対照薬：プラセボフィルムコーティング錠（ロット番号:[redacted]）を水 240 mL とともに経口投与した。

治療期間：

被験者は投与日（Day 1）の前日（Day -1）に治験実施施設に入院し、治験薬の最終投与 72 時間後の採血が完了するまで計 5 日間滞在した。

評価項目：

主要評価項目：

安全性及び忍容性として以下を評価：バイタルサイン（血圧、心拍数）、身体所見、臨床検査（血液学的検査、血液生化学的検査、尿検査［顕微鏡検査を含む］）、心電図、有害事象の評価。また、24 時間連続 12 誘導心電図（ホルター心電図）。

副次評価項目：

1. 血漿中濃度データからアコラミジス及びその代謝物アコラミジス-アシルグルクロニド（アコラミジス-AG）の PK パラメータとして、必要に応じて以下を算出：時間 0 から投与 24 時間後までの濃度時間曲線下面積（AUC_{0-24}）、時間 0 から投与 72 時間後までの濃度時間曲線下面積（AUC_{0-72}）、時間 0 から血漿中濃度測定可能最終時点（t）までの濃度時間曲線下面積（AUC_{0-t}）、時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0-\infty}$）、最高血漿中濃度（C_{max}）、最高血漿中濃度到達時間（t_{max}）、分布相の消失半減期（$t_{1/2,d}$）及び終末相の消失半減期（$t_{1/2,t}$）、みかけの全身クリアランス（CL/F）並びに終末相のみかけの分布容積（V_z/F）。また、用量補正した AUC_{0-24} 及び C_{max} を算出。尿中データから以下の PK パラメータを算出：腎クリアランス（CLr）及び尿中総排泄量（Ae）。
2. 蛍光プローブ排除（FPE）アッセイ及びウェスタンブロット分析を用いた TTR 安定化の確立されたアッセイによってアコラミジスの PD 特性を評価。

統計手法：

薬物動態：

PK 解析対象集団は「アコラミジス塩酸塩を 1 回以上投与され、定量可能な血漿中濃度を示す PK 血液検体を 1 つ以上有する被験者」と定義した。PK 評価可能集団は「治験実施計画書からの重大な逸脱がなく、評価可能な PK プロファイルを有する被験者」と定義した。

PK パラメータはノンコンパートメント法により算出した。すべてのアコラミジス及びアコラミジス-AG の PK 濃度及び PK パラメータの要約統計量は SAS® Version 9.3 以上を用いて算出した。PK 解析対象集団のすべての被験者のアコラミジス及びアコラミジス-AG の血漿中濃度及び尿中回収率を一覧表に示し、コホート別及び時点別に要約した。全ての名目上の評価時点に対し、n、算術平均値、標準偏差（SD）、変動係数（CV%）、平均値の標準誤差（SEM）、最小値、中央値及び最大値を含む要約統計量を算出した。PK 解析対象集団から除外された被験者は濃度の一覧表に含めたが、要約統計量からは除外し、その旨を表中に記載した。濃度の一覧表では、定量下限値未満（BLQ）の値は「BLQ」として示し、その旨を脚注に記載した。また、血漿中及び尿中アコラミジス及びアコラミジス-AG の PK パラメータも同様に一覧表に示し、コホート別に要約し、要約統計量（n、算術平均値、SD、CV%、SEM、最小値、中央値、最大値、幾何平均値及び幾何 CV%）を算出した。PK 解析対象集団から除外された被験者は PK パラメータの一覧表には含めたが、要約統計量からは除外し、その旨を表中に記載した。

<u>用量比例性解析</u>

アコラミジス塩酸塩の単回漸増投与後に、アコラミジス及びアコラミジス-AG の自然対数（ln）変換した AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} の用量比例性を評価した。ln 変換した PK パラメータと ln 変換した用量間の線形関係は、線形回帰モデルを用いて当てはめた。

$$\ln(Y) = \ln b0 + b \ln \text{用量} + e$$

ここで、Y は PK パラメータ AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} を、e は誤差項を表す。この方法は通常、パワーモデルと呼ばれ、これは指数変換後の次の理由による。

$Y = b0 (用量)^{b}$

用量比例性を示すには b=1 となる必要がある。したがって、これらのパラメータの 95%信頼区間に用量依存的なパラメータの値として 1 が含まれる場合、用量比例性が確認されることとした。Step 1 として、二次効果に相当する（ln 用量）^{2} 項をモデルに含めることにより、ln 変換した PK パラメータと ln 変換した用量との線形関係を検証した。二次効果の検定には有意水準 5%を用いた（第 I 種の過誤）。二次項が統計的に有意でない場合、線形関係が結論付けられた。Step 1 で線形関係が成立した後、Step 2 を実施した。Step 2 として、線形モデルを用いて上記の ln 変換した PK パラメータの傾きの 95%信頼区間を算出した。直線の傾き、標準誤差、傾きの 95%信頼区間及び p 値を示した。

薬力学的作用：

PD は PD 評価可能集団を対象に解析し、その定義は「安全性解析対象集団のうち、投与前及び投与後の定量可能な PD バイオマーカー値を 1 つ以上有する被験者」とした。

TTR へのアコラミジス結合に関する個々のデータを示す表には、プローブ前蛍光強度、キネティクスデータ蛍光強度及びベースライン補正値を示した。キネティクスデータ蛍光強度及びベースライン補正値は 2 回の繰り返しで示した。さらに、同じ表（15 分間隔）を用いて、6 時間 FPE 試験中の各血液検体のベースライン補正値の平均値及び SD を示した。TTR へのアコラミジス結合に関する個々の数値を、各被験者の 6 時間 FPE 試験中の全血液試料採取時点に対して SD とともに線形スケールで示した。

TTR の安定化に関する個々のデータを示す表には、TTR 及び IgG の生デンシトメトリー値を記載した。TTR 及び IgG の生デンシトメトリー値は 2 回の繰り返しで示した。酸性化時間は、0 時間又は 72 時間のいずれかで、各血液試料採取時点も示した。IgG デンシトメトリー値に対する TTR の正常化も示した。各血液試料採取時点の生データ及び酸性化に関する平均値及び SD を示した。酸性化に関する各血液試料採取時点の標準化 TTR-IgG 値の平均値及び SD を示した。TTR 安定化の個別の棒グラフを、各被験者の標準化及び生データの SD とともに示した。

ベースライン値、投与後値及びベースラインからの変化量は、要約統計量を用いて表に示した。ベースラインからの個々の変化が 0 未満の場合、SAS プログラムではこの値を欠測に設定した。

安全性：

安全性は安全性解析対象集団を対象に解析し、その定義は治験薬を 1 回以上投与された被験者とした。

すべての安全性データは被験者別及び評価時期別に一覧に示した。連続変数は n、平均値、SD、最小値、中央値及び最大値を示した。カテゴリカルデータは必要に応じて頻度を示した。各コホートのプラセボ群のデータは併合した。

すべての有害事象は ICH 国際医薬用語集（MedDRA）Version 21.1 を用いてコード化し、器官別大分類及び基本語別、並びにコホート別に要約した。重篤な有害事象（発現した場合）、治験薬との関連性が否定できない有害事象、重症度別の有害事象も同様に要約することとした。

臨床検査（血液学的検査、血液生化学的検査、尿検査）及びバイタルサインは評価時点及びコホート別に要約統計量（n、平均値、SD、最小値、中央値、最大値）を示した。また、ベースライン

からの変化をシフトテーブルで示した。

結果の要約：

薬物動態：

アコラミジス

血漿中アコラミジスの PK パラメータの要約を以下に示す。

アコラミジス塩酸塩を単回経口投与したときの血漿中アコラミジスの薬物動態パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	1200 mg AG10	1600 mg AG10	2000 mg AG10
AUC_{0-t} (ng*hr/mL)	111000 (23.6) [n=6]	173000 (40.1) [n=6]	165000 (40.2) [n=6]
AUC_{0-24} (ng*hr/mL)	55000 (19.6) [n=6]	73900 (8.90) [n=6]	69900 (34.7) [n=6]
$AUC_{0-\infty}$ (ng*hr/mL)	112000 (23.2) [n=6]	176000 (42.0) [n=6]	166000 (40.8) [n=6]
C_{max} (ng/mL)	8880 (48.1) [n=6]	16800 (23.0) [n=6]	15100 (89.5) [n=6]
T_{max} (hr)	1.00 (0.501, 1.04) [n=6]	1.00 (1.00, 2.03) [n=6]	1.01 (0.999, 2.01) [n=6]
$t_{½,d}$ (hr)	2.75 ± 1.85 [n=6]	1.45 ± 0.744 [n=6]	2.42 ± 1.63 [n=6]
$t_{½,t}$ (hr)	19.6 ± 3.05 [n=6]	26.5 ± 9.74 [n=6]	22.0 ± 8.07 [n=6]
CL/F (L/hr)	9.75 ± 2.29 [n=6]	8.66 ± 3.40 [n=6]	11.4 ± 4.20 [n=6]
V_z/F (L)	272 ± 55.4 [n=6]	304 ± 83.0 [n=6]	332 ± 77.6 [n=6]
DN_AUC_{0-24} (ng*hr/mL/mg)	51.5 (19.6) [n=6]	51.9 (8.90) [n=6]	39.3 (34.7) [n=6]
DN_C_{max} (ng/mL/mg)	8.32 (48.1) [n=6]	11.8 (23.0) [n=6]	8.48 (89.5) [n=6]

1200 mg AG10: Administration of a Single Oral Dose of 1200 mg AG10 (Cohort 1) (PK Population)
1600 mg AG10: Administration of a Single Oral Dose of 1600 mg AG10 (Cohort 2) (PK Population)
2000 mg AG10: Administration of a Single Oral Dose of 2000 mg AG10 (Cohort 3) (PK Population)
AUCs and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.2項AG10-005 CSR Tables 14.2.1.1.2.1 ~ 14.2.1.1.2.3

アコラミジス塩酸塩 1200～2000 mg を単回経口投与したとき、AUC_{0-24}、AUC_{0-t} 及び $AUC_{0-\infty}$の幾何平均値に基づく血漿中アコラミジスの総曝露量並びに C_{max} の幾何平均値に基づく血漿中アコラミジスのピーク曝露量は、1200 mg から 1600 mg では用量増加に伴って増加したが、1600 mg から 2000 mg では用量増加に伴う増加はみられなかった。AUC 及び C_{max} パラメータのばらつき（幾何 CV%に基づく）は、1600 mg コホートの AUC_{0-24} を除き、すべてのコホートで比較的大きかった。特に 2000 mg コホートの C_{max} の幾何平均値は、すべての PK パラメータの中で最もばらつきが大きく、幾何 CV%値は約 89.5%であった。ばらつきが比較的大きく、また、各投与の被験者数が少ないため、これらの結果の解釈には注意が必要である。用量で補正した血漿中アコラミジスの AUC_{0-24}（DN_AUC_{0-24}）の算術平均値は、1200 及び 1600 mg コホートで同程度であった。しかし、2000 mg コホートの DN_AUC_{0-24} の算術平均値は他の 2 つのコホートと比較して低かった。用量で補正した血漿中 C_{max}（DN_C_{max}）の算術平均値は 1200 及び 2000 mg コホートでは同程度であったが、1600 mg コホートでは他の 2 つのコホートより高かった。アコラミジスの t_{max} の中央値は､すべてのコホートで同程度であった｡1200 及び 2000 mg を単回経口投与したときの $t_{1/2,d}$ の算術平均値は同程度であり、それぞれ 2.75 及び 2.42 時間であった。1600 mg コホートの $t_{1/2,d}$ はこれよりも短かった（1.45 時間）。$t_{1/2,t}$ の算術平均値も 3 つのコホートで同程度であり、平均値は 19.6～26.5 時間の範囲であった。

アコラミジス塩酸塩 1200～2000 mg を単回漸増経口投与したときの血漿中アコラミジスの PK パラメータの用量比例性解析の結果を以下に要約する。

アコラミジス塩酸塩 1200～2000 mg を単回漸増経口投与したときの血漿中アコラミジスの用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	0.8010	0.3939	(-0.0341, 1.6361)
$AUC_{0-\infty}$ (ng*hr/mL)	0.8036	0.4039	(-0.0527, 1.6599)
C_{max} (ng/mL)	1.0938	0.6112	(-0.2020, 2.3896)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * $Dose^b$ which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.2 項 AG10-005 CSR Table 14.2.1.1.2.6

用量比例性を評価する統計モデルに基づくと、1200～2000 mg の範囲で単回漸増経口投与後、血漿中アコラミジスの AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} は用量に比例して増加すると考えられた。しかし、95%信頼区間の幅が広いことからデータのばらつきが大きいことが示唆されるため、これらの結果の解釈には注意が必要である。最初に AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} に対して二次項の検定を行ったが、いずれも有意ではなかった。
また、AG10-001 試験（50～800 mg）及び本試験（1200～2000 mg）のデータを用いた、アコラミジス塩酸塩 50～2000 mg を単回経口投与したときの血漿中アコラミジスの PK パラメータの用量比例性解析の結果を以下に要約する。

アコラミジス塩酸塩 50～2000 mg を単回漸増経口投与したときの血漿中アコラミジスの用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	0.4983	0.0361	(0.4252, 0.5714)
$AUC_{0-\infty}$ (ng*hr/mL)	0.4970	0.0369	(0.4225, 0.5716)
C_{max} (ng/mL)	0.5687	0.0510	(0.4656, 0.6719)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * $Dose^b$ which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.2 項 AG10-005 CSR Table 14.2.1.1.2.7

アコラミジス塩酸塩 50～2000 mg を単回漸増経口投与したとき（AG10-001 試験で得られたデータ：50、150、300 及び 800 mg；本試験のデータ：1200、1600 及び 2000 mg）、血漿中アコラミジスの AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} は用量比を下回って増加した。最初に AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} に対して二次項の検定を行ったが、いずれも有意ではなかった。
さらに、尿中アコラミジスの PK パラメータの要約を以下に示す。

アコラミジス塩酸塩を単回経口投与したときの尿中アコラミジスの PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	1200 mg AG10	1600 mg AG10	2000 mg AG10
Ae (mg)	80.4 ± 30.7 [n=6]	135 ± 31.5 [n=6]	161 ± 68.9 [n=6]
CLr (mL/hr)	819 ± 304 [n=6]	1030 ± 249 [n=6]	1170 ± 478 [n=6]

1200 mg AG10: Administration of a Single Oral Dose of 1200 mg AG10 (Cohort 1) (PK Population)
1600 mg AG10: Administration of a Single Oral Dose of 1600 mg AG10 (Cohort 2) (PK Population)
2000 mg AG10: Administration of a Single Oral Dose of 2000 mg AG10 (Cohort 3) (PK Population)
Parameters presented as arithmetic mean ± SD.
Source: 5.3.3.1.2 項 AG10-005 CSR Tables 14.2.1.1.4.1 ~14.2.1.1.4.3

投与 72 時間後までのアコラミジスの Ae 及び CLr の平均値は投与量の増加に伴って増加し、それぞれ約 80.4～161 mg 及び約 819～1170 mL/hr の範囲であった。平均総排泄量は比較的少なく、1200～2000 mg を投与したときの投与量の約 7.5%～9.5%に相当した。

アコラミジス-AG

血漿中アコラミジス-AG の PK パラメータの要約を以下に示す。

アコラミジス塩酸塩を単回経口投与したときの血漿中アコラミジス-AG の PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	1200 mg AG10	1600 mg AG10	2000 mg AG10
$AUC_{0\text{-}t}$ (ng*hr/mL)	28900 (15.0) [n=6]	41400 (21.8) [n=6]	42500 (36.0) [n=6]
$AUC_{0\text{-}24}$ (ng*hr/mL)	25800 (15.5) [n=6]	34000 (11.0) [n=6]	36300 (38.2) [n=6]
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	28900 (15.0) [n=6]	41500 (21.9) [n=6]	42500 (36.0) [n=6]
C_{max} (ng/mL)	5750 (35.3) [n=6]	8290 (20.2) [n=6]	8890 (86.9) [n=6]
T_{max} (hr)	1.50 (1.00, 4.01) [n=6]	1.01 (1.00, 2.03) [n=6]	2.00 (1.00, 6.00) [n=6]
$t_{½,d}$ (hr)	1.69 ± 0.597 [n=6]	1.67 ± 0.710 [n=6]	1.85 ± 0.612 [n=6]
$t_{½,t}$ (hr)	12.8 ± 4.40 [n=6]	18.8 ± 8.50 [n=6]	15.8 ± 5.85 [n=6]
DN_$AUC_{0\text{-}24}$ (ng*hr/mL/mg)	24.2 (15.5) [n=6]	23.9 (11.0) [n=6]	20.4 (38.2) [n=6]
DN_C_{max} (ng/mL/mg)	5.39 (35.3) [n=6]	5.82 (20.2) [n=6]	4.99 (86.9) [n=6]

1200 mg AG10: Administration of a Single Oral Dose of 1200 mg AG10 (Cohort 1) (PK Population)
1600 mg AG10: Administration of a Single Oral Dose of 1600 mg AG10 (Cohort 2) (PK Population)
2000 mg AG10: Administration of a Single Oral Dose of 2000 mg AG10 (Cohort 3) (PK Population)
AUCs and C_{max} are presented as geometric mean and geometric CV%.
T_{max} values are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Source: 5.3.3.1.2 項 AG10-005 CSR Tables 14.2.1.2.2.1 ~ 14.2.1.2.2.3

アコラミジス塩酸塩 1200～2000 mg を単回経口投与したとき、$AUC_{0\text{-}24}$、$AUC_{0\text{-}t}$ 及び $AUC_{0\text{-}\infty}$の幾何平均値に基づく血漿中アコラミジス-AG の総曝露量並びに C_{max} の幾何平均値に基づく血漿中アコラミジス-AG のピーク曝露量は、用量増加に伴って増加すると考えられた。DN_$AUC_{0\text{-}24}$ 及び DN_C_{max} の算術平均値は、これらのパラメータのばらつきを考慮すると、3 用量すべてで同程度であった。アコラミジス-AG の t_{max} の中央値は、アコラミジス塩酸塩 1200～2000 mg の単回経口投与約 1.01～2.00 時間後の範囲であった。$t_{1/2,d}$ の算術平均値はすべてのコホート間で同程度であり、約 1.67～1.85 時間の範囲であった。$t_{1/2,t}$ の算術平均値もデータのばらつきを考慮すると、すべての用量（コホート）で同程度であり、約 12.8～18.8 時間の範囲であった。
アコラミジス塩酸塩 1200～2000 mg を単回漸増経口投与したときの血漿中アコラミジス-AG の PK パラメータの用量比例性解析の結果を以下に要約する。

アコラミジス塩酸塩 1200～2000 mg を単回漸増経口投与したときの血漿中アコラミジス-AG の用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
$AUC_{0\text{-}t}$ (ng*hr/mL)	0.7790	0.2866	(0.1714, 1.3865)
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	0.7775	0.2871	(0.1689, 1.3860)
C_{max} (ng/mL)	0.8726	0.5390	(-0.2700, 2.0151)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * $Dose^b$ which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Source: 5.3.3.1.2 項 AG10-005 CSR Table 14.2.1.2.2.6

アコラミジス塩酸塩 1200～2000 mg を単回漸増経口投与したとき、血漿中アコラミジス-AG の $AUC_{0\text{-}t}$、$AUC_{0\text{-}\infty}$及び C_{max} は用量に比例して増加すると考えられた。最初に $AUC_{0\text{-}t}$、$AUC_{0\text{-}\infty}$及び C_{max} に対して二次項の検定を行ったが、いずれも有意ではなかった。
また、AG10-001 試験（50～800 mg）及び本試験（1200～2000 mg）のデータを用いた、アコラミジス塩酸塩 50～2000 mg を単回経口投与したときの血漿中アコラミジス-AG の PK パラメータの用量比例性解析の結果を以下に要約する。

アコラミジス塩酸塩 50～2000 mg を単回漸増投与したときの血漿中アコラミジス-AG の用量比例性解析（PK 評価可能集団）

Pharmacokinetic Parameter	Estimate of Slope (b)	Standard Error	95% Confidence Interval for Slope
AUC_{0-t} (ng*hr/mL)	1.0052	0.0317	(0.9412, 1.0692)
$AUC_{0-\infty}$ (ng*hr/mL)	0.9963	0.0321	(0.9314, 1.0612)

Parameters were ln-transformed prior to analysis.
The following statistical model using PROC MIXED of SAS was used to test dose proportionality:
Parameter = a * $Dose^b$ which was equivalent to ln(Parameter) = ln(a) + b[ln(Dose)]
Dose proportionality is not rejected if the 95% CI for b contains 1.
Dose proportionality is rejected for C_{max} due to non-linear relationship (p-value of quadratic term = 0.0114 for C_{max}).
Source: 5.3.3.1.2 項 AG10-005 CSR Table 14.2.1.2.2.7

アコラミジス塩酸塩 50～2000 mg を単回漸増経口投与したとき（AG10-001 試験で得られたデータ：50、150、300 及び 800 mg；本試験のデータ：1200、1600 及び 2000 mg）、血漿中アコラミジス-AG の AUC_{0-t} 及び $AUC_{0-\infty}$は用量に比例して増加すると考えられた。C_{max} は非線形性を示したため、用量比例性は棄却された（C_{max} の二次項 p 値=0.0114）。
さらに、尿中アコラミジス-AG の PK パラメータの要約を以下に示す。

アコラミジス塩酸塩を単回経口投与したときの尿中アコラミジス-AG の PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	1200 mg AG10	1600 mg AG10	2000 mg AG10
Ae (mg)	502 ± 89.7 [n=6]	662 ± 92.5 [n=6]	783 ± 242 [n=6]
CLr (mL/hr)	17600 ± 4040 [n=6]	17000 ± 4400 [n=6]	18000 ± 2230 [n=6]

1200 mg AG10: Administration of a Single Oral Dose of 1200 mg AG10 (Cohort 1) (PK Population)
1600 mg AG10: Administration of a Single Oral Dose of 1600 mg AG10 (Cohort 2) (PK Population)
2000 mg AG10: Administration of a Single Oral Dose of 2000 mg AG10 (Cohort 3) (PK Population)
Parameters presented as arithmetic mean ± SD.
Source: 5.3.3.1.2 項 AG10-005 CSR Tables 14.2.1.2.4.1 ~ 14.2.1.2.4.3

投与 72 時間後までのアコラミジス-AG の Ae の平均値は、アコラミジス塩酸塩 1200 から 2000 mg への用量増加に伴って増加し、約 502～783 mg の範囲であった。アコラミジス塩酸塩 1200～2000 mg を投与したときのアコラミジス-AG の平均総排泄量は、投与量の約 27.5%～29.3%であった。

安全性：

本試験では、死亡、重篤な有害事象及び中止に至った有害事象は認められなかった。全体として、有害事象はアコラミジス塩酸塩群（併合）の 39%に、プラセボ群（併合）の 56%に発現し、アコラミジス塩酸塩のいずれの用量でも有害事象の発現者数は同程度であった。ほとんどの有害事象の重症度は軽度であった。アコラミジス塩酸塩群（併合）で 2 名以上に発現した有害事象は、浮動性めまい（3 名）及び咽頭炎（2 名）であった。プラセボ群（併合）で 2 名以上に発現した有害事象は頭痛（2 名）であった（アコラミジス塩酸塩群では 1 名）。アコラミジス群（1600 mg）の 1 名では、軽度で一過性のバイタルサイン関連の有害事象として低血圧が発現した。その他に臨床検査、バイタルサイン、心電図又は身体所見の安全性評価に、臨床的に重要な所見は認められなかった。

結論：

- 本試験の健康成人被験者で、治療用量よりも高用量のアコラミジス塩酸塩の単回経口投与は安全であり、概して忍容性が良好であると考えられた。
- 用量比例性を評価する統計モデルに基づくと、アコラミジス塩酸塩 1200～2000 mg を単回経

口投与したとき、血漿中アコラミジス及びアコラミジス-AG の AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} は用量に比例して増加すると考えられた。しかし、95%信頼区間の幅が広いことからデータのばらつきが大きいことが示唆されるため、これらの結果の解釈には注意が必要である。

- AG10-001 試験の過去のデータ（アコラミジス塩酸塩 50、150、300 及び 800 mg）に基づき、アコラミジス塩酸塩 50～2000 mg を単回経口投与したとき、血漿中アコラミジスの AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} は用量比を下回って増加した。血漿中アコラミジス-AG では、AUC_{0-t} 及び $AUC_{0-\infty}$は用量増加に比例して増加したが、C_{max} は非線形性を示したため、用量比例性は棄却された（C_{max} の二次項 p 値=0.0114）。
- 投与 72 時間後までに尿中排泄されたアコラミジス及びアコラミジス-AG の平均総排泄量は、投与量が 1200 mg から 2000 mg への増加に伴い増加した。
- アコラミジスの血漿クリアランスに対する尿中排泄の寄与は小さく、アコラミジス-AG の尿中排泄の寄与は大きくないと考えられた。アコラミジス塩酸塩 1200～2000 mg を投与したときの尿中に排泄されたアコラミジスの平均総排泄量は投与量の約 7.5%～9.5%であり、アコラミジス-AG の平均総排泄量は、投与量の約 27.5%～29.3%であった。

報告書作成日：20[redacted] 年 [redacted] 月 [redacted] 日

3.2 有害事象

すべての有害事象及び治験薬との関連性が否定できない有害事象を以下に示す。本試験で重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Table 14.3.1.1
治験薬との関連性が否定できない有害事象	Table 14.3.1.3
重篤な有害事象	Table 14.3.2.1（該当なし）
治験薬の投与中止に至った有害事象	該当なし

3.3 個別被験者の詳細

本試験で死亡又は重篤な有害事象は発現していないため、該当なし。

Table 14.3.1.1 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Subjects Reporting Events (% of Subjects Dosed) (Safety Population)

Adverse Event*	Placebo	AG10 1200 mg (Cohort 1)	AG10 1600 mg (Cohort 2)	AG10 2000 mg (Cohort 3)	AG10 Total
Number of Subjects Dosed	9 (100%)	6 (100%)	6 (100%)	6 (100%)	18 (100%)
Number of Subjects With TEAEs	5 (56%)	2 (33%)	3 (50%)	2 (33%)	7 (39%)
Number of Subjects Without TEAEs	4 (44%)	4 (67%)	3 (50%)	4 (67%)	11 (61%)
胃腸障害	2 (22%)	1 (17%)	0 (0%)	1 (17%)	2 (11%)
上腹部痛	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (6%)
下痢	1 (11%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
悪心	1 (11%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
嘔吐	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
一般・全身障害および投与部位の状態	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
熱感	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
感染症および寄生虫症	1 (11%)	0 (0%)	2 (33%)	1 (17%)	3 (17%)
膀胱炎	0 (0%)	0 (0%)	0 (0%)	1 (17%)	1 (6%)
咽頭炎	0 (0%)	0 (0%)	2 (33%)	0 (0%)	2 (11%)
上気道感染	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
神経系障害	2 (22%)	2 (33%)	1 (17%)	0 (0%)	3 (17%)
浮動性めまい	0 (0%)	2 (33%)	1 (17%)	0 (0%)	3 (17%)
頭痛	2 (22%)	1 (17%)	0 (0%)	0 (0%)	1 (6%)
生殖系および乳房障害	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
不正子宮出血	1 (11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
血管障害	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)
低血圧	0 (0%)	0 (0%)	1 (17%)	0 (0%)	1 (6%)

Note: * Adverse events are classified according to MedDRA Version 21.1.
In each category (cell), a subject, if present, is counted only once.
TEAE = Treatment-Emergent Adverse Event

Table 14.3.1.3 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Study Drug - Number of Adverse Events (Safety Population)

Adverse Event*	AG10	Number of Adverse Events	Severity#			Relationship to Study Drug			
			Mild	Moderate	Severe	Probable	Possible	Unlikely	Unrelated
上腹部痛	2000 mg	1	1	0	0	0	0	1	0
膀胱炎	2000 mg	1	1	0	0	0	0	0	1
下痢	1200 mg	1	1	0	0	0	1	0	0
	Placebo	1	1	0	0	0	1	0	0
浮動性めまい	1200 mg	2	2	0	0	0	1	0	1
	1600 mg	1	1	0	0	0	1	0	0
熱感	Placebo	1	1	0	0	0	0	1	0
頭痛	1200 mg	1	0	1	0	0	1	0	0
	Placebo	2	0	2	0	0	1	1	0
低血圧	1600 mg	1	1	0	0	0	1	0	0
不正子宮出血	Placebo	1	1	0	0	0	1	0	0
悪心	1200 mg	1	1	0	0	0	1	0	0
	Placebo	1	1	0	0	0	0	1	0
咽頭炎	1600 mg	2	1	1	0	0	0	0	2
上気道感染	Placebo	1	1	0	0	0	0	0	1
嘔吐	Placebo	1	1	0	0	0	0	1	0
Placebo		8	6	2	0	0	3	4	1
1200 mg		5	4	1	0	0	4	0	1
1600 mg		4	3	1	0	0	2	0	2
2000 mg		2	2	0	0	0	0	1	1
Total (AG10 Dose)		11	9	2	0	0	6	1	4

Note: * Adverse events are classified according to MedDRA Version 21.1.
No subject experienced a potentially life-threatening or fatal adverse event.

Table 14.3.2.1 Serious Adverse Events (Safety Population)

No serious adverse event was reported.

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4　第 1 相試験【AG10-007】（海外）［参考資料］

4.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-007】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-007】

治験の標題：健康成人男性を対象に[^{14}C]-アコラミジスを経口投与したときの吸収、代謝、排泄及びマスバランスを評価する第 1 相、オープンラベル試験	
治験実施計画書番号：AG10-007	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の完了日：20[redacted] 年 [redacted] 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： • 健康成人男性に[^{14}C]-アコラミジス塩酸塩を単回経口投与したときのアコラミジスの排泄経路及びマスバランスを評価する。 • 健康成人男性に[^{14}C]-アコラミジス塩酸塩を単回経口投与したときの血漿中及び全血中の総放射能（TRA）濃度を定量する。 • 健康成人男性に[^{14}C]-アコラミジス塩酸塩を単回経口投与したときの血漿中及び尿中のアコラミジス及びその代謝物アコラミジス-アシルグルクロニド（アコラミジス-AG）の薬物動態（PK）プロファイルを明らかにする。 • 健康成人男性に[^{14}C]-アコラミジス塩酸塩を単回経口投与したときのアコラミジスの代謝を検討し、生体試料中の代謝物を同定する。 • 全血中の細胞成分に対する TRA の割合（全血／血漿分配比など）を経時的に測定する。 副次目的： • 健康成人男性に[^{14}C]-アコラミジス塩酸塩を単回投与したときの安全性及び忍容性を評価する。	
方法： 本試験は、オープンラベル、単回投与、吸収、代謝、排泄及びマスバランス試験であった。健康成人男性 6 名を登録した。被験者のスクリーニングは投与前 28 日以内に実施し、被験者は Day -1 に治験実施施設に入院した。 被験者には Day 1 に[^{14}C]-アコラミジス塩酸塩 800 mg（約 450 µCi）を単回投与した。投与後 216 時間（すなわち Day 10）以上、血漿、尿及び糞便検体を採取し、TRA（すべてのマトリックス中）、アコラミジス及びアコラミジス-AG の濃度（血漿及び尿中のみ）を測定し、代謝物をプロファイリング（すべてのマトリックス中）した。投与後 24 時間（すなわち Day 2）まで全血検体を採取し、TRA を測定した。厳密に管理し、被験者が採尿を忘れないよう、指定されたトイレのみ使用することとし、さらに、シャワーを浴びる前にも採尿した。 被験者は投与 216 時間後（Day 10）以降、以下のいずれかの退院基準を満たした場合、治験実施施設から退院した。	

- 投与した総放射能の 90%以上が尿及び糞便中に回収された又は
- 2回の連続する24時間間隔で採取された各尿及び糞便検体で検出された放射能が投与した総放射能の 1%以下

投与 216 時間後（Day 10）までにいずれの退院基準も満たさなかった場合、被験者は少なくとも一つの基準を満たすまで又は投与後最長 14 日間（すなわち Day 15）まで入院した。投与 216 時後（Day 10）を超えて入院した被験者は、TRA 及び代謝物プロファイリング測定用の尿及び糞便検体の採取を 24 時間間隔で、TRA 測定及び代謝物プロファイリング用の血漿検体の採取を 72 時間間隔（Day 13［該当する場合］）で継続することとした。ただし、本試験では実際にはすべての被験者は投与 216 時間後（Day 10）に退院した。

安全性は、繰り返しの臨床評価及び臨床検査で試験期間をとおしてモニタリングした。治験薬が投与されたすべての被験者と治験薬の投与から約 14 日後に連絡を取り、最終来院以降の有害事象の発現の有無を確認した。

被験者数（計画時及び解析時）：

計画時：6 名

解析時：6 名（PK 評価可能集団：6 名、安全性解析対象集団：6 名）

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす被験者を本試験の組入れ対象とした。

1. スクリーニング時に 19～55 歳の健康成人男性。
2. 被験者の自己報告に基づき、治験薬投与前 3 ヵ月以上ニコチン含有製品を使用しておらず、試験期間中も使用しない、継続的な非喫煙者。
3. スクリーニング時の体格指数が 18.0 kg/m^2 以上、32.0 kg/m^2 以下の者。
4. 医学的に健康であり、臨床的に重要な病歴、身体所見、臨床検査プロファイル、バイタルサイン又は心電図の所見がないと治験責任医師等が判断した者。
5. 試験期間中及び治験薬投与後 90 日間は殺精子剤付きコンドームを使用するか、性交を控えることに同意できる者。
6. 治験薬投与開始から投与 90 日後まで精子を提供しないことに同意できる者。
7. 同意説明文書の試験手順を理解し、治験実施計画書を遵守する意思及び能力がある者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. 治験責任医師等の判断で、スクリーニング時に精神的又は法的に能力がない又は重大な情緒的問題がある、あるいは試験実施中に予想される者。
2. 治験責任医師等の判断で、臨床的に重要な医学的又は精神的状態若しくは疾患の既往歴又は現病歴がある者。
3. 治験責任医師等の判断で、試験結果に影響を及ぼす可能性がある又は試験参加により被験者にさらなるリスクをもたらす可能性がある疾患の既往歴を有する者。
4. 被験者の自己報告に基づき、治験薬投与前 2 年以内にアルコール依存症又は薬物乱用の既往歴又は現病歴がある者。
5. 治験薬又は関連化合物に対する過敏症又は特異体質反応の既往歴又は現病歴を有する者。

6. 治験薬の吸収、代謝又は排泄に影響を及ぼす可能性のある疾患又は処置の既往歴（胃又は腸の手術若しくは切除、経頸静脈的肝内門脈大循環シャント又は外科的シャントの既往歴を含む）を有する者。虫垂切除、胆嚢摘出及びヘルニア修復は、合併症を伴わない場合は許容される。
7. 排便が 2 日に 1 回未満の者。
8. 治験薬投与前 2 週間以内に下痢、軟便、便秘などの便通異常の既往がある者。
9. スクリーニング時に Fridericia 式を用いて補正した QT 間隔が 460 msec 超又は治験責任医師等の判断で心電図所見に臨床的に重要な異常がある者。
10. 心筋梗塞、急性冠症候群、脳血管発作、一過性脳虚血発作、心室頻拍、心房細動の既往歴、先天性 QT 延長症候群の既往歴若しくは既知の家族歴又は原因不明の突然死の既知の家族歴、ペースメーカー若しくは植込み型除細動器、心臓若しくは脳のステント留置若しくは血管形成又は臨床的に重要な心臓弁膜症の既往歴を有する者。
11. 治験責任医師等の判断で、臨床的に重要な以下のいずれかの臨床検査値異常が認められる者：スクリーニング時又は入院時に肝機能検査値（アラニンアミノトランスフェラーゼ、アスパラギン酸アミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限（ULN）超；トロポニンが ULN 超；甲状腺刺激ホルモンが ULN 超、低カリウム血症、低マグネシウム血症又は低カルシウム血症が認められる。
12. 治験薬投与前 4 週間以内に処方薬を使用した者。
13. Day -1 前 7 日以内又は半減期の 5 倍の期間内（いずれか長い方）に、ハーブ、定期的なビタミン、ミネラル若しくはその他のサプリメントを含む何らかの市販薬を使用した者又は試験参加中に処方薬又は市販薬の継続的な使用を必要とする者。ただし、治験薬投与後は、治験責任医師等の判断でアセトアミノフェン（24 時間あたり最大 2 g）を投与してもよい。また、治験責任医師等の判断で、治験薬投与 24 時間後にマグネシアミルク（すなわち、水酸化マグネシウム）（≤ 60 mL/日）又はプルーンジュースを摂取してもよい。
14. 治験薬投与前 24 時間以内にキサンチン類／カフェインを含む飲食物を摂取した者。ただし、通常の食品に由来する少量のカフェイン（例：ディカフェのコーヒー又はその他のカフェイン抜き飲料［エスプレッソを除く］1 杯 250 mL/8 オンス/日又はチョコレートバー45 g/1.5 オンス/日）は、この制限の逸脱とはみなされない。
15. 治験薬投与前 48 時間以内にアルコールを含む飲食物を摂取した者。
16. 治験薬投与前 14 日間にグレープフルーツ／セビリアオレンジを含む飲食物を摂取した者。
17. スクリーニング時の座位血圧で収縮期血圧が 90 mmHg 未満、140 mmHg 超、拡張期血圧が 40 mmHg 未満、90 mmHg 超の者。
18. スクリーニング時の座位心拍数が 40 bpm 未満又は 99 bpm 超の者。
19. スクリーニング時又は入院時の尿中薬物乱用又はアルコール検査結果が陽性の者。
20. スクリーニング時にヒト免疫不全ウイルス、B 型肝炎表面抗原又は C 型肝炎ウイルスの検査結果が陽性の者。
21. 治験薬投与前 30 日以内及び試験期間を通じて、治験責任医師等の判断で、治験薬の食事内容と一致しない食事を摂っている者。
22. 治験薬投与前 56 日以内に献血又は大量失血した者。
23. 治験薬投与前 7 日以内に血漿を提供した者。
24. 治験薬投与前 12 ヵ月以内に放射性標識物質を投与した若しくは放射線源に曝露した者又は

治験薬投与後 12 ヵ月以内に放射線曝露若しくは放射性同位元素の投与を受ける可能性が高く、本試験へ参加することで総曝露量が安全と考えられる推奨レベル（すなわち、国際放射線防護委員会が推奨する加重年間限界値 3000 mrem）を超えて増加する可能性がある者。

25. 治験薬投与前 30 日以内に他の臨床試験に参加した者。30 日間の許容期間は、前試験の最終採血日又は投与日のいずれか遅い方から本試験の Day 1 までとする。

治験薬、用法・用量：

アコラミジス塩酸塩経口懸濁液は調製後 2 時間以内に各被験者に投与した。投与ボトルは 2 × 60 mL の水で洗浄し、被験者には洗浄水に加えて、さらに 120 mL の水を投与した。

治療期間：

被験者は Day -1 に治験実施施設に入院し、投与 216 時間後（Day 10）に退院した（すべての被験者が退院基準を満たした）。

評価項目：

主要評価項目：

- 回収された TRA、並びに尿及び糞便中に排泄された放射能の割合：マスバランスは、投与した放射能から嘔吐により失われた放射能（嘔吐があった場合）を差し引いた量に対する、尿及び糞便中に回収された TRA の割合の合計として算出した。
- 尿中 TRA 濃度相当量及び以下の PK パラメータ：尿中総排泄量（Ae［u］）、尿中累積排泄量（CumAe［u］）、投与量に占める尿中排泄量の割合（%Dose［u］）、投与量に占める尿中累積排泄量の割合（Cum%Dose［u］）及び腎クリアランス（CLr）。
- 糞便中 TRA 濃度相当量及び以下の PK パラメータ：糞便中総排泄量（Ae［f］）、糞便中累積排泄量（CumAe［f］）、投与量に占める糞便中排泄量の割合（%Dose［f］）及び投与量に占める糞便中累積排泄量の割合（Cum%Dose［f］）。
- 全血中及び血漿中の TRA 濃度相当量、並びに血漿中 TRA 濃度相当量に対応する以下の PK パラメータ：時間 0 から血漿中濃度測定可能最終時点までの濃度時間曲線下面積（$AUC_{0\text{-last}}$）、時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0\text{-}\infty}$）、$AUC_{0\text{-}\infty}$の外挿部分の割合（$AUC_{\%extrap}$）、最高血漿中濃度（C_{max}）、最高血漿中濃度到達時間（t_{max}）、消失速度定数（λ_z）、消失半減期（$t_{1/2}$）及び時間を一致させた時間 0 から血漿中濃度測定可能最終時間（t）までの濃度時間曲線下面積（$AUC_{0\text{-}t}$）（t は全被験者で TRA、血漿中アコラミジス及びアコラミジス-AG が定量可能であった最後の共通の時点）。
- 血漿中アコラミジス及びアコラミジス AG の以下のパラメータ：$AUC_{0\text{-last}}$、$AUC_{0\text{-}\infty}$、$AUC_{0\text{-}t}$、$AUC_{\%extrap}$、C_{max}、t_{max}、λ_z 、$t_{1/2}$、みかけの全身クリアランス（CL/F）（アコラミジスのみ）及び終末相のみかけの分布容積（V_z/F）（アコラミジスのみ）。
- 尿中アコラミジス及びアコラミジス-AG 濃度並びに以下の PK パラメータ：Ae（u）、CumAe（u）、%Dose（u）、Cum%Dose（u）及び CLr。
- C_{max} 及び時間を一致させた $AUC_{0\text{-}t}$ での血漿中 TRA に対するアコラミジス及びアコラミジス-AG 濃度の割合。
- 血漿、尿及び糞便中のアコラミジス代謝物プロファイリング。
- 時間を一致させた全血中及び血漿中 TRA 濃度測定結果から推定した血漿中 TRA 濃度に対する全血中 TRA 濃度の割合（B:P 比）。

副次評価項目：

- 有害事象、12 誘導心電図、バイタルサイン及び臨床検査。

統計手法：

薬物動態：

PK 解析対象集団は「治験薬が投与され、評価可能な血漿濃度を有する PK 検体を 1 つ以上有する被験者」と定義した。PK 評価可能集団は「PK 解析対象集団のうち、治験実施計画書を遵守し、評価可能な PK プロファイルを有する被験者（すなわち、治験薬が投与され、評価可能な測定値を有し、治験実施計画書からの重大な逸脱がない被験者）」と定義した。

血漿中及び全血中のアコラミジス及びアコラミジス-AG の血漿中濃度／濃度相当量並びに TRA 濃度／濃度相当量を一覧表に示し、PK 解析対象集団の全被験者を測定時点別に要約した。アコラミジス及びアコラミジス-AG の血漿中濃度並びに血漿中及び全血中の TRA 濃度／濃度相当量は、生体試料分析データの精度に基づいて示した。n、算術平均値、標準偏差（SD）、変動係数（CV%）、平均値の標準誤差（SEM）、最小値、中央値及び最大値を含む要約統計量をすべての名目上の測定時点に対して算出した。濃度一覧表ではすべての定量下限値未満（BLQ）の値を「BLQ」として示し、脚注にその旨を記載した。

PK 解析対象集団の全被験者で、尿中アコラミジス及びアコラミジス-AG 濃度並びに尿中及び糞便中 TRA 濃度相当量を一覧表に示し、名目上の採取時間別に要約した。尿中アコラミジス及びアコラミジス-AG 濃度、並びに尿中及び糞便中の TRA 濃度相当量及び回収量は有効数字 3 桁以上で示した。すべての名目上の採取時間で、n、算術平均値、SD、CV%、SEM、最小値、中央値及び最大値を含む要約統計量を算出した。濃度一覧表ではすべての BLQ 値を「BLQ」として示し、脚注にその旨を記載した。

血漿中及び全血中濃度／濃度相当量時間プロファイル（平均値及び個々）を線形スケール及び片対数スケールで示した。線形平均プロットは SD の有無別で示した。尿中及び糞便中の TRA 累積回収率プロファイル（平均値［SD の有無別］及び個々）は線形スケールのみで示した。B:P 比プロファイル（平均値［SD の有無別］）は線形スケールのみで示した。尿及び糞便中回収率は、投与前の採取間隔の値を 0 としてプロットし、その後は投与後のすべての採取間隔をプロットした。

PK パラメータは、小数点以下第 2 位まで表示した t_{max}、定量可能な濃度が検出された最終時点（t_{last}）、$t_{1/2}$、%Dose 及び Cum%Dose を除き、その他のパラメータは有効数字 3 桁で示した。全血、血漿、尿及び糞便中の血漿中アコラミジス及びアコラミジス-AG 並びに TRA の PK パラメータを被験者別に一覧にした。TRA の B:P 比は有効数字 3 桁で示し、被験者別及び測定時点別に一覧を作成した。血漿中アコラミジス及びアコラミジス-AG 並びに血漿、全血、尿及び糞便中 TRA の PK パラメータの要約統計量（n、算術平均値、SD、CV%、SEM、最小値、中央値、最大値、幾何平均値、幾何 CV%）を算出した。

安全性：

安全性は安全性解析対象集団を対象に解析し、その定義は、治験薬が投与されたすべての被験者とした。

すべての安全性及び忍容性データを被験者別及び評価時点別に一覧にした。連続変数は要約統計量（n、算術平均値、SD、最小値、中央値及び最大値）を算出した。カテゴリーデータは必要に応じて頻度を報告した。すべての有害事象は ICH 国際医薬用語集（MedDRA®）Version 24.0 を用

いてコード化した。収集したすべての有害事象を、報告用語、器官別大分類（SOC）、基本語（PT）、発現時期、重篤度、重症度、治験責任医師が評価した治験薬との因果関係、治験責任医師が評価した治験薬以外との因果関係、治験薬に対して取られた処置及び治験薬以外に対する処置を含む被験者別のデータ一覧表に示した。ただし、要約には治験薬投与後に発現した有害事象のみを含めた。数値で表されるすべての臨床検査値は、各臨床検査の評価時点別及び投与別に要約統計量を示した。ベースラインからの変化を比較するため、シフトテーブルを作成した。バイタルサイン及び心電図の測定値及びベースラインからの変化量の要約統計量を評価時点及び投与別に算出した。前治療薬及び併用薬はすべて World Health Organization（WHO）Dictionary Version 01-Mar-2021_b3 を用いてコード化し、一覧表を作成した。

結果の要約：

薬物動態：

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したときの全血中 TRA の血漿中濃度に対する割合（B:P 比）を以下に要約する。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したときの全血中 TRA の血漿中濃度に対する割合（全血:血漿分配比）の要約（PK 評価可能集団）

Nominal Sample Times (hr)	Whole Blood:Plasma Ratio (N=6)
1	0.4940 ± 0.022354
4	0.5084 ± 0.015235
24	0.5198 ± 0.028986

Values presented as arithmetic mean ± SD
Whole Blood:Plasma Partitioning Ratio (B:P Ratio) = Cb/Cp, where Cb = total radioactivity concentration equivalents (ng eq/g) in whole blood and Cp = total radioactivity concentration equivalents in plasma converted from ng eq/mL to ng eq/g.
eq = Equivalents
Source: 5.3.3.1.3 項 AG10-007 CSR Table 14.2.1.2.5

注：投与量は[^{14}C]-アコラミジス塩酸塩経口懸濁系 800 mg（約 450 μCi）。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したときの各評価時点での TRA 濃度の B:P 比の算術平均値は各評価時点間で類似しており、0.4940～0.5198 の範囲であった。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したときの血漿中アコラミジス、アコラミジス-AG 及び TRA の PK パラメータを以下に要約する。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したときの血漿中アコラミジス及びアコラミジス-AG 並びに血漿中 TRA の PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	Acoramidis in Plasma (N=6)	Acoramidis-AG in Plasma (N=6)	Total Radioactivity in Plasma (N=6)
$AUC_{0\text{-}168(parent)}$ (ng*hr/mL)	132700 (21.0)	NC	211600 (15.3)
$AUC_{0\text{-}96(metab)}$ (ng*hr/mL)	NC	22690 (28.4)	191800 (14.4)
$AUC_{0\text{-}last}$ (ng*hr/mL)	133800 (21.3)	22810 (28.2)	217300 (15.4)
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	134500 (21.3)	22850 (28.1)	227000 (15.4)
$AUC_{\%extrap}$ (%)	0.5637 (± 0.28352)	0.1751 (± 0.094960)	4.251 (± 0.43467)
C_{max} (ng/mL)	16260 (45.0)	9352 (41.2)	30010 (28.1)
T_{max} (hr)	0.749 (0.51, 0.76)	0.997 (0.54, 1.50)	0.755 (0.52, 1.01)
T_{last} (hr)	216.004 (168.02, 216.06)	132.000 (96.00, 144.01)	NC
λ_z (1/hr)	0.02361 (± 0.0039754)	0.04163 (± 0.010997)	0.01014 (± 0.0014350)
$t_{½}$ (hr)	30.003 (± 4.5997)	17.397 (± 3.4273)	69.694 (± 11.2365)
CL/F (L/hr)	5.430 (± 1.1929)	NC	NC
V_z/F (L)	230.7 (± 36.319)	NC	NC
PE $AUC_{0\text{-}last}$ (ng eq*hr/mL)	NC	14240 (28.2)	NC
PE $AUC_{0\text{-}t}$ (ng eq*hr/mL)	NC	14160 (28.4)	NC

PE $AUC_{0-\infty}$ (ng eq*hr/mL)	NC	14260 (28.1)	NC
PE C_{max} (ng eq/mL)	NC	5836 (41.2)	NC
MPR C_{max}	NC	0.4433 (± 0.20991)	NC
MPR $AUC_{0-\infty}$	NC	0.1267 (± 0.043714)	NC
C_{max} Ratio	0.5510 (± 0.10317)	0.2017 (± 0.056474)	NC
AUC Ratio	0.6306 (± 0.071278)	0.07643 (± 0.020780)	NC

AUCs and C_{max} values are presented as geometric mean (geometric CV%).
T_{max} and T_{last} values are presented as median (min, max).
Other parameters are presented as arithmetic mean (± SD).
TRA concentrations (dpm/mL) were normalized to acoramidis concentrations (ng eq "acoramidis"/mL) based the quotient of the µCi/dpm conversion factor (1 µCi/2220000 dpm) and the radiochemical purity-corrected Specific Activity of the dose of 88.209 µCi/mg acoramidis.
The C_{max} and AUC ratios for acoramidis-AG represent the ratio of the PE parameter of plasma acoramidis-AG (ng eq) to plasma TRA parameter (ng eq).
MPR C_{max} = (C_{max},acoramidis-AG / C_{max},acoramidis) x (MW,acoramidis / MW,acoramidis-AG)
MPR $AUC_{0-\infty}$ = ($AUC_{0-\infty}$,acoramidis-AG / $AUC_{0-\infty}$,acoramidis) x (MW,acoramidis / MW,acoramidis-AG)
NC = Not calculated; PE = Parent equivalent; MW = Molecular weight
Source: 5.3.3.1.3 項 AG10-007 CSR Tables 14.2.1.2.1 ~ 14.2.1.2.3

注：投与量は[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの血漿中アコラミジスの $AUC_{\%extrap}$ の算術平均値は 1%未満であり、PK プロファイルは良好に特徴付けられた。血漿中 AUC_{0-last} 及び $AUC_{0-\infty}$の幾何平均値は同程度で、それぞれ 133800 及び 134500 ng*hr/mL であり、血漿中 C_{max} の幾何平均値は 16260 ng/mL であった。t_{max} の中央値は 0.749 時間、$t_{1/2}$ の算術平均値は約 30.0 時間と推定された。また、血漿中アコラミジス及び血漿中 TRA の投与開始後 168 時間までの AUC（AUC_{0-168}）及び C_{max} の比（血漿中アコラミジス／血漿中 TRA）の算術平均値はそれぞれ 0.631 及び 0.551 であった。アコラミジスの CL/F 及び V_z/F の算術平均値はそれぞれ 5.430 L/hr 及び 230.7 L であった。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの血漿中アコラミジス-AG の $AUC_{\%extrap}$ の算術平均値は 1%未満であり、アコラミジス-AG の PK プロファイルは良好に特徴付けられた。血漿中 AUC_{0-last} 及び $AUC_{0-\infty}$の幾何平均値は同程度で、それぞれ 22810 及び 22850 ng*hr/mL であり（アコラミジス換算値［PE 値］はそれぞれ 14240 及び 14260 ng eq*hr/mL）、血漿中 C_{max} の幾何平均値は 9352 ng/mL であった（PE 値は 5836 ng eq/mL）。t_{max} の中央値は 0.997 時間であり、$t_{1/2}$ の算術平均値は約 17.4 時間と推定された。血漿中アコラミジス-AG 及び血漿中 TRA の投与開始後 96 時間までの AUC（AUC_{0-96}）及び C_{max} の比（血漿中アコラミジス-AG／血漿中 TRA）の算術平均値はそれぞれ約 0.0764 及び 0.202 であった。MPR $AUC_{0-\infty}$ 及び MPR C_{max} 値がそれぞれ約 0.127 及び 0.443 であることから示されるように、血漿中アコラミジス-AG 曝露量はアコラミジスよりも著しく低かった。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの血漿中 TRA の $AUC_{\%extrap}$ の算術平均は 5%未満であり、TRA の PK プロファイルは良好に特徴付けられた。血漿中 AUC_{0-last} 及び $AUC_{0-\infty}$の幾何平均値は同程度で、それぞれ 217300 及び 227000 ng eq*hr/mL であり、血漿中 C_{max} の幾何平均値は 30010 ng eq/mL であった。血漿中 TRA 曝露量（AUC 及び C_{max}）はアコラミジスとアコラミジス-AG の合計よりも大きく、更なる代謝物が生成されていることが示唆された。t_{max} の中央値は 0.755 時間で、これはアコラミジスの t_{max} と同程度であった。$t_{1/2}$ の算術平均値は約 69.7 時間と推定され、これはアコラミジス及びアコラミジス-AG のいずれの $t_{1/2}$ よりも長かった。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの尿中アコラミジス及びアコラミジス-AG の PK パラメータの要約を以下に示す。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの尿中アコラミジス及びアコラミジス-AG の PK パラメータの要約（PK 評価可能集団）

Pharmacokinetic Parameters	Acoramidis in Urine (N=6)	Acoramidis-AG in Urine (N=6)
CumAe (mg)	56.95 ± 22.244	353.6 ± 37.950
Cum%Dose (%)	7.939 ± 3.0816	30.786 ± 3.3369
CL_r (L/hr)	0.4302 ± 0.17777	15.61 ± 2.9958

Values presented as arithmetic mean ± SD.
The CL_r for Participants 1 and 2 was calculated using the acoramidis Ae and plasma AUC up to 216 hours. The CL_r for Participant 4 was calculated using the acoramidis Ae and AUC up to 192 hours. The CL_r for Participant 6 was calculated using the acoramidis Ae and plasma AUC up to 168 hours. The CL_r for Participants 3 and 5 was calculated using the acoramidis Ae and plasma AUC up to 144 hours.
The CL_r for Participants 1, 4, and 6 was calculated using the acoramidis-AG Ae and plasma AUC up to 144 hours. The CL_r for Participants 2 and 5 was calculated using the acoramidis-AG Ae and plasma AUC up to 120 hours. The CL_r for Participant 3 was calculated using the acoramidis-AG Ae and plasma AUC up to 96 hours.
Source: 5.3.3.1.3 項 AG10-007 CSR Tables 14.2.1.3.1, 14.2.1.3.2

注：投与量は[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの尿中アコラミジス及びアコラミジス-AG の CumAe の算術平均値はそれぞれ約 57 及び 354 mg であった。CLr の算術平均値は、アコラミジス-AG の方がアコラミジスよりも高かった（それぞれ約 15.6 及び 0.43 L/hr）。検体採取期間中全体で尿中に排泄されたアコラミジス及びアコラミジス-AG の Cum%Dose の算術平均値は、それぞれ投与量の約 7.9%及び 30.8%であった。
[^{14}C]-アコラミジス塩酸塩の尿中、糞便中及び尿糞中の TRA 累積回収量並びに TRA 累積回収率の要約を以下に示す。

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 µCi）を単回経口投与したときの総放射能回収率及びマスバランスの要約（PK 評価可能集団）

		Arithmetic Mean ± SD		
Parameter	Collection Interval (hrs)	Urine (N=6)	Feces (N=6)	Total (N=6)
CumAe (mg eq)	0-4	293.1 ± 50.514	NC	293.1 ± 50.514
	0-8	346.5 ± 43.659	NC	346.5 ± 43.659
	0-12	381.1 ± 46.877	NC	381.1 ± 46.877
	0-24	425.1 ± 47.400	20.59 ± 32.949	445.7 ± 54.856
	0-48	464.1 ± 44.649	51.88 ± 93.093	516.0 ± 99.027
	0-72	478.6 ± 45.292	183.5 ± 102.94	662.2 ± 67.455
	0-96	483.8 ± 47.281	204.4 ± 104.86	688.2 ± 68.552
	0-120	485.8 ± 47.863	230.4 ± 49.691	716.2 ± 17.169
	0-144	486.6 ± 48.031	244.2 ± 49.094	730.9 ± 9.9038
	0-168	487.1 ± 48.066	244.9 ± 49.888	732.0 ± 10.482
	0-192	487.4 ± 48.121	245.2 ± 49.954	732.6 ± 10.341
	0-216	487.5 ± 48.168	246.6 ± 48.211	734.1 ± 11.371
Cum%Dose (%)	0-4	40.880 ± 7.0044	NC	40.880 ± 7.0044
	0-8	48.340 ± 6.0818	NC	48.340 ± 6.0818
	0-12	53.156 ± 6.5079	NC	53.156 ± 6.5079
	0-24	59.299 ± 6.5939	2.885 ± 4.6251	62.184 ± 7.7675
	0-48	64.747 ± 6.1970	7.267 ± 13.0659	72.014 ± 14.0370
	0-72	66.768 ± 6.2758	25.622 ± 14.3759	92.390 ± 9.5624
	0-96	67.488 ± 6.5431	28.535 ± 14.6301	96.023 ± 9.7059
	0-120	67.764 ± 6.6197	32.143 ± 6.9487	99.907 ± 2.3911
	0-144	67.883 ± 6.6419	34.072 ± 6.8628	101.955 ± 1.2145
	0-168	67.944 ± 6.6461	34.168 ± 6.9723	102.112 ± 1.2881
	0-192	67.983 ± 6.6536	34.212 ± 6.9819	102.195 ± 1.2737
	0-216	68.009 ± 6.6599	34.401 ± 6.7370	102.410 ± 1.3731

NC = Not calculated
Source: 5.3.3.1.3 項 AG10-007 CSR Tables 14.2.1.4.1, 14.2.1.4.3

[^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したとき、尿中、糞便中及び尿糞中に投与した放射能量のそれぞれ約 68.0%、34.4%及び 102.4%が回収された。個々の被験者の TRA の回収率は 100.72%～104.16%の範囲であった。すべての被験者が投与 192～216 時間後の採取時点で退院基準を満たした。1 名を除くすべての被験者で、投与した放射能の大部分（算術平均値約 92.4%）が投与後最初の 72 時間の排泄物中に回収され、これは退院基準である「総投与放射能の 90%以上の排泄」よりも高かった。

安全性：

本試験中に死亡、重篤な有害事象及び中止に至った有害事象は認められなかった。1 名（17%）に計 5 件の有害事象が報告された。これらの有害事象はすべて軽度で、回復し、治験責任医師によって治験薬と関連なしと判断された。本試験では、臨床検査、バイタルサイン、心電図又は身体所見の結果に臨床的に注目すべき傾向は認められなかった。

結論：

薬物動態

- [^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したとき、尿中、糞便中及び尿糞中に投与した放射能量のそれぞれ約 68.0%、34.4%及び 102.4%が回収された。
- 未変化体の尿中への平均累積排泄割合は低く、投与量の約 7.9%であった。アコラミジス-AG の尿中への平均累積排泄割合は投与量の約 30.8%であった。
- [^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したとき、血漿中アコラミジスの $AUC_{0\text{-last}}$、$AUC_{0\text{-}\infty}$及び C_{max} の幾何平均値は、それぞれ 133800 ng*/mL、134500 ng*hr/mL 及び 16260 ng/mL であった。
- [^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したとき、血漿中アコラミジス-AG の $AUC_{0\text{-last}}$、$AUC_{0\text{-}\infty}$及び C_{max} の幾何平均値は、それぞれ 22810 ng*hr/mL、22850 ng*hr/mL 及び 9352 ng/mL であった。
- [^{14}C]-アコラミジス塩酸塩経口懸濁液 800 mg（約 450 μCi）を単回経口投与したとき、血漿中 TRA の $AUC_{0\text{-last}}$、$AUC_{0\text{-}\infty}$及び C_{max} の幾何平均値は、それぞれ 217300 ng eq*hr/mL、227000 ng eq*hr/mL 及び 30010 ng eq/mL であった。
- 血漿中 TRA の $AUC_{0\text{-}168}$ 及び C_{max} のそれぞれ約 63.1%及び 55.1%がアコラミジスであった。血漿中 TRA の $AUC_{0\text{-}96}$ 及び C_{max} のそれぞれ約 7.64%及び 20.2%がアコラミジス-AG であった。これらの結果から、TRA の総曝露量には他の循環血中代謝物が寄与していることが示唆された。
- 血漿中アコラミジスの t_{max} は、血漿中 TRA で認められた値（それぞれ 0.749 及び 0.755）と同程度であったが、血漿中アコラミジス-AG の t_{max} は血漿中 TRA に比べて遅延した（0.997 時間）。
- 血漿中アコラミジスの $t_{1/2}$（平均値約 30.0 時間）及びアコラミジス-AG の $t_{1/2}$（平均値約 17.4 時間）はいずれも血漿中 TRA の $t_{1/2}$（平均値約 69.7 時間）よりも短かったことから、TRA の総曝露量には他の循環代謝物が寄与していることが示唆された。
- 血漿中アコラミジス-AG の総曝露量はアコラミジスより低く、MPR $AUC_{0\text{-}\infty}$及び MPR C_{max} 値はそれぞれ約 0.127 及び 0.443 であった。
- TRA の B:P 比の算術平均値は約 0.49～0.52 の範囲であり、アコラミジス関連物質と全血の細

胞成分との結合はほとんど又は全くないと考えられた。

- アコラミジスは、AUC_{0-120}に該当する血漿プール抽出物に含まれるTRAの69.5%を占める主要放射能成分であった。主要代謝物はアコラミジス-β-D-グルクロニドであり、循環中 TRAの 13.54%を占めた。アコラミジス-β-D-グルクロニドは 2 つの異性体ピークとして溶出し、M468a（35.5 分で溶出）が血漿中 TRA の 4.76%、M468b（36.2 分で溶出）が 8.78%を占めた。これらの値は、TRA/液体クロマトグラフィー質量分析法（LC-MS/MS）のデータ（血漿中 TRA の AUC の約 63.1%及び 7.64%がそれぞれアコラミジス及びアコラミジス-AG であった）とよく一致している。血漿中の他の代謝物は、血漿中 TRA のそれぞれ 6%未満であった。
- 尿中の主要代謝物はアコラミジス-β-D-グルクロニドであり、投与量の 37.46%を占めた。アコラミジス-β-D-グルクロニドは 2 つの異性体ピークとして溶出し、M468a（34.4 分で溶出）が投与量の 2.52%、M468b（34.8 分で溶出）が投与量の 34.94%を占めた。アコラミジスは尿中で 2 番目に多い成分であり、投与量の 10.04%を占めた。これらの値は、TRA/LC-MS/MS データ（尿中に排泄されるアコラミジス及びアコラミジス-AG 平均累積排泄割合がそれぞれ投与量の約 7.9%及び 30.8%であった）とよく一致している。その他の尿中代謝物はいずれも投与量の 10%未満であった。
- 糞便中の主要放射能成分としてアコラミジスが検出され、投与量の 15.39%を占めた。M308（酸化体）は糞便中で 2 番目に多く、総投与量の 9.24%を占めた。糞便中の他の代謝物は、いずれも投与量のそれぞれ 5%未満であった。

安全性

- 本試験の健康男性被験者で、[^{14}C]-アコラミジス塩酸塩の単回経口投与の忍容性は良好であった。

報告書作成日：20[redacted]年[redacted]月[redacted]日（Errata 20[redacted]年[redacted]月[redacted]日、20[redacted]年[redacted]月[redacted]日）

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5　第 1 相試験【AG10-004】（海外）［評価資料］

5.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-004】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-004】

治験の標題：日本人及び外国人の健康成人被験者を対象に AG10 の安全性、忍容性及び薬物動態を検討する第 1 相、ランダム化、オープンラベル、2 期クロスオーバー、単回投与試験	
治験実施計画書番号：AG10-004	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の完了日：20[redacted] 年 [redacted] 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： 日本人及び外国人の健康成人被験者を対象に、アコラミジス塩酸塩を異なる 2 用量で投与したときの薬物動態（PK）を比較する。 副次目的： 日本人及び外国人の健康成人被験者を対象に、アコラミジス塩酸塩を異なる 2 用量で投与したときの安全性及び忍容性を比較する。	
方法： 本試験は、日本人及び外国人の健康成人被験者を対象に、アコラミジス塩酸塩を単回投与したときの PK を検討するオープンラベル、ランダム化、2 期クロスオーバー試験であった。本試験は、スクリーニング期、間に 7 日間のウォッシュアウトを含む 2 つの投与期及び追跡調査来院で構成された。検討用量は 400 及び 800 mg の 2 用量であり、スクリーニング期に適格性が確認された被験者を順序 1 又は順序 2 のいずれかにランダム割付けした。 • 順序 1：投与期 1 に 400 mg、投与期 2 に 800 mg のアコラミジス塩酸塩をそれぞれ単回経口投与 • 順序 2：投与期 1 に 800 mg、投与期 2 に 400 mg のアコラミジス塩酸塩をそれぞれ単回経口投与	
被験者数（計画時及び解析時）： 計画時：最大 20 名（日本人 10 名、外国人 10 名） 解析時：19 名（日本人 9 名、外国人 10 名）がランダム割付けされ、全 19 名が PK 解析対象集団及び安全性解析対象集団に含まれた。19 名中 18 名が試験を完了し、外国人 1 名は投与期 1 の投与（800 mg）後に有害事象（肉離れ、アコラミジス塩酸塩との関連なし）のために試験を中止した。	
診断及び組入れ基準： ［選択基準］ 以下のすべての基準を満たす被験者を本試験の組入れ対象とした。 1.　同意書に署名できる者。	

2. 同意書への署名時点で 18 歳以上 55 歳以下の男性又は女性。
3. 既往歴、身体所見、臨床検査、バイタルサイン及び心電図に基づき明らかに健康と判断される者。
4. 体格指数が 18 kg/m^2 以上 32.0 kg/m^2 以下かつ体重が 50 kg 以上の者。
5. 非喫煙者又は過去 6 ヵ月を超えて喫煙していない元喫煙者。
6. 男性で精管切除術を受けていない場合、試験期間中から治験薬の最終投与 90 日後まで殺精子剤付きコンドームを使用するか、性交渉を控えることに同意する者（治験薬の初回投与 4 ヵ月以上前に精管切除術を受けた男性は、この制限を設けない。精管切除術を受けた時期が治験薬の初回投与前 4 ヵ月未満の場合は、精管切除術を受けていない男性と同様の制限を設ける）。
7. 男性の場合、治験薬の初回投与から最終投与 90 日後まで精子を提供しないことに同意する者。
8. 女性の場合、治験薬の初回投与 6 ヵ月以上前に以下のいずれかの避妊術を受けている、妊娠の可能性がない者：
   - 子宮鏡下避妊術
   - 両側卵管結紮術又は両側卵管切除術
   - 子宮摘出術
   - 両側卵巣摘出術

   又は、治験薬の初回投与前 1 年以上無月経で、スクリーニング時の卵胞刺激ホルモン血清中濃度が閉経後の状態と一致する女性。
9. ［日本人被験者のみ］以下に定義される第一世代の日本人である者：
   - 日本生まれである。
   - 生物学上の両親 2 名及び生物学上の祖父母 4 名が日本人である。
   - 海外での生活が 5 年未満である。
   - 日本を離れてから、食事を含む生活習慣に大きな変化はない。

［除外基準］
以下のいずれかの基準に抵触する被験者は本試験から除外した。
1. スクリーニング来院時に精神的若しくは法的な能力がない、又は重大な感情的問題を有する者、又は試験実施中にそのような状態が予測される者。
2. 治験責任医師等の判断で、臨床的に重要な医学的若しくは精神的状態又は疾患の既往歴若しくは現病歴を有する者。
3. 治験責任医師等の判断で、試験結果に影響を及ぼす可能性がある、又は試験参加により被験者にさらなるリスクをもたらす可能性がある疾患の既往歴を有する者。
4. 治験薬の初回投与前 2 年以内にアルコール依存症又は薬物乱用の既往歴又は現病歴がある者。
5. 治験薬又は関連化合物に対する過敏症又は特異体質反応の既往歴又は現病歴を有する者。
6. スクリーニング時の心電図で第二度若しくは第三度房室ブロックを示す臨床的に重要な異常が認められた者、又は以下の 1 項目以上に該当する者：QRS が 110 msec 超、Fridericia 式を用いた補正 QC 間隔が 450 msec 超（男性及び女性）、PR 間隔が 220 msec 超。軽度の非特異的 T

波変化以外に、QT 解析を妨げる又は臨床的に重要であると治験責任医師等が判断した重大な形態学的変化（平坦 T 波を含む）が認められる。

7. 心筋梗塞、急性冠症候群、脳血管発作、一過性脳虚血発作、心室頻拍、心房細動の既往歴、先天性 QT 延長症候群の既往歴若しくは既知の家族歴、又は原因不明の突然死の既知の家族歴、ペースメーカー若しくは植込み型除細動器、心臓若しくは脳へのステント留置若しくは血管形成術、又は臨床的に重要な心臓弁膜症の既往歴を有する者。
8. 以下のいずれかの臨床検査値異常が認められる者：肝機能検査値（アラニンアミノトランスフェラーゼ、アスパラギン酸アミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限［ULN］超、トロポニンが ULN 超、甲状腺刺激ホルモンが ULN 超、クレアチニンクリアランスが基準値下限未満、スクリーニング時に臨床的に重要な低カリウム血症、低マグネシウム血症又は低カルシウム血症を有する者。
9. 妊娠する可能性のある女性。
10. 妊娠検査陽性又は授乳中の女性。
11. スクリーニング時又は初回入院時の尿中薬物又はアルコール検査結果が陽性の者。
12. スクリーニング時にヒト免疫不全ウイルス、B 型肝炎表面抗原又は C 型肝炎ウイルスの検査結果が陽性の者。
13. スクリーニング時の座位の収縮期血圧が 90 mmHg 未満、140 mmHg 超；拡張期血圧が 40 mmHg 未満、90 mmHg 超の者。
14. スクリーニング時の座位心拍数が 40 bpm 未満又は 99 bpm 超の者。
15. 治験薬の初回投与前 4 週間以内に、ホルモン補充療法を含む処方薬を使用した者。
16. Day -1 前の 7 日間又は半減期の 5 倍（いずれか長い方）以内に、ハーブ又は定期的にビタミン、ミネラル、若しくはその他のサプリメントを含む市販薬を使用した者、又は試験参加中に処方薬又は市販薬の継続的な使用を必要とする者。ランダム化後、治験責任医師等の判断でアセトアミノフェン（24 時間あたり 2 g まで）は投与可能とする。
17. 胆嚢摘出術の既往がある者。
18. 治験責任医師等の判断で、治験薬の初回投与前 30 日以内に試験期間中の食事内容と一致しない食事を摂っていた、又は試験期間中に摂る予定の者。
19. 治験薬の初回投与前 56 日以内に献血又は重大な失血をした者。
20. 治験薬の初回投与前 7 日以内に血漿を提供した者。
21. 治験薬の初回投与前 30 日以内に他の臨床試験に参加した者。30 日間の許容期間は、前の試験の最終採血日又は投与日のいずれか遅い方から本試験の投与期 1Day 1 までとする。

治験薬、用法・用量：

アコラミジス塩酸塩 200 mg フィルムコーティング錠として、400 及び 800 mg をそれぞれ単回経口投与した（ロット番号：[redacted]）。

治療期間：

各被験者の総試験期間は約 52 日間であった（スクリーニング 28 日間、2 回の投与、各単回投与間の 7 日間のウォッシュアウト、初回投与約 24 日後の追跡調査来院）。

評価項目：

主要評価項目

- 以下の PK パラメータを評価する：時間 0 から血漿中濃度測定可能最終時点までの濃度時間

曲線下面積（$AUC_{0\text{-}last}$）、時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0\text{-}\infty}$）、最高血漿中濃度（C_{max}）、最高血漿中濃度到達時間（t_{max}）、消失半減期（$t_{1/2}$）、みかけの全身クリアランス（CL/F）及びみかけの分布容積（V_d/F）

副次評価項目

- 以下の安全性項目を評価する：有害事象の発現頻度、臨床検査値、身体所見、バイタルサイン及び心電図

統計手法：

薬物動態：

PK は PK 解析対象集団を対象に解析し、その定義は治験実施計画書を遵守し、評価可能な PK プロファイルを有する（すなわち、治験薬が 1 回以上投与され、PK の測定値を有し、治験実施計画書からの重大な逸脱がない）被験者とした。PK パラメータは、要約統計量（平均値、標準偏差、変動係数%、中央値、最小値、最大値）を用いて要約した。関連するアコラミジス-アシルグルクロニド（アコラミジス-AG）の PK パラメータも同様に要約した。アコラミジス及びアコラミジス-AG の濃度時間曲線をグラフで示した。

安全性：

安全性は安全性解析対象集団を対象に解析し、その定義は治験薬が 1 回以上投与されたすべての被験者とした。安全性の評価は、有害事象の発現頻度、並びに身体所見、臨床検査、バイタルサイン及び心電図の変化に基づいて評価した。

結果の要約：

薬物動態：

アコラミジス塩酸塩 400 及び 800 mg を単回経口投与したとき、血漿中アコラミジス及びアコラミジス-AG 濃度の平均値は用量比例性を示さずに増加し、投与 48 時間後まで同様のプロファイルを維持すると考えられた。血漿中アコラミジス及びアコラミジス-AG 濃度は投与 48 時間後まで定量可能であった。

400 mg を投与したときの血漿中アコラミジス及びアコラミジス-AG 濃度プロファイルは、評価したすべての時点で日本人と外国人との間で同等であった。800 mg を投与したとき、アコラミジスの血漿中濃度の平均値は、投与 2 時間後まで日本人の方が外国人よりも高かったが、投与 4 時間後までに同等となり、投与 48 時間後まで同様であった。用量及び体重で補正した事後解析の結果、投与 2 時間後までの血漿中濃度時間プロファイルは日本人と外国人で類似していた。

アコラミジス塩酸塩 400 及び 800 mg を単回経口投与したときの $AUC_{0\text{-}last}$、$AUC_{0\text{-}\infty}$及び C_{max} の幾何平均値に基づくアコラミジスの曝露量は日本人と外国人で同程度であり、その幾何平均比（日本人／外国人）は 1.01～1.20 の範囲であった。アコラミジス-AG の曝露量の幾何平均比（日本人／外国人）は 1.18～1.46 の範囲であった。用量及び体重で補正したアコラミジス及びアコラミジス-AG の曝露量の幾何平均比はそれぞれ 0.85～1.00 及び 0.99～1.22 の範囲であった。

安全性：

本試験で重篤な有害事象又は死亡は報告されなかった。また、2 名以上に発現した有害事象はなく、治験薬との関連性が否定できない有害事象も認められなかった。有害事象の重症度は上気道感染及び肉離れが中等度であったほかは、いずれも軽度であった。外国人の 1 名では投与期 1 の

投与後に治験薬と関連のない有害事象（肉離れ）を発現し、投与期 2 の投与を受けることなく試験を中止した。臨床検査パラメータの平均値及びベースラインからの変化に臨床的に重要な変化は認められず、心電図及びバイタルサインにも臨床的に重要な変化は認められなかった。日本人と外国人でアコラミジス塩酸塩の安全性プロファイルに臨床的に意味のある差は認められなかった。

結論：

日本人と外国人との間でアコラミジスの PK プロファイルに意味のある差は認められなかった。アコラミジス塩酸塩 400 及び 800 mg 単回投与の忍容性は概して良好であり、安全性上の懸念は認められなかった。日本人と外国人の安全性プロファイルの間に臨床的に意味のある差は認められなかった。

報告書作成日：20[redacted] 年 [redacted] 月 [redacted] 日（Errata：20[redacted] 年 [redacted] 月 [redacted] 日、20[redacted] 年 [redacted] 月 [redacted] 日、20[redacted] 年 [redacted] 月 [redacted] 日）

5.2 有害事象

すべての有害事象を以下に示す。本試験で治験薬との関連性が否定できない有害事象、重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Table 14.3.1.2
治験薬との関連性が否定できない有害事象	Table 14.3.1.4（該当なし）
重篤な有害事象	該当なし
治験薬の投与中止に至った有害事象	該当なし

5.3 個別被験者の詳細

本試験で死亡又は重篤な有害事象は発現していないため、該当なし。

Eidos Therapeutics, Inc.
AG10-004

Table 14.3.1.2 Number (%) of Subjects with TEAEs by System Organ Class and Preferred Term by Dose and Race - Safety Population

	400 mg AG10		800 mg AG10	
MedDRA SYSTEM ORGAN CLASS PREFERRED TERM#	Japanese (N = 9)	Non-Japanese (N = 9)	Japanese (N = 9)	Non-Japanese (N = 10)
Subjects with at least one TEAE	0 (0.0%)	1 (11.1%)	1 (11.1%)	2 (20.0%)
耳および迷路障害	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)
耳鳴	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)
胃腸障害	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
悪心	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
感染症および寄生虫症	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
上気道感染	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
傷害、中毒および処置合併症	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
肉離れ	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (10.0%)
神経系障害	0 (0.0%)	1 (11.1%)	1 (11.1%)	0 (0.0%)
浮動性めまい	0 (0.0%)	0 (0.0%)	1 (11.1%)	0 (0.0%)
視野欠損	0 (0.0%)	1 (11.1%)	0 (0.0%)	0 (0.0%)

N = Number of subjects in specific group; n = Number of subjects with a particular AE; Calculation of percentages based on N.
# Coded according to MedDRA, version 21.1.
TEAE = Treatment Emergent Adverse event.
TEAEs are defined as AEs that increased in severity or newly developed during the treatment-emergent period.
A subject with more than one AE within a preferred term was counted once for each intensity category of the preferred term. A subject with more than one AE within a SOC was counted once for each intensity category of the SOC

SOURCE: t-14.3.1.2.sas

Eidos Therapeutics, Inc.
AG10-004

Table 14.3.1.4 Number (%) of Subjects with Drug-related TEAEs by Dose and Race - Safety Population

	400 mg AG10		800 mg AG10	
MedDRA SYSTEM ORGAN CLASS PREFERRED TERM#	Japanese (N = 9)	Non-Japanese (N = 9)	Japanese (N = 9)	Non-Japanese (N = 10)
There were no Subjects in this category				

N = Number of subjects in specific group; n = Number of subjects with a particular AE; Calculation of percentages based on N.
# Coded according to MedDRA, version 21.1.
TEAE = Treatment Emergent Adverse event.
TEAEs are defined as AEs that increased in severity or newly developed during the treatment-emergent period.
A subject with more than one AE within a preferred term was counted once for each intensity category of the preferred term. A subject with more than one AE within a SOC was counted once for each intensity category of the SOC

SOURCE: t-14.3.1.4.sas

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6　第 1 相試験【AG10-008】（海外）［参考資料］

6.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 1 相試験【治験実施計画書番号：AG10-008】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 1 相試験【治験実施計画書番号：AG10-008】

治験の標題：健康成人被験者を対象にアデホビル及びオセルタミビルカルボン酸の薬物動態に対するアコラミジスの影響を評価する第 1 相、オープンラベル、2 パート、2 期試験	
治験実施計画書番号：AG10-008	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：20[redacted] 年 [redacted] 月 [redacted] 日 最後の被験者の完了日：20[redacted] 年 [redacted] 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： Part 1： • 健康成人被験者を対象に、有機アニオントランスポーター（OAT）1 に対するアコラミジスの阻害作用を評価する。 Part 2： • 健康成人被験者を対象に、OAT 3 に対するアコラミジスの阻害作用を評価する。 副次目的： Part 1： • 健康成人被験者を対象に、アデホビル単回投与と併用したときのアコラミジス反復投与の安全性及び忍容性を評価する。 Part 2： • 健康成人被験者を対象に、オセルタミビル単回投与と併用したときのアコラミジス反復投与の安全性及び忍容性を評価する。	
方法： 本試験は、オープンラベル、2 パート、固定順序、2 期、薬物相互作用試験であった。両パートは並行して実施され、被験者はいずれかのパートのみに登録された。健康成人男女 32 名を登録した。 Part 1： 第 1 期の Day 1（Study Day 1）にアデホビルを単回投与した。アデホビルの薬物動態（PK）用検体を投与前及び投与 48 時間後（第 1 期 Day 3 = Study Day 3）まで採取した。 第 2 期では、アコラミジスを約 12 時間間隔（q12h）で 8 日間連続投与し（第 2 期 Day 1～8 = Study Day 3～10）、第 2 期 Day 7（Study Day 9）の朝にアデホビルを単回併用投与した。アデホビルの投与前及び投与 48 時間後まで PK 用検体を採取した（すなわち、第 2 期 Day 9 = Study Day 11 まで）。アコラミジス濃度評価用の血液検体は、第 2 期 Day 1、5～7 及び 9 の朝投与前に採取した（Study Day 3、7～9 及び 11）。	

Part 2：
第 1 期 Day 1（Study Day 1）にオセルタミビルを単回投与した。投与前及び投与 72 時間後（第 1 期 Day 4 = Study Day 4）まで、オセルタミビル及びその代謝物であるオセルタミビルカルボン酸の PK 用検体を採取した。
第 2 期では、アコラミジスを q12h で 9 日間連続投与し（第 2 期 Day 1～9 = Study Day 4～12）、第 2 期 Day 7（Study Day 10）の朝にオセルタミビルを単回併用投与した。オセルタミビル及びその代謝物オセルタミビルカルボン酸の PK 用検体を、投与前及びオセルタミビル投与 72 時間後（すなわち、第 2 期 Day 10 = Study Day 13）まで採取した。アコラミジス濃度評価用の血液検体は、第 2 期 Day 1、5～7 及び 10 の朝投与前に採取した（Study Day 4、8～10 及び 13）。
Part 1 及び Part 2：
治験薬が 1 回以上投与されたすべての被験者（試験を早期中止した被験者を含む）に対し、最終投与約 14 日後に連絡し、最終来院以降の有害事象の発現状況を確認した。安全性は、繰り返しの臨床評価及び臨床検査によって試験期間をとおしてモニタリングした。

被験者数（計画時及び解析時）：
計画時：32 名（Part 1：14 名、Part 2：18 名）
解析時 : 安全性解析対象集団 32 名（Part 1 : 14 名、Part 2 : 18 名）、PK 解析対象集団 32 名（Part 1：14 名、Part 2：18 名）、PK 評価可能集団 32 名（Part 1：14 名、Part 2：18 名）

診断及び組入れ基準：
［選択基準］
以下のすべての基準を満たす被験者を本試験の組入れ対象とした。
1. スクリーニング時に 19～55 歳の健康成人男女（妊娠の可能性がない女性*のみ）。
   *妊娠の可能性がない女性は以下のように定義される。
   - 治験薬の初回投与 6 ヵ月以上前に以下のいずれかの避妊術を受けている。
     - 子宮鏡下避妊術
     - 両側卵管結紮術又は両側卵管切除術
     - 子宮摘出術
     - 両側卵巣摘出術

   又は
   - 治験薬の初回投与前 1 年以上無月経であり、スクリーニング時の卵胞刺激ホルモンの血清中濃度が閉経後状態の基準を満たす閉経後の女性。
2. 男性被験者の場合、治験実施計画書に規定された避妊ガイダンスに従うことができる者。
3. 被験者の自己報告に基づき、治験薬初回投与前の少なくとも 3 ヵ月間、ニコチン含有製品を使用していない、また試験期間を通じて使用しない、継続的な非喫煙者。
4. スクリーニング時の体格指数が 18.0 kg/m^2 以上、32.0 kg/m^2 以下の者。
5. 医学的に健康であり、以下を含む臨床的に重要な病歴、身体所見、臨床検査プロファイル、バイタルサイン又は心電図所見がないと治験責任医師等が判断した者。
   - スクリーニング時の座位の収縮期血圧が 90 mmHg 以上、140 mmHg 以下、拡張期血圧が 40 mmHg 以上、90 mmHg 以下
   - スクリーニング時の座位心拍数が 40 bpm 以上、99 bpm 以下
   - Fridericia 式を用いた補正 QT 間隔が 460 msec 以下（男性）又は 470 msec 以下（女性）

であり、スクリーニング時に治験責任医師等が異常又は臨床的に重要と判断した心電図所見がない。

- Cockcroft-Gault 式を用いて算出したスクリーニング時の推算クレアチニンクリアランスが 90 mL/min 以上。
- スクリーニング時及び入院時の肝機能検査（すなわち、アラニンアミノトランスフェラーゼ、アスパラギン酸アミノトランスフェラーゼ、アルカリホスファターゼ、総ビリルビン）が基準値上限（ULN）以下；スクリーニング時及び入院時のマグネシウム、カルシウム及びカリウムが基準値下限以上；スクリーニング時の甲状腺刺激ホルモンが ULN 以下。

6. 同意説明文書の試験手順を理解し、治験実施計画書を遵守する意思及び能力がある者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. 治験責任医師等の判断で、スクリーニング時に精神的若しくは法的な能力がない又は重大な情緒的問題を有する、あるいは試験実施中にそのような状態になることが予想される者。
2. 治験責任医師等の判断で、臨床的に重要な医学的若しくは精神的状態又は疾患の既往歴若しくは現病歴を有する者。
3. 治験責任医師等の判断で、試験結果に影響を及ぼす可能性がある又は試験参加により被験者にさらなるリスクをもたらす可能性がある疾患の既往歴を有する者。
4. 被験者の自己報告に基づき、治験薬の初回投与前 2 年以内にアルコール依存症又は薬物乱用の既往歴又は現病歴を有する者。
5. 治験薬又は関連化合物に対する過敏症又は特異体質反応の既往歴又は現病歴を有する者。
6. 心筋梗塞、急性冠症候群、脳血管発作、一過性脳虚血発作、心室頻拍、心房細動の既往歴若しくは現病歴、先天性 QT 延長症候群の既往歴若しくは既知の家族歴又は原因不明の突然死の既知の家族歴、ペースメーカー若しくは植込み型除細動器、心臓若しくは脳のステント留置若しくは血管形成術又は臨床的に重要な心臓弁膜症の既往歴を有する者。
7. 治験薬の吸収、代謝及び／又は排泄に影響を及ぼす可能性のある疾患又は処置の既往歴（胃又は腸の手術若しくは切除、経頸静脈的肝内門脈大循環シャント又は外科的シャントの既往歴を含む）を有する者。合併症を伴わない虫垂切除、胆嚢摘出及びヘルニア修復は許容される。
8. 妊娠可能な女性。
9. スクリーニング時又は入院時の妊娠検査で陽性又は授乳中の女性。
10. スクリーニング時又は入院時の尿中薬物乱用又はアルコール検査結果が陽性の者。
11. スクリーニング時にヒト免疫不全ウイルス、B 型肝炎表面抗原又は C 型肝炎ウイルスの検査結果が陽性の者。
12. 治験薬の初回投与前 4 週間以内に、ホルモン補充療法を含む処方薬を使用した者。
13. Day -1 前 7 日以内又は半減期の 5 倍の期間内（いずれか長い方）に、ハーブ、定期的なビタミン、ミネラル若しくはその他のサプリメントを含む何らかの市販薬を使用した者又は試験参加中に処方薬又は市販薬の継続的な使用を必要とする者。ただし、治験薬の初回投与後、治験責任医師等の判断でアセトアミノフェン（24 時間あたり 2 g まで）は投与可能とする。
14. 治験責任医師等の判断で、治験薬の初回投与前 30 日以内に、試験の食事内容と一致しない

食事を摂取していた者。

15. 治験薬の初回投与前 56 日以内に献血又は大量失血した者。
16. 治験薬の初回投与前 7 日以内に血漿を提供した者。
17. 治験薬の初回投与前 30 日以内に他の臨床試験に参加した者。30 日間とは、前の試験の最終採血日又は投与日のいずれか遅い方から本試験の第 1 期 Day 1（Study Day 1）までの期間とする。

Part 1 のみ：

18. 乳酸アシドーシスの既往歴を有する者。

Part 2 のみ：

19. 遺伝性フルクトース不耐症の既往歴を有する者。
20. 中毒性表皮壊死融解症、スティーヴンス・ジョンソン症候群、多形紅斑などの重篤な皮膚反応の既往歴又は所見を有する者。

治験薬、用法・用量：

アコラミジス：アコラミジス塩酸塩錠 400 mg、ロット番号：[redacted]

アデホビル：Hepsera®（アデホビルジピボキシル 10 mg 錠）、ロット番号：[redacted]

オセルタミビル：Tamiflu®（オセルタミビルリン酸塩カプセル 75 mg）、ロット番号：[redacted]

すべての被験薬は、以下の投与に従って約 240 mL の水とともに経口投与した。

Part 1

投与 A：第 1 期 Day 1 の 0 時間目にアデホビル 10 mg（1 × 10 mg）を投与する。

投与 B：第 2 期 Day 1～8 に q12h でアコラミジス 712 mg（2 × 356 mg［アコラミジス塩酸塩 400 mg に相当］）を投与し、Day 7 の朝（0 時間目）にはアデホビル 10 mg（1 × 10 mg）を併用投与する。

Part 2

投与 C：第 1 期 Day 1 の 0 時間目にオセルタミビル 75 mg（1 × 75 mg）を投与する。

投与 D：第 2 期 Day 1～9 に q12h でアコラミジス 712 mg（2 × 356 mg［アコラミジス塩酸塩 400 mg に相当］）を投与し、Day 7 の朝（0 時間目）にはオセルタミビル 75 mg（1 × 75 mg）を併用投与する。

治療期間：

各被験者の試験期間は Part 1 で約 39 日、Part 2 で約 41 日であった。

評価項目：

主要評価項目：

Part 1：アコラミジス反復投与前及び後にアデホビルを投与したときのアデホビルの時間 0 から血漿中濃度測定可能最終時点（t）までの濃度時間曲線下面積（AUC_{0-t}）、時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0-\infty}$）及び最高血漿中濃度（C_{max}）。

Part 2：アコラミジス反復投与前及び後にオセルタミビルを投与したときのオセルタミビルカルボン酸の AUC_{0-t}、$AUC_{0-\infty}$及び C_{max}。

副次評価項目：

Part 1：治験薬投与後に発現した有害事象、12 誘導心電図、バイタルサイン及び臨床検査。

Part 2：治験薬投与後に発現した有害事象、12 誘導心電図、バイタルサイン及び臨床検査。

統計手法：

薬物動態：

PK 解析対象集団には、治験薬が 1 回以上投与され、PK 血液検体が 1 つ以上採取され、評価可能な血漿中濃度を 1 つ以上有する被験者を含めた。

PK 評価可能集団には、PK 解析対象集団のうち、治験実施計画書から重大な逸脱のない、評価可能な PK プロファイルを有する被験者を含めた。PK パラメータの要約統計量を含む統計解析は PK 評価可能集団を対象に行った。

アデホビル、オセルタミビル、オセルタミビルカルボン酸及びアコラミジスの血漿中濃度を一覧に示し、PK 解析対象集団の全被験者に対して試験パート、投与及び測定時点別に要約した。すべての名目上の濃度時点に対して、n、算術平均値、標準偏差（SD）、変動係数（CV%）、平均値の標準誤差（SEM）、最小値、中央値及び最大値を含む要約統計量を算出した。PK 評価可能集団から除外された被験者は濃度一覧表に含めたが、要約統計量からは除外し、その旨を表に記載した。濃度一覧表では、定量下限値未満（BLQ）の値はすべて「BLQ」と表記し、その旨を脚注に記載した。

アデホビル、オセルタミビル及びオセルタミビルカルボン酸の血漿中濃度-時間プロファイルの平均値及び個別データを線形スケール及び片対数スケールで示した。血漿中アコラミジスのトラフ濃度（C_{trough}）-時間プロファイルの平均値も各試験パート別に線形スケールで示した。線形平均プロットは SD の有無別に示した。個々の血漿中アコラミジスの C_{trough}-時間プロファイルのスパゲッティ・プロットを線形スケールで示した。

血漿中 PK パラメータは、最高血漿中濃度到達時間（t_{max}）及び定量可能な濃度が検出された最終時点（t_{last}）は小数点以下第 2 位まで、その他のパラメータは有効数字 3 桁で表示した。血漿中アデホビル、オセルタミビル及びオセルタミビルカルボン酸の PK パラメータの要約統計量（n、算術平均値、SD、CV%、SEM、最小値、中央値、最大値、幾何平均値及び幾何 CV%）を算出した。PK 評価可能集団から除外された被験者は要約統計量からは除外し、その旨を記載した。

<u>PK パラメータの統計解析</u>

各試験パートで、SAS®の PROC MIXED を用いた分散分析（ANOVA）モデルによって、自然対数（ln）に変換した PK パラメータの比較を行った。比較には AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} を用いた。ANOVA モデルには、投与を固定効果、被験者を変量効果として含め、同じ被験者の対応する測定値間の関係を検討した。推測結果（最小二乗平均値［LSM］、LSM 間の差及び差の 90%信頼区間）を元のスケールに指数変換した。幾何 LSM、幾何平均比（GMR）及び 90%信頼区間を示した。信頼区間は、投与 A（Part 1、アデホビル単独）又は投与 C（Part 2、オセルタミビル単独）に対する割合として示した。以下の比較を実施した。

Part 1：

- アデホビル：アコラミジス q12h＋アデホビル（投与 B）とアデホビル単独（投与 A）の比較
  注：Part 1 では、投与 B の $AUC_{0-\infty}$の外挿部分の割合（$AUC_{\%extrap}$）が 20%を超えた被験者の血漿中アデホビル $AUC_{0-\infty}$を含めた場合と除外した場合の 2 回の ANOVA を実施した。

Part 2：

- オセルタミビル及びオセルタミビルカルボン酸：アコラミジス q12h＋オセルタミビル（投与 D）とオセルタミビル単独（投与 C）の比較

<u>定常状態解析</u>

血漿中アコラミジスの C_{trough} 値を試験パートごとに集計・プロットし、定常状態の濃度に達して

いることを目視で確認した。

安全性：

安全性解析対象集団には、治験薬が 1 回以上投与された被験者を含めた。

すべての安全性及び忍容性データは、被験者及び評価時点別に一覧にした。連続変数は n、算術平均値、SD、最小値、中央値及び最大値を用いて要約した。カテゴリーデータは適宜頻度を示した。本試験で発現したすべての有害事象は、ICH 国際医薬用語集 （MedDRA ®）Version 24.1 を用いてコード化した。データベースに記録されたすべての有害事象に対して、報告用語、器官別大分類、基本語、発現時期、重篤度、重症度、治験責任医師が評価した治験薬との因果関係、治験薬以外の薬剤との因果関係、治験薬に対する処置及び治験薬以外の薬剤に対する処置を含む被験者別のデータ一覧表に示した。ただし、要約表には治験薬投与後に発現した有害事象のみを含めた。すべての臨床検査値（数値）は、評価時点及びパート別に要約統計量を示し、ベースラインからの変化量も同様に要約した。各臨床検査は、結果（高値、低値、正常）の頻度のシフトテーブルを作成し、ベースラインからの変化を要約した。バイタルサイン及び 12 誘導心電図は各パートの評価時点での測定値及びベースラインからの変化の要約統計量を算出した。試験中に記録されたすべての前治療薬及び併用薬は、World Health Organization（WHO）Dictionary Version 01-SEP-2021 b 3 を用いてコード化し、一覧表を作成した。

結果の要約：

薬物動態：

Part 1

血漿中アデホビルの PK パラメータの要約を以下に示す。

アデホビル 10 mg 単独投与時（投与 A）及びアコラミジス 712 mg q12h + アデホビル 10 mg 併用投与時（投与 B）の血漿中アデホビルの PK パラメータの要約－Part 1（PK 評価可能集団）

Pharmacokinetic Parameters	Adefovir Alone	Acoramidis Q12h + Adefovir
AUC_{0-t} (ng*hr/mL)	217.1 (26.0) [n=14]	247.0 (25.1) [n=11]
$AUC_{0-\infty}$ (ng*hr/mL)	227.1 (26.0) [n=14]	256.5 (24.1) [n=11]
$AUC_{\%extrap}$ (%)	4.374 ± 1.0665 [n=14]	3.708 ± 1.2960 [n=11]
C_{max} (ng/mL)	18.42 (19.7) [n=14]	17.03 (24.0) [n=13]
C_{last} (ng/mL)	0.7830 (32.8) [n=14]	0.7031 (25.4) [n=11]
T_{max} (hr)	0.752 (0.57, 1.50) [n=14]	2.000 (0.75, 6.00) [n=13]
T_{last} (hr)	36.046 (36.00, 47.89) [n=14]	47.999 (35.85, 48.02) [n=11]
λ_z (1/hr)	0.08187 ± 0.012498 [n=14]	0.08018 ± 0.017527 [n=11]
$t_{½}$ (hr)	8.659 ± 1.3765 [n=14]	9.030 ± 1.9894 [n=11]
CL/F (L/hr)	24.73 ± 6.2941 [n=14]	21.78 ± 4.9346 [n=11]
V_z/F (L)	304.3 ± 70.971 [n=14]	280.4 ± 74.378 [n=11]

Adefovir Alone: 10 mg adefovir (1 x 10 mg adefovir dipivoxil tablet) at Hour 0 on Day 1 of Period 1
Acoramidis Q12h + Adefovir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 8 with 10 mg adefovir (1 x 10 mg adefovir dipivoxil tablet) coadministered in the morning at Hour 0 on Day 7 of Period 2
AUCs, C_{max}, and C_{last} are presented as geometric mean (geometric CV%).
T_{max} and T_{last} are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
Participants 12 and 14 were excluded from summary statistics for AUC_{0-t}, C_{last}, and T_{last} for Acoramidis Q12h + Adefovir since both participants had truncated PK profiles.
Participant 14 had $AUC_{\%extrap}$ > 20% for Acoramidis Q12h + Adefovir, and therefore, was excluded from summary statistics for $AUC_{0-\infty}$, $AUC_{\%extrap}$, λ_z, $t_{½}$, CL/F, and V_z/F.
n = Sample size; Q12h = Every 12 hours; λ_z = Apparent first-order terminal elimination rate constant.
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.1.2.1, Table 14.2.1.2.2

血漿中アデホビルのPKプロファイルが明らかとなり、両投与後の$AUC_{\%extrap}$の算術平均値は4.5%未満であった。アコラミジス q12h + アデホビルを併用投与したとき、アデホビル単独投与したときの値と比較して、血漿中 AUC の幾何平均値は 10%をわずかに上回ったが、血漿中 C_{max} 及び t_{last} に相当する最終測定可能濃度（C_{last}）の幾何平均値は同程度であった。t_{max} の中央値と t_{last} の中央値はいずれも、アコラミジス q12h + アデホビル併用投与時（それぞれ 2 時間及び約 48 時間）の方がアデホビル単独投与時（それぞれ約 0.75 時間及び約 36 時間）よりも遅かったが、t_{last} の範囲は両投与で類似していた（約 36～48 時間；すなわち、最後の 2 測定時点）。終末相の消失半減期（$t_{1/2}$）、みかけの全身クリアランス（CL/F）及び終末相のみかけの分布容積（V_z/F）の算術平均値は両投与で同程度であった。

血漿中アデホビルの PK パラメータの統計学的比較を以下に示す。

アコラミジス 712 mg q12h + アデホビル 10 mg 併用投与時（投与 B）とアデホビル 10 mg 単独投与時（投与 A）の血漿中アデホビルの PK パラメータの統計学的比較の要約－Part 1（PK 評価可能集団）

	Acoramidis Q12h + Adefovir (Test)		Adefovir Alone (Reference)				
Pharmacokinetic Parameter	**Geometric LSM**	**n**	**Geometric LSM**	**n**	**GMR (%)**	**90% Confidence Interval**	**Intra-participant CV%**
AUC_{0-t} (ng*hr/mL)	259.4	11	217.1	14	119.45	110.55 - 129.06	10.09
$AUC_{0-\infty}$ (ng*hr/mL)	269.4	11	227.1	14	118.63	110.30 - 127.59	9.48
C_{max} (ng/mL)	16.99	13	18.42	14	92.27	83.51 - 101.94	14.48

Acoramidis Q12h + Adefovir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 8 with 10 mg adefovir (1 x 10 mg adefovir dipivoxil tablet) coadministered in the morning at Hour 0 on Day 7 of Period 2 (Test)
Adefovir Alone: 10 mg adefovir (1 x 10 mg adefovir dipivoxil tablet) at Hour 0 on Day 1 of Period 1 (Reference)
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio (GMR) = 100 x (Test/Reference)
Intra-participant CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
Participants 12 and 14 were excluded from statistical comparison for AUC_{0-t} for Acoramidis Q12h + Adefovir since both participants had truncated PK profiles.
Participant 14 was excluded from the statistical comparison for $AUC_{0-\infty}$ for Acoramidis Q12h + Adefovir, because $AUC_{\%extrap}$ > 20%.
CV% = Coefficient of variation; GMR = Geometric mean ratio; n = Sample size; Q12h = Every 12 hours
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.1.2.5

アコラミジス q12h + アデホビルを併用投与したとき、血漿中アデホビルの AUC_{0-t} 及び $AUC_{0-\infty}$の幾何 LSM 値は、アデホビル単独投与したときと比較していずれも約 19%高く、90%信頼区間は影響がないと判断される範囲（80%～125%）からわずかに外れた。血漿中アデホビルの C_{max} は両投与で同程度であり、C_{max} の GMR の 90%信頼区間は影響がないと判断される範囲（80%～125%）の範囲内であった。

1 名では、併用投与時の $AUC_{\%extrap}$ が 20%を超えたため、当該被験者は $AUC_{0-\infty}$の比較解析から除外したが、当該被験者を含めた場合の血漿中 $AUC_{0-\infty}$はアデホビル単独投与時と比較して約 16%大きかった。したがって、当該被験者を解析に含めるか否かにかかわらず、統計学的結論は類似していた。なお、当該被験者では、第 2 期の最後の採取検体が投与 12 時間後であったため、$AUC_{0-\infty}$ 値の頑健な推定値が得られなかった。

Part 2：

オセルタミビルカルボン酸の血漿中 PK パラメータの要約を以下に示す。

オセルタミビル 75 mg 単独投与時（投与 C）及びアコラミジス 712 mg q12h + オセルタミビル 75 mg 投与時（投与 D）の血漿中オセルタミビルカルボン酸の PK パラメータの要約－Part 2（PK 評価可能集団）

Pharmacokinetic Parameters	Oseltamivir Alone	Acoramidis Q12h + Oseltamivir
AUC_{0-t} (ng*hr/mL)	3135 (17.4) [n=18]	3261 (19.1) [n=18]
$AUC_{0-\infty}$ (ng*hr/mL)	3229 (16.7) [n=18]	3343 (18.3) [n=18]
$AUC_{\%extrap}$ (%)	2.906 ± 1.4952 [n=18]	2.449 ± 1.1057 [n=18]
C_{max} (ng/mL)	291.0 (22.8) [n=18]	271.3 (27.7) [n=18]
C_{last} (ng/mL)	8.511 (38.1) [n=18]	7.301 (27.6) [n=18]
T_{max} (hr)	3.757 (3.00, 6.00) [n=18]	5.497 (3.00, 7.07) [n=18]
T_{last} (hr)	36.016 (24.02, 48.00) [n=18]	35.864 (35.84, 47.91) [n=18]
λ_z (1/hr)	0.1023 ± 0.017933 [n=18]	0.09999 ± 0.019792 [n=18]
$t_{½}$ (hr)	6.976 ± 1.2865 [n=18]	7.257 ± 1.8137 [n=18]
MPR $AUC_{0-\infty}$	28.38 ± 6.2162 [n=18]	24.28 ± 5.8830 [n=18]
MPR C_{max}	6.423 ± 2.7288 [n=18]	7.391 ± 2.6229 [n=18]

Oseltamivir Alone: 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) at Hour 0 on Day 1 of Period 1
Acoramidis Q12h + Oseltamivir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 9 with 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) coadministered in the morning at Hour 0 on Day 7 of Period 2
AUCs, C_{max}, and C_{last} are presented as geometric mean (geometric CV%).
T_{max} and T_{last} are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
n = Sample size; Q12h = Every 12 hours
MPR = Metabolite-to-parent ratio
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.2.4.1, Table 14.2.2.4.2

オセルタミビルカルボン酸の血漿中 PK プロファイルは十分に明らかにされ、両投与後の $AUC_{\%extrap}$ の算術平均値は 3%未満であった。アコラミジス q12h + オセルタミビル併用投与時の血漿中 AUC 及び C_{max} の幾何平均値は、オセルタミビル単独投与時の値と同程度であった。t_{max} の中央値は、アコラミジス q12h + オセルタミビル併用投与時（約 5.5 時間）の方が、オセルタミビル単独投与時（約 3.8 時間）よりも長かった。

血漿中オセルタミビルカルボン酸の PK パラメータの統計学的比較を以下に示す。

アコラミジス 712 mg q12h + オセルタミビル 75 mg 併用投与時（投与 D）とオセルタミビル 75 mg 単独投与時（投与 C）の血漿中オセルタミビルカルボン酸の PK パラメータの統計学的比較の要約－Part 2（PK 評価可能集団）

	Acoramidis Q12h + Oseltamivir (Test)		Oseltamivir Alone (Reference)				
Pharmacokinetic Parameter	Geometric LSM	n	Geometric LSM	n	GMR (%)	90% Confidence Interval	Intra-participant CV%
AUC_{0-t} (ng*hr/mL)	3261	18	3135	18	104.02	99.92 - 108.28	6.94
$AUC_{0-\infty}$ (ng*hr/mL)	3343	18	3229	18	103.52	99.44 - 107.78	6.95
C_{max} (ng/mL)	271.3	18	291.0	18	93.23	88.32 - 98.42	9.35

Acoramidis Q12h + Oseltamivir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 9 with 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) coadministered in the morning at Hour 0 on Day 7 of Period 2 (Test)
Oseltamivir Alone: 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) at Hour 0 on Day 1 of Period 1 (Reference)
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio (GMR) = 100 x (Test/Reference)
Intra-participant CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
CV% = Coefficient of variation; GMR = Geometric mean ratio; n = Sample size; Q12h = Every 12 hours
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.2.4.5

アコラミジス q12h + オセルタミビル併用投与時の血漿中オセルタミビルカルボン酸の AUC_{0-t}、$AUC_{0-\infty}$及び C_{max} は、オセルタミビル単独投与時の値と同程度であった（評価したすべてのパラメータの GMR の 90%信頼区間は、影響がないと判断される範囲の 80%～125%の範囲内であった）。

血漿中オセルタミビルの PK パラメータの要約を以下に示す。

オセルタミビル 75 mg 単独投与時（投与 C）及びアコラミジス 712 mg q12h + オセルタミビル 75 mg 併用投与時（投与 D）の血漿中オセルタミビルの PK パラメータの要約－Part 2（PK 評価可能集団）

Pharmacokinetic Parameters	Oseltamivir Alone	Acoramidis Q12h + Oseltamivir
AUC_{0-t} (ng*hr/mL)	125.3 (24.3) [n=18]	151.7 (25.3) [n=18]
$AUC_{0-\infty}$ (ng*hr/mL)	127.5 (24.1) [n=18]	155.2 (25.0) [n=18]
$AUC_{\%extrap}$ (%)	1.743 ± 0.55256 [n=18]	2.214 ± 0.87756 [n=18]
C_{max} (ng/mL)	54.24 (52.9) [n=18]	43.10 (46.6) [n=18]
C_{last} (ng/mL)	0.7030 (25.4) [n=18]	0.7073 (29.9) [n=18]
T_{max} (hr)	0.696 (0.25, 4.00) [n=18]	0.998 (0.50, 5.00) [n=18]
T_{last} (hr)	12.000 (8.00, 16.05) [n=18]	16.000 (10.06, 23.93) [n=18]
λ_z (1/hr)	0.3579 ± 0.13064 [n=18]	0.2476 ± 0.11561 [n=18]
$t_{½}$ (hr)	2.264 ± 1.0031 [n=18]	3.559 ± 1.8953 [n=18]
CL/F (L/hr)	604.9 ± 158.38 [n=18]	497.6 ± 126.36 [n=18]
V_z/F (L)	1903 ± 778.76 [n=18]	2476 ± 1389.5 [n=18]

Oseltamivir Alone: 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) at Hour 0 on Day 1 of Period 1
Acoramidis Q12h + Oseltamivir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 9 with 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) coadministered in the morning at Hour 0 on Day 7 of Period 2
AUCs, C_{max}, and C_{last} are presented as geometric mean (geometric CV%).
T_{max} and T_{last} are presented as median (minimum, maximum).
Other parameters are presented as arithmetic mean ± SD.
n = Sample size; Q12h = Every 12 hours
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.2.2.1, Table 14.2.2.2.2

血漿中オセルタミビルの PK プロファイルは十分に明らかにされ、両投与後の $AUC_{\%extrap}$ の算術平均値は 2.5%未満であった。アコラミジス q12h + オセルタミビル併用投与したとき、オセルタミビル単独投与したときの値と比較して、血漿中 AUC の幾何平均値は約 20%高く、血漿中 C_{max} の幾何平均値は約 20%低かった。アコラミジス q12h + オセルタミビル併用投与時とオセルタミビル単独投与時の t_{max} 及び t_{last} の中央値はいずれも同程度であった。アコラミジス q12h + オセルタミビル併用投与したとき、オセルタミビル単独投与時と比較して、$t_{1/2}$ 及び V_z/F の算術平均値は高かったが、CL/F 値は低かった。
血漿中オセルタミビルの PK パラメータの統計学的比較を以下に示す。

アコラミジス 712 mg q12h + オセルタミビル 75 mg 併用投与時（投与 D）とオセルタミビル 75 mg 単独投与時（投与 C）の血漿中オセルタミビルの PK パラメータの統計学的比較の要約－Part 2（PK 評価可能集団）

	Acoramidis Q12h + Oseltamivir (Test)		Oseltamivir Alone (Reference)				
Pharmacokinetic Parameter	Geometric LSM	n	Geometric LSM	n	GMR (%)	90% Confidence Interval	Intra-participant CV%
AUC_{0-t} (ng*hr/mL)	151.7	18	125.3	18	121.07	114.04 - 128.53	10.34
$AUC_{0-\infty}$ (ng*hr/mL)	155.2	18	127.5	18	121.66	114.67 - 129.07	10.23
C_{max} (ng/mL)	43.10	18	54.24	18	79.46	69.03 - 91.46	24.62

Acoramidis Q12h + Oseltamivir: 712 mg acoramidis (2 x 356 mg acoramidis tablets [equivalent to 400 mg acoramidis HCl]) administered q12h on Days 1 to 9 with 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) coadministered in the morning at Hour 0 on Day 7 of Period 2 (Test)
Oseltamivir Alone: 75 mg oseltamivir (1 x 75 mg oseltamivir phosphate capsule) at Hour 0 on Day 1 of Period 1 (Reference)
Geometric least-squares means (LSMs) are calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio (GMR) = 100 x (Test/Reference)
Intra-participant CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
CV% = Coefficient of variation; GMR = Geometric mean ratio; n = Sample size; Q12h = Every 12 hours
Source: 5.3.3.4.1 項 AG10-008 CSR Table 14.2.2.2.5

アコラミジス q12h + オセルタミビル併用投与後、オセルタミビル単独投与後と比較して、血漿中オセルタミビルの AUC_{0-t} 及び $AUC_{0-\infty}$はそれぞれ約 21%及び約 22%高かったが、C_{max} は約 21%低かった。AUC の GMR の 90%信頼区間は、影響がないと判断される範囲（80%～125%）からわずかに外れたのみであったが、C_{max} 比は明らかに範囲外であった。

安全性：

Part 1

本試験の Part 1 で死亡及び重篤な有害事象は認められなかった。中止に至った有害事象は 3 名に発現し、その内訳は 2 名（14%）が治験薬との関連性がない軽度の COVID-19 感染、1 名（7%）が治験薬との関連性が否定できないと判断された軽度の上腹部痛であった。治験責任医師によると、被験者は投与継続可能であったが、投与中止を決定した。全体で軽度な有害事象が 5 名（36%）に計 7 件発現した。2 名（14%）に発現した 2 件の有害事象（上腹部痛 1 名、頭痛 1 名）は治験薬との関連性が否定できないと判断され、残りの 5 件の有害事象は関連なしと判断された。
頭痛が発現した 1 名（7%）では頭痛は 2 件報告され、このうち 1 件はアコラミジス q12h 投与後に発現し、治験薬と関連なしと判断され、1 件はアコラミジス q12h + アデホビル併用投与後に発現し、治験薬との関連性が否定できないと判断された。いずれの頭痛も軽度であった。
試験終了時に軽快と判断された COVID-19 感染の 1 件を除き、すべての有害事象は回復した。本試験の Part 1 では、臨床検査、バイタルサイン、心電図及び身体所見の結果に臨床的に注目すべき傾向は認められなかった。

Part 2

本試験の Part 2 では、死亡、重篤な有害事象及び中止に至った有害事象は認められなかった。全体で 7 名（39%）に計 17 件の有害事象が認められた。軽度の頭痛は 2 名（11%）に 4 件認められ、このうち 1 名（6%）で 3 件認められた。当該 3 件のうち 2 件はアコラミジス q12h 投与後に発現し、治験薬との関連性が否定できないと判断され、残りの 1 件はオセルタミビル単独投与後に発現し、治験薬と関連なしと判断された。別の 1 名（6%）では、軽度の頭痛がアコラミジス q12h 投与後に発現し、治験薬との関連性が否定できないと判断された。
悪心は 1 名（6%）に 3 件認められ、このうち 2 件はアコラミジス q12h 投与後に発現し、1 件はアコラミジス q12h + オセルタミビル投与後に発現した。悪心のうち 1 件は中等度であり、Day 4 に治験薬の投与を 1 回中断した後、投与を再開した。残りの 2 件の悪心は軽度であり、悪心は 3 件ともすべて治験薬との関連性が否定できないと判断された。当該被験者ではその他にアコラミジス q12h 投与後に軽度の下痢が 1 件、アコラミジス q12h +オセルタミビル投与後に軽度の嘔吐が 1 件報告された。いずれの事象も治験薬との関連性が否定できないと判断された。その他に悪心、嘔吐及び下痢の有害事象が報告された被験者はいなかった。
Part 2 で認められたその他の有害事象はすべて治験薬と関連なしと判断された。本試験の Part 2 で発現したすべての有害事象は試験終了時までに回復した。臨床検査、バイタルサイン、心電図又は身体所見の結果に臨床的に注目すべき傾向は認められなかった。

結論：

薬物動態

Part 1

- アコラミジス q12h + アデホビル併用投与時、アデホビルの総曝露量（AUC_{0-t} 及び $AUC_{0-\infty}$に基づく）は、アデホビル単独投与と比較して約 19%高かったが、アデホビルの最高曝露量（C_{max} に基づく）は同程度であった。これらのデータに基づき、アコラミジスは検討した用量で OAT1 に対してわずかな阻害作用を示すと結論された。
- アコラミジス q12h + アデホビル併用投与時の血漿中アデホビルの $t_{1/2}$（算術平均値でそれぞれ約 9 時間及び約 8.7 時間）はアデホビル単独投与時と同程度であった。

Part 2

- オセルタミビルカルボン酸（活性代謝物）の総曝露量（AUC_{0-t} 及び $AUC_{0-\infty}$に基づく）及び最大曝露量（C_{max} に基づく）は、アコラミジス q12h + オセルタミビル併用投与時とオセルタミビル単独投与時で同程度であった。オセルタミビルカルボン酸は OAT3 の薬物相互作用試験に推奨される基質であることから、検討した用量でアコラミジスは OAT3 に対する阻害作用を示さないことが示唆された。
- 血漿中オセルタミビルカルボン酸の $t_{1/2}$（算術平均値でそれぞれ約 7.3 時間及び約 7.0 時間）は、アコラミジス q12h + オセルタミビル併用投与時とオセルタミビル単独投与時で同程度であった。

安全性

- 本試験の健康成人被験者で、アデホビル単回投与と併用したアコラミジス反復経口投与の忍容性はおおむね良好であった。
- 本試験の健康成人被験者で、オセルタミビル単回投与と併用したアコラミジス反復経口投与の忍容性はおおむね良好であった。

報告書作成日：20[redacted]年[redacted]月[redacted]日（Errata　20[redacted]年[redacted]月[redacted]日）

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7　第 1 相試験【ALXN2060-HV-101】（海外）［評価資料］

7.1　試験の概要

海外で実施した第 1 相試験【治験実施計画書番号：ALXN2060-HV-101】の概要を Table 1 に示す。

Table 1:　　第 1 相試験【治験実施計画書番号：ALXN2060-HV-101】

治験の標題：健康被験者を対象にアコラミジス単回投与時の薬物動態に及ぼす食事の影響を評価する第 1 相、ランダム化、オープンラベル、2 期、2 順序、2 方向クロスオーバー試験	
治験実施計画書番号：ALXN2060-HV-101	
治験実施施設：米国 1 施設	
治験期間： 最初の被験者の登録日：2021 年 7 月 [redacted] 日 最後の被験者の完了日：2021 年 8 月 [redacted] 日	**開発段階：**第 1 相
目的： 主要目的： • 健康成人被験者にアコラミジス塩酸塩 800 mg を単回経口投与したときのアコラミジスの薬物動態（PK）に及ぼす高脂肪・高カロリー食の影響を検討する。 副次目的： • 健康成人被験者にアコラミジス塩酸塩 800 mg を単回経口投与したときのアコラミジス-アシルグルクロニド（アコラミジス-AG）の PK に及ぼす高脂肪・高カロリー食の影響を検討する。 • 健康成人被験者にアコラミジス塩酸塩 800 mg を単回経口投与したときの安全性及び忍容性を評価する。	
方法： 本試験は、健康被験者を対象に高脂肪・高カロリー食がアコラミジス塩酸塩単回経口投与時の PK に及ぼす影響を評価するランダム化、オープンラベル、2 期、2 順序、2 方向クロスオーバー試験であった。計 18 名を単一施設で登録した。 本試験は、スクリーニング期（Day -28～Day -2）、各 11 日間の 2 つの投与期（各期 Day 1～Day 11、アコラミジス塩酸塩の投与間には 14 日間以上のウォッシュアウト期を設けた）及び第 2 期の投与後の試験終了時（EOS）来院（Day 15 ± 2 日）で構成された。被験者は第 1 期の Day -1～Day 11 まで治験実施施設に入院、第 1 期完了後に退院し、治験薬の投与後 14 日間以上経過してから第 2 期のために再度治験実施施設に入院した。 被験者は各期に治験薬が 1 回投与され、投与順はランダム割付けに基づいて決定した。 • 投与 A（空腹時）：一晩（10 時間以上）絶食後、アコラミジス塩酸塩 2 × 400 mg 錠を水 240 mL とともに服用する。 • 投与 B（食後）：一晩（10 時間以上）絶食後、治験薬投与の 30 分前に高脂肪・高カロリー食を開始し（食事は 30 分以内に終えることとした）、食事開始 30 分後にアコラミジス塩酸塩 2 × 400 mg 錠を水 240 mL とともに服用する。 アコラミジス塩酸塩単回経口投与後のアコラミジス及びその代謝物であるアコラミジス-AG の	

PK プロファイルを約 5 半減期以上かけて測定した。PK 評価用の採血は、経時的な曝露を広範に評価するため、各期の投与前、投与 0.5、1、2、3、4、6、8、12（Day 1）、24（Day 2）、48（Day 3）、72（Day 4）、120（Day 6）、168（Day 8）、216（Day 10）、240（Day 11）及び 336 時間後（Day 15、第 2 期では投与 288 時間後）に実施した。第 2 期の EOS 来院は、第 2 期の Day 15 ± 2 日に実施し、投与 336 時間後（実際には、被験者の早期完了のため治験実施計画書で許容される± 2 日の許容期間内である 288 時間後に採取）の PK 検体を採取した。PK 検体採取に加えて、有害事象、重篤な有害事象、身体所見、バイタルサイン、12 誘導心電図及び臨床検査パラメータのモニタリングにより、安全性及び忍容性を評価した。

被験者数（計画時及び解析時）：

計画時：18 名

解析時：18 名（安全性解析対象集団 18 名、PK 解析対象集団 18 名）

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす被験者を本試験の組入れ対象とした。

1. 同意取得時の年齢が 18 歳以上 55 歳以下の者。
2. 病歴、身体所見、バイタルサイン、12 誘導心電図及び臨床検査（血液学的検査、血液生化学的検査、尿検査及び血液凝固検査）に基づく医学的評価により、試験参加若しくは試験を完了する能力に支障を来す可能性が高い、又は試験結果の解釈に影響を及ぼす可能性がある臨床的に重要若しくは関連する異常がないと治験責任医師等が判断した健康である者。
3. 体重が 50 kg 以上 100 kg 以下、かつ体格指数（BMI）が 18 kg/m^2 以上 32 kg/m^2 未満の者。
4. 男性又は女性。
5. 妊娠可能な女性被験者及び男性被験者の場合、治験実施計画書に規定された避妊ガイダンスに従うことに同意できる者。
6. 同意説明文書及び治験実施計画書に記載されている要件及び制限の遵守を含め、同意説明文書に署名できる者。

［除外基準］

以下のいずれかの基準に抵触する被験者は本試験から除外した。

1. 治験責任医師等の判断に基づき、臨床検査で正常値からの臨床的に重要な逸脱が認められる者。
2. 治験責任医師等の判断で、本試験の完了若しくは参加を制限する、治験結果に影響を及ぼす、又は本試験への参加により被験者に新たなリスクをもたらす可能性がある医学的若しくは精神的状態又は疾患の既往歴を有する者。
3. 治験薬若しくは関連化合物に対する臨床的に重要な過敏症又は特異体質反応の既往歴若しくは現病歴を有する者。治験責任医師等は、その他の薬剤又は食物に対するアレルギーの既往歴を個別に評価し、治験責任医師等の判断で状況に応じて組入れを決定する。
4. 呼吸器系、腎臓系、肝臓系、消化器系、血液系、リンパ系、神経系及び心血管疾患の臨床的に重要な既往歴又は現病歴を有する者。
5. Day 1 の投与前 90 日以内に大手術又は入院した者。
6. 本試験の実施を妨げる可能性がある、又は本試験に参加することで被験者に容認できないリ

スクをもたらす可能性があると治験責任医師等が判断する合併症若しくは病態を有する又は治療を受けている者。
7. 治験実施計画書に規定する薬剤の使用を控えることができない又は使用が予想される者。
8. 治験薬の初回投与前 30 日間又は半減期の 5 倍の期間（いずれか長い方）内に他の治験薬が投与された者。
9. 過去にアコラミジスに曝露したことがある者。
10. スクリーニング時の血清妊娠検査が陽性であり、妊娠していることが確認された女性又は授乳中の女性。
11. 治験薬の初回投与前 3 ヵ月以内にあらゆる形態のタバコ（例：喫煙、咀嚼、吸引）又はその他のニコチン含有製品（例：ガム、パッチ、電子タバコ又は蒸気）を使用した者。
12. 予定している治験薬の初回投与前 6 ヵ月以内に薬物乱用が確認されている者。
13. 試験前 6 ヵ月以内に定期的にアルコール摂取している者。すなわち、週平均摂取量が男性で > 14 単位/週、女性で > 7 単位/週の者。1 単位はアルコール 8 g に相当し、ビールでは半パイント（約 240 mL）、ワインでは約 4 オンス（125 mL）、蒸留酒では 1 メジャー（25 mL）である。
14. スクリーニング時又は入院時（Day -1）の尿中薬物検査が陽性の者。
15. 治験薬の初回投与前 72 時間以内のアルコール摂取又はスクリーニング時若しくは入院時（Day -1）の呼気アルコール検査で陽性の者。
16. 治験薬又はその成分に対する過敏症、あるいは治験責任医師等又はメディカルモニターが本試験への参加を禁忌と判断した薬物又はその他のアレルギーを有する者。

治験薬、用法・用量：

各期で、一晩（10 時間以上）絶食後、空腹時又は食後にアコラミジス塩酸塩 2 × 400 mg（ロット番号：[redacted]）を水 240 mL とともに 1 回服用する。

治療期間：

スクリーニング期：第 1 期の Day -28～Day -2

投与期：各期約 11 日間（各期の投与間のウォッシュアウトは 14 日間以上）

追跡調査来院：治験薬の最終投与後 15（± 2）日

評価項目：

主要評価項目：

- 空腹時投与（対照）に対する食後投与（被験）のアコラミジスの最高血漿中濃度（C_{max}）、時間 0 から血漿中濃度測定可能最終時点（t）までの濃度時間曲線下面積（AUC_{0-t}）及び時間 0 から無限時間までの濃度時間曲線下面積（$AUC_{0-\infty}$）の最小二乗幾何平均値の比。

副次評価項目：

- 空腹時投与（対照）に対する食後投与（被験）のアコラミジス-AG の C_{max}、AUC_{0-t} 及び $AUC_{0-\infty}$ の最小二乗幾何平均値の比。
- 有害事象及び重篤な有害事象の発現頻度、身体所見、バイタルサイン、臨床検査、12 誘導心電図所見。

統計手法：

薬物動態：

PK は PK 解析対象集団を対象に解析し、その定義は「治験薬が 1 回以上投与され、評価可能な

PK データを有する被験者」とした。
すべての PK 結果を一覧表に示し、該当する場合は要約統計量を用いて要約した。
自然対数変換した PK パラメータに、投与条件、投与順序及び投与期を固定効果、投与順序内でネストした被験者を変量効果とした線形混合効果モデルを当てはめた。

安全性：
安全性は安全性解析対象集団を対象に解析し、その定義は「治験薬が 1 回以上投与された被験者」とした。
すべての安全性の結果を一覧にし、該当する場合は要約統計量を用いて示した。
有害事象は、ICH 国際医薬用語集（MedDRA®）Version 24.0 を用いてコード化し、有害事象発現者数及び発現件数を投与別に要約した。有害事象は治験薬との因果関係別（関連あり、関連なし）でも要約した。報告された用語、コード化した用語、投与、重症度及び治験薬との因果関係を含む、被験者ごとの有害事象データ一覧を示した。重篤な有害事象及び中止に至った有害事象を一覧表に示した。同一カテゴリー内で複数の有害事象を発現した被験者は、そのカテゴリーで 1 回のみカウントした。重症度の表では、各カテゴリー内の被験者の最も重度の事象を集計した。
心電図、臨床検査、身体所見及びバイタルサイン測定値を含むその他の安全性データも投与別に要約した。

結果の要約：

本試験に登録された 18 名のうち、男性が 13 名（72%）、女性が 5 名（28%）であった。被験者の大多数は白人であり（10 名［56%］）、全 18 名が非ヒスパニック／非ラテン系であった。スクリーニング時の平均年齢は 39.2 歳、平均 BMI は約 25.9 kg/m^2 であった。
全 18 名に治験薬が 1 回以上投与され、安全性解析対象集団に含まれた。治験実施計画書に従って試験を完了した被験者は 17 名で、1 名は早期中止により第 1 期（空腹時）のみ投与された。当該 1 名は PK 解析対象集団に含まれたが、推測統計からは除外した。

薬物動態

PK 解析対象集団で、空腹時（投与 A）及び食後（投与 B）にアコラミジス塩酸塩 800 mg を単回経口投与したときの血漿中アコラミジス及びアコラミジス-AG の曝露量パラメータ（AUC 及び C_{max}）の統計学的比較をそれぞれ以下に示す。

血漿中アコラミジスの PK パラメータの統計学的比較の要約：アコラミジス塩酸塩錠 800 mg の食後投与（投与 B）と空腹時投与（投与 A）（PK 解析対象集団）

	Treatment B (Test)		Treatment A (Reference)				
Parameter	Geometric LSM	n	Geometric LSM	n	Geometric Mean Ratio (%)	90% Confidence Interval	Intra-participant CV%
AUC_{0-t} (ng*hr/mL)	127200	17	137030	17	92.83	86.33 - 99.82	12.10
$AUC_{0-\infty}$ (ng*hr/mL)	128030	17	137860	17	92.87	86.41 - 99.82	12.02
C_{max} (ng/mL)	6986	17	9004	17	77.59	62.20 - 96.78	37.97

Treatment A: Administration of 2 x 400 mg acoramidis HCl salt tablets under fasting conditions (reference)
Treatment B: Administration of 2 x 400 mg acoramidis HCl salt tablets under fed conditions (test)
Participant 3 terminated early and was excluded from inferential statistics.
Geometric least-squares means (LSMs) were calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio (%) = 100 x (test/reference)
Intra-participant CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
Source: 5.3.3.4.2 項 ALXN2060-HV-101 CSR Table 14.2.1.7.1

血漿中アコラミジス-AG の PK パラメータの統計学的比較の要約:アコラミジス塩酸塩錠 800 mg の食後投与（投与 B）と空腹時投与（投与 A）（PK 解析対象集団）

	Treatment B (Test)		Treatment A (Reference)				
Parameter	Geometric LSM	n	Geometric LSM	n	Geometric Mean Ratio (%)	90% Confidence Interval	Intra-participant CV%
$AUC_{0\text{-}t}$ (ng*hr/mL)	16386	17	18508	17	88.53	84.65 - 92.60	7.46
$AUC_{0\text{-}\infty}$ (ng*hr/mL)	16449	17	18578	17	88.54	84.69 - 92.56	7.38
C_{max} (ng/mL)	3878	17	4643	17	83.51	74.51 - 93.60	19.10

Treatment A: Administration of 2 x 400 mg acoramidis HCl salt tablets under fasting conditions (reference)
Treatment B: Administration of 2 x 400 mg acoramidis HCl salt tablets under fed conditions (test)
Participant 3 terminated early and was excluded from inferential statistics.
Geometric least-squares means (LSMs) were calculated by exponentiating the LSMs from ANOVA.
Geometric Mean Ratio (%) = 100 x (test/reference)
Intra-participant CV% was calculated as 100 x square root(exp[MSE]-1), where MSE = Residual variance from ANOVA.
Acoramidis-AG = Acoramidis-Acylglucuronide
Source: 5.3.3.4.2 項 ALXN2060-HV-101 CSR Table 14.2.2.7.1

アコラミジス塩酸塩 800 mg を食後（高脂肪・高カロリー食）に単回経口投与したとき、血漿中アコラミジスの全身曝露量（$AUC_{0\text{-}t}$ 及び $AUC_{0\text{-}\infty}$）は空腹時投与と同程度であったが（幾何平均比［GMR］はいずれも 93%）、ピーク曝露量（C_{max}）は食後投与の方が約 22%低かった。アコラミジスの最高血漿中濃度到達時間（t_{max}）の中央値は、空腹時投与と比較して食後投与で約 1 時間遅延した。アコラミジスの消失半減期（$t_{1/2}$）、全身クリアランス（CL/F）及びみかけの分布容積（V_z/F）に投与間で顕著な差は認められなかった。
血漿中アコラミジス-AG の全身曝露量（AUC）は食後投与と空腹時投与で同程度であった（GMR はいずれも 89%）。しかし、ピーク曝露量は食後投与の方が約 16%低かった。また、t_{max} は食後投与で約 1 時間遅延した。代謝物アコラミジス-AG の未変化体に対する AUC 及び C_{max} のモル比（$MR_AUC_{0\text{-}t}$、$MR_AUC_{0\text{-}\infty}$及び MR_C_{max}）並びに $t_{1/2}$ の推定値は投与間で同程度であった。

安全性

本試験では、死亡、重篤な有害事象及び中止に至った有害事象は報告されなかった。
全体で 6 名（33%）に 23 件の有害事象が認められた。その内訳はアコラミジス塩酸塩 800 mg の空腹時投与で 4 名（22%）、食後投与で 4 名（24%）であった。最も多く認められた有害事象（2 名以上）は、悪心、背部痛及び頭痛であった。1 件を除くすべての事象で重症度は軽度（グレード 1）であり、1 件を除くすべての事象が治験責任医師により治験薬と関連なしと判断された。
心電図、バイタルサイン及び臨床検査パラメータに注目すべき所見は認められなかった。

結論：

薬物動態：

- アコラミジス塩酸塩 800 mg を単回経口投与したとき、アコラミジスの曝露量（AUC）は食後（高脂肪・高カロリー食）投与と空腹時投与で同程度であった。しかし、アコラミジスのピーク曝露量（C_{max}）は食後投与で約 22%低かった。アコラミジスの t_{max} の中央値は、空腹時投与と比較して食後投与で約 1 時間遅延した。
- アコラミジス塩酸塩 800 mg を単回経口投与したときのアコラミジス-AG の曝露量は、食後投与と空腹時投与で同程度であった。しかし、アコラミジス-AG のピーク曝露量は食後投与では空腹時投与と比較して約 16%低く、t_{max} の中央値は約 1 時間遅延した。

安全性： • 本試験では、死亡、重篤な有害事象及び中止に至った有害事象は報告されなかった。 • 本試験の健康成人被験者にアコラミジス塩酸塩 800 mg を空腹時又は食後に単回経口投与したときの安全性プロファイルは許容可能であり、忍容性はおおむね良好であった。
報告書作成日：20[redacted] 年 [redacted] 月 [redacted] 日（Erratum：20[redacted] 年 [redacted] 月 [redacted] 日）

7.2 有害事象

すべての有害事象及び治験薬との関連性が否定できない有害事象を以下に示す。本試験で重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Table 14.3.1.2
治験薬との関連性が否定できない有害事象	Table 14.3.1.5
重篤な有害事象	Table 14.3.2.1（該当なし）
治験薬の投与中止に至った有害事象	該当なし

7.3 個別被験者の詳細

本試験で死亡又は重篤な有害事象は発現していないため、該当なし。

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Participants Reporting the Event (% of Participants Dosed) (Safety Set)

	Treatment		
	A n(%)	B n(%)	Overall n(%)
Number of Participants Dosed	18 (100%)	17 (100%)	18 (100%)
Number of Participants With TEAEs	4 (22%)	4 (24%)	6 (33%)
Number of Participants Without TEAEs	14 (78%)	13 (76%)	12 (67%)
胃腸障害	3 (17%)	0 (0%)	3 (17%)
上腹部痛	1 (6%)	0 (0%)	1 (6%)
胃食道逆流性疾患	1 (6%)	0 (0%)	1 (6%)
悪心	2 (11%)	0 (0%)	2 (11%)
一般・全身障害および投与部位の状態	0 (0%)	1 (6%)	1 (6%)
血管穿刺部位疼痛	0 (0%)	1 (6%)	1 (6%)
感染症および寄生虫症	1 (6%)	1 (6%)	1 (6%)
腟感染	1 (6%)	1 (6%)	1 (6%)
傷害、中毒および処置合併症	1 (6%)	0 (0%)	1 (6%)
皮膚擦過傷	1 (6%)	0 (0%)	1 (6%)
代謝および栄養障害	1 (6%)	0 (0%)	1 (6%)
食欲減退	1 (6%)	0 (0%)	1 (6%)
筋骨格系および結合組織障害	1 (6%)	2 (12%)	3 (17%)
関節痛	0 (0%)	1 (6%)	1 (6%)
背部痛	1 (6%)	1 (6%)	2 (11%)
神経系障害	2 (11%)	1 (6%)	3 (17%)
味覚消失	1 (6%)	0 (0%)	1 (6%)
体位性めまい	1 (6%)	0 (0%)	1 (6%)
頭痛	1 (6%)	1 (6%)	2 (11%)
精神障害	1 (6%)	0 (0%)	1 (6%)
不眠症	1 (6%)	0 (0%)	1 (6%)

Treatment A: Administration of 2 x 400 mg acoramidis HCl salt tablets under fasting conditions
Treatment B: Administration of 2 x 400 mg acoramidis HCl salt tablets under fed conditions
Although a participant may have had 2 or more clinical adverse experiences, the participant is counted only once within a category.
The same participant may appear in different categories.
Adverse events are classified according to MedDRA Version 24.0.
TEAEs = Treatment-emergent adverse events

Table 14.3.1.2 Treatment-Emergent Adverse Event Frequency by Treatment - Number of Participants Reporting the Event (% of Participants Dosed) (Safety Set)

	Treatment		
	A n(%)	B n(%)	Overall n(%)
生殖系および乳房障害	1 (6%)	0 (0%)	1 (6%)
腟分泌物	1 (6%)	0 (0%)	1 (6%)
呼吸器、胸郭および縦隔障害	1 (6%)	0 (0%)	1 (6%)
咳嗽	1 (6%)	0 (0%)	1 (6%)
咽喉乾燥	1 (6%)	0 (0%)	1 (6%)

Treatment A: Administration of 2 x 400 mg acoramidis HCl salt tablets under fasting conditions
Treatment B: Administration of 2 x 400 mg acoramidis HCl salt tablets under fed conditions
Although a participant may have had 2 or more clinical adverse experiences, the participant is counted only once within a category.
The same participant may appear in different categories.
Adverse events are classified according to MedDRA Version 24.0.
TEAEs = Treatment-emergent adverse events

Table 14.3.1.5 Treatment-Emergent Adverse Event Frequency by Treatment, Severity, and Relationship to Drug - Number of Participants (Safety Set)

Adverse Event	Treatment	Number of Participants with TEAEs	Severity					Relationship to Study Product	
			Grade 1: Mild	Grade 2: Mod.	Grade 3: Sev.	Grade 4: Life-threat.	Grade 5: Fatal	Not Related	Related
上腹部痛	A	1	1	0	0	0	0	1	0
味覚消失	A	1	1	0	0	0	0	1	0
関節痛	B	1	1	0	0	0	0	1	0
背部痛	A	1	1	0	0	0	0	1	0
	B	1	1	0	0	0	0	1	0
咳嗽	A	1	1	0	0	0	0	1	0
食欲減退	A	1	1	0	0	0	0	1	0
体位性めまい	A	1	1	0	0	0	0	1	0
咽喉乾燥	A	1	1	0	0	0	0	1	0
胃食道逆流性疾患	A	1	1	0	0	0	0	1	0
頭痛	A	1	1	0	0	0	0	1	0
	B	1	1	0	0	0	0	0	1
不眠症	A	1	1	0	0	0	0	1	0
悪心	A	2	2	0	0	0	0	2	0
皮膚擦過傷	A	1	0	1	0	0	0	1	0
腟分泌物	A	1	1	0	0	0	0	1	0
腟感染	A	1	1	0	0	0	0	1	0
	B	1	1	0	0	0	0	1	0
血管穿刺部位疼痛	B	1	1	0	0	0	0	1	0
	A	4	3	1	0	0	0	4	0
	B	4	4	0	0	0	0	3	1
	Overall	6	5	1	0	0	0	5	1

Treatment A: Administration of 2 x 400 mg acoramidis HCl salt tablets under fasting conditions
Treatment B: Administration of 2 x 400 mg acoramidis HCl salt tablets under fed conditions
Adverse events are classified according to MedDRA Version 24.0.
TEAEs = Treatment-emergent adverse events
Grade 2: Mod. = Moderate; Grade 3: Sev. = Severe; Grade 4: Life-threat. = Life-threatening

Table 14.3.2.1 Serious Adverse Events (Safety Set)

No serious adverse event was reported.

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8　第 2 相試験【AG10-201】（海外）［評価資料］

8.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 2 相試験【治験実施計画書番号：AG10-201】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 2 相試験【治験実施計画書番号：AG10-201】

治験の標題：症候性トランスサイレチン型心アミロイドーシス患者を対象に AG10 の安全性、忍容性、薬物動態及び薬力学的作用を評価する第 2 相、ランダム化、プラセボ対照、用量設定試験	
治験実施計画書番号：AG10-201	
治験実施施設：米国 12 施設（このうち 9 施設で患者を登録）	
治験期間： 最初の患者の登録日：2018 年 5 月 [redacted] 日 最後の患者の完了日：2018 年 8 月 [redacted] 日	**開発段階：**第 2 相
目的： 主要目的：本試験の主要目的は以下のとおりであった。 • 症候性トランスサイレチン型心アミロイドーシス（ATTR-CM）の成人患者にアコラミジス塩酸塩を投与したときの安全性及び忍容性を評価する。 副次目的：本試験の副次目的は以下のとおりであった。 • 症候性 ATTR-CM 患者にアコラミジス塩酸塩を 1 日 2 回（BID）経口投与したときの薬物動態（PK）の特性を明らかにする。 • 症候性 ATTR-CM 患者にアコラミジス塩酸塩を投与したときの、プレアルブミンレベル並びに蛍光プローブ排除（FPE）アッセイ及びウェスタンブロットを含むトランスサイレチン（TTR）安定化の確立されたアッセイを用いて評価したアコラミジスの薬力学的作用（PD）の特性、並びに PK-PD 関係を明らかにする。	
方法： 本試験では前向き、ランダム化、多施設共同、二重盲検、並行群間、プラセボ対照、用量設定デザインを用いて、安定した心不全療法下でアコラミジス塩酸塩の安全性、忍容性、PK 及び PD をプラセボと比較した。本試験はスクリーニング期、二重盲検投与期及び追跡調査来院で構成された。スクリーニング期に適格性が確認された患者は、以下のいずれかに 1：1：1 の比でランダム割付けされた。 ・アコラミジス塩酸塩 400 mg：2 × 200 mg 錠 + 2 × プラセボ錠 BID ・アコラミジス塩酸塩 800 mg：4 × 200 mg 錠 BID ・プラセボ：4 × プラセボ錠 BID	
患者数（計画時及び解析時）： 計画時：約 55 名（各群約 18 名；全体の約 30%が遺伝性 ATTR-CM［ATTRm-CM］） 登録時：49 名（400 mg 群 16 名、800 mg 群 16 名、プラセボ群 17 名；全体で 14 名［28.6%］が ATTRm-CM） 解析時：安全性解析対象集団：49 名（400 mg 群 16 名、800 mg 群 16 名、プラセボ群 17 名）、PK 解析対象集団：32 名（400 mg 群 16 名、800 mg 群 16 名）、PD 解析対象集団：49 名（400 mg 群	

16 名、800 mg 群 16 名、プラセボ群 17 名）

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす患者を本試験の組入れ対象とした。

1. 同意説明文書を理解し、署名できる者（試験手順の開始前に取得しなければならない）。
2. 18 歳以上 90 歳以下の男女。
3. 心内膜心筋生検陽性又はピロリン酸テクネチウムスキャン陽性のいずれかにより定義される、野生型 ATTR-CM（ATTRwt-CM）又は ATTRm-CM と確定診断された者（ジェノタイピングによる評価。意義不明の単クローン性高ガンマグロブリン血症を併発している患者では質量分析による確認検査を必要とする）。
4. 過去に心不全のために 1 回以上入院又は医学的管理を必要とする心不全の臨床的エビデンス（入院なし）によって確認される心不全の既往歴を有する者。
5. New York Heart Association（NYHA）分類クラス II-III の症状を有する者。
6. 男性患者及び妊娠可能な女性患者の場合、異性間性交渉を行う際に適切な避妊法を使用することに同意できる者。
7. 心血管系の薬物療法を受けている患者の場合、利尿薬の投与を除き、スクリーニング前 2 週間以上にわたって用量が安定（用量調節が 50%以下であり、薬剤のカテゴリー変更がないものと定義）している者。

［除外基準］

以下のいずれかの基準に抵触する患者は本試験から除外した。

1. スクリーニング前 90 日以内に急性心筋梗塞若しくは急性冠症候群を発症又は冠動脈血行再建を施術された者。
2. スクリーニング前 90 日以内に脳卒中を発症した者。
3. スクリーニング時又はランダム化時に血行動態が不安定であり、試験参加によるリスクが非常に大きいと治験責任医師等が判断した者。
4. スクリーニング時の推算糸球体濾過量が 30 mL/min/1.73 m^2 未満の者。
5. 1 年以内に心臓移植を受ける可能性が高い者。
6. 免疫グロブリン軽鎖アミロイドーシスの確定診断を受けている者。
7. スクリーニング時に肝機能検査値異常が認められた者（アラニンアミノトランフェラーゼ若しくはアスパラギン酸アミノトランスフェラーゼが基準値上限［ULN］）の 3 倍超又は総ビリルビンが ULN の 2 倍超と定義）。
8. スクリーニング時又はランダム化時の臨床検査で異常が認められ、試験参加のリスクが非常に大きいと治験責任医師等が判断した者。
9. 治験薬（アコラミジス又はプラセボ）、その代謝物又は製剤の賦形剤に対する過敏症が確認されている者。
10. 治験薬投与前 14 日間又は該当薬の半減期の 5 倍の期間（いずれか長い方）以内にジフルニサル、タファミジス、緑茶、ドキシサイクリン、tauroursodeoxycholic acid/ウルソデオキシコール酸、パチシラン又は inotersen による治療を受けた者。
11. 妊娠中又は授乳中の女性。授乳中の女性は、治験薬の投与前に授乳を中止することに同意し

なければならない。妊娠可能な女性は、スクリーニング時の血清妊娠検査が陰性であり、ランダム化時の尿妊娠検査が陰性でなければならない。

12. スクリーニング前 30 日以内に他の治験薬又は治験機器の試験に参加し、本試験の結果に影響を及ぼす可能性のある後遺症があるなど、患者の安全を脅かす又は本試験の実施を妨げる可能性がある臨床的に重要な医学的状態が継続していると治験責任医師等が判断した者。
13. 患者の安全性に悪影響を及ぼす又は試験結果の評価を損なう可能性があると治験責任医師等が判断した臨床検査値異常若しくは状態を有する者。
14. 薬物乱用歴、アルコール依存症又は精神疾患など、治験実施計画書の遵守を妨げる可能性があると治験責任医師等が判断した者。
15. 治験薬投与前 14 日間又は他の治験薬の半減期の 5 倍の期間（いずれか長い方）以内に別の試験に参加した者。観察研究及び／又は登録研究の場合は、メディカルモニターと協議の上、例外として組入れることができる。

治験薬、用法・用量：

アコラミジス塩酸塩 400 mg BID 及び 800 mg BID：アコラミジス錠を経口投与（ロット番号：[redacted]）

プラセボ：アコラミジス錠と外観が同一のプラセボ錠を経口投与（ロット番号：[redacted]、[redacted] 及び [redacted]）。

治療期間：

試験期間：35～42 日間（スクリーニング期：28 日間、二重盲検投与期：Day 1～Day 28、追跡調査来院：Day 28 の 7～14 日後）

評価項目：

主要評価項目：

- 安全性及び忍容性：試験治療下で発現した有害事象、ランダム化後の身体所見、臨床事象（死亡、心筋梗塞、脳卒中、心不全による入院、心不全の悪化による緊急受診を含む）、バイタルサイン、心電図データ（PR、RR、QRS 及び QT 間隔）及び臨床検査パラメータの収集により評価する。

副次評価項目：

- PK：アコラミジス及びその代謝物アコラミジス-アシルグルクロニド（アコラミジス-AG）の PK 測定は、初回投与後及び定常状態時（Day 14、Day 28）に指定の生体試料分析機関で実施する。
- PD：FPE アッセイ及びウェスタンブロットを含む確立された TTR 安定化アッセイを用いてアコラミジスの PD 測定を評価し、症候性 ATTR-CM の成人患者でのアコラミジスの PK-PD 関連性を明らかにする。循環血中プレアルブミン濃度の変化も PD マーカーとして測定する。

統計手法：

すべての要約統計量の解析は、SAS Version 9.4 以上（SAS Institute, Inc.）を用いて実施した。図の作成には別のソフトウェアを用いた。PK パラメータは Phoenix WinNonlin を用いて算出した。ベースライン値は初回投与日前の直前の測定値とした。

薬物動態：

PK の解析は PK 解析対象集団を対象に実施し、その定義は「アコラミジス塩酸塩が 1 回以上投与され、投与後の評価可能な濃度を 1 つ以上有するすべての患者」とした。血漿中アコラミジス及びアコラミジス-AG 濃度を患者ごとに測定し、用量別に要約した。初回投与時及び定常状態（Day 14 及び Day 28）でのパラメータを示した。

薬力学的作用：

PD の解析は PD 解析対象集団を対象に実施し、その定義は「治験薬が 1 回以上投与され、投与後の評価可能な値を 1 つ以上有するすべての患者」とした。各患者の TTR 安定化の程度は、FPE アッセイとウェスタンブロットの両方を用いて、投与前の測定値と比較して算出した。循環血中の血清中 TTR（プレアルブミン）濃度の変化も用量及び時点別に報告した。また、血清中 TTR の増加率が特定の閾値（10%、25%及び 50%）に達した患者の要約を示した。
なお、PK 及び PD 用の血液検体は Day 1、14 及び 28 に採取した。

安全性：

安全性の解析は安全性解析対象集団を対象に実施し、その定義は「治験薬が 1 回以上投与されたすべての患者」とした。有害事象は ICH 国際医薬用語集（MedDRA）version 21.0 を用いてコード化した。有害事象の発現頻度は、器官別大分類、基本語（PT）及び投与群別に集計した。同一の患者に同一の PT が複数回発現した場合は 1 とカウントした。併用薬は、WHO Drug Dictionary を用いて、一般名及び治療的使用（ATC コード）とともにコード化し、ATC コード、WHO 一般名及び治療別に要約した。早期中止の理由を投与群別に要約した。安全性に関する臨床検査所見、バイタルサイン及び 12 誘導心電図データの記述的要約を示し、投与群別及び来院別に一覧にした。規定された時点での値及びベースラインからの変化量を要約した。臨床検査データを一覧表に示し、各来院時の値及びベースラインからの変化量を要約した。試験治療下で発現した臨床検査値異常の一覧を追加した。主要な臨床イベントの総数を投与群別に要約し、イベント発生までの期間の解析も実施した。

結果の要約：

薬物動態

Day 28 のアコラミジスのトラフ濃度の平均値及び中央値は、400 mg BID 群でそれぞれ 1841.3 及び 1955.0 ng/mL、800 mg BID 群でそれぞれ 2439.4 及び 2360.0 ng/mL であった。800 mg BID の定常状態では、健康成人被験者で示された TTR の完全な安定化のためのアコラミジスの目標治療濃度である 8 μM（2340 ng/mL）を上回るアコラミジスのトラフ濃度の平均値及び中央値が得られた。

薬力学的作用

データが得られたアコラミジス投与群の全患者で Day 14 及び Day 28 の両方で TTR 値がベースラインを上回って増加した。プラセボ群の患者では、血清 TTR 値に変化は認められなかったか又は低下が認められた。800 mg BID 群では、400 mg BID 群と比較して、ATTRwt-CM 又は ATTRm-CM のいずれでも、ベースラインからの TTR レベルの変化率が大きかった。概して、アコラミジス投与患者では、血清 TTR レベルの変化率は ATTRwt-CM 患者（データを有する患者 21 名）よりも ATTRm-CM 患者（11 名）で大きかった。

ATTRm-CM 患者の数は限られているものの（11 名）、ATTRm-CM 患者では ATTRwt-CM 患者と比較して、概してアコラミジスの血漿中濃度が高い方がより大きな血清 TTR の変化を示した。ATTRm-CM 患者で TTR の変化が大きかった理由として、ATTRm-CM 患者では ATTRwt-CM 患者と比較して、ベースラインの TTR 値が低かったことが一因の可能性がある。ATTRm-CM/ATTRwt-CM にかかわらず、800 mg BID では 400 mg BID と比較して、2 倍高い頻度で血清中 TTR 濃度の 50%以上の増加が認められた。

FPE アッセイ及びウェスタンブロットの結果から、400 mg BID 又は 800 mg BID のいずれの用量でもアコラミジス塩酸塩の投与に起因する TTR 安定化の薬理学的作用機序及び程度が確認された。これらのアッセイはいずれも TTR4 量体のほぼ完全な ex vivo 安定化を示した。FPE アッセイの結果、800 mg BID が投与された患者では、400 mg BID が投与された患者と比較して患者間変動が小さかった。

800 mg BID が投与された患者では、400 mg BID が投与された患者と比較して、TTR の完全な安定化（90%以上）が得られる可能性が高く、目標治療濃度である 8 μM を上回るアコラミジスのトラフ濃度が維持されていた。

安全性

症候性 ATTR-CM 患者にアコラミジス塩酸塩を 400 mg BID 及び 800 mg BID の用量で 28 日間経口投与したときの忍容性はおおむね良好であった。本試験では、臨床的に問題となる可能性のあるアコラミジス塩酸塩関連の安全性の兆候は認められず、400 mg BID 投与と 800 mg BID 投与との間に臨床的に重要な安全性プロファイルの差は認められなかった。また、死亡、治験薬の投与中止又は試験中止に至った有害事象は認められなかった。

重篤な有害事象は 3 名に 4 件発現した。重篤な有害事象のうち、アコラミジス塩酸塩投与群で認められたのは、心不全の悪化を示し入院に至った軽度の呼吸困難の 1 件のみであった。その他の 3 件はプラセボ群での発現であり、1 名に蜂巣炎、1 名に心房細動及びうっ血性心不全が発現した。治験薬との関連性が否定できない（関連あるかもしれない又は関連あり）と判断された重篤な有害事象はなかった。

有害事象は全体の 73.5%で認められ、その発現割合はアコラミジス塩酸塩の投与群間で同程度であり（400 mg BID 群：62.5%、800 mg BID 群：68.8%）、いずれもプラセボ群（88.2%）よりも低かった。また、有害事象の発現件数も、アコラミジス塩酸塩の投与群間では同程度であったのに対し（400 mg BID 群：32 件、800 mg BID 群：36 件）、プラセボ群では 66 件であった。

全体で最も多く認められた有害事象は、便秘（12.2%）、下痢（10.2%）、筋痙縮（8.2%）及び心房細動（8.2%）であった。いずれかの投与群で 3 名以上に認められた PT 別の有害事象は 3 件のみであり、このうち便秘の発現割合はアコラミジス塩酸塩群（両投与群で 4/32 名、12.5%）とプラセボ群（2/17 名、11.8%）で同程度、下痢はアコラミジス塩酸塩群のみに発現（両投与群で 5/32 名、15.6%）、動悸はプラセボ群のみに発現（3/17 名、17.6%）した。

全体で 3 名以上に発現した治験薬との関連性が否定できない（関連あるかもしれない又は関連あり）有害事象は 2 件であり、このうち便秘の発現割合は 800 mg BID 群（3/16 名、18.8%）でプラセボ群（1/17 名、5.9%）より高く、400 mg BID 群では認められなかった。また、下痢はアコラミジス塩酸塩群でのみ認められた（400 mg BID 群 : 1/16 名、6.3%、800 mg BID 群 : 2/16 名、12.5%）。

2018 年 10 月 5 日版の統計解析計画書に基づき、関連性の定義に「おそらく関連なし」を含めて関連性を解析したところ、治験薬との関連性が否定できない有害事象発現者数及び有害事象発現

件数の両方が、すべての投与群で増加したが、データの全体的な解釈に変更はなかった。
重度の有害事象が 3 件（蜂巣炎、急性腎障害、感音性難聴）発現し、いずれも治験薬と関連なし又はおそらく関連なしと判断された。全体として、有害事象の重症度は 34.7%が軽度、34.7%が中等度、4.1%が重度であった。
試験期間中に 1 名以上に発現した注目すべき臨床的事象は心房細動のみであり、全体では 8.2%で何らかの注目すべき臨床的事象が認められた。

結論：
症候性 ATTR-CM の成人患者を対象にアコラミジス塩酸塩 400 mg BID 又は 800 mg BID を 28 日間経口投与したときの忍容性は良好であった。臨床的に問題となる可能性のあるアコラミジス塩酸塩関連の安全性の兆候は認められず、400 mg BID 及び 800 mg BID の両群間の安全性プロファイルに臨床的に重要な差は認められなかった。
PK 解析の結果、800 mg BID の定常状態では、健康成人で TTR の完全な安定化が示された目標治療濃度である 8 μM（2340 ng/mL）を上回るアコラミジスのトラフ濃度（平均値及び中央値）が得られた。800 mg BID が投与された患者では、400 mg BID が投与された患者と比較して、50%以上の TTR 増加を示す可能性が高く、また、TTR の完全な安定化（90%以上）を示す可能性が高く、目標治療濃度である 8 μM を上回るアコラミジスのトラフ濃度が維持された。

報告書作成日：20[redacted]年[redacted]月[redacted]日（Errata　20[redacted]年[redacted]月[redacted]日、20[redacted]年[redacted]月[redacted]日）

8.2　有害事象

すべての有害事象、治験薬との関連性が否定できない有害事象及び重篤な有害事象を以下に示す。本試験で治験薬の投与中止に至った有害事象は認められなかった。

すべての有害事象	Table 14.3.2.2
治験薬との関連性が否定できない有害事象	Table 14.3.2.4.1
重篤な有害事象	Table 14.3.2.7
治験薬の投与中止に至った有害事象	Table 14.3.2.9（該当なし）

8.3　個別被験者の詳細

本試験で死亡は認められなかった。重篤な有害事象を発現した患者の詳細を以下に示す。

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
Any Adverse Events	10	(62.5)	32	11	(68.8)	36	15	(88.2)	66	36	(73.5)	134
胃腸障害	3	(18.8)	7	7	(43.8)	11	2	(11.8)	3	12	(24.5)	21
便秘	1	(6.3)	1	3	(18.8)	3	2	(11.8)	2	6	(12.2)	6
下痢	2	(12.5)	3	3	(18.8)	3	0			5	(10.2)	6
腹痛	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
腹部不快感	1	(6.3)	1	0			0			1	(2.0)	1
腹部膨満	0			1	(6.3)	1	0			1	(2.0)	1
上腹部痛	1	(6.3)	1	0			0			1	(2.0)	1
排便回数増加	1	(6.3)	1	0			0			1	(2.0)	1
悪心	0			1	(6.3)	1	0			1	(2.0)	1
口腔粘膜水疱形成	0			1	(6.3)	2	0			1	(2.0)	2
筋骨格系および結合組織障害	2	(12.5)	3	4	(25.0)	5	3	(17.6)	6	9	(18.4)	14
筋痙縮	1	(6.3)	1	1	(6.3)	1	2	(11.8)	2	4	(8.2)	4
四肢痛	0			2	(12.5)	2	1	(5.9)	1	3	(6.1)	3
鼡径部痛	1	(6.3)	1	0			1	(5.9)	1	2	(4.1)	2
関節痛	0			1	(6.3)	1	0			1	(2.0)	1
背部痛	0			0			1	(5.9)	1	1	(2.0)	1
筋骨格硬直	0			0			1	(5.9)	1	1	(2.0)	1

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
筋骨格系および結合組織障害												
滑液嚢腫	0			1	(6.3)	1	0			1	(2.0)	1
開口障害	1	(6.3)	1	0			0			1	(2.0)	1
感染症および寄生虫症	1	(6.3)	1	4	(25.0)	5	3	(17.6)	4	8	(16.3)	10
蜂巣炎	0			1	(6.3)	2	1	(5.9)	1	2	(4.1)	3
結膜炎	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
気管支炎	0			0			1	(5.9)	1	1	(2.0)	1
耳感染	0			1	(6.3)	1	0			1	(2.0)	1
上咽頭炎	1	(6.3)	1	0			0			1	(2.0)	1
気道感染	0			1	(6.3)	1	0			1	(2.0)	1
尿路感染	0			0			1	(5.9)	1	1	(2.0)	1
臨床検査	5	(31.3)	5	0			3	(17.6)	5	8	(16.3)	10
頚静脈圧上昇	2	(12.5)	2	0			0			2	(4.1)	2
抗凝固薬濃度治療量以上	1	(6.3)	1	0			0			1	(2.0)	1
血中クレアチニン増加	0			0			1	(5.9)	1	1	(2.0)	1
血中甲状腺刺激ホルモン減少	1	(6.3)	1	0			0			1	(2.0)	1
体温上昇	0			0			1	(5.9)	1	1	(2.0)	1
Ｃ－反応性蛋白増加	0			0			1	(5.9)	1	1	(2.0)	1
国際標準比増加	1	(6.3)	1	0			0			1	(2.0)	1

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
臨床検査												
肝機能検査値上昇	0			0			1	(5.9)	1	1	(2.0)	1
白血球数減少	0			0			1	(5.9)	1	1	(2.0)	1
代謝および栄養障害	0			2	(12.5)	2	5	(29.4)	9	7	(14.3)	11
体液貯留	0			1	(6.3)	1	2	(11.8)	2	3	(6.1)	3
水分過負荷	0			1	(6.3)	1	1	(5.9)	2	2	(4.1)	3
食欲減退	0			0			1	(5.9)	1	1	(2.0)	1
耐糖能障害	0			0			1	(5.9)	1	1	(2.0)	1
痛風	0			0			1	(5.9)	1	1	(2.0)	1
高カリウム血症	0			0			1	(5.9)	1	1	(2.0)	1
低ナトリウム血症	0			0			1	(5.9)	1	1	(2.0)	1
心臓障害	1	(6.3)	4	2	(12.5)	2	3	(17.6)	7	6	(12.2)	13
心房細動	1	(6.3)	2	2	(12.5)	2	1	(5.9)	1	4	(8.2)	5
動悸	0			0			3	(17.6)	3	3	(6.1)	3
狭心症	0			0			1	(5.9)	1	1	(2.0)	1
うっ血性心不全	0			0			1	(5.9)	1	1	(2.0)	1
上室性頻脈	1	(6.3)	1	0			0			1	(2.0)	1
頻脈	0			0			1	(5.9)	1	1	(2.0)	1
心室性頻脈	1	(6.3)	1	0			0			1	(2.0)	1

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
一般・全身障害および投与部位の状態	2	(12.5)	2	1	(6.3)	1	3	(17.6)	3	6	(12.2)	6
疲労	0			1	(6.3)	1	2	(11.8)	2	3	(6.1)	3
末梢性浮腫	2	(12.5)	2	0			0			2	(4.1)	2
腫脹	0			0			1	(5.9)	1	1	(2.0)	1
神経系障害	1	(6.3)	1	3	(18.8)	5	2	(11.8)	4	6	(12.2)	10
頭痛	0			1	(6.3)	2	2	(11.8)	2	3	(6.1)	4
浮動性めまい	0			2	(12.5)	2	0			2	(4.1)	2
体位性めまい	0			1	(6.3)	1	0			1	(2.0)	1
記憶障害	1	(6.3)	1	0			0			1	(2.0)	1
失神	0			0			1	(5.9)	2	1	(2.0)	2
傷害、中毒および処置合併症	1	(6.3)	1	0			4	(23.5)	8	5	(10.2)	9
挫傷	0			0			2	(11.8)	2	2	(4.1)	2
転倒	0			0			2	(11.8)	2	2	(4.1)	2
損傷	0			0			1	(5.9)	1	1	(2.0)	1
四肢損傷	0			0			1	(5.9)	2	1	(2.0)	2
肉離れ	1	(6.3)	1	0			0			1	(2.0)	1
皮膚擦過傷	0			0			1	(5.9)	1	1	(2.0)	1
呼吸器、胸郭および縦隔障害	1	(6.3)	2	1	(6.3)	1	3	(17.6)	5	5	(10.2)	8

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
呼吸器、胸郭および縦隔障害												
呼吸困難	1	(6.3)	1	0			2	(11.8)	2	3	(6.1)	3
咳嗽	0			0			2	(11.8)	2	2	(4.1)	2
鼻出血	1	(6.3)	1	0			0			1	(2.0)	1
起坐呼吸	0			0			1	(5.9)	1	1	(2.0)	1
副鼻腔うっ血	0			1	(6.3)	1	0			1	(2.0)	1
腎および尿路障害	0			1	(6.3)	1	2	(11.8)	3	3	(6.1)	4
頻尿	0			0			2	(11.8)	2	2	(4.1)	2
急性腎障害	0			1	(6.3)	1	0			1	(2.0)	1
排尿困難	0			0			1	(5.9)	1	1	(2.0)	1
生殖系および乳房障害	1	(6.3)	1	0			2	(11.8)	2	3	(6.1)	3
良性前立腺肥大症	0			0			1	(5.9)	1	1	(2.0)	1
乳房圧痛	0			0			1	(5.9)	1	1	(2.0)	1
女性化乳房	1	(6.3)	1	0			0			1	(2.0)	1
眼障害	1	(6.3)	1	0			1	(5.9)	1	2	(4.1)	2
複視	0			0			1	(5.9)	1	1	(2.0)	1
眼充血	1	(6.3)	1	0			0			1	(2.0)	1
精神障害	1	(6.3)	2	0			1	(5.9)	1	2	(4.1)	3
不眠症	1	(6.3)	1	0			1	(5.9)	1	2	(4.1)	2

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
精神障害												
うつ病	1	(6.3)	1	0			0			1	(2.0)	1
皮膚および皮下組織障害	1	(6.3)	2	0			1	(5.9)	2	2	(4.1)	4
光線角化症	0			0			1	(5.9)	1	1	(2.0)	1
脱毛症	1	(6.3)	1	0			0			1	(2.0)	1
冷汗	1	(6.3)	1	0			0			1	(2.0)	1
発疹	0			0			1	(5.9)	1	1	(2.0)	1
血管障害	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
低血圧	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
耳および迷路障害	0			1	(6.3)	1	0			1	(2.0)	1
感音性難聴	0			1	(6.3)	1	0			1	(2.0)	1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0			0			1	(5.9)	2	1	(2.0)	2
扁平上皮癌	0			0			1	(5.9)	1	1	(2.0)	1
皮膚有棘細胞癌	0			0			1	(5.9)	1	1	(2.0)	1
外科および内科処置	0			1	(6.3)	1	0			1	(2.0)	1
股関節形成	0			1	(6.3)	1	0			1	(2.0)	1

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.4.1 Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term*
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
Any Treatment-Related Adverse Events	5	(31.3)	13	6	(37.5)	22	3	(17.6)	15	14	(28.6)	50
胃腸障害	2	(12.5)	6	6	(37.5)	8	1	(5.9)	2	9	(18.4)	16
便秘	0			3	(18.8)	3	1	(5.9)	1	4	(8.2)	4
下痢	2	(12.5)	3	2	(12.5)	2	0			4	(8.2)	5
腹部不快感	1	(6.3)	1	0			0			1	(2.0)	1
腹部膨満	0			1	(6.3)	1	0			1	(2.0)	1
腹痛	0			0			1	(5.9)	1	1	(2.0)	1
上腹部痛	1	(6.3)	1	0			0			1	(2.0)	1
排便回数増加	1	(6.3)	1	0			0			1	(2.0)	1
口腔粘膜水疱形成	0			1	(6.3)	2	0			1	(2.0)	2
筋骨格系および結合組織障害	0			2	(12.5)	3	2	(11.8)	5	4	(8.2)	8
筋痙縮	0			1	(6.3)	1	2	(11.8)	2	3	(6.1)	3
四肢痛	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
関節痛	0			1	(6.3)	1	0			1	(2.0)	1

n = Number of subjects; m = Number of events
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.
Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.
*Treatment-relatedness is defined as any event with relationship of ‘Possibly Related’, 'Unlikely Related' or ‘Related’ on AE CRF page. Missing relationship is considered as ‘Related’.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.4.1 Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term*
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
筋骨格系および結合組織障害												
背部痛	0			0			1	(5.9)	1	1	(2.0)	1
筋骨格硬直	0			0			1	(5.9)	1	1	(2.0)	1
一般・全身障害および投与部位の状態	0			1	(6.3)	1	2	(11.8)	2	3	(6.1)	3
疲労	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
腫脹	0			0			1	(5.9)	1	1	(2.0)	1
神経系障害	1	(6.3)	1	2	(12.5)	3	0			3	(6.1)	4
浮動性めまい	0			1	(6.3)	1	0			1	(2.0)	1
体位性めまい	0			1	(6.3)	1	0			1	(2.0)	1
頭痛	0			1	(6.3)	1	0			1	(2.0)	1
記憶障害	1	(6.3)	1	0			0			1	(2.0)	1
呼吸器、胸郭および縦隔障害	1	(6.3)	1	1	(6.3)	1	1	(5.9)	1	3	(6.1)	3
呼吸困難	1	(6.3)	1	0			1	(5.9)	1	2	(4.1)	2
副鼻腔うっ血	0			1	(6.3)	1	0			1	(2.0)	1
心臓障害	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2

n = Number of subjects; m = Number of events
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.
Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.
*Treatment-relatedness is defined as any event with relationship of ‘Possibly Related’, 'Unlikely Related' or ‘Related’ on AE CRF page. Missing relationship is considered as ‘Related’.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.4.1 Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term*
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
心臓障害												
心房細動	0			1	(6.3)	1	0			1	(2.0)	1
動悸	0			0			1	(5.9)	1	1	(2.0)	1
臨床検査	2	(12.5)	2	0			0			2	(4.1)	2
抗凝固薬濃度治療量以上	1	(6.3)	1	0			0			1	(2.0)	1
国際標準比増加	1	(6.3)	1	0			0			1	(2.0)	1
精神障害	1	(6.3)	1	0			1	(5.9)	1	2	(4.1)	2
うつ病	1	(6.3)	1	0			0			1	(2.0)	1
不眠症	0			0			1	(5.9)	1	1	(2.0)	1
腎および尿路障害	0			1	(6.3)	1	1	(5.9)	1	2	(4.1)	2
急性腎障害	0			1	(6.3)	1	0			1	(2.0)	1
頻尿	0			0			1	(5.9)	1	1	(2.0)	1
耳および迷路障害	0			1	(6.3)	1	0			1	(2.0)	1
感音性難聴	0			1	(6.3)	1	0			1	(2.0)	1
眼障害	0			0			1	(5.9)	1	1	(2.0)	1

n = Number of subjects; m = Number of events
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.
Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.
*Treatment-relatedness is defined as any event with relationship of ‘Possibly Related’, 'Unlikely Related' or ‘Related’ on AE CRF page. Missing relationship is considered as ‘Related’.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.4.1 Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term*
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
眼障害												
複視	0			0			1	(5.9)	1	1	(2.0)	1
感染症および寄生虫症	0			1	(6.3)	2	0			1	(2.0)	2
蜂巣炎	0			1	(6.3)	2	0			1	(2.0)	2
代謝および栄養障害	0			0			1	(5.9)	1	1	(2.0)	1
食欲減退	0			0			1	(5.9)	1	1	(2.0)	1
皮膚および皮下組織障害	1	(6.3)	2	0			0			1	(2.0)	2
脱毛症	1	(6.3)	1	0			0			1	(2.0)	1
冷汗	1	(6.3)	1	0			0			1	(2.0)	1
血管障害	0			1	(6.3)	1	0			1	(2.0)	1
低血圧	0			1	(6.3)	1	0			1	(2.0)	1

n = Number of subjects; m = Number of events
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term.
Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.
*Treatment-relatedness is defined as any event with relationship of ‘Possibly Related’, 'Unlikely Related' or ‘Related’ on AE CRF page. Missing relationship is considered as ‘Related’.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.7 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)			AG10 800 mg (N=16)			Placebo (N=17)			Total (N=49)		
Any Serious Adverse Events	1	(6.3)	1	0			2	(11.8)	3	3	(6.1)	4
心臓障害	0			0			1	(5.9)	2	1	(2.0)	2
心房細動	0			0			1	(5.9)	1	1	(2.0)	1
うっ血性心不全	0			0			1	(5.9)	1	1	(2.0)	1
感染症および寄生虫症	0			0			1	(5.9)	1	1	(2.0)	1
蜂巣炎	0			0			1	(5.9)	1	1	(2.0)	1
呼吸器、胸郭および縦隔障害	1	(6.3)	1	0			0			1	(2.0)	1
呼吸困難	1	(6.3)	1	0			0			1	(2.0)	1

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

Table 14.3.2.9 Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term
(Safety Set)

System Organ Class Preferred Term [n (%) m]	AG10 400 mg (N=16)	AG10 800 mg (N=16)	Placebo (N=17)	Total (N=49)
No Adverse Events Leading to Discontinuation				

n = Number of subjects; m = Number of events.
Note: Adverse events were coded using MedDRA version 21.0. For each system organ class and preferred term, subjects are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergence is defined as any event with onset date on or after the first dose of study drug and not more than 30 days after the last dose of study drug.

Source: Listing 16.2.7.1, Dataset: ADAE

8.3.1. 死亡に至った有害事象の詳細

なし

8.3.2. その他の重篤な有害事象の詳細

Patient ID: [redacted]							
Treatment Arm: AG10 400 mg	Race: Black or African American	Country: US	Sex: F	Age: 7[redacted]			
Medical History [1]: HYPERTENSION, MIGRAINE, HYSTERECTOMY, HYPERCHOLESTEROLAEMIA, PARTIAL SEIZURES, COGNITIVE DISORDER, SLEEP APNOEA SYNDROME, SPINAL COLUMN STENOSIS, MICROALBUMINURIA, GLAUCOMA, OSTEOARTHRITIS, CARPAL TUNNEL SYNDROME, FALL, OSTEOARTHRITIS, CHRONIC KIDNEY DISEASE, BLOOD ALKALINE PHOSPHATASE INCREASED, ARTHROPATHY, ANAEMIA, HAEMATURIA, CEREBROVASCULAR ACCIDENT, CARDIAC FAILURE CONGESTIVE, HAEMANGIOMA OF LIVER, ATRIAL FIBRILLATION, FLUID OVERLOAD							
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 28					
Concomitant Medication [3]: COLECALCIFEROL, PARACETAMOL, AMLODIPINE, POTASSIUM CHLORIDE, AMIODARONE, APIXABAN, LEVETIRACETAM, LAMOTRIGINE, TORASEMIDE							
Non-Serious Adverse Event [4]: VENOUS PRESSURE JUGULAR INCREASED, EPISTAXIS							
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship [5]	Action Taken [6]	Other Action Taken [7]	Outcome [8]	Severity
呼吸困難	SHORTNESS OF BREATH	Day 14/ Day 14	2	1	NA	3	Mild
治験責任医師の見解：「呼吸困難」は、入院又は入院延長のため重篤、治験薬とおそらく関連なしと判断した。							

F = female; M = male; MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; US = United States; WHO = World Health Organization.

[1] Medical history preferred terms are coded using MedDRA version 21.0.

[2] Relative to the first study drug administration.

[3] Concomitant Medication is defined as any medication taken by a patient on or after the first dose of study drug. Medications are coded using WHO Drug Dictionary version 2018MAR01 DDE+HD B3 (Enhanced + Herbal).

[4] Adverse Event preferred terms are coded using MedDRA version 21.0.

[5] 1 = Not related; 2 = Unlikely related; 3 = Possibly related; 4 = Related.

[6] 1 = Dose not changed; 2 = Drug interrupted; 3 = Drug withdrawn; 4 = Not applicable; 5 = Unknown.

[7] M = Medication; NA = Not applicable.

[8] 1 = Fatal; 2 = Not recovered/not resolved; 3 = Recovered/resolved; 4 = Recovered/resolved with sequelae; 5 = Recovering/resolving; 6 = Unknown.

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: DEPRESSION, ANXIETY, HYPOKALAEMIA, INSOMNIA, LEFT VENTRICULAR FAILURE, AMYLOIDOSIS, ARTHRALGIA, BACK PAIN, GLAUCOMA, HYPERCHOLESTEROLAEMIA, BLOOD CREATININE INCREASED, ATRIAL FIBRILLATION, HYPERPARATHYROIDISM, HYPERTENSION, IRON DEFICIENCY ANAEMIA				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 28		
Concomitant Medication [3]: PAROXETINE, CLONAZEPAM, TRAZODONE, CODEINE;PARACETAMOL, ATORVASTATIN, DORZOLAMIDE, POTASSIUM, AMIODARONE, CALCITRIOL, FERROUS SULFATE, TORASEMIDE, CLOPIDOGREL, WARFARIN, MIDODRINE, METOLAZONE, WARFARIN, APIXABAN, POTASSIUM, POTASSIUM, TORASEMIDE, ACETYLSALICYLIC ACID, CEFTRIAXONE, FUROSEMIDE, TICAGRELOR, GLYCERYL TRINITRATE, AMIODARONE, ONDANSETRON, AMIODARONE, AMIODARONE, AMIODARONE				
Non-Serious Adverse Event [4]: FALL, HEADACHE, SYNCOPE, SYNCOPE, WHITE BLOOD CELL COUNT DECREASED, HYPERKALAEMIA, COUGH, ANGINA PECTORIS, PALPITATIONS, TACHYCARDIA, FATIGUE, DYSURIA, POLLAKIURIA, DYSPNOEA, ORTHOPNOEA, HYPOTENSION, URINARY TRACT INFECTION, BLOOD CREATININE INCREASED, C-REACTIVE PROTEIN INCREASED				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship [5]	Action Taken [6]	Other Action Taken [7]	Outcome [8]	Severity
心房細動	WORSENING A-FIB	Day 39/ Day 42	1	4	M	3	Moderate
うっ血性心不全	CONGESTIVE HEART FAILURE EXACERBATION	Day 39/ Day 42	1	4	M	3	Moderate

治験責任医師の見解：「心房細動」及び「うっ血性心不全」は、入院又は入院延長のため重篤、治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: TONSILLECTOMY, APPENDICECTOMY, SEASONAL ALLERGY, BORDERLINE GLAUCOMA, LUMBAR SPINAL STENOSIS, GLAUCOMA, CARPAL TUNNEL SYNDROME, HYPERLIPIDAEMIA, BURSITIS, CERVICAL SPINAL STENOSIS, ANAL FISSURE, CARDIAC FAILURE CONGESTIVE, FATIGUE, DYSPNOEA, THROMBOCYTOPENIA, IMPLANTABLE DEFIBRILLATOR INSERTION, FALL, CATARACT OPERATION, POSTERIOR LENS CAPSULOTOMY				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 29		
Concomitant Medication [3]: DORZOLAMIDE HYDROCHLORIDE;TIMOLOL MALEATE, DIPHENHYDRAMINE, EPLERENONE, FUROSEMIDE, EPLERENONE, EPLERENONE, FUROSEMIDE, FUROSEMIDE, EPLERENONE, FUROSEMIDE, PARACETAMOL, VANCOMYCIN, IPRATROPIUM;SALBUTAMOL, CEFTRIAXONE, FUROSEMIDE, CODEINE;GUAIFENESIN, LACTOBACILLUS NOS;SACCHAROMYCES BOULARDII, PSYLLIUM HYDROPHILIC MUCILLOID, PSYLLIUM HYDROPHILIC MUCILLOID, FUROSEMIDE, VANCOMYCIN, BUMETANIDE, BUMETANIDE, POTASSIUM CHLORIDE, VANCOMYCIN, DOCUSATE SODIUM, DOXYCYCLINE, EPLERENONE, FUROSEMIDE, EPLERENONE, FUROSEMIDE, EPLERENONE, TORASEMIDE				
Non-Serious Adverse Event [4]: FLUID OVERLOAD, CONTUSION, FLUID OVERLOAD, BRONCHITIS, BODY TEMPERATURE INCREASED, HYPONATRAEMIA, CONSTIPATION, FLUID RETENTION				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship [5]	Action Taken [6]	Other Action Taken [7]	Outcome [8]	Severity
蜂巣炎	LEFT LEG CELLULITIS	Day 52/ Day 59	1	4	M	3	Severe
治験責任医師の見解：「蜂巣炎」は、入院又は入院延長のため重篤、治験薬と関連なしと判断した。							

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9　第 3 相試験【AG10-301】（海外）［評価資料］

9.1　試験の概要

Eidos Therapeutics, Inc.（Eidos 社）が海外で実施した第 3 相試験【治験実施計画書番号：AG10-301】の概要を Table 1 に示す。AG10 は ALXN2060（アコラミジス塩酸塩）の Eidos 社での呼称である。

Table 1:　　第 3 相試験【治験実施計画書番号：AG10-301】

治験の標題：症候性トランスサイレチン型心アミロイドーシス患者を対象に AG10 の有効性及び安全性を評価する第 3 相、ランダム化、二重盲検、プラセボ対照試験（ATTRibute-CM 試験）	
治験実施計画書番号：AG10-301	
治験実施施設：18 ヵ国（オーストラリア、ベルギー、ブラジル、カナダ、チェコ共和国、デンマーク、ギリシャ、アイルランド、イスラエル、イタリア、オランダ、ニュージーランド、ポーランド、ポルトガル、韓国、スペイン、英国及び米国）117 施設。このうち 95 施設で実際に患者がランダム化。	
治験期間： 最初の患者の登録日：2019 年 4 月 [redacted] 日 最後の患者の最終来院日（安全性追跡調査）： 2023 年 5 月 [redacted] 日	**開発段階：**第 3 相
目的： 主要目的：本試験の主要目的は以下のとおりであった。 ● 複合評価項目（全死因死亡割合、心血管症状に関連する入院の累積頻度、N 末端プロ脳性ナトリウム利尿ペプチド［NT-proBNP］濃度のベースラインからの変化量及び 6 分間歩行試験［6MWT］の歩行距離のベースラインからの変化量）に関して、アコラミジス群とプラセボ群の差異を評価することによって、症候性トランスサイレチン型心アミロイドーシス（ATTR-CM）患者にアコラミジス塩酸塩を投与したときの有効性を検討する。 主な副次目的：本試験の主な副次目的は以下のとおりであった。 ● 6MWT の歩行距離に及ぼすアコラミジス塩酸塩の治療効果を評価する。 ● 症候性 ATTR-CM 患者を対象に、心不全の評価指標（Kansas City Cardiomyopathy Questionnaire［KCCQ］）を用いて測定した健康関連生活の質（QOL）に及ぼすアコラミジス塩酸塩の治療効果を評価する。 ● 循環血中プレアルブミン（トランスサイレチン［TTR］）濃度を TTR 安定化の *in vivo* バイオマーカーとして測定し、アコラミジスの薬力学的作用（PD）を評価する。 ● 全死因死亡割合に及ぼすアコラミジス塩酸塩の治療効果を評価する。 その他の副次目的：：本試験のその他の副次目的は以下のとおりであった。 ● 主要評価項目の各構成要素及びそれらの階層的解析結果によって、アコラミジス塩酸塩の有効性を検討する。 ● 症候性 ATTR-CM 患者を対象に、心血管関連死の低下に及ぼすアコラミジス塩酸塩の有効性を検討する。 ● 症候性 ATTR-CM 患者を対象に、アコラミジス塩酸塩を 30 ヵ月間投与したときの安全性及び	

忍容性を評価する。

- アコラミジスの PD に関して以下を指標に評価する：
  - 循環血中 TTR 値（TTR 安定化の *in vivo* バイオマーカー）
  - TTR 安定化の確立された *ex vivo* アッセイ

探索的目的：本試験の探索的目的は以下のとおりであった。

- 症候性 ATTR-CM 患者を対象に、アコラミジス塩酸塩が微小血管虚血の循環血中バイオマーカーに及ぼす治療効果を評価する。
- 症候性 ATTR-CM 患者を対象に、アコラミジス塩酸塩 800 mg を 1 日 2 回（BID）経口投与したときのアコラミジス（及びその主要代謝物）の薬物動態（PK）の特性を明らかにする。
- ATTR-CM 患者を対象に、アコラミジスのポピュレーション PK（PopPK）を示す。
- 循環血中 TTR 値（TTR 安定化の *in vivo* バイオマーカー）及び TTR 安定化の確立された *ex vivo* アッセイ、並びにこれらの測定値とアコラミジスの PK との相関を指標として、アコラミジスの PD 特性及び PK-PD 関連性を示す。
- 症候性 ATTR-CM 患者を対象に、EuroQOL 5-dimensions 5-levels Health Outcomes Assessment（EQ-5D-5L）評価尺度を指標として、アコラミジス塩酸塩が健康関連 QOL に及ぼす治療効果を評価する。
- 広範な臨床所見の原因となるアミノ酸置換が TTR 配列中に認められ、病原性である又は病原性である可能性が高い多種多様な変異型 TTR 四量体に対するアコラミジス塩酸塩の結合・安定化能を、ATTR-CM 患者から採取した血漿及び／又は血清検体を用いて評価する。

方法：

本試験は前向き、第 3 相、二重盲検、ランダム化、多施設共同、並行群間試験であり、症候性 ATTR-CM 患者を対象に、安定した心不全療法下でアコラミジス塩酸塩の有効性及び安全性をプラセボと比較評価した。スクリーニングで適格性が確認され、ランダム化された患者は、盲検下で計 30 ヵ月間、アコラミジス塩酸塩又はプラセボを投与した。New York Heart Association（NYHA）心機能分類 II 又は III の心不全が認められた ATTR-CM 患者を対象に実施された第 2 相試験のデータに基づき、本試験ではアコラミジス塩酸塩の用量として 800 mg BID を選択した。

慢性的かつ安定した症候性（NYHA 分類クラス I～III）ATTR-CM が認められた 18～90 歳の男女約 510 名の登録を計画し、これらの患者を 2：1 の比でアコラミジス群及びプラセボ群にランダム割付することとした。ランダム化の際には患者を遺伝子型（野生型 ATTR-CM［ATTRwt-CM］又は遺伝性 ATTR-CM［ATTRm-CM、以降は variant ATTR-CM（ATTRv-CM）］）、スクリーニング時の NT-proBNP 濃度（3000 pg/mL 以下 vs. 3000 pg/mL 超）及び腎機能（推算糸球体濾過量［eGFR］が 45 mL/min/1.73 m^2 以上 vs. 45 mL/min/1.73 m^2 未満）を層別因子とした。なお、ATTRv-CM 患者は全体の 20%となることを目標とした。

本試験では、12 ヵ月間の機能評価（Part A）、並びに 30 ヵ月間の死亡、疾患状態及び機能評価（Part B）を含む試験デザインを採用し、主要評価項目は各パートで異なった。α 消費分量は全体で 0.05 とし、Part A 及び Part B それぞれの消費分量を 0.01 及び 0.04 とした。12 ヵ月間の投与（Month 12）完了時点（Part A）で Part A の主要評価項目である機能評価（6MWT の歩行距離）及び主な副次評価項目である健康関連 QOL（KCCQ-Overall Summary Score［OS］）を解析し、アコラミジス塩酸塩の有効性を評価した。Part A の評価の結果、Part A の主要評価項目を達成しなかったた

め、計画どおり試験を継続した（Part A の結果の要約は Part A synoptic Clinical Study Report に示す）。

本項では、計 30 ヵ月間の投与（Month 30）完了時点（Part B）で得られた結果を示す。アコラミジス塩酸塩の有効性は、Month 30 までの全死因死亡、心血管症状に関連する入院の累積頻度、NT-proBNP 濃度のベースラインからの変化量及び 6MWT の歩行距離のベースラインからの変化量を階層的に解析することによって評価した。主要評価項目は、臨床的重要度に基づき評価項目を階層化する、確立されたノンパラメトリック検定である Finkelstein-Schoenfeld（F-S）法を用いて解析した。本解析法では重要度の高い臨床転帰ほど優先される。

全死因死亡及び心血管症状に関連する入院は、階層的複合エンドポイントのうち患者のベネフィットを評価するうえで臨床的に最も重要な評価項目であると判断されたため、それぞれを F-S 法の階層では 1 番目及び 2 番目の構成要素とした。近年、ベースライン時の NT-proBNP 濃度及び NT-proBNP 濃度の推移が、ATTR-CM による心不全の優れた予後評価指標であることを示した有力なエビデンスが示された。そのため、NT-proBNP 濃度を疾患進行に関連する疾患状態の臨床的に重要なマーカーとして、F-S 法の階層では 3 番目の構成要素とした。6MWT の歩行距離は、最大下運動負荷の確立された指標であるため、F-S 法の階層では最後の構成要素として、臨床的に重要な身体機能評価であると判断された。

30 ヵ月間の盲検下での治験薬投与期間及び二重盲検投与期間の最終評価（Month 30 の来院日）を完了し、適格基準を満たしたすべての患者は、アコラミジス塩酸塩を長期投与するオープンラベル継続投与（OLE）試験（AG10-304 試験）に移行できることとした。

独立したデータモニタリング委員会（DMC）が安全性、有効性及び試験の実施をモニタリングした。また、独立した臨床イベント判定委員会（CEC）で、治験責任医師等が報告した死亡、心臓移植、心臓補助装置（CMAD）、心血管症状に関連する入院及び臨床的に注目すべき事象が治験実施計画書で規定した有効性評価項目の定義に合致しているかどうかを評価及び審査した。さらに、独立した学術データ報告センターが、DMC のために盲検解除したデータを解析した。その際に DMC をサポートした非盲検統計解析専門チームは、その他の点で本試験の実施に関与することはなかった。

患者数（計画時及び解析時）：

計画時：510 名（アコラミジス群 340 名、プラセボ群 170 名）。

解析時：632 名が登録され、治験薬が投与された（アコラミジス群 421 名、プラセボ群 211 名）。有効性評価項目の主解析対象集団（modified Intent-to-Treat［mITT］集団）には 611 名（アコラミジス群：409 名、プラセボ群：202 名）が含まれた。

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす患者を本試験の組入れ対象とした。

1. 同意説明文書を理解し、署名できる者（試験手順の開始前に取得しなければならない）。
2. ランダム化時点で 18 歳以上 90 歳以下の男女。
3. 以下のいずれかの診断法により野生型 TTR 又は変異型 TTR（ジェノタイピングにより確認）を示す ATTR-CM と確定診断された者：
   a. 心筋生検で、質量分析、免疫電子顕微鏡法又は免疫組織化学による TTR アミロイドタイピングの確認。

b. ピロリン酸テクネチウム（^{99m}Tc）若しくは ^{99m}Tc-ビスホスホネートシンチグラフィ（DPD 又は HMDP/HDP）による陽性確認、及びアミロイド軽鎖（AL）アミロイドーシスの診断（血清及び尿両方の免疫固定電気泳動［IFE］、並びに血清遊離軽鎖測定に基づく）を除く一般的な検査基準の組み合わせ。

意義不明の単クローン性高ガンマグロブリン血症を併発している患者は、組織生検で質量分析、免疫電子顕微鏡法又は免疫組織化学による TTR アミロイド分類確認検査による ATTR-CM の確定診断を必要とする場合がある。

4. 以下のいずれかの条件に該当する者：
   a. 心不全による入院歴に基づく心不全の既往歴。
   b. 心不全による入院歴はないが、容量負荷や心内圧上昇の兆候又は症状による心不全の臨床的エビデンス（例：頸静脈圧上昇、息切れ、X 線検査又は聴診での肺うっ血の徴候、末梢浮腫）。
   c. 利尿薬による治療を必要とした、又は継続的に必要とする心不全の症状。
5. ATTR-CM による NYHA 心機能分類 I～III の症状を有する者。
6. 妊娠可能な女性患者の場合、ランダム化から治験薬の最終投与 30 日後までの間、異性間性交渉時には効果の高い避妊法を使用することに同意する者。妊娠可能な女性との性交渉があり、精管切除術を受けていない男性患者の場合、ダブルバリア避妊法を使用することに同意する者。
7. 心血管系の薬物療法を受けている患者の場合、利尿薬の投与を除き、スクリーニング前 2 週間以上にわたって用量が安定している者。
8. ランダム化前に 24 時間超 3 週間以下の間隔を空けて 2 回以上実施した 6MWT で歩行距離が 150 m 以上であり、2 回の歩行距離の差が 15%以内である者。

   最初の 2 回の試験のうちの 1 回で歩行距離が 150 m 未満又は最初の 2 回の歩行距離の差が 15%を超えた場合、1 回目の試験から 3 週間以内に 3 回目の試験を実施し、3 回目の試験でも歩行距離が 150 m 未満又は過去 2 回の試験のいずれとの歩行距離の差も 15%以内でない場合、当該患者は試験参加不適格とする。
9. スクリーニング時に NT-proBNP 濃度が 300 pg/mL 以上の者。
10. スクリーニング前 10 年以内に受けた（病歴に記載）経胸壁心エコー若しくは心臓磁気共鳴（CMR）、又はスクリーニング時に受けた心エコー若しくは CMR で、左室壁（心室中隔又は左室後壁）厚が 12 mm 以上である者。

［除外基準］

以下のいずれかの基準に抵触する患者は本試験から除外した。

1. スクリーニング前 90 日以内に急性心筋梗塞若しくは急性冠症候群を発症、又は冠動脈血行再建を施術された者。
2. スクリーニング前 90 日以内に脳卒中又は一過性脳虚血発作を発症した者。
3. スクリーニング時又はランダム化時に血行動態が不安定であり、試験参加のリスクが非常に大きいと治験責任医師等が判断した者。
4. スクリーニング後 1 年以内に心臓移植を受ける可能性が高い者。
5. AL アミロイドーシスの確定診断を受けている者。
6. スクリーニング時に肝機能検査値異常が認められた者（アラニンアミノトランスフェラーゼ

［ALT］若しくはアスパラギン酸アミノトランスフェラーゼ［AST］が基準値上限［ULN］の 3 倍超、又は総ビリルビンが ULN の 3 倍超と定義)。

7. スクリーニング時に NT-proBNP 濃度が 8500 pg/mL 以上の者。
8. スクリーニング時に eGFR が Modification of Diet for Renal Disease（MDRD）式で 15 mL/min/1.73 m^2 未満である者。
9. 治験薬（アコラミジス又はプラセボ)、その代謝物又は製剤の賦形剤に対する過敏症が確認されている者。
10. ATTR-CM の治療のために、治験薬の投与前 14 日以内にタファミジス、添付文書に適応症として ATTR-CM の記載がない市販製剤（例：ジフルニサル、ドキシサイクリン）又は ATTR-CM の療法として実証されていない天然物若しくは天然物誘導体（例：緑茶抽出物、タウロウルソデオキシコール酸／ウルソディオール)、投与前 90 日以内にパチシラン、投与前 180 日以内にイノテルセン、投与前（該当薬の半減期の 5 倍の期間以内）にその他の遺伝子抑制（すなわちノックダウン）剤の投与を受けた者。
    ただし、試験期間中にタファミジスが入手可能となった場合、盲検下で 12 ヵ月以上治験薬の投与を完了した患者は、併用薬としてタファミジスによる治療を開始できることとする。
11. 伝導系に影響を及ぼすカルシウムチャネル遮断薬（例：ベラパミル、ジルチアゼム）による治療を必要とする者。ジヒドロピリジンカルシウムチャネル遮断薬の使用は許可する。ジギタリスの使用は、頻拍性の心房細動を管理する必要がある場合に限り許可する。
12. 妊娠中又は授乳中の女性。授乳中の女性は、治験薬の投与前に授乳を中止することに同意しなければならない。妊娠可能な女性は、スクリーニング時及びランダム化時の尿妊娠検査が陰性でなければならない。
13. 臨床的に重要な医学的状態若しくは臨床検査値異常が継続している、又は患者の安全を脅かす、本試験への参加により患者のリスクが高まる若しくは本試験の実施を妨げる可能性がある状態にあると治験責任医師等又はメディカルモニターが判断した者。
14. 治験薬の投与前 30 日以内に他の治験に参加し、本試験の結果に影響を及ぼす可能性のある後遺症がある者。観察研究及び／又はレジストリ研究への参加に関しては、メディカルモニターと協議する。
15. 薬物乱用、アルコール依存症又は精神疾患の病歴など、治験実施計画書の遵守を妨げる可能性があると治験責任医師等又はメディカルモニターが判断した者。

治験薬、用法・用量：

アコラミジス群：アコラミジス塩酸塩 800 mg（アコラミジス塩酸塩錠 400 mg［アコラミジス活性成分 356 mg に相当］×2）を BID 経口投与した。

プラセボ群　：アコラミジス塩酸塩錠と外観が同一のプラセボ錠×2 を BID 経口投与した。

治療期間：

投与期間：30 ヵ月間（治験薬の投与中止又は試験中止に至った患者も含め、全患者の生存状況を Month 30 に収集した）

試験期間：最長約 32 ヵ月間（スクリーニング期：最長 35 日間、投与期：30 ヵ月間［固定投与期間］、追跡調査期：治験薬最終投与から最長 1 ヵ月間）

評価項目：

有効性：

主要評価項目：

- Month 30 までの固定投与期間での全死因死亡割合、心血管症状に関連する入院の累積頻度、NT-proBNP 濃度のベースラインからの変化量、及び 6MWT の歩行距離のベースラインからの変化量による階層的複合エンドポイント

主な副次評価項目：

- 6MWT の歩行距離のベースラインから Month 30 までの変化量
- KCCQ-OS のベースラインから Month 30 までの変化量
- 血清中 TTR 値（*in vivo* での TTR 安定化の指標）のベースラインから Month 30 までの変化量
- Month 30 までの全死因死亡（死因を問わないすべての死亡、心臓移植及び CMAD を含む）

その他の副次評価項目：

- Month 30 までの固定投与期間での全死因死亡及び心血管症状に関連する入院の累積頻度の階層的複合エンドポイント
- Month 30 までの固定投与期間での全死因死亡、心血管症状に関連する入院の累積頻度及び 6MWT の歩行距離のベースラインからの変化量の階層的複合エンドポイント
- Month 30 までの心血管関連死
- Month 30 までの心血管症状に関連する入院の累積頻度
- TTR 値のベースラインから Month 30 までの変化量
- 確立された *ex vivo* アッセイ（蛍光プローブ排除［FPE］アッセイ及びウェスタンブロット）を用いて測定した PK-PD サブスタディでの TTR 安定化
- NT-proBNP 濃度のベースラインから Month 30 までの変化量

探索的評価項目：

- トロポニン I（TnI）のベースラインからの変化量
- PK-PD サブスタディに参加した治験実施施設の患者から成るサブグループを対象として、症候性 ATTR-CM 患者にアコラミジス塩酸塩 800 mg を BID 経口投与したときの、アコラミジス及びその主要代謝物の定常状態（3 ヵ月ごと）での PK データ
- PK-PD サブスタディでのアコラミジスの PopPK 解析
- PK-PD サブスタディでの症候性 ATTR-CM 成人患者を対象としたアコラミジスの PK-PD 関係
- EQ-5D-5L スコアのベースラインからの変化量
- 複数の変異型 TTR に対するアコラミジスの活性を比較する追加アッセイ

安全性：

副次評価項目：

- 安全性パラメータとして、有害事象及び重篤な有害事象、治験薬の投与中止に至った有害事象、臨床的に重要な身体検査の異常所見、臨床的に重要なバイタルサインの異常、臨床的に重要な心電図（ECG）パラメータの異常、及び潜在的な臨床的懸念がある臨床安全性検査パ

ラメータの変化を評価した。

解析概要：

本試験では、試験終了までの患者データを使用し、これには規定来院、規定外来院及び早期試験終了時の来院、公記録由来のデータ（生存状況の評価用）並びに通話記録が含まれた。

連続変数はすべて平均値（標準偏差［SD］）、中央値（第一及び第三四分位数）、最小値及び最大値として要約した。カテゴリー変数は患者数及び割合としてカテゴリーごとに示した。

有効性の主要評価項目及び主な副次評価項目の正式な統計的検定は、Part B の消費分量（α_B）0.04 で順次調整した。その他の第一種の過誤の調整が不要な評価項目では、統計学的比較の際に有意水準 5%（両側）で検定した。

試験終了までの生存状況のデータを収集し、これを用いて有効性評価項目である死亡割合を算出した。全死因死亡に関するすべての解析では、心臓移植及び CMAD 埋め込みも死亡と同様に扱った。有効性評価の目的では、心血管症状に関連する入院には CEC によって判定された「心血管症状に関連する非選択的入院」又は臨床的に注目すべき事象が含まれた。臨床的に注目すべき事象の定義は心不全による 24 時間未満の規定外来院とした。臨床的に注目すべき事象のための来院時の診断及び治療に関しては、来院の目的が非代償性心不全を管理するための利尿薬静脈内投与又は心不全の一次診断であり、その他の点で心不全による入院の基準を満たさないことを記載する必要があった。

統計手法：

有効性：

Intent-to-Treat（ITT）集団の定義は、ランダム化後に治験薬が 1 回以上投与され、ベースライン後の有効性評価結果を 1 つ以上有するすべての患者とした。有効性評価項目の主要解析対象集団は mITT 集団とし、その定義は、ITT 集団の定義に合致し、ベースライン時の eGFR が 30 mL/min/1.73 m^2 以上の患者とした。

有効性の主解析では、F-S 法により各階層の構成要素に関して各患者とその他すべての患者を対比較した。解析は段階的に進め、全死因死亡を 1 番目、心血管症状に関連する入院頻度を 2 番目、NT-proBNP 濃度のベースラインからの変化量（患者間で臨床的に意味のある差は 500 pg/mL 以上）を 3 番目、6MWT の歩行距離のベースラインからの変化量を 4 番目（最後）に解析した。この段階的な解析法では、前の段階で変数を患者間で対比較した結果、差が認められなかった場合のみ、次の段階を検討した。

投与群間差の点推定値及びその信頼区間を算出し、F-S 法のスコアリングアルゴリズム（p 値は得られるが、点推定値は得られない）による有効性の主解析結果を補完するために、Win Ratio を算出した。層別化 non-matched Win Ratio 法では、F-S 法の階層構造に倣い各階層の評価項目に関してアコラミジス群の全患者とプラセボ群の全患者を対比較した。Win Ratio は、階層ごとにアコラミジス群の全 Win の和をプラセボ群の全 Win の和で割って算出した。

主解析では欠測値の補完は行わなかった。

主な副次評価項目は、α_B を維持するために、多重性を調整し検定した。

安全性：

安全性の解析は安全性解析対象集団を対象に実施し、その定義は、治験薬が 1 回以上投与された

すべての患者とした。
安全性評価パラメータは、有害事象及び重篤な有害事象（治験責任医師等により有害事象／重篤な有害事象と報告された心血管事象を含む）、治験薬の投与中止に至った有害事象、臨床的に重要な身体検査の異常所見、臨床的に重要なバイタルサインの異常、臨床的に重要な ECG パラメータの異常、並びに潜在的な臨床的懸念がある臨床安全性検査パラメータの変化であった。有害事象、臨床検査パラメータ、肝機能検査、バイタルサイン及び ECG の要約に関して、スクリーニング時の eGFR 別（30 mL/min/1.73 m^2 以上 vs. 30 mL/min/1.73 m^2 未満）の解析結果を示した。

盲検性：
試験期間中は試験完了まで、患者、治験責任医師等、CEC、治験依頼者が指定した治験実施施設のモニタリング担当者に対し、各患者の投与群への割付けの盲検性は維持された。

結果の要約：

人口統計学的特性及びベースラインの疾患特性：

全体として、ランダム化時の平均年齢は 77 歳であり、ほぼすべての患者（96.6%）が 65 歳以上であった。ほとんどの患者が男性（90.8%）、白人（87.9%）、ATTR-CM と診断されて間もない患者（診断からの期間の平均値 1.2 年［範囲：0～10.1 年］）であり、NYHA 心機能分類 II（72.7%）であった。全体で、NYHA 心機能分類 III の患者は 99 名（16.2%）、黒人の患者は 29 名（4.7%）であった。投与群間で層別因子に顕著な不均衡は認められず、試験実施時点の患者集団は、一般的な ATTR-CM 患者集団を反映していた。
全体として、ATTRv-CM 患者は 56 名（mITT 集団の 9.2%）であり、56 名の 62.5%で V122I 変異が認められた。全体として、TTR 変異ホモ接合体を有していたのは 4 名（いずれも V122I 変異）であった。ほとんどの患者（75.9%）は心内膜心筋生検を実施せず、非侵襲的に診断された。これらのベースラインの疾患特性は、投与群間でおおむねバランスがとれていた。
全体として、患者の 57.8%で心房細動、18.8%で永久的ペースメーカー留置、43.4%で手根管開放術歴が認められた。このような ATTR-CM 患者の病歴に関するベースライン特性は、投与群間でおおむねバランスがとれていた。
各評価項目のベースライン値は、投与群間でおおむねバランスがとれていた。
前治療薬及び併用薬の使用頻度は、投与群間でバランスがとれており、本試験の対象疾患及び対象患者集団で見られる併存疾患と整合していた。
本試験のいずれかの時点（Month 12 の来院前も含む）でタファミジス投与を開始した患者数は、アコラミジス群（14.9%）と比較してプラセボ群（22.8%）で多かった。全体として、ランダム化からタファミジス投与開始までの期間及び本試験でのタファミジスの曝露期間の中央値は、それぞれ 17.22 及び 11.40 ヵ月であり、投与群間で同程度であった。

有効性：

本試験の Part B の主要評価項目は達成され、プラセボと比較してアコラミジスで統計学的に有意な（$p < 0.0001$）治療効果が認められた。主解析の Win Ratio は 1.772［96%信頼区間：1.402～2.240］であり、この結果は、プラセボ群の患者と比較してアコラミジス群の患者で治療ベネフィットを得られる可能性が 77.2%高いことを示している。
F-S 法に基づく解析では、4 構成要素による全ての患者間比較のうち、最初の 2 構成要素である

全死因死亡及び心血管症状に関連する入院の比較によって約 55%で勝敗が決定した（Win Ratio 法では 58%）。また、いずれの階層的解析（2、3 又は 4 つの構成要素による F-S 主解析）でも Win Ratio 法に基づき、一貫して良好な結果が認められた。

主要評価項目の各構成要素の解析でも、プラセボ群と比較してアコラミジス群で Month 30 時点での良好な治療効果が一貫して示された：

- その他の副次評価項目である心血管症状に関連する入院頻度：臨床的に意義のある、プラセボ群に対するアコラミジス群の相対リスク比（約 50%、名目上の p 値：$p < 0.0001$）が認められた。
- その他の副次評価項目である NT-proBNP 濃度:プラセボ群と比較してアコラミジス群で良好な治療効果（調整後の幾何平均倍率変化率：0.529［95%信頼区間：0.463～0.604］、名目上の p 値：$p < 0.0001$）が認められた。
- 主な副次評価項目である 6MWT の歩行距離：プラセボ群と比較してアコラミジス群で統計学的に有意かつ臨床的に意義のある治療効果（最小二乗平均の群間差：39.64 m［96%信頼区間：20.18～59.10 m］、$p < 0.0001$）が認められた。
- 主な副次評価項目である全死因死亡：プラセボ群と比較してアコラミジス群で数値的に良好かつ臨床的に意義のある治療効果（ハザード比：0.772［96%信頼区間：0.532～1.121］、$p = 0.1543$）が認められた。生存割合は、アコラミジス群では約 81%であったのに対しプラセボ群では約 74%であった（リスクは絶対値で 6.4%低下、相対リスクは 25%低下）。eGFR が 30 mL/min/1.73 m^2 未満の患者でも、全死因死亡の相対リスクは同様に 25%低下した。

主要評価項目、並びに心血管症状に関連する入院、6MWT の歩行距離及び NT-proBNP 濃度（主要評価項目の構成要素）に関する F-S 法及び Win Ratio のサブグループ解析の結果、すべてのサブグループ（年齢、ATTRwt-CM vs. ATTRv-CM、ベースライン時の NT-proBNP 濃度、登録した国、ベースライン時の腎機能及び NYHA 心機能分類）で一貫してアコラミジス群の治療効果が良好であり、これらの結果の頑健性が示された。全死因死亡では、治療効果の点推定値（ハザード比）は NYHA 心機能分類 III を除き、すべての部分集団で一貫して 1 を下回った。

非盲検化でのタファミジス併用投与（Month 12 の来院後に使用可）の潜在的効果を検討するために実施した補足的解析の結果は、主解析の結果と整合していた（名目上の p 値：$p < 0.0001$）。タファミジスの投与開始によりアコラミジスの治療効果が低下した可能性があるにもかかわらず、複数の解析でタファミジス併用下でもプラセボ群と比較してアコラミジス群で臨床的に意義のある治療効果が認められた。

主要評価項目の構成要素に含まれない以下の主な（有意水準を調整した）副次評価項目に関しても、Month 30 時点でプラセボ群と比較してアコラミジス群で統計学的に有意な治療効果が認められた：

- KCCQ-OS:プラセボ群と比較してアコラミジス群で統計学的に有意かつ臨床的に意義のある治療ベネフィット（最小二乗平均の群間差:9.94 点［96%信頼区間:5.79～14.10 点］、$p < 0.0001$）が認められた。
- TTR 濃度のベースラインからの変化量 : プラセボ群と比較してアコラミジス群で統計学的に有意な臨床的ベネフィットに関連する治療効果（最小二乗平均の群間差：7.10 mg/dL［96%信頼区間：5.73～8.46 mg/dL］、$p < 0.0001$）が認められた。

Month 30 時点の KCCQ-OS 及び TTR 濃度のサブグループ解析の結果、プラセボ群と比較してアコラミジス群で良好な治療効果がすべてのサブグループで一貫して認められた。

その他の副次評価項目（有意水準の調整なし、及び主要評価項目の構成要素に含まれない）でも、プラセボ群と比較してアコラミジス群で Month 30 時点での良好な治療効果が認められた：

- Month 30 までの全死因死亡、心血管症状に関連する入院頻度及び 6MWT の歩行距離のベースラインからの変化量の階層的複合エンドポイント：3 つの構成要素に基づく F-S 法による検定結果は良好であった（名目上の p 値：p = 0.0024、Win Ratio：1.409［95%信頼区間：1.129～1.760］）。
- Month 30 までの全死因死亡及び心血管症状に関連する入院頻度の階層的複合エンドポイント:2 つの構成要素に基づく F-S 法による検定結果は良好であった（名目上の p 値:p = 0.0182、Win Ratio：1.464［95%信頼区間：1.067～2.009］）。
- 心血管関連死：死亡イベントの大部分（約 79%）は心血管症状に関連していた。心血管関連死は、アコラミジス群で 14.9%、プラセボ群で 21.3%であった（リスクは絶対値で 6.4%低下、相対リスクは 30%低下）。心血管関連死の Cox 比例ハザードモデルで得られたプラセボ群に対するアコラミジス群のハザード比は 0.709［95%信頼区間：0.476～1.054］であり、この結果はアコラミジス群の治療効果が良好である傾向を示している（プラセボ群と比較してアコラミジス群で心血管関連死のリスク［ハザード比］が 29.1%低下［名目上の p 値:p = 0.0889］）。

探索的評価項目でも、プラセボ群と比較してアコラミジス群で Month 30 時点での良好な治療効果が認められた：

- TnI（心不全及び急性心筋虚血イベントに関連する心筋細胞傷害及び心筋細胞死のバイオマーカー）のベースラインからの変化量：高感度 TnI は 1 施設のみで測定され、当該施設の患者で TnI はアコラミジス群で低下し、プラセボ群で上昇した（ベースラインからの平均変化率：アコラミジス群は−2.08%、プラセボ群は 39.56%）。
- EQ-5D-5L スコア（視覚的アナログ尺度）のベースラインからの変化量：プラセボ群と比較してアコラミジス群で臨床的に意味のある治療ベネフィット（最小二乗平均の群間差：9.55 点［95%信頼区間：5.50～13.59 点］、名目上の p 値：p < 0.0001）が認められた。
- PK：Month 30 時点でアコラミジスの定常状態（平均濃度：2358.0 ng/mL［約 8 μM］）のトラフ濃度は維持されていた。定常状態のトラフ濃度は Month 30 以前（Day 28～Month 27）も同程度であった。FPE アッセイ及びウェスタンブロットによりほぼ完全な（90%以上）TTR 安定化が示された。

Month 30 時点で NYHA 心機能分類のベースラインからの変化に関して、良好な治療効果（NYHA 心機能分類が改善した患者の割合：アコラミジス群 12.5%、プラセボ群 4.5%、名目上の p 値：p < 0.0001）が認められた。

安全性：

30 ヵ月間の試験期間でアコラミジスは安全であり、その忍容性は概して良好であった。全体として、有害事象の発現傾向は本試験の対象疾患及び ATTR-CM 患者集団で予測された併存疾患と整合していた。

全体で有害事象の発現割合は 97.9%（アコラミジス群：98.1%、プラセボ群：97.6%、以下同順）であった。全体で重篤な有害事象の発現割合（54.6%、64.9%）、重度の有害事象の発現割合（37.3%、45.5%）、死亡に至った有害事象の発現割合（14.3%、17.1%）及び入院に至った有害事象の発現割合（50.4%、60.7%）は、アコラミジス群でプラセボ群と比較して低かった。治験薬の投与中止に至った有害事象の発現割合（9.3%、8.5%）は、両投与群で同程度であった。

治験薬との関連性が否定できない有害事象の発現割合（11.9%、5.2%）はアコラミジス群の方が高く、この結果は主に ICH 国際医薬用語集（MedDRA）の器官別大分類（SOC）「胃腸障害」（4.8%、0.5%［群間差：4.3%］）及び「臨床検査」（2.4%、0.5%［群間差：1.9%］）に起因していた。報告された有害事象は本試験の対象疾患及び ATTR-CM 患者集団で予測された併存疾患と整合していた。
有害事象の重症度は、過半数で軽度又は中等度（60.8%、52.1%）であった。重度の有害事象は、アコラミジス群の 37.3%、プラセボ群の 45.5%で報告された。両投与群で最も多く認められた（5%超）重度の有害事象は、心不全（7.6%、12.8%）であった。
死亡に至った有害事象の発現割合は、アコラミジス群でプラセボ群と比較して低かった（14.3%、17.1%）。両投与群で最も多く認められた死亡に至った有害事象は、SOC「心臓障害」に分類される事象であり、基本語（PT）としては特に心不全（4.3%、3.8%）が多く認められた。その他すべての SOC に関して、死亡に至った有害事象の発現割合の群間差は 1%未満であった。死亡に至った重篤な有害事象は、ATTR-CM の進行及び ATTR-CM 患者集団で予測された併存疾患と整合していた。治験責任医師等により治験薬との関連性が否定できないと判定された死亡に至った有害事象は認められなかった。
治験薬の投与中止に至った有害事象の発現割合は、両投与群で同程度（9.3%、8.5%）であった。最も多く認められた治験薬の投与中止に至った有害事象は、アコラミジス群では心不全（1.2%）、プラセボ群では心不全及び心腎症候群（各 0.9%）であった。
重篤な有害事象の発現割合は、アコラミジス群でプラセボ群と比較して低かった（54.6%、64.9%）。ほとんどの重篤な有害事象は基礎疾患に起因していた。最も多く認められた重篤な有害事象（SOC 別、両投与群で 20%超）は「心臓障害」（全体で 31.6%［27.8%、39.3%］）であった。最も多く認められた重篤な有害事象（PT 別、いずれかの投与群で 3%超）は、心不全（10.7%、18.5%）、急性心不全（5.0%、6.6%）、心房細動（4.5%、7.1%）、急性腎障害（5.0%、3.8%）、転倒（3.1%、0.9%）及び COVID-19 肺炎（0.5%、3.8%）であった。全体として、重篤な有害事象の発現傾向は本試験の対象疾患及び ATTR-CM 患者集団で予測された併存疾患と整合していた。
臨床検査、バイタルサイン、ECG 及び身体検査の各所見は、本試験の患者集団と整合していた。甲状腺機能低下症（報告された有害事象により評価）の発現割合に臨床的に意味のある群間差は認められなかった。肝臓の安全性データは本試験の患者集団と整合していた。ALT 若しくは AST が ULN の 3 倍以上かつ総ビリルビンが ULN の 2 倍超であった患者、又は規定されたスケジュールで臨床検査評価中に ALT 若しくは AST が ULN の 10 倍超変化した患者はいなかった。
アコラミジスに関して、潜在的な臨床的懸念を示す安全上のシグナルは認められなかった。

結論：
アコラミジスは、ほぼ完全に TTR を安定化させる、次世代の強力な経口の TTR 安定化薬である。本試験（ATTRibute-CM 試験）では、死亡割合、疾患状態、身体機能及び QOL のいずれでもアコラミジス投与に関連したベネフィットが一貫して示された。アコラミジスが心血管症状に関連する入院頻度に及ぼす影響が明確であることは、効果の大きさ（入院頻度が 50%低下）及び早さ（Kaplan-Meier 曲線で投与開始 3 ヵ月後から）、並びに主なサブグループをとおしての一貫性により示された。また、ATTR-CM は従来、進行が避けられない疾患であるが、患者の多く（40%～45%）で身体機能、QOL 及び心臓バイオマーカーである NT-proBNP 濃度が投与開始 30 ヵ月後にプラセボ群と比較して改善した。このようなアコラミジスの臨床転帰及び疾患進行の指標に対す

る有効な治療効果は、*in vivo* での TTR 安定化による血清中 TTR 濃度の上昇と関連していた。アコラミジスは ATTRwt-CM 及び ATTRv-CM のいずれにも有効であり、その忍容性はおおむね良好で、潜在的な臨床的懸念を示す安全上のシグナルは認められなかった。これらのデータは、アコラミジスが ATTR-CM 患者にとって有効で安全な治療選択肢であることを裏付けている。
報告書作成日：20[redacted] 年 [redacted] 月 [redacted] 日

9.2 有害事象

すべての有害事象、治験薬との関連性が否定できない有害事象、重篤な有害事象及び治験薬の投与中止に至った有害事象を以下に示す。

すべての有害事象	Table 14.3.1.2
治験薬との関連性が否定できない有害事象	Table 14.3.1.5
重篤な有害事象	Table 14.3.1.9
治験薬の投与中止に至った有害事象	Table 14.3.1.16

9.3 個別被験者の詳細

死亡に至った有害事象及び重篤な有害事象を発現した患者の詳細を以下に示す。

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
Any treatment emergent adverse event	413 (98.1%) 4234	206 (97.6%) 2314	619 (97.9%) 6548
心臓障害	230 (54.6%) 498	144 (68.2%) 397	374 (59.2%) 895
心不全	101 (24.0%) 167	83 (39.3%) 166	184 (29.1%) 333
心房細動	70 (16.6%) 77	46 (21.8%) 59	116 (18.4%) 136
急性心不全	27 (6.4%) 34	17 (8.1%) 24	44 (7.0%) 58
徐脈	23 (5.5%) 23	9 (4.3%) 10	32 (5.1%) 33
心室性頻脈	17 (4.0%) 20	14 (6.6%) 24	31 (4.9%) 44
心房粗動	22 (5.2%) 22	9 (4.3%) 11	31 (4.9%) 33
慢性心不全	17 (4.0%) 21	11 (5.2%) 14	28 (4.4%) 35
うっ血性心不全	10 (2.4%) 10	7 (3.3%) 7	17 (2.7%) 17
狭心症	10 (2.4%) 13	5 (2.4%) 9	15 (2.4%) 22
完全房室ブロック	8 (1.9%) 8	3 (1.4%) 3	11 (1.7%) 11
動悸	9 (2.1%) 10	1 (0.5%) 2	10 (1.6%) 12
急性心筋梗塞	5 (1.2%) 7	4 (1.9%) 4	9 (1.4%) 11
心停止	4 (1.0%) 4	4 (1.9%) 4	8 (1.3%) 8
心房頻脈	6 (1.4%) 10	1 (0.5%) 1	7 (1.1%) 11
心腎症候群	4 (1.0%) 4	3 (1.4%) 4	7 (1.1%) 8
頻脈	5 (1.2%) 5	2 (0.9%) 3	7 (1.1%) 8
上室性頻脈	6 (1.4%) 6	1 (0.5%) 1	7 (1.1%) 7

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
急性左室不全	3 (0.7%) 3	3 (1.4%) 5	6 (0.9%) 8
房室ブロック	3 (0.7%) 4	3 (1.4%) 3	6 (0.9%) 7
心アミロイドーシス	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
冠動脈疾患	1 (0.2%) 1	4 (1.9%) 4	5 (0.8%) 5
心原性ショック	1 (0.2%) 1	3 (1.4%) 5	4 (0.6%) 6
第一度房室ブロック	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
心筋虚血	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
心嚢液貯留	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
右室不全	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
三束ブロック	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
心室性期外収縮	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
心房血栓症	1 (0.2%) 2	2 (0.9%) 2	3 (0.5%) 4
第二度房室ブロック	1 (0.2%) 1	2 (0.9%) 3	3 (0.5%) 4
慢性左室不全	2 (0.5%) 2	1 (0.5%) 2	3 (0.5%) 4
不整脈	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
洞性徐脈	3 (0.7%) 3	0	3 (0.5%) 3
洞結節機能不全	3 (0.7%) 3	0	3 (0.5%) 3
徐脈性不整脈	0	2 (0.9%) 2	2 (0.3%) 2
伝導障害	2 (0.5%) 2	0	2 (0.3%) 2
僧帽弁閉鎖不全症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
三尖弁閉鎖不全症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
心膜炎	0	1 (0.5%) 2	1 (0.2%) 2
大動脈弁石灰化	1 (0.2%) 1	0	1 (0.2%) 1
大動脈弁狭窄	1 (0.2%) 1	0	1 (0.2%) 1
大動脈弁肥厚	1 (0.2%) 1	0	1 (0.2%) 1
冠動脈硬化症	1 (0.2%) 1	0	1 (0.2%) 1
二束ブロック	1 (0.2%) 1	0	1 (0.2%) 1
脚ブロック	1 (0.2%) 1	0	1 (0.2%) 1
左脚ブロック	0	1 (0.5%) 1	1 (0.2%) 1
右脚ブロック	0	1 (0.5%) 1	1 (0.2%) 1
心粗動	1 (0.2%) 1	0	1 (0.2%) 1
心タンポナーデ	0	1 (0.5%) 1	1 (0.2%) 1
心室血栓症	1 (0.2%) 1	0	1 (0.2%) 1
心肺停止	0	1 (0.5%) 1	1 (0.2%) 1
左室機能不全	0	1 (0.5%) 1	1 (0.2%) 1
僧帽弁肥厚	1 (0.2%) 1	0	1 (0.2%) 1
心筋梗塞	0	1 (0.5%) 1	1 (0.2%) 1
陰性心筋変力作用	1 (0.2%) 1	0	1 (0.2%) 1
結節性調律	1 (0.2%) 1	0	1 (0.2%) 1
肺動脈弁閉鎖不全症	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
上室性期外収縮	1 (0.2%) 1	0	1 (0.2%) 1
頻脈性不整脈	1 (0.2%) 1	0	1 (0.2%) 1
心室性不整脈	1 (0.2%) 1	0	1 (0.2%) 1
心室細動	1 (0.2%) 1	0	1 (0.2%) 1
感染症および寄生虫症	246 (58.4%) 501	116 (55.0%) 240	362 (57.3%) 741
COVID-19	89 (21.1%) 89	30 (14.2%) 32	119 (18.8%) 121
尿路感染	51 (12.1%) 62	28 (13.3%) 34	79 (12.5%) 96
上気道感染	24 (5.7%) 26	12 (5.7%) 12	36 (5.7%) 38
上咽頭炎	21 (5.0%) 23	11 (5.2%) 12	32 (5.1%) 35
下気道感染	20 (4.8%) 37	10 (4.7%) 14	30 (4.7%) 51
肺炎	16 (3.8%) 18	14 (6.6%) 17	30 (4.7%) 35
蜂巣炎	19 (4.5%) 22	10 (4.7%) 12	29 (4.6%) 34
気管支炎	14 (3.3%) 15	5 (2.4%) 5	19 (3.0%) 20
帯状疱疹	12 (2.9%) 12	4 (1.9%) 4	16 (2.5%) 16
インフルエンザ	8 (1.9%) 8	6 (2.8%) 7	14 (2.2%) 15
歯感染	11 (2.6%) 13	1 (0.5%) 1	12 (1.9%) 14
気道感染	8 (1.9%) 9	3 (1.4%) 3	11 (1.7%) 12
COVID-19肺炎	2 (0.5%) 2	8 (3.8%) 8	10 (1.6%) 10
丹毒	6 (1.4%) 7	3 (1.4%) 4	9 (1.4%) 11

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
口腔カンジダ症	5 (1.2%) 5	4 (1.9%) 5	9 (1.4%) 10
胃腸炎	7 (1.7%) 8	1 (0.5%) 1	8 (1.3%) 9
創傷感染	5 (1.2%) 6	3 (1.4%) 3	8 (1.3%) 9
敗血症	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
結膜炎	5 (1.2%) 5	2 (0.9%) 2	7 (1.1%) 7
副鼻腔炎	5 (1.2%) 8	1 (0.5%) 2	6 (0.9%) 10
限局性感染	4 (1.0%) 5	2 (0.9%) 2	6 (0.9%) 7
ウイルス性上気道感染	4 (1.0%) 5	2 (0.9%) 2	6 (0.9%) 7
膀胱炎	3 (0.7%) 3	3 (1.4%) 3	6 (0.9%) 6
無症候性COVID-19	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
ウイルス性胃腸炎	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
処置後感染	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
医療機器関連感染	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
細菌性肺炎	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
術後創感染	4 (1.0%) 4	0	4 (0.6%) 4
敗血症性ショック	4 (1.0%) 4	0	4 (0.6%) 4
ブドウ球菌感染	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
尿路性敗血症	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
菌血症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
眼感染	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
口腔ヘルペス	0	3 (1.4%) 3	3 (0.5%) 3
皮膚感染	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
歯膿瘍	3 (0.7%) 3	0	3 (0.5%) 3
四肢膿瘍	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
急性副鼻腔炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
肛門カンジダ症	2 (0.5%) 2	0	2 (0.3%) 2
体部白癬	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
クロストリジウム・ディフィシレ感染	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
憩室炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
耳感染	2 (0.5%) 2	0	2 (0.3%) 2
精巣上体炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
大腸菌性尿路感染	2 (0.5%) 2	0	2 (0.3%) 2
真菌感染	0	2 (0.9%) 2	2 (0.3%) 2
皮膚真菌感染	2 (0.5%) 2	0	2 (0.3%) 2
血腫感染	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
ヘリコバクター性胃炎	2 (0.5%) 2	0	2 (0.3%) 2
ヘルペス眼感染	2 (0.5%) 2	0	2 (0.3%) 2
外耳炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
誤嚥性肺炎	2 (0.5%) 2	0	2 (0.3%) 2
ブドウ球菌性菌血症	2 (0.5%) 2	0	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
ブドウ球菌性敗血症	0	2 (0.9%) 2	2 (0.3%) 2
足部白癬	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
ウイルス感染	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
精巣膿瘍	1 (0.2%) 2	0	1 (0.2%) 2
細菌性尿路感染	1 (0.2%) 2	0	1 (0.2%) 2
腹部敗血症	0	1 (0.5%) 1	1 (0.2%) 1
ダニ皮膚炎	0	1 (0.5%) 1	1 (0.2%) 1
真菌性肛門感染	1 (0.2%) 1	0	1 (0.2%) 1
感染性関節炎	1 (0.2%) 1	0	1 (0.2%) 1
細菌性敗血症	1 (0.2%) 1	0	1 (0.2%) 1
細菌尿	1 (0.2%) 1	0	1 (0.2%) 1
カンジダ性亀頭炎	0	1 (0.5%) 1	1 (0.2%) 1
ブラストシスティス感染	0	1 (0.5%) 1	1 (0.2%) 1
カンピロバクター感染	1 (0.2%) 1	0	1 (0.2%) 1
カンジダ感染	1 (0.2%) 1	0	1 (0.2%) 1
感染性胆嚢炎	1 (0.2%) 1	0	1 (0.2%) 1
慢性副鼻腔炎	1 (0.2%) 1	0	1 (0.2%) 1
医療機器関連敗血症	0	1 (0.5%) 1	1 (0.2%) 1
赤痢	1 (0.2%) 1	0	1 (0.2%) 1
ウイルス性耳感染	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
心内膜炎	0	1 (0.5%) 1	1 (0.2%) 1
腸球菌感染	1 (0.2%) 1	0	1 (0.2%) 1
大腸菌性菌血症	0	1 (0.5%) 1	1 (0.2%) 1
眼膿瘍	1 (0.2%) 1	0	1 (0.2%) 1
毛包炎	1 (0.2%) 1	0	1 (0.2%) 1
真菌性咽頭炎	1 (0.2%) 1	0	1 (0.2%) 1
ウイルス性消化管感染	0	1 (0.5%) 1	1 (0.2%) 1
鼠径部感染	1 (0.2%) 1	0	1 (0.2%) 1
B型肝炎	0	1 (0.5%) 1	1 (0.2%) 1
C型肝炎	1 (0.2%) 1	0	1 (0.2%) 1
単純ヘルペス	1 (0.2%) 1	0	1 (0.2%) 1
埋込み部位感染	1 (0.2%) 1	0	1 (0.2%) 1
切開部位蜂巣炎	1 (0.2%) 1	0	1 (0.2%) 1
感染性腱膜瘤	0	1 (0.5%) 1	1 (0.2%) 1
感染性嚢腫	0	1 (0.5%) 1	1 (0.2%) 1
感染による気管支拡張症の増悪	1 (0.2%) 1	0	1 (0.2%) 1
感染性腱鞘炎	0	1 (0.5%) 1	1 (0.2%) 1
椎間板炎	1 (0.2%) 1	0	1 (0.2%) 1
肺膿瘍	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
医療機器使用部位感染	1 (0.2%) 1	0	1 (0.2%) 1
医療機器使用部位関節感染	0	1 (0.5%) 1	1 (0.2%) 1
爪床感染	0	1 (0.5%) 1	1 (0.2%) 1
食道カンジダ症	1 (0.2%) 1	0	1 (0.2%) 1
爪真菌症	0	1 (0.5%) 1	1 (0.2%) 1
眼帯状疱疹	1 (0.2%) 1	0	1 (0.2%) 1
口腔真菌感染	0	1 (0.5%) 1	1 (0.2%) 1
精巣炎	1 (0.2%) 1	0	1 (0.2%) 1
骨髄炎	1 (0.2%) 1	0	1 (0.2%) 1
中耳炎	1 (0.2%) 1	0	1 (0.2%) 1
歯周炎	1 (0.2%) 1	0	1 (0.2%) 1
咽頭炎	1 (0.2%) 1	0	1 (0.2%) 1
肺炎球菌感染	0	1 (0.5%) 1	1 (0.2%) 1
ブドウ球菌性肺炎	1 (0.2%) 1	0	1 (0.2%) 1
ウイルス感染後疲労症候群	1 (0.2%) 1	0	1 (0.2%) 1
急性COVID-19後症候群	1 (0.2%) 1	0	1 (0.2%) 1
急性腎盂腎炎	1 (0.2%) 1	0	1 (0.2%) 1
ウイルス性気道感染	0	1 (0.5%) 1	1 (0.2%) 1
後腹膜膿瘍	0	1 (0.5%) 1	1 (0.2%) 1
鼻炎	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
SARS-CoV-2キャリアー	1 (0.2%) 1	0	1 (0.2%) 1
パスツレラ菌性敗血症	0	1 (0.5%) 1	1 (0.2%) 1
レンサ球菌性化膿性関節炎	1 (0.2%) 1	0	1 (0.2%) 1
皮膚カンジダ	1 (0.2%) 1	0	1 (0.2%) 1
植皮感染	0	1 (0.5%) 1	1 (0.2%) 1
股部白癬	1 (0.2%) 1	0	1 (0.2%) 1
感染後尿道狭窄	0	1 (0.5%) 1	1 (0.2%) 1
シュードモナス性尿路感染	1 (0.2%) 1	0	1 (0.2%) 1
胃腸障害	221 (52.5%) 445	98 (46.4%) 185	319 (50.5%) 630
便秘	52 (12.4%) 58	32 (15.2%) 38	84 (13.3%) 96
下痢	49 (11.6%) 56	16 (7.6%) 17	65 (10.3%) 73
悪心	24 (5.7%) 26	11 (5.2%) 11	35 (5.5%) 37
上腹部痛	23 (5.5%) 23	3 (1.4%) 5	26 (4.1%) 28
腹痛	18 (4.3%) 19	5 (2.4%) 6	23 (3.6%) 25
胃食道逆流性疾患	15 (3.6%) 16	7 (3.3%) 8	22 (3.5%) 24
鼠径ヘルニア	15 (3.6%) 15	6 (2.8%) 8	21 (3.3%) 23
腹部膨満	14 (3.3%) 15	4 (1.9%) 4	18 (2.8%) 19
嚥下障害	9 (2.1%) 9	7 (3.3%) 7	16 (2.5%) 16
消化不良	12 (2.9%) 16	3 (1.4%) 3	15 (2.4%) 19

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
嘔吐	12 (2.9%) 13	3 (1.4%) 3	15 (2.4%) 16
腹部不快感	8 (1.9%) 8	5 (2.4%) 6	13 (2.1%) 14
痔核	9 (2.1%) 9	4 (1.9%) 4	13 (2.1%) 13
直腸出血	10 (2.4%) 12	2 (0.9%) 2	12 (1.9%) 14
メレナ	7 (1.7%) 9	4 (1.9%) 4	11 (1.7%) 13
腹水	4 (1.0%) 5	7 (3.3%) 7	11 (1.7%) 12
憩室	8 (1.9%) 8	1 (0.5%) 1	9 (1.4%) 9
口内乾燥	7 (1.7%) 7	1 (0.5%) 1	8 (1.3%) 8
鼓腸	7 (1.7%) 7	1 (0.5%) 1	8 (1.3%) 8
大腸ポリープ	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
胃腸出血	5 (1.2%) 6	2 (0.9%) 2	7 (1.1%) 8
胃炎	4 (1.0%) 4	3 (1.4%) 3	7 (1.1%) 7
裂孔ヘルニア	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
肛門失禁	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
おくび	4 (1.0%) 4	0	4 (0.6%) 4
胃腸障害	4 (1.0%) 4	0	4 (0.6%) 4
過敏性腸症候群	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
口腔内潰瘍形成	4 (1.0%) 4	0	4 (0.6%) 4
上部消化管出血	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
胃潰瘍	2 (0.5%) 3	1 (0.5%) 1	3 (0.5%) 4

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
下腹部痛	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
腸憩室	3 (0.7%) 3	0	3 (0.5%) 3
歯肉出血	3 (0.7%) 3	0	3 (0.5%) 3
小腸閉塞	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
歯痛	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
変色便	2 (0.5%) 3	0	2 (0.3%) 3
腹部ヘルニア	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
バレット食道	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
便習慣変化	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
慢性胃炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
大腸炎	2 (0.5%) 2	0	2 (0.3%) 2
十二指腸潰瘍	2 (0.5%) 2	0	2 (0.3%) 2
十二指腸炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
びらん性胃炎	2 (0.5%) 2	0	2 (0.3%) 2
消化器痛	2 (0.5%) 2	0	2 (0.3%) 2
血便排泄	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
絞扼性鼠径ヘルニア	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
腸閉塞	2 (0.5%) 2	0	2 (0.3%) 2
嚥下痛	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
直腸ポリープ	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
臍ヘルニア	2 (0.5%) 2	0	2 (0.3%) 2
流涎過多	1 (0.2%) 2	0	1 (0.2%) 2
腹部脂肪エプロン	0	1 (0.5%) 1	1 (0.2%) 1
腹部圧痛	0	1 (0.5%) 1	1 (0.2%) 1
腹壁障害	0	1 (0.5%) 1	1 (0.2%) 1
異常便	0	1 (0.5%) 1	1 (0.2%) 1
裂肛	0	1 (0.5%) 1	1 (0.2%) 1
便通不規則	1 (0.2%) 1	0	1 (0.2%) 1
セリアック病	1 (0.2%) 1	0	1 (0.2%) 1
潰瘍性大腸炎	1 (0.2%) 1	0	1 (0.2%) 1
齲歯	1 (0.2%) 1	0	1 (0.2%) 1
出血性腸憩室	0	1 (0.5%) 1	1 (0.2%) 1
腸炎	1 (0.2%) 1	0	1 (0.2%) 1
びらん性十二指腸炎	1 (0.2%) 1	0	1 (0.2%) 1
硬便	1 (0.2%) 1	0	1 (0.2%) 1
大腿ヘルニア	1 (0.2%) 1	0	1 (0.2%) 1
排便回数増加	0	1 (0.5%) 1	1 (0.2%) 1
機能性胃腸障害	1 (0.2%) 1	0	1 (0.2%) 1
胃障害	1 (0.2%) 1	0	1 (0.2%) 1
出血性胃潰瘍	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
胃腸管血管異形成	1 (0.2%) 1	0	1 (0.2%) 1
消化管運動障害	1 (0.2%) 1	0	1 (0.2%) 1
胃食道括約筋機能不全	0	1 (0.5%) 1	1 (0.2%) 1
歯肉障害	0	1 (0.5%) 1	1 (0.2%) 1
歯肉痛	1 (0.2%) 1	0	1 (0.2%) 1
舌炎	0	1 (0.5%) 1	1 (0.2%) 1
痔出血	1 (0.2%) 1	0	1 (0.2%) 1
イレウス	1 (0.2%) 1	0	1 (0.2%) 1
腸管虚血	1 (0.2%) 1	0	1 (0.2%) 1
腸上皮化生	1 (0.2%) 1	0	1 (0.2%) 1
腸管穿孔	1 (0.2%) 1	0	1 (0.2%) 1
腸管ポリープ	1 (0.2%) 1	0	1 (0.2%) 1
腹腔内液貯留	1 (0.2%) 1	0	1 (0.2%) 1
大腸出血	0	1 (0.5%) 1	1 (0.2%) 1
口唇腫脹	1 (0.2%) 1	0	1 (0.2%) 1
下部消化管出血	1 (0.2%) 1	0	1 (0.2%) 1
マロリー・ワイス症候群	0	1 (0.5%) 1	1 (0.2%) 1
機械的イレウス	1 (0.2%) 1	0	1 (0.2%) 1
腸間膜動脈血栓症	0	1 (0.5%) 1	1 (0.2%) 1
口腔内出血	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
口腔血性水疱	0	1 (0.5%) 1	1 (0.2%) 1
口腔障害	1 (0.2%) 1	0	1 (0.2%) 1
口腔粘膜水疱形成	1 (0.2%) 1	0	1 (0.2%) 1
口腔粘膜剥脱	0	1 (0.5%) 1	1 (0.2%) 1
口腔内色素沈着	1 (0.2%) 1	0	1 (0.2%) 1
耳下腺腫大	1 (0.2%) 1	0	1 (0.2%) 1
ひだ舌	1 (0.2%) 1	0	1 (0.2%) 1
肛門周囲痛	0	1 (0.5%) 1	1 (0.2%) 1
直腸脱	0	1 (0.5%) 1	1 (0.2%) 1
吐き戻し	1 (0.2%) 1	0	1 (0.2%) 1
後腹膜腫瘤	1 (0.2%) 1	0	1 (0.2%) 1
小腸出血	1 (0.2%) 1	0	1 (0.2%) 1
舌変色	1 (0.2%) 1	0	1 (0.2%) 1
舌障害	1 (0.2%) 1	0	1 (0.2%) 1
舌粘膜剥脱	0	1 (0.5%) 1	1 (0.2%) 1
地図状舌	1 (0.2%) 1	0	1 (0.2%) 1
舌血腫	0	1 (0.5%) 1	1 (0.2%) 1
舌出血	0	1 (0.5%) 1	1 (0.2%) 1
歯槽出血	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
筋骨格系および結合組織障害	184 (43.7%) 336	83 (39.3%) 165	267 (42.2%) 501
関節痛	48 (11.4%) 62	23 (10.9%) 32	71 (11.2%) 94
背部痛	39 (9.3%) 44	14 (6.6%) 15	53 (8.4%) 59
筋痙縮	34 (8.1%) 42	15 (7.1%) 15	49 (7.8%) 57
四肢痛	30 (7.1%) 40	11 (5.2%) 15	41 (6.5%) 55
変形性関節症	12 (2.9%) 16	12 (5.7%) 15	24 (3.8%) 31
滑液包炎	10 (2.4%) 11	6 (2.8%) 6	16 (2.5%) 17
筋肉痛	8 (1.9%) 8	8 (3.8%) 9	16 (2.5%) 17
関節炎	7 (1.7%) 8	6 (2.8%) 6	13 (2.1%) 14
頚部痛	7 (1.7%) 7	4 (1.9%) 6	11 (1.7%) 13
関節腫脹	4 (1.0%) 4	7 (3.3%) 7	11 (1.7%) 11
筋骨格系胸痛	7 (1.7%) 7	3 (1.4%) 3	10 (1.6%) 10
肩回旋筋腱板症候群	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
筋力低下	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
運動性低下	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
脊柱管狭窄症	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
痛風性関節炎	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
椎間板突出	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
筋骨格痛	4 (1.0%) 4	0	4 (0.6%) 4
骨粗鬆症	4 (1.0%) 4	0	4 (0.6%) 4

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
脊椎痛	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
滑液嚢腫	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
弾発指	4 (1.0%) 4	0	4 (0.6%) 4
関節障害	3 (0.7%) 3	0	3 (0.5%) 3
腰部脊柱管狭窄症	3 (0.7%) 3	0	3 (0.5%) 3
筋萎縮	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
筋骨格硬直	3 (0.7%) 3	0	3 (0.5%) 3
関節リウマチ	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
変形性脊椎症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
腱鞘炎	1 (0.2%) 1	1 (0.5%) 2	2 (0.3%) 3
頚部脊柱管狭窄症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
ピロリン酸カルシウム結晶性軟骨石灰化症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
足変形	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
四肢不快感	2 (0.5%) 2	0	2 (0.3%) 2
骨減少症	2 (0.5%) 2	0	2 (0.3%) 2
横紋筋融解症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
腱炎	2 (0.5%) 2	0	2 (0.3%) 2
狭窄性腱鞘炎	2 (0.5%) 2	0	2 (0.3%) 2
乾癬性関節症	1 (0.2%) 2	0	1 (0.2%) 2
足関節インピンジメント	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
滑液包障害	1 (0.2%) 1	0	1 (0.2%) 1
指炎	1 (0.2%) 1	0	1 (0.2%) 1
デュプイトラン拘縮	1 (0.2%) 1	0	1 (0.2%) 1
腱付着部症	0	1 (0.5%) 1	1 (0.2%) 1
椎間関節症候群	1 (0.2%) 1	0	1 (0.2%) 1
側腹部痛	0	1 (0.5%) 1	1 (0.2%) 1
痛風結節	0	1 (0.5%) 1	1 (0.2%) 1
鼠径部痛	0	1 (0.5%) 1	1 (0.2%) 1
出血性関節症	1 (0.2%) 1	0	1 (0.2%) 1
高クレアチン血症	1 (0.2%) 1	0	1 (0.2%) 1
椎間板障害	1 (0.2%) 1	0	1 (0.2%) 1
関節可動域低下	0	1 (0.5%) 1	1 (0.2%) 1
関節硬直	0	1 (0.5%) 1	1 (0.2%) 1
中足骨痛	0	1 (0.5%) 1	1 (0.2%) 1
筋肉疲労	1 (0.2%) 1	0	1 (0.2%) 1
筋攣縮	1 (0.2%) 1	0	1 (0.2%) 1
筋骨格不快感	0	1 (0.5%) 1	1 (0.2%) 1
筋炎	1 (0.2%) 1	0	1 (0.2%) 1
頚部腫瘤	1 (0.2%) 1	0	1 (0.2%) 1
顎痛	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
病的骨折	1 (0.2%) 1	0	1 (0.2%) 1
リウマチ性多発筋痛	0	1 (0.5%) 1	1 (0.2%) 1
リウマチ熱	1 (0.2%) 1	0	1 (0.2%) 1
脊椎炎	1 (0.2%) 1	0	1 (0.2%) 1
脊椎すべり症	1 (0.2%) 1	0	1 (0.2%) 1
滑膜炎	1 (0.2%) 1	0	1 (0.2%) 1
全身性強皮症	1 (0.2%) 1	0	1 (0.2%) 1
腱痛	1 (0.2%) 1	0	1 (0.2%) 1
胸部脊柱管狭窄症	1 (0.2%) 1	0	1 (0.2%) 1
斜頚	0	1 (0.5%) 1	1 (0.2%) 1
椎間孔狭窄	1 (0.2%) 1	0	1 (0.2%) 1
神経系障害	182 (43.2%) 283	77 (36.5%) 128	259 (41.0%) 411
浮動性めまい	46 (10.9%) 55	23 (10.9%) 24	69 (10.9%) 79
失神	21 (5.0%) 23	15 (7.1%) 22	36 (5.7%) 45
頭痛	17 (4.0%) 19	8 (3.8%) 8	25 (4.0%) 27
錯感覚	15 (3.6%) 16	4 (1.9%) 4	19 (3.0%) 20
失神寸前の状態	15 (3.6%) 16	4 (1.9%) 4	19 (3.0%) 20
末梢性ニューロパチー	11 (2.6%) 12	4 (1.9%) 4	15 (2.4%) 16
認知障害	10 (2.4%) 10	4 (1.9%) 4	14 (2.2%) 14

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
感覚鈍麻	10 (2.4%) 10	4 (1.9%) 4	14 (2.2%) 14
体位性めまい	9 (2.1%) 9	3 (1.4%) 3	12 (1.9%) 12
手根管症候群	5 (1.2%) 5	5 (2.4%) 5	10 (1.6%) 10
平衡障害	8 (1.9%) 8	1 (0.5%) 1	9 (1.4%) 9
坐骨神経痛	8 (1.9%) 8	1 (0.5%) 1	9 (1.4%) 9
振戦	5 (1.2%) 6	2 (0.9%) 2	7 (1.1%) 8
脳血管発作	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
認知症	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
嗜眠	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
傾眠	5 (1.2%) 5	1 (0.5%) 1	6 (0.9%) 6
下肢静止不能症候群	1 (0.2%) 1	4 (1.9%) 7	5 (0.8%) 8
記憶障害	5 (1.2%) 6	0	5 (0.8%) 6
味覚不全	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
意識消失	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
神経痛	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
パーキンソン病	1 (0.2%) 1	2 (0.9%) 5	3 (0.5%) 6
失語症	3 (0.7%) 3	0	3 (0.5%) 3
脳梗塞	3 (0.7%) 3	0	3 (0.5%) 3
灼熱感	2 (0.5%) 3	0	2 (0.3%) 3
神経系障害	2 (0.5%) 3	0	2 (0.3%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
ジスキネジア	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
塞栓性脳卒中	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
虚血性脳卒中	2 (0.5%) 2	0	2 (0.3%) 2
多発ニューロパチー	2 (0.5%) 2	0	2 (0.3%) 2
痙攣発作	0	2 (0.9%) 2	2 (0.3%) 2
くも膜下出血	2 (0.5%) 2	0	2 (0.3%) 2
一過性脳虚血発作	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
三叉神経痛	2 (0.5%) 2	0	2 (0.3%) 2
舞踏病	1 (0.2%) 2	0	1 (0.2%) 2
てんかん	0	1 (0.5%) 2	1 (0.2%) 2
不随意性筋収縮	1 (0.2%) 2	0	1 (0.2%) 2
味覚消失	0	1 (0.5%) 1	1 (0.2%) 1
健忘	0	1 (0.5%) 1	1 (0.2%) 1
反射消失	0	1 (0.5%) 1	1 (0.2%) 1
軸索型ニューロパチー	1 (0.2%) 1	0	1 (0.2%) 1
頚動脈狭窄	0	1 (0.5%) 1	1 (0.2%) 1
脳出血	1 (0.2%) 1	0	1 (0.2%) 1
頚髄神経根障害	1 (0.2%) 1	0	1 (0.2%) 1
脳神経麻痺	1 (0.2%) 1	0	1 (0.2%) 1
意識レベルの低下	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
糖尿病性ニューロパチー	1 (0.2%) 1	0	1 (0.2%) 1
よだれ	1 (0.2%) 1	0	1 (0.2%) 1
異常感覚	1 (0.2%) 1	0	1 (0.2%) 1
構語障害	1 (0.2%) 1	0	1 (0.2%) 1
脳症	1 (0.2%) 1	0	1 (0.2%) 1
本態性振戦	0	1 (0.5%) 1	1 (0.2%) 1
顔面麻痺	1 (0.2%) 1	0	1 (0.2%) 1
前頭側頭型認知症	1 (0.2%) 1	0	1 (0.2%) 1
不全片麻痺	0	1 (0.5%) 1	1 (0.2%) 1
肝性脳症	0	1 (0.5%) 1	1 (0.2%) 1
知覚過敏	1 (0.2%) 1	0	1 (0.2%) 1
過眠症	1 (0.2%) 1	0	1 (0.2%) 1
低酸素性虚血性脳症	0	1 (0.5%) 1	1 (0.2%) 1
虚血性脳梗塞	1 (0.2%) 1	0	1 (0.2%) 1
腰髄神経根障害	1 (0.2%) 1	0	1 (0.2%) 1
腰仙部神経根障害	1 (0.2%) 1	0	1 (0.2%) 1
マイクロスリープ	1 (0.2%) 1	0	1 (0.2%) 1
脊髄症	1 (0.2%) 1	0	1 (0.2%) 1
神経圧迫	1 (0.2%) 1	0	1 (0.2%) 1
非24時間睡眠覚醒障害	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
小発作てんかん	0	1 (0.5%) 1	1 (0.2%) 1
ヘルペス後神経痛	1 (0.2%) 1	0	1 (0.2%) 1
老年認知症	0	1 (0.5%) 1	1 (0.2%) 1
感覚障害	0	1 (0.5%) 1	1 (0.2%) 1
会話障害	1 (0.2%) 1	0	1 (0.2%) 1
味覚障害	0	1 (0.5%) 1	1 (0.2%) 1
緊張性頭痛	1 (0.2%) 1	0	1 (0.2%) 1
声帯麻痺	0	1 (0.5%) 1	1 (0.2%) 1
代謝および栄養障害	149 (35.4%) 262	85 (40.3%) 158	234 (37.0%) 420
痛風	47 (11.2%) 67	17 (8.1%) 23	64 (10.1%) 90
血液量増加症	23 (5.5%) 34	18 (8.5%) 26	41 (6.5%) 60
低カリウム血症	22 (5.2%) 26	12 (5.7%) 18	34 (5.4%) 44
食欲減退	19 (4.5%) 21	11 (5.2%) 11	30 (4.7%) 32
高カリウム血症	16 (3.8%) 19	10 (4.7%) 11	26 (4.1%) 30
脱水	11 (2.6%) 11	7 (3.3%) 8	18 (2.8%) 19
高尿酸血症	12 (2.9%) 13	4 (1.9%) 4	16 (2.5%) 17
低ナトリウム血症	8 (1.9%) 9	5 (2.4%) 6	13 (2.1%) 15
2型糖尿病	7 (1.7%) 7	5 (2.4%) 5	12 (1.9%) 12

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
鉄欠乏	6 (1.4%) 6	5 (2.4%) 7	11 (1.7%) 13
ビタミンD欠乏	6 (1.4%) 6	4 (1.9%) 4	10 (1.6%) 10
糖尿病	3 (0.7%) 3	3 (1.4%) 3	6 (0.9%) 6
低カルシウム血症	5 (1.2%) 5	1 (0.5%) 1	6 (0.9%) 6
低血糖	5 (1.2%) 5	1 (0.5%) 1	6 (0.9%) 6
体液貯留	1 (0.2%) 1	4 (1.9%) 4	5 (0.8%) 5
高コレステロール血症	5 (1.2%) 5	0	5 (0.8%) 5
高血糖	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
血液量減少症	1 (0.2%) 1	4 (1.9%) 4	5 (0.8%) 5
ビタミンB12欠乏	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
異常体重減少	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
悪液質	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
高ナトリウム血症	1 (0.2%) 1	1 (0.5%) 2	2 (0.3%) 3
葉酸欠乏	0	2 (0.9%) 2	2 (0.3%) 2
耐糖能障害	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
高カルシウム血症	0	2 (0.9%) 2	2 (0.3%) 2
低アルブミン血症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
低マグネシウム血症	2 (0.5%) 2	0	2 (0.3%) 2
代謝性アシドーシス	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
脂質異常症	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
高アンモニア血症	1 (0.2%) 1	0	1 (0.2%) 1
高乳酸血症	0	1 (0.5%) 1	1 (0.2%) 1
高脂血症	0	1 (0.5%) 1	1 (0.2%) 1
高リン血症	1 (0.2%) 1	0	1 (0.2%) 1
高トリグリセリド血症	1 (0.2%) 1	0	1 (0.2%) 1
過小食	0	1 (0.5%) 1	1 (0.2%) 1
食欲亢進	1 (0.2%) 1	0	1 (0.2%) 1
乳酸アシドーシス	1 (0.2%) 1	0	1 (0.2%) 1
栄養障害	1 (0.2%) 1	0	1 (0.2%) 1
ステロイド糖尿病	0	1 (0.5%) 1	1 (0.2%) 1
ビタミンB群欠乏	1 (0.2%) 1	0	1 (0.2%) 1
呼吸器、胸郭および縦隔障害	146 (34.7%) 263	86 (40.8%) 142	232 (36.7%) 405
呼吸困難	52 (12.4%) 62	40 (19.0%) 56	92 (14.6%) 118
咳嗽	32 (7.6%) 37	18 (8.5%) 20	50 (7.9%) 57
鼻出血	22 (5.2%) 25	7 (3.3%) 7	29 (4.6%) 32
胸水	11 (2.6%) 16	13 (6.2%) 15	24 (3.8%) 31
労作性呼吸困難	13 (3.1%) 14	6 (2.8%) 6	19 (3.0%) 20
口腔咽頭痛	7 (1.7%) 7	4 (1.9%) 4	11 (1.7%) 11
肺腫瘤	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
湿性咳嗽	6 (1.4%) 7	1 (0.5%) 1	7 (1.1%) 8
睡眠時無呼吸症候群	4 (1.0%) 4	3 (1.4%) 3	7 (1.1%) 7
鼻漏	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
鼻閉	3 (0.7%) 5	2 (0.9%) 2	5 (0.8%) 7
慢性閉塞性肺疾患	3 (0.7%) 4	2 (0.9%) 2	5 (0.8%) 6
発声障害	4 (1.0%) 5	1 (0.5%) 1	5 (0.8%) 6
肺水腫	3 (0.7%) 5	1 (0.5%) 1	4 (0.6%) 6
呼吸不全	3 (0.7%) 5	1 (0.5%) 1	4 (0.6%) 6
気胸	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
ラ音	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
喘鳴	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
喀血	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
起坐呼吸	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
胸膜炎	3 (0.7%) 3	0	3 (0.5%) 3
鼻茸	2 (0.5%) 3	0	2 (0.3%) 3
アレルギー性鼻炎	2 (0.5%) 3	0	2 (0.3%) 3
急性呼吸不全	2 (0.5%) 2	0	2 (0.3%) 2
喘息	2 (0.5%) 2	0	2 (0.3%) 2
気管支痙攣	2 (0.5%) 2	0	2 (0.3%) 2
咽喉乾燥	2 (0.5%) 2	0	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
安静時呼吸困難	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
間質性肺疾患	0	2 (0.9%) 2	2 (0.3%) 2
胸膜痛	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
肺うっ血	2 (0.5%) 2	0	2 (0.3%) 2
肺塞栓症	0	2 (0.9%) 2	2 (0.3%) 2
急性肺水腫	1 (0.2%) 1	0	1 (0.2%) 1
失声症	0	1 (0.5%) 1	1 (0.2%) 1
無気肺	1 (0.2%) 1	0	1 (0.2%) 1
前屈呼吸困難	1 (0.2%) 1	0	1 (0.2%) 1
気管支反応性亢進	1 (0.2%) 1	0	1 (0.2%) 1
息詰まり	1 (0.2%) 1	0	1 (0.2%) 1
血胸	1 (0.2%) 1	0	1 (0.2%) 1
しゃっくり	1 (0.2%) 1	0	1 (0.2%) 1
低酸素症	0	1 (0.5%) 1	1 (0.2%) 1
特発性間質性肺炎	1 (0.2%) 1	0	1 (0.2%) 1
喉頭刺激感	0	1 (0.5%) 1	1 (0.2%) 1
肺障害	1 (0.2%) 1	0	1 (0.2%) 1
肺浸潤	1 (0.2%) 1	0	1 (0.2%) 1
肺陰影	1 (0.2%) 1	0	1 (0.2%) 1
鼻部不快感	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
鼻乾燥	0	1 (0.5%) 1	1 (0.2%) 1
副鼻腔の炎症	0	1 (0.5%) 1	1 (0.2%) 1
咽頭出血	1 (0.2%) 1	0	1 (0.2%) 1
胸膜肥厚	1 (0.2%) 1	0	1 (0.2%) 1
肺臓炎	1 (0.2%) 1	0	1 (0.2%) 1
肺アミロイドーシス	1 (0.2%) 1	0	1 (0.2%) 1
肺線維症	1 (0.2%) 1	0	1 (0.2%) 1
肺高血圧症	1 (0.2%) 1	0	1 (0.2%) 1
逆流性喉頭炎	1 (0.2%) 1	0	1 (0.2%) 1
気道うっ血	1 (0.2%) 1	0	1 (0.2%) 1
拘束性肺疾患	1 (0.2%) 1	0	1 (0.2%) 1
副鼻腔うっ血	0	1 (0.5%) 1	1 (0.2%) 1
くしゃみ	1 (0.2%) 1	0	1 (0.2%) 1
いびき	1 (0.2%) 1	0	1 (0.2%) 1
咽喉絞扼感	1 (0.2%) 1	0	1 (0.2%) 1
一般・全身障害および投与部位の状態	144 (34.2%) 219	79 (37.4%) 130	223 (35.3%) 349
疲労	42 (10.0%) 48	26 (12.3%) 28	68 (10.8%) 76
末梢性浮腫	33 (7.8%) 36	25 (11.8%) 28	58 (9.2%) 64
無力症	22 (5.2%) 23	9 (4.3%) 9	31 (4.9%) 32

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
非心臓性胸痛	14 (3.3%) 16	7 (3.3%) 10	21 (3.3%) 26
末梢腫脹	7 (1.7%) 7	14 (6.6%) 15	21 (3.3%) 22
発熱	13 (3.1%) 14	2 (0.9%) 2	15 (2.4%) 16
胸痛	9 (2.1%) 10	5 (2.4%) 6	14 (2.2%) 16
胸部不快感	8 (1.9%) 11	1 (0.5%) 1	9 (1.4%) 12
インフルエンザ様疾患	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
全身健康状態悪化	4 (1.0%) 4	3 (1.4%) 3	7 (1.1%) 7
倦怠感	6 (1.4%) 6	1 (0.5%) 1	7 (1.1%) 7
歩行障害	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
運動耐性低下	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
医薬品副作用	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
死亡	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
疼痛	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
悪寒	3 (0.7%) 4	0	3 (0.5%) 4
炎症	0	3 (1.4%) 3	3 (0.5%) 3
浮腫	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
腫脹	0	2 (0.9%) 3	2 (0.3%) 3
医療機器関連合併症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
薬物不耐性	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
限局性浮腫	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
医療機器使用部位血腫	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
多臓器機能不全症候群	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
異常感	1 (0.2%) 2	0	1 (0.2%) 2
ヘルニア痛	1 (0.2%) 2	0	1 (0.2%) 2
腋窩痛	1 (0.2%) 1	0	1 (0.2%) 1
嚢胞	0	1 (0.5%) 1	1 (0.2%) 1
疾患進行	0	1 (0.5%) 1	1 (0.2%) 1
熱感	1 (0.2%) 1	0	1 (0.2%) 1
全身性浮腫	1 (0.2%) 1	0	1 (0.2%) 1
過形成	1 (0.2%) 1	0	1 (0.2%) 1
低体温	1 (0.2%) 1	0	1 (0.2%) 1
医療機器使用部位壊死	0	1 (0.5%) 1	1 (0.2%) 1
粘膜の炎症	0	1 (0.5%) 1	1 (0.2%) 1
体調不良	1 (0.2%) 1	0	1 (0.2%) 1
突然死	1 (0.2%) 1	0	1 (0.2%) 1
ワクチン接種部位不快感	0	1 (0.5%) 1	1 (0.2%) 1
傷害、中毒および処置合併症	137 (32.5%) 292	81 (38.4%) 180	218 (34.5%) 472
転倒	67 (15.9%) 96	39 (18.5%) 62	106 (16.8%) 158
四肢損傷	16 (3.8%) 18	10 (4.7%) 13	26 (4.1%) 31

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
挫傷	16 (3.8%) 16	10 (4.7%) 10	26 (4.1%) 26
皮膚裂傷	13 (3.1%) 17	11 (5.2%) 13	24 (3.8%) 30
頭部損傷	8 (1.9%) 8	6 (2.8%) 6	14 (2.2%) 14
肋骨骨折	10 (2.4%) 12	2 (0.9%) 2	12 (1.9%) 14
皮膚擦過傷	6 (1.4%) 8	3 (1.4%) 3	9 (1.4%) 11
靱帯捻挫	6 (1.4%) 6	3 (1.4%) 3	9 (1.4%) 9
関節損傷	8 (1.9%) 10	0	8 (1.3%) 10
創傷	4 (1.0%) 4	4 (1.9%) 4	8 (1.3%) 8
処置後出血	4 (1.0%) 5	3 (1.4%) 5	7 (1.1%) 10
腱断裂	4 (1.0%) 6	2 (0.9%) 2	6 (0.9%) 8
脊椎圧迫骨折	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
顔面骨骨折	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
大腿骨頚部骨折	4 (1.0%) 4	0	4 (0.6%) 4
大腿骨骨折	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
処置後血腫	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
手首関節骨折	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
足関節部骨折	3 (0.7%) 3	0	3 (0.5%) 3
節足動物咬傷	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
骨挫傷	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
頭蓋脳損傷	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
手骨折	0	3 (1.4%) 3	3 (0.5%) 3
肉離れ	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
人工関節周囲骨折	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
処置による疼痛	0	3 (1.4%) 3	3 (0.5%) 3
軟部組織損傷	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
硬膜下血腫	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
上肢骨折	3 (0.7%) 3	0	3 (0.5%) 3
偶発的過量投与	2 (0.5%) 2	0	2 (0.3%) 2
動物咬傷	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
背部損傷	0	2 (0.9%) 2	2 (0.3%) 2
頚椎骨折	0	2 (0.9%) 2	2 (0.3%) 2
胸部損傷	2 (0.5%) 2	0	2 (0.3%) 2
鎖骨骨折	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
脳振盪	2 (0.5%) 2	0	2 (0.3%) 2
耳部損傷	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
眼挫傷	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
仙骨骨折	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
外傷性血尿	2 (0.5%) 2	0	2 (0.3%) 2
瘢痕ヘルニア	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
関節脱臼	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
靱帯断裂	2 (0.5%) 2	0	2 (0.3%) 2
腰椎骨折	2 (0.5%) 2	0	2 (0.3%) 2
筋損傷	2 (0.5%) 2	0	2 (0.3%) 2
ワクチン接種後症候群	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
交通事故	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
外傷性血腫	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
尺骨神経損傷	2 (0.5%) 2	0	2 (0.3%) 2
ワクチン接種合併症	2 (0.5%) 2	0	2 (0.3%) 2
創傷出血	2 (0.5%) 2	0	2 (0.3%) 2
ストーマ合併症	0	1 (0.5%) 2	1 (0.2%) 2
アルコール中毒	0	1 (0.5%) 1	1 (0.2%) 1
大動脈損傷	1 (0.2%) 1	0	1 (0.2%) 1
殿部損傷	1 (0.2%) 1	0	1 (0.2%) 1
放射線性膀胱炎	1 (0.2%) 1	0	1 (0.2%) 1
上顎炎	0	1 (0.5%) 1	1 (0.2%) 1
焼痂	1 (0.2%) 1	0	1 (0.2%) 1
顔面損傷	0	1 (0.5%) 1	1 (0.2%) 1
腓骨骨折	0	1 (0.5%) 1	1 (0.2%) 1
足骨折	1 (0.2%) 1	0	1 (0.2%) 1
尾骨骨折	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
上腕骨骨折	1 (0.2%) 1	0	1 (0.2%) 1
角膜損傷	1 (0.2%) 1	0	1 (0.2%) 1
企図的過量投与	1 (0.2%) 1	0	1 (0.2%) 1
正中神経損傷	1 (0.2%) 1	0	1 (0.2%) 1
投薬過誤	0	1 (0.5%) 1	1 (0.2%) 1
半月板損傷	0	1 (0.5%) 1	1 (0.2%) 1
多発性外傷	1 (0.2%) 1	0	1 (0.2%) 1
神経損傷	1 (0.2%) 1	0	1 (0.2%) 1
開放性眼球外傷	0	1 (0.5%) 1	1 (0.2%) 1
過量投与	1 (0.2%) 1	0	1 (0.2%) 1
骨盤骨折	1 (0.2%) 1	0	1 (0.2%) 1
処置後紅斑	0	1 (0.5%) 1	1 (0.2%) 1
処置後血尿	1 (0.2%) 1	0	1 (0.2%) 1
処置によるめまい	1 (0.2%) 1	0	1 (0.2%) 1
再狭窄	1 (0.2%) 1	0	1 (0.2%) 1
陰嚢血腫	1 (0.2%) 1	0	1 (0.2%) 1
脊椎骨折	0	1 (0.5%) 1	1 (0.2%) 1
放射線口内炎	0	1 (0.5%) 1	1 (0.2%) 1
ストレス骨折	1 (0.2%) 1	0	1 (0.2%) 1
硬膜下出血	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
サンバーン	1 (0.2%) 1	0	1 (0.2%) 1
腱損傷	0	1 (0.5%) 1	1 (0.2%) 1
熱傷	1 (0.2%) 1	0	1 (0.2%) 1
歯牙破折	1 (0.2%) 1	0	1 (0.2%) 1
外傷性血胸	0	1 (0.5%) 1	1 (0.2%) 1
外傷性頭蓋内出血	1 (0.2%) 1	0	1 (0.2%) 1
外傷性潰瘍	0	1 (0.5%) 1	1 (0.2%) 1
術後尿閉	1 (0.2%) 1	0	1 (0.2%) 1
第7神経損傷	1 (0.2%) 1	0	1 (0.2%) 1
腎および尿路障害	142 (33.7%) 216	64 (30.3%) 99	206 (32.6%) 315
急性腎障害	52 (12.4%) 64	22 (10.4%) 30	74 (11.7%) 94
腎機能障害	37 (8.8%) 42	17 (8.1%) 17	54 (8.5%) 59
血尿	18 (4.3%) 24	16 (7.6%) 18	34 (5.4%) 42
慢性腎臓病	16 (3.8%) 20	2 (0.9%) 2	18 (2.8%) 22
尿閉	12 (2.9%) 14	2 (0.9%) 2	14 (2.2%) 16
腎不全	7 (1.7%) 7	3 (1.4%) 3	10 (1.6%) 10
蛋白尿	5 (1.2%) 5	3 (1.4%) 4	8 (1.3%) 9
尿失禁	3 (0.7%) 3	3 (1.4%) 3	6 (0.9%) 6
排尿困難	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
ミクロアルブミン尿	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
腎結石症	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
夜間頻尿	4 (1.0%) 4	0	4 (0.6%) 4
腎嚢胞	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
膀胱痙縮	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
中毒性腎症	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
頻尿	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
尿道狭窄	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
末期腎疾患	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
失禁	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
下部尿路症状	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
アルブミン尿	0	1 (0.5%) 1	1 (0.2%) 1
膀胱壁肥厚	1 (0.2%) 1	0	1 (0.2%) 1
膀胱結石	1 (0.2%) 1	0	1 (0.2%) 1
巣状分節性糸球体硬化症	1 (0.2%) 1	0	1 (0.2%) 1
糖尿	0	1 (0.5%) 1	1 (0.2%) 1
尿路出血	1 (0.2%) 1	0	1 (0.2%) 1
尿意切迫	1 (0.2%) 1	0	1 (0.2%) 1
腎症	0	1 (0.5%) 1	1 (0.2%) 1
多尿	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
腎前性腎不全	1 (0.2%) 1	0	1 (0.2%) 1
腎仙痛	1 (0.2%) 1	0	1 (0.2%) 1
腎損傷	0	1 (0.5%) 1	1 (0.2%) 1
尿道脱	1 (0.2%) 1	0	1 (0.2%) 1
尿道症候群	0	1 (0.5%) 1	1 (0.2%) 1
排尿躊躇	1 (0.2%) 1	0	1 (0.2%) 1
尿路閉塞	1 (0.2%) 1	0	1 (0.2%) 1
臨床検査	127 (30.2%) 234	68 (32.2%) 117	195 (30.9%) 351
血中クレアチニン増加	26 (6.2%) 31	4 (1.9%) 5	30 (4.7%) 36
体重減少	16 (3.8%) 17	13 (6.2%) 13	29 (4.6%) 30
脳性ナトリウム利尿ペプチド前駆体N端フラグメント増加	9 (2.1%) 9	8 (3.8%) 9	17 (2.7%) 18
尿中アルブミン／クレアチニン比増加	11 (2.6%) 12	5 (2.4%) 6	16 (2.5%) 18
血中クレアチンホスホキナーゼ増加	11 (2.6%) 12	4 (1.9%) 4	15 (2.4%) 16
国際標準比増加	9 (2.1%) 10	3 (1.4%) 3	12 (1.9%) 13
SARS-CoV-2検査陽性	8 (1.9%) 9	3 (1.4%) 3	11 (1.7%) 12
頚静脈圧上昇	7 (1.7%) 7	4 (1.9%) 5	11 (1.7%) 12
前立腺特異性抗原増加	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
血中カリウム減少	4 (1.0%) 4	3 (1.4%) 5	7 (1.1%) 9
血中カリウム増加	5 (1.2%) 6	2 (0.9%) 2	7 (1.1%) 8

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
心電図QT延長	5 (1.2%) 5	2 (0.9%) 3	7 (1.1%) 8
血中甲状腺刺激ホルモン増加	3 (0.7%) 4	3 (1.4%) 3	6 (0.9%) 7
血中尿酸増加	3 (0.7%) 3	3 (1.4%) 3	6 (0.9%) 6
ヘモグロビン減少	6 (1.4%) 6	0	6 (0.9%) 6
血中ビリルビン増加	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
血中尿素増加	5 (1.2%) 5	0	5 (0.8%) 5
γ-グルタミルトランスフェラーゼ増加	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
肝機能検査値上昇	2 (0.5%) 2	2 (0.9%) 3	4 (0.6%) 5
血小板数減少	4 (1.0%) 5	0	4 (0.6%) 5
血中鉄減少	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
血中甲状腺刺激ホルモン減少	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
C-反応性蛋白増加	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
心拍数増加	4 (1.0%) 4	0	4 (0.6%) 4
肝機能検査異常	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
便潜血陽性	4 (1.0%) 4	0	4 (0.6%) 4
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
抱合ビリルビン増加	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
血中ブドウ糖増加	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
尿中血陽性	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
駆出率減少	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
糸球体濾過率減少	3 (0.7%) 3	0	3 (0.5%) 3
尿中蛋白陽性	3 (0.7%) 3	0	3 (0.5%) 3
体重増加	3 (0.7%) 3	0	3 (0.5%) 3
血中マグネシウム減少	0	2 (0.9%) 3	2 (0.3%) 3
血中アルブミン減少	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
血中アルカリホスファターゼ増加	0	2 (0.9%) 2	2 (0.3%) 2
血中カルシウム減少	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
血圧上昇	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
心拍出量低下	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
好酸球数増加	2 (0.5%) 2	0	2 (0.3%) 2
心拍数減少	2 (0.5%) 2	0	2 (0.3%) 2
心拍数不整	2 (0.5%) 2	0	2 (0.3%) 2
血清フェリチン減少	0	2 (0.9%) 2	2 (0.3%) 2
トランスアミナーゼ上昇	2 (0.5%) 2	0	2 (0.3%) 2
トロポニン増加	0	2 (0.9%) 2	2 (0.3%) 2
尿中白血球陽性	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
アラニンアミノトランスフェラーゼ増加	1 (0.2%) 1	0	1 (0.2%) 1
尿中アルブミン陽性	1 (0.2%) 1	0	1 (0.2%) 1
細菌検査	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
細菌検査陽性	1 (0.2%) 1	0	1 (0.2%) 1
血中重炭酸塩増加	0	1 (0.5%) 1	1 (0.2%) 1
血中カルシウム増加	0	1 (0.5%) 1	1 (0.2%) 1
血中クレアチニン異常	1 (0.2%) 1	0	1 (0.2%) 1
血中ブドウ糖減少	0	1 (0.5%) 1	1 (0.2%) 1
血中副甲状腺ホルモン増加	1 (0.2%) 1	0	1 (0.2%) 1
血圧低下	1 (0.2%) 1	0	1 (0.2%) 1
収縮期血圧上昇	1 (0.2%) 1	0	1 (0.2%) 1
血中ナトリウム減少	1 (0.2%) 1	0	1 (0.2%) 1
血中テストステロン減少	1 (0.2%) 1	0	1 (0.2%) 1
血中テストステロン増加	1 (0.2%) 1	0	1 (0.2%) 1
血中尿素異常	1 (0.2%) 1	0	1 (0.2%) 1
体温上昇	1 (0.2%) 1	0	1 (0.2%) 1
脳性ナトリウム利尿ペプチド増加	1 (0.2%) 1	0	1 (0.2%) 1
呼吸音異常	0	1 (0.5%) 1	1 (0.2%) 1
心臓負荷試験異常	0	1 (0.5%) 1	1 (0.2%) 1
中心静脈圧上昇	1 (0.2%) 1	0	1 (0.2%) 1
心電図PR延長	0	1 (0.5%) 1	1 (0.2%) 1
好酸球数異常	1 (0.2%) 1	0	1 (0.2%) 1
糸球体濾過率増加	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
グリコヘモグロビン増加	1 (0.2%) 1	0	1 (0.2%) 1
ヘマトクリット減少	1 (0.2%) 1	0	1 (0.2%) 1
ヘマトクリット増加	0	1 (0.5%) 1	1 (0.2%) 1
炎症マーカー上昇	0	1 (0.5%) 1	1 (0.2%) 1
国際標準比変動	1 (0.2%) 1	0	1 (0.2%) 1
肝触知	0	1 (0.5%) 1	1 (0.2%) 1
リンパ球数増加	0	1 (0.5%) 1	1 (0.2%) 1
便潜血	0	1 (0.5%) 1	1 (0.2%) 1
酸素飽和度低下	1 (0.2%) 1	0	1 (0.2%) 1
身体的診察結果異常	0	1 (0.5%) 1	1 (0.2%) 1
総蛋白減少	1 (0.2%) 1	0	1 (0.2%) 1
赤血球数減少	1 (0.2%) 1	0	1 (0.2%) 1
血沈亢進	1 (0.2%) 1	0	1 (0.2%) 1
腎機能検査異常	0	1 (0.5%) 1	1 (0.2%) 1
トランスフェリン飽和度低下	0	1 (0.5%) 1	1 (0.2%) 1
トロポニンT増加	1 (0.2%) 1	0	1 (0.2%) 1
尿円柱	0	1 (0.5%) 1	1 (0.2%) 1
尿検査異常	0	1 (0.5%) 1	1 (0.2%) 1
尿量減少	0	1 (0.5%) 1	1 (0.2%) 1
振動検査異常	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
白血球数増加	0	1 (0.5%) 1	1 (0.2%) 1
皮膚および皮下組織障害	108 (25.7%) 154	53 (25.1%) 77	161 (25.5%) 231
そう痒症	25 (5.9%) 27	8 (3.8%) 11	33 (5.2%) 38
発疹	21 (5.0%) 24	11 (5.2%) 13	32 (5.1%) 37
皮膚潰瘍	11 (2.6%) 12	5 (2.4%) 6	16 (2.5%) 18
皮膚病変	11 (2.6%) 12	5 (2.4%) 5	16 (2.5%) 17
光線角化症	5 (1.2%) 8	3 (1.4%) 3	8 (1.3%) 11
紅斑	3 (0.7%) 4	4 (1.9%) 4	7 (1.1%) 8
蕁麻疹	4 (1.0%) 4	3 (1.4%) 3	7 (1.1%) 7
過角化	3 (0.7%) 4	2 (0.9%) 2	5 (0.8%) 6
脱毛症	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
そう痒性皮疹	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
多汗症	4 (1.0%) 5	0	4 (0.6%) 5
斑状出血	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
湿疹	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
水疱	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
皮膚炎	3 (0.7%) 3	0	3 (0.5%) 3
薬疹	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
皮膚乾燥	3 (0.7%) 3	0	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
皮膚変色	0	3 (1.4%) 3	3 (0.5%) 3
うっ滞性皮膚炎	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
皮脂欠乏性湿疹	2 (0.5%) 2	0	2 (0.3%) 2
斑状丘疹状皮疹	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
丘疹性皮疹	0	2 (0.9%) 2	2 (0.3%) 2
痂皮	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
皮膚腫瘤	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
日光黒子	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
毛細血管拡張症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
ざ瘡	1 (0.2%) 1	0	1 (0.2%) 1
血管浮腫	1 (0.2%) 1	0	1 (0.2%) 1
眉毛下垂	0	1 (0.5%) 1	1 (0.2%) 1
皮膚血管炎	0	1 (0.5%) 1	1 (0.2%) 1
褥瘡性潰瘍	0	1 (0.5%) 1	1 (0.2%) 1
アレルギー性皮膚炎	0	1 (0.5%) 1	1 (0.2%) 1
接触皮膚炎	1 (0.2%) 1	0	1 (0.2%) 1
顔のやせ	1 (0.2%) 1	0	1 (0.2%) 1
毛髪障害	1 (0.2%) 1	0	1 (0.2%) 1
扁平苔癬	1 (0.2%) 1	0	1 (0.2%) 1
苔癬化	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
爪変色	1 (0.2%) 1	0	1 (0.2%) 1
神経皮膚炎	0	1 (0.5%) 1	1 (0.2%) 1
神経障害性潰瘍	1 (0.2%) 1	0	1 (0.2%) 1
寝汗	1 (0.2%) 1	0	1 (0.2%) 1
爪破損	1 (0.2%) 1	0	1 (0.2%) 1
天疱瘡	1 (0.2%) 1	0	1 (0.2%) 1
血管周囲細胞浸潤性皮膚炎	1 (0.2%) 1	0	1 (0.2%) 1
点状出血	1 (0.2%) 1	0	1 (0.2%) 1
紫斑	0	1 (0.5%) 1	1 (0.2%) 1
老人性紫斑	1 (0.2%) 1	0	1 (0.2%) 1
紅斑性皮疹	1 (0.2%) 1	0	1 (0.2%) 1
酒さ	0	1 (0.5%) 1	1 (0.2%) 1
脂漏	1 (0.2%) 1	0	1 (0.2%) 1
脂漏性皮膚炎	0	1 (0.5%) 1	1 (0.2%) 1
皮膚色素脱失	1 (0.2%) 1	0	1 (0.2%) 1
皮膚剥脱	1 (0.2%) 1	0	1 (0.2%) 1
皮膚亀裂	1 (0.2%) 1	0	1 (0.2%) 1
皮膚脆弱性	0	1 (0.5%) 1	1 (0.2%) 1
皮膚出血	1 (0.2%) 1	0	1 (0.2%) 1
皮膚刺激	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
皮膚軟化	1 (0.2%) 1	0	1 (0.2%) 1
皮膚局面	1 (0.2%) 1	0	1 (0.2%) 1
皮下気腫	1 (0.2%) 1	0	1 (0.2%) 1
血管障害	88 (20.9%) 116	49 (23.2%) 56	137 (21.7%) 172
低血圧	33 (7.8%) 36	14 (6.6%) 14	47 (7.4%) 50
起立性低血圧	14 (3.3%) 15	7 (3.3%) 7	21 (3.3%) 22
血腫	8 (1.9%) 8	10 (4.7%) 10	18 (2.8%) 18
高血圧	10 (2.4%) 10	2 (0.9%) 2	12 (1.9%) 12
大動脈狭窄	5 (1.2%) 5	3 (1.4%) 4	8 (1.3%) 9
動脈硬化症	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
末梢動脈閉塞性疾患	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
末梢静脈疾患	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
出血性静脈瘤	3 (0.7%) 3	0	3 (0.5%) 3
上腕動脈捕捉症候群	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
深部静脈血栓症	3 (0.7%) 3	0	3 (0.5%) 3
レイノー現象	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
ほてり	2 (0.5%) 4	0	2 (0.3%) 4
高血圧クリーゼ	0	2 (0.9%) 3	2 (0.3%) 3
間欠性跛行	2 (0.5%) 2	0	2 (0.3%) 2

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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
鎖骨下静脈血栓症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
血栓性静脈炎	2 (0.5%) 2	0	2 (0.3%) 2
静脈瘤	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
静脈瘤破裂	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
末梢動脈狭窄	1 (0.2%) 2	0	1 (0.2%) 2
チアノーゼ	1 (0.2%) 1	0	1 (0.2%) 1
塞栓症	1 (0.2%) 1	0	1 (0.2%) 1
本態性高血圧症	1 (0.2%) 1	0	1 (0.2%) 1
大腿動脈塞栓症	1 (0.2%) 1	0	1 (0.2%) 1
巨細胞性動脈炎	1 (0.2%) 1	0	1 (0.2%) 1
リンパ浮腫	1 (0.2%) 1	0	1 (0.2%) 1
微小塞栓症	0	1 (0.5%) 1	1 (0.2%) 1
蒼白	1 (0.2%) 1	0	1 (0.2%) 1
末梢動脈閉塞	1 (0.2%) 1	0	1 (0.2%) 1
末梢冷感	1 (0.2%) 1	0	1 (0.2%) 1
末梢血管障害	1 (0.2%) 1	0	1 (0.2%) 1
末梢静脈血栓進展	0	1 (0.5%) 1	1 (0.2%) 1
ショック	1 (0.2%) 1	0	1 (0.2%) 1
鎖骨下静脈閉塞	1 (0.2%) 1	0	1 (0.2%) 1
表在性静脈血栓症	1 (0.2%) 1	0	1 (0.2%) 1

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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
上大静脈閉塞	1 (0.2%) 1	0	1 (0.2%) 1
血栓症	0	1 (0.5%) 1	1 (0.2%) 1
血管炎	0	1 (0.5%) 1	1 (0.2%) 1
精神障害	57 (13.5%) 72	39 (18.5%) 48	96 (15.2%) 120
不眠症	20 (4.8%) 21	16 (7.6%) 16	36 (5.7%) 37
うつ病	13 (3.1%) 15	9 (4.3%) 9	22 (3.5%) 24
不安	7 (1.7%) 7	7 (3.3%) 7	14 (2.2%) 14
錯乱状態	5 (1.2%) 6	4 (1.9%) 4	9 (1.4%) 10
譫妄	5 (1.2%) 5	3 (1.4%) 3	8 (1.3%) 8
抑うつ気分	3 (0.7%) 4	3 (1.4%) 4	6 (0.9%) 8
睡眠障害	4 (1.0%) 4	0	4 (0.6%) 4
無感情	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
易刺激性	2 (0.5%) 2	0	2 (0.3%) 2
異常な夢	1 (0.2%) 1	0	1 (0.2%) 1
激越	1 (0.2%) 1	0	1 (0.2%) 1
不安障害	0	1 (0.5%) 1	1 (0.2%) 1
双極性障害	1 (0.2%) 1	0	1 (0.2%) 1
白日夢	0	1 (0.5%) 1	1 (0.2%) 1
失見当識	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
感情的苦悩	1 (0.2%) 1	0	1 (0.2%) 1
幻覚	1 (0.2%) 1	0	1 (0.2%) 1
リビドー減退	1 (0.2%) 1	0	1 (0.2%) 1
躁病	1 (0.2%) 1	0	1 (0.2%) 1
神経過敏	0	1 (0.5%) 1	1 (0.2%) 1
血液およびリンパ系障害	61 (14.5%) 91	29 (13.7%) 38	90 (14.2%) 129
貧血	37 (8.8%) 45	17 (8.1%) 19	54 (8.5%) 64
鉄欠乏性貧血	15 (3.6%) 18	8 (3.8%) 11	23 (3.6%) 29
血小板減少症	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
リンパ節症	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
白血球増加症	4 (1.0%) 4	0	4 (0.6%) 4
白血球減少症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
凝血異常	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
好酸球増加症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
内出血発生の増加傾向	2 (0.5%) 2	0	2 (0.3%) 2
正球性貧血	2 (0.5%) 2	0	2 (0.3%) 2
失血性貧血	1 (0.2%) 1	0	1 (0.2%) 1
出血性素因	1 (0.2%) 1	0	1 (0.2%) 1
免疫性血小板減少症	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
縦隔リンパ節腫脹	1 (0.2%) 1	0	1 (0.2%) 1
リンパ球浸潤	1 (0.2%) 1	0	1 (0.2%) 1
リンパ球減少症	0	1 (0.5%) 1	1 (0.2%) 1
好中球減少症	1 (0.2%) 1	0	1 (0.2%) 1
正色素性貧血	1 (0.2%) 1	0	1 (0.2%) 1
正色素性正球性貧血	1 (0.2%) 1	0	1 (0.2%) 1
網状赤血球増加症	0	1 (0.5%) 1	1 (0.2%) 1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	54 (12.8%) 74	36 (17.1%) 46	90 (14.2%) 120
基底細胞癌	16 (3.8%) 16	13 (6.2%) 13	29 (4.6%) 29
扁平上皮癌	7 (1.7%) 10	4 (1.9%) 4	11 (1.7%) 14
前立腺癌	2 (0.5%) 2	4 (1.9%) 4	6 (0.9%) 6
脂漏性角化症	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
皮膚有棘細胞癌	5 (1.2%) 5	0	5 (0.8%) 5
再発膀胱癌	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
ケラトアカントーマ	3 (0.7%) 3	0	3 (0.5%) 3
ボーエン病	1 (0.2%) 3	1 (0.5%) 1	2 (0.3%) 4
慢性リンパ性白血病	0	2 (0.9%) 2	2 (0.3%) 2
悪性黒子	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
悪性黒色腫	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
メラノサイト性母斑	2 (0.5%) 2	0	2 (0.3%) 2
骨髄異形成症候群	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
遠隔転移を伴う前立腺癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
皮膚癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
扁桃癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
移行上皮癌	2 (0.5%) 2	0	2 (0.3%) 2
遠隔転移を伴う扁桃癌	0	1 (0.5%) 2	1 (0.2%) 2
棘細胞腫	0	1 (0.5%) 1	1 (0.2%) 1
結腸腺癌	1 (0.2%) 1	0	1 (0.2%) 1
膵腺癌	0	1 (0.5%) 1	1 (0.2%) 1
脈絡膜の良性新生物	0	1 (0.5%) 1	1 (0.2%) 1
皮膚良性新生物	1 (0.2%) 1	0	1 (0.2%) 1
甲状腺の良性新生物	1 (0.2%) 1	0	1 (0.2%) 1
膀胱癌	1 (0.2%) 1	0	1 (0.2%) 1
遠隔転移を伴う骨癌	0	1 (0.5%) 1	1 (0.2%) 1
大腸腺腫	1 (0.2%) 1	0	1 (0.2%) 1
結腸直腸癌	1 (0.2%) 1	0	1 (0.2%) 1
びまん性大細胞型B細胞性リンパ腫	1 (0.2%) 1	0	1 (0.2%) 1
外耳の悪性新生物	0	1 (0.5%) 1	1 (0.2%) 1
遠隔転移を伴う消化器癌	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
皮膚血管腫	1 (0.2%) 1	0	1 (0.2%) 1
良性単クローン性高γグロブリン血症	1 (0.2%) 1	0	1 (0.2%) 1
再発肺腺癌	0	1 (0.5%) 1	1 (0.2%) 1
遠隔転移を伴う肺癌	1 (0.2%) 1	0	1 (0.2%) 1
悪性胸水	0	1 (0.5%) 1	1 (0.2%) 1
甲状腺髄様癌	1 (0.2%) 1	0	1 (0.2%) 1
肝転移	1 (0.2%) 1	0	1 (0.2%) 1
神経線維腫	0	1 (0.5%) 1	1 (0.2%) 1
乳頭腫	1 (0.2%) 1	0	1 (0.2%) 1
良性副甲状腺腫瘍	0	1 (0.5%) 1	1 (0.2%) 1
再発前立腺癌	1 (0.2%) 1	0	1 (0.2%) 1
腎細胞癌	1 (0.2%) 1	0	1 (0.2%) 1
皮膚乳頭腫	1 (0.2%) 1	0	1 (0.2%) 1
小腸腺癌	1 (0.2%) 1	0	1 (0.2%) 1
悪性度不明の脾臓新生物	1 (0.2%) 1	0	1 (0.2%) 1
頭頚部扁平上皮癌	1 (0.2%) 1	0	1 (0.2%) 1
再発甲状腺癌	0	1 (0.5%) 1	1 (0.2%) 1
尿道腺腫	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
眼障害	46 (10.9%) 62	26 (12.3%) 40	72 (11.4%) 102
白内障	14 (3.3%) 19	4 (1.9%) 5	18 (2.8%) 24
結膜出血	5 (1.2%) 5	1 (0.5%) 1	6 (0.9%) 6
ドライアイ	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
霧視	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
眼出血	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
緑内障	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
眼の炎症	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
黄斑円孔	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
視力障害	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
加齢黄斑変性	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
眼瞼炎	2 (0.5%) 2	0	2 (0.3%) 2
複視	2 (0.5%) 2	0	2 (0.3%) 2
眼刺激	0	2 (0.9%) 2	2 (0.3%) 2
眼そう痒症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
注視麻痺	2 (0.5%) 2	0	2 (0.3%) 2
角膜炎	2 (0.5%) 2	0	2 (0.3%) 2
黄斑変性	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
新生血管加齢黄斑変性	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
網膜出血	0	2 (0.9%) 2	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
水晶体脱臼	1 (0.2%) 2	0	1 (0.2%) 2
一過性黒内障	1 (0.2%) 1	0	1 (0.2%) 1
乱視	0	1 (0.5%) 1	1 (0.2%) 1
脈絡膜滲出	1 (0.2%) 1	0	1 (0.2%) 1
乾性加齢黄斑変性	0	1 (0.5%) 1	1 (0.2%) 1
眼痛	1 (0.2%) 1	0	1 (0.2%) 1
眼潰瘍	1 (0.2%) 1	0	1 (0.2%) 1
眼瞼刺激	1 (0.2%) 1	0	1 (0.2%) 1
眼瞼下垂	0	1 (0.5%) 1	1 (0.2%) 1
遠視	0	1 (0.5%) 1	1 (0.2%) 1
流涙増加	0	1 (0.5%) 1	1 (0.2%) 1
黄斑浮腫	1 (0.2%) 1	0	1 (0.2%) 1
近視	0	1 (0.5%) 1	1 (0.2%) 1
眼充血	0	1 (0.5%) 1	1 (0.2%) 1
眼静脈血栓症	0	1 (0.5%) 1	1 (0.2%) 1
後嚢部混濁	1 (0.2%) 1	0	1 (0.2%) 1
老視	0	1 (0.5%) 1	1 (0.2%) 1
網膜動脈閉塞	0	1 (0.5%) 1	1 (0.2%) 1
網膜剥離	1 (0.2%) 1	0	1 (0.2%) 1
網膜裂孔	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
網膜下線維症	1 (0.2%) 1	0	1 (0.2%) 1
視力低下	0	1 (0.5%) 1	1 (0.2%) 1
硝子体剥離	0	1 (0.5%) 1	1 (0.2%) 1
硝子体出血	0	1 (0.5%) 1	1 (0.2%) 1
生殖系および乳房障害	28 (6.7%) 30	23 (10.9%) 26	51 (8.1%) 56
良性前立腺肥大症	8 (1.9%) 8	6 (2.8%) 6	14 (2.2%) 14
女性化乳房	7 (1.7%) 7	4 (1.9%) 4	11 (1.7%) 11
勃起不全	3 (0.7%) 3	6 (2.8%) 6	9 (1.4%) 9
乳頭痛	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
前立腺腫大	2 (0.5%) 2	0	2 (0.3%) 2
前立腺炎	1 (0.2%) 2	0	1 (0.2%) 2
亀頭包皮炎	0	1 (0.5%) 1	1 (0.2%) 1
乳房圧痛	0	1 (0.5%) 1	1 (0.2%) 1
精巣上体嚢胞	0	1 (0.5%) 1	1 (0.2%) 1
骨盤血腫	0	1 (0.5%) 1	1 (0.2%) 1
前立腺嚢胞	0	1 (0.5%) 1	1 (0.2%) 1
前立腺障害	1 (0.2%) 1	0	1 (0.2%) 1
陰嚢皮膚炎	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
陰嚢腫脹	0	1 (0.5%) 1	1 (0.2%) 1
性機能不全	1 (0.2%) 1	0	1 (0.2%) 1
精巣嚢胞	1 (0.2%) 1	0	1 (0.2%) 1
精巣痛	1 (0.2%) 1	0	1 (0.2%) 1
精巣腫脹	1 (0.2%) 1	0	1 (0.2%) 1
精索静脈瘤	0	1 (0.5%) 1	1 (0.2%) 1
外陰腟紅斑	0	1 (0.5%) 1	1 (0.2%) 1
耳および迷路障害	22 (5.2%) 29	10 (4.7%) 10	32 (5.1%) 39
回転性めまい	8 (1.9%) 11	4 (1.9%) 4	12 (1.9%) 15
聴力低下	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
耳鳴	3 (0.7%) 3	0	3 (0.5%) 3
頭位性回転性めまい	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
耳垢栓塞	0	2 (0.9%) 2	2 (0.3%) 2
耳不快感	2 (0.5%) 2	0	2 (0.3%) 2
耳痛	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
両耳難聴	1 (0.2%) 1	0	1 (0.2%) 1
感音性難聴	1 (0.2%) 1	0	1 (0.2%) 1
耳閉	1 (0.2%) 1	0	1 (0.2%) 1
耳出血	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
耳管機能障害	1 (0.2%) 1	0	1 (0.2%) 1
外耳痛	1 (0.2%) 1	0	1 (0.2%) 1
メニエール病	0	1 (0.5%) 1	1 (0.2%) 1
前庭障害	1 (0.2%) 1	0	1 (0.2%) 1
内分泌障害	22 (5.2%) 25	9 (4.3%) 9	31 (4.9%) 34
甲状腺機能低下症	15 (3.6%) 18	6 (2.8%) 6	21 (3.3%) 24
甲状腺機能亢進症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
副甲状腺機能亢進症	2 (0.5%) 2	0	2 (0.3%) 2
急性副腎皮質機能不全	1 (0.2%) 1	0	1 (0.2%) 1
自己免疫性甲状腺炎	0	1 (0.5%) 1	1 (0.2%) 1
甲状腺腫	1 (0.2%) 1	0	1 (0.2%) 1
続発性副甲状腺機能亢進症	0	1 (0.5%) 1	1 (0.2%) 1
甲状腺腫瘤	1 (0.2%) 1	0	1 (0.2%) 1
肝胆道系障害	11 (2.6%) 17	10 (4.7%) 15	21 (3.3%) 32
胆石症	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
胆管炎	2 (0.5%) 6	0	2 (0.3%) 6
胆道仙痛	0	2 (0.9%) 3	2 (0.3%) 3
胆嚢炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
高ビリルビン血症	0	2 (0.9%) 2	2 (0.3%) 2
胆管結石	1 (0.2%) 2	0	1 (0.2%) 2
心臓性肝硬変	1 (0.2%) 1	0	1 (0.2%) 1
うっ血性肝障害	0	1 (0.5%) 1	1 (0.2%) 1
肉芽腫性肝疾患	1 (0.2%) 1	0	1 (0.2%) 1
肝嚢胞	0	1 (0.5%) 1	1 (0.2%) 1
肝不全	0	1 (0.5%) 1	1 (0.2%) 1
肝機能異常	1 (0.2%) 1	0	1 (0.2%) 1
肝病変	1 (0.2%) 1	0	1 (0.2%) 1
肝腫瘤	1 (0.2%) 1	0	1 (0.2%) 1
胆汁うっ滞性肝炎	0	1 (0.5%) 1	1 (0.2%) 1
肝腫大	0	1 (0.5%) 1	1 (0.2%) 1
高トランスアミナーゼ血症	1 (0.2%) 1	0	1 (0.2%) 1
虚血性肝炎	0	1 (0.5%) 1	1 (0.2%) 1
黄疸	0	1 (0.5%) 1	1 (0.2%) 1
肝損傷	1 (0.2%) 1	0	1 (0.2%) 1
免疫系障害	5 (1.2%) 6	4 (1.9%) 4	9 (1.4%) 10
季節性アレルギー	3 (0.7%) 4	2 (0.9%) 2	5 (0.8%) 6
薬物過敏症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
アミロイドーシス	0	1 (0.5%) 1	1 (0.2%) 1
先天性、家族性および遺伝性障害	4 (1.0%) 5	1 (0.5%) 1	5 (0.8%) 6
包茎	1 (0.2%) 2	1 (0.5%) 1	2 (0.3%) 3
発育性股関節形成不全	1 (0.2%) 1	0	1 (0.2%) 1
遺伝性神経障害性アミロイドーシス	1 (0.2%) 1	0	1 (0.2%) 1
陰嚢水瘤	1 (0.2%) 1	0	1 (0.2%) 1
製品の問題	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
医療機器位置異常	0	1 (0.5%) 1	1 (0.2%) 1
医療機器不具合	1 (0.2%) 1	0	1 (0.2%) 1
医療機器のゆるみ	1 (0.2%) 1	0	1 (0.2%) 1
医療機器機能不良	0	1 (0.5%) 1	1 (0.2%) 1
リードの位置ずれ	1 (0.2%) 1	0	1 (0.2%) 1
外科および内科処置	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
心臓アブレーション	1 (0.2%) 1	0	1 (0.2%) 1
安楽死	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.5
Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
Any related treatment emergent adverse event	50 (11.9%) 76	11 (5.2%) 15	61 (9.7%) 91
胃腸障害	20 (4.8%) 26	1 (0.5%) 3	21 (3.3%) 29
悪心	6 (1.4%) 6	1 (0.5%) 1	7 (1.1%) 7
消化不良	3 (0.7%) 4	1 (0.5%) 1	4 (0.6%) 5
下痢	4 (1.0%) 4	0	4 (0.6%) 4
腹部不快感	3 (0.7%) 3	0	3 (0.5%) 3
上腹部痛	3 (0.7%) 3	0	3 (0.5%) 3
便秘	2 (0.5%) 2	0	2 (0.3%) 2
鼓腸	2 (0.5%) 2	0	2 (0.3%) 2
腹部膨満	1 (0.2%) 1	0	1 (0.2%) 1
口腔粘膜水疱形成	1 (0.2%) 1	0	1 (0.2%) 1
嘔吐	0	1 (0.5%) 1	1 (0.2%) 1
臨床検査	10 (2.4%) 11	1 (0.5%) 1	11 (1.7%) 12
血中クレアチニン増加	3 (0.7%) 3	0	3 (0.5%) 3
血中クレアチンホスホキナーゼ増加	2 (0.5%) 2	0	2 (0.3%) 2
尿中アルブミン／クレアチニン比増加	2 (0.5%) 2	0	2 (0.3%) 2
抱合ビリルビン増加	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Relatedness as assessed by investigator.

Table 14.3.1.5
Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
心電図QT延長	0	1 (0.5%) 1	1 (0.2%) 1
国際標準比変動	1 (0.2%) 1	0	1 (0.2%) 1
国際標準比増加	1 (0.2%) 1	0	1 (0.2%) 1
体重減少	1 (0.2%) 1	0	1 (0.2%) 1
皮膚および皮下組織障害	7 (1.7%) 9	2 (0.9%) 2	9 (1.4%) 11
発疹	4 (1.0%) 5	1 (0.5%) 1	5 (0.8%) 6
そう痒症	2 (0.5%) 2	0	2 (0.3%) 2
斑状出血	0	1 (0.5%) 1	1 (0.2%) 1
爪変色	1 (0.2%) 1	0	1 (0.2%) 1
紅斑性皮疹	1 (0.2%) 1	0	1 (0.2%) 1
神経系障害	5 (1.2%) 8	2 (0.9%) 2	7 (1.1%) 10
振戦	1 (0.2%) 2	1 (0.5%) 1	2 (0.3%) 3
浮動性めまい	1 (0.2%) 2	0	1 (0.2%) 2
体位性めまい	1 (0.2%) 1	0	1 (0.2%) 1
頭痛	0	1 (0.5%) 1	1 (0.2%) 1
記憶障害	1 (0.2%) 1	0	1 (0.2%) 1
傾眠	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Relatedness as assessed by investigator.

Table 14.3.1.5
Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
失神	1 (0.2%) 1	0	1 (0.2%) 1
一般・全身障害および投与部位の状態	5 (1.2%) 6	1 (0.5%) 1	6 (0.9%) 7
疲労	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
倦怠感	1 (0.2%) 1	0	1 (0.2%) 1
末梢性浮腫	1 (0.2%) 1	0	1 (0.2%) 1
発熱	1 (0.2%) 1	0	1 (0.2%) 1
腎および尿路障害	2 (0.5%) 2	2 (0.9%) 3	4 (0.6%) 5
腎機能障害	2 (0.5%) 2	0	2 (0.3%) 2
蛋白尿	0	1 (0.5%) 2	1 (0.2%) 2
腎不全	0	1 (0.5%) 1	1 (0.2%) 1
代謝および栄養障害	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
食欲減退	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
高乳酸血症	0	1 (0.5%) 1	1 (0.2%) 1
精神障害	3 (0.7%) 3	0	3 (0.5%) 3
錯乱状態	1 (0.2%) 1	0	1 (0.2%) 1
譫妄	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Relatedness as assessed by investigator.

Table 14.3.1.5
Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
易刺激性	1 (0.2%) 1	0	1 (0.2%) 1
呼吸器、胸郭および縦隔障害	1 (0.2%) 2	1 (0.5%) 1	2 (0.3%) 3
呼吸困難	0	1 (0.5%) 1	1 (0.2%) 1
鼻出血	1 (0.2%) 1	0	1 (0.2%) 1
ラ音	1 (0.2%) 1	0	1 (0.2%) 1
筋骨格系および結合組織障害	2 (0.5%) 2	0	2 (0.3%) 2
高クレアチン血症	1 (0.2%) 1	0	1 (0.2%) 1
筋力低下	1 (0.2%) 1	0	1 (0.2%) 1
内分泌障害	1 (0.2%) 2	0	1 (0.2%) 2
甲状腺機能低下症	1 (0.2%) 2	0	1 (0.2%) 2
心臓障害	1 (0.2%) 1	0	1 (0.2%) 1
急性心不全	1 (0.2%) 1	0	1 (0.2%) 1
生殖系および乳房障害	1 (0.2%) 1	0	1 (0.2%) 1
前立腺障害	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Relatedness as assessed by investigator.

Table 14.3.1.5
Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
血管障害	1 (0.2%) 1	0	1 (0.2%) 1
低血圧	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Relatedness as assessed by investigator.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
Any treatment emergent serious adverse event	230 (54.6%) 592	137 (64.9%) 376	367 (58.1%) 968
心臓障害	117 (27.8%) 193	83 (39.3%) 177	200 (31.6%) 370
心不全	45 (10.7%) 64	39 (18.5%) 77	84 (13.3%) 141
急性心不全	21 (5.0%) 28	14 (6.6%) 19	35 (5.5%) 47
心房細動	19 (4.5%) 19	15 (7.1%) 18	34 (5.4%) 37
徐脈	11 (2.6%) 11	2 (0.9%) 2	13 (2.1%) 13
心室性頻脈	6 (1.4%) 6	5 (2.4%) 11	11 (1.7%) 17
完全房室ブロック	8 (1.9%) 8	3 (1.4%) 3	11 (1.7%) 11
急性心筋梗塞	5 (1.2%) 7	4 (1.9%) 4	9 (1.4%) 11
慢性心不全	6 (1.4%) 6	3 (1.4%) 4	9 (1.4%) 10
心停止	4 (1.0%) 4	4 (1.9%) 4	8 (1.3%) 8
うっ血性心不全	5 (1.2%) 5	3 (1.4%) 3	8 (1.3%) 8
心腎症候群	3 (0.7%) 3	3 (1.4%) 4	6 (0.9%) 7
心房粗動	3 (0.7%) 3	3 (1.4%) 3	6 (0.9%) 6
急性左室不全	3 (0.7%) 3	2 (0.9%) 4	5 (0.8%) 7
心原性ショック	1 (0.2%) 1	3 (1.4%) 5	4 (0.6%) 6
房室ブロック	2 (0.5%) 3	2 (0.9%) 2	4 (0.6%) 5
心アミロイドーシス	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
狭心症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
右室不全	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
洞結節機能不全	3 (0.7%) 3	0	3 (0.5%) 3
三束ブロック	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
心房頻脈	2 (0.5%) 2	0	2 (0.3%) 2
慢性左室不全	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
大動脈弁狭窄	1 (0.2%) 1	0	1 (0.2%) 1
心房血栓症	1 (0.2%) 1	0	1 (0.2%) 1
二束ブロック	1 (0.2%) 1	0	1 (0.2%) 1
徐脈性不整脈	0	1 (0.5%) 1	1 (0.2%) 1
脚ブロック	1 (0.2%) 1	0	1 (0.2%) 1
心粗動	1 (0.2%) 1	0	1 (0.2%) 1
心タンポナーデ	0	1 (0.5%) 1	1 (0.2%) 1
心肺停止	0	1 (0.5%) 1	1 (0.2%) 1
冠動脈疾患	0	1 (0.5%) 1	1 (0.2%) 1
僧帽弁閉鎖不全症	0	1 (0.5%) 1	1 (0.2%) 1
心筋梗塞	0	1 (0.5%) 1	1 (0.2%) 1
心筋虚血	1 (0.2%) 1	0	1 (0.2%) 1
動悸	1 (0.2%) 1	0	1 (0.2%) 1
心膜炎	0	1 (0.5%) 1	1 (0.2%) 1
上室性頻脈	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
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Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
心室細動	1 (0.2%) 1	0	1 (0.2%) 1
感染症および寄生虫症	62 (14.7%) 91	37 (17.5%) 44	99 (15.7%) 135
肺炎	12 (2.9%) 13	6 (2.8%) 6	18 (2.8%) 19
COVID-19	9 (2.1%) 9	4 (1.9%) 4	13 (2.1%) 13
尿路感染	7 (1.7%) 8	3 (1.4%) 3	10 (1.6%) 11
COVID-19肺炎	2 (0.5%) 2	8 (3.8%) 8	10 (1.6%) 10
蜂巣炎	7 (1.7%) 7	3 (1.4%) 3	10 (1.6%) 10
敗血症	4 (1.0%) 4	2 (0.9%) 2	6 (0.9%) 6
敗血症性ショック	4 (1.0%) 4	0	4 (0.6%) 4
下気道感染	3 (0.7%) 6	0	3 (0.5%) 6
丹毒	2 (0.5%) 3	1 (0.5%) 1	3 (0.5%) 4
尿路性敗血症	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
四肢膿瘍	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
気管支炎	2 (0.5%) 2	0	2 (0.3%) 2
医療機器関連感染	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
胃腸炎	2 (0.5%) 2	0	2 (0.3%) 2
誤嚥性肺炎	2 (0.5%) 2	0	2 (0.3%) 2
細菌性肺炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
処置後感染	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
気道感染	2 (0.5%) 2	0	2 (0.3%) 2
ブドウ球菌性菌血症	2 (0.5%) 2	0	2 (0.3%) 2
ブドウ球菌性敗血症	0	2 (0.9%) 2	2 (0.3%) 2
上気道感染	2 (0.5%) 2	0	2 (0.3%) 2
腹部敗血症	0	1 (0.5%) 1	1 (0.2%) 1
菌血症	1 (0.2%) 1	0	1 (0.2%) 1
細菌性敗血症	1 (0.2%) 1	0	1 (0.2%) 1
感染性胆嚢炎	1 (0.2%) 1	0	1 (0.2%) 1
クロストリジウム・ディフィシレ感染	1 (0.2%) 1	0	1 (0.2%) 1
膀胱炎	1 (0.2%) 1	0	1 (0.2%) 1
医療機器関連敗血症	0	1 (0.5%) 1	1 (0.2%) 1
大腸菌性菌血症	0	1 (0.5%) 1	1 (0.2%) 1
血腫感染	1 (0.2%) 1	0	1 (0.2%) 1
埋込み部位感染	1 (0.2%) 1	0	1 (0.2%) 1
感染による気管支拡張症の増悪	1 (0.2%) 1	0	1 (0.2%) 1
感染性腱鞘炎	0	1 (0.5%) 1	1 (0.2%) 1
インフルエンザ	0	1 (0.5%) 1	1 (0.2%) 1
椎間板炎	1 (0.2%) 1	0	1 (0.2%) 1
肺膿瘍	1 (0.2%) 1	0	1 (0.2%) 1
精巣炎	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
ブドウ球菌性肺炎	1 (0.2%) 1	0	1 (0.2%) 1
後腹膜膿瘍	0	1 (0.5%) 1	1 (0.2%) 1
パスツレラ菌性敗血症	0	1 (0.5%) 1	1 (0.2%) 1
レンサ球菌性化膿性関節炎	1 (0.2%) 1	0	1 (0.2%) 1
副鼻腔炎	1 (0.2%) 1	0	1 (0.2%) 1
植皮感染	0	1 (0.5%) 1	1 (0.2%) 1
皮膚感染	0	1 (0.5%) 1	1 (0.2%) 1
ブドウ球菌感染	0	1 (0.5%) 1	1 (0.2%) 1
細菌性尿路感染	1 (0.2%) 1	0	1 (0.2%) 1
シュードモナス性尿路感染	1 (0.2%) 1	0	1 (0.2%) 1
ウイルス性上気道感染	1 (0.2%) 1	0	1 (0.2%) 1
傷害、中毒および処置合併症	41 (9.7%) 55	16 (7.6%) 18	57 (9.0%) 73
転倒	13 (3.1%) 13	2 (0.9%) 2	15 (2.4%) 15
肋骨骨折	5 (1.2%) 5	0	5 (0.8%) 5
大腿骨頚部骨折	4 (1.0%) 4	0	4 (0.6%) 4
大腿骨骨折	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
足関節部骨折	3 (0.7%) 3	0	3 (0.5%) 3
頭部損傷	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
人工関節周囲骨折	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
硬膜下血腫	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
頭蓋脳損傷	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
四肢損傷	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
交通事故	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
皮膚裂傷	2 (0.5%) 2	0	2 (0.3%) 2
偶発的過量投与	1 (0.2%) 1	0	1 (0.2%) 1
背部損傷	0	1 (0.5%) 1	1 (0.2%) 1
骨挫傷	1 (0.2%) 1	0	1 (0.2%) 1
頚椎骨折	0	1 (0.5%) 1	1 (0.2%) 1
脳振盪	1 (0.2%) 1	0	1 (0.2%) 1
放射線性膀胱炎	1 (0.2%) 1	0	1 (0.2%) 1
焼痂	1 (0.2%) 1	0	1 (0.2%) 1
尾骨骨折	1 (0.2%) 1	0	1 (0.2%) 1
仙骨骨折	1 (0.2%) 1	0	1 (0.2%) 1
外傷性血尿	1 (0.2%) 1	0	1 (0.2%) 1
企図的過量投与	1 (0.2%) 1	0	1 (0.2%) 1
靱帯捻挫	1 (0.2%) 1	0	1 (0.2%) 1
腰椎骨折	1 (0.2%) 1	0	1 (0.2%) 1
投薬過誤	0	1 (0.5%) 1	1 (0.2%) 1
半月板損傷	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
骨盤骨折	1 (0.2%) 1	0	1 (0.2%) 1
処置後血腫	0	1 (0.5%) 1	1 (0.2%) 1
処置後血尿	1 (0.2%) 1	0	1 (0.2%) 1
処置後出血	1 (0.2%) 1	0	1 (0.2%) 1
処置による疼痛	0	1 (0.5%) 1	1 (0.2%) 1
硬膜下出血	1 (0.2%) 1	0	1 (0.2%) 1
外傷性血胸	0	1 (0.5%) 1	1 (0.2%) 1
外傷性頭蓋内出血	1 (0.2%) 1	0	1 (0.2%) 1
術後尿閉	1 (0.2%) 1	0	1 (0.2%) 1
創傷出血	1 (0.2%) 1	0	1 (0.2%) 1
胃腸障害	34 (8.1%) 41	16 (7.6%) 18	50 (7.9%) 59
鼠径ヘルニア	6 (1.4%) 6	2 (0.9%) 2	8 (1.3%) 8
胃腸出血	4 (1.0%) 5	1 (0.5%) 1	5 (0.8%) 6
便秘	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
上部消化管出血	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
腹痛	2 (0.5%) 2	1 (0.5%) 2	3 (0.5%) 4
直腸出血	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
小腸閉塞	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3
胃食道逆流性疾患	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
絞扼性鼠径ヘルニア	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
腸閉塞	2 (0.5%) 2	0	2 (0.3%) 2
上腹部痛	1 (0.2%) 1	0	1 (0.2%) 1
腹水	0	1 (0.5%) 1	1 (0.2%) 1
大腸炎	1 (0.2%) 1	0	1 (0.2%) 1
下痢	1 (0.2%) 1	0	1 (0.2%) 1
出血性腸憩室	0	1 (0.5%) 1	1 (0.2%) 1
十二指腸炎	1 (0.2%) 1	0	1 (0.2%) 1
嚥下障害	1 (0.2%) 1	0	1 (0.2%) 1
腸炎	1 (0.2%) 1	0	1 (0.2%) 1
胃炎	1 (0.2%) 1	0	1 (0.2%) 1
歯肉出血	1 (0.2%) 1	0	1 (0.2%) 1
血便排泄	0	1 (0.5%) 1	1 (0.2%) 1
裂孔ヘルニア	1 (0.2%) 1	0	1 (0.2%) 1
イレウス	1 (0.2%) 1	0	1 (0.2%) 1
腸管虚血	1 (0.2%) 1	0	1 (0.2%) 1
腸上皮化生	1 (0.2%) 1	0	1 (0.2%) 1
腸管穿孔	1 (0.2%) 1	0	1 (0.2%) 1
下部消化管出血	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
マロリー・ワイス症候群	0	1 (0.5%) 1	1 (0.2%) 1
機械的イレウス	1 (0.2%) 1	0	1 (0.2%) 1
メレナ	0	1 (0.5%) 1	1 (0.2%) 1
神経系障害	32 (7.6%) 35	13 (6.2%) 17	45 (7.1%) 52
失神	6 (1.4%) 6	4 (1.9%) 5	10 (1.6%) 11
失神寸前の状態	5 (1.2%) 5	1 (0.5%) 1	6 (0.9%) 6
脳血管発作	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
脳梗塞	3 (0.7%) 3	0	3 (0.5%) 3
浮動性めまい	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
塞栓性脳卒中	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
虚血性脳卒中	2 (0.5%) 2	0	2 (0.3%) 2
くも膜下出血	2 (0.5%) 2	0	2 (0.3%) 2
舞踏病	1 (0.2%) 2	0	1 (0.2%) 2
神経系障害	1 (0.2%) 2	0	1 (0.2%) 2
パーキンソン病	0	1 (0.5%) 2	1 (0.2%) 2
下肢静止不能症候群	0	1 (0.5%) 2	1 (0.2%) 2
脳出血	1 (0.2%) 1	0	1 (0.2%) 1
頚髄神経根障害	1 (0.2%) 1	0	1 (0.2%) 1
脳神経麻痺	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
認知症	0	1 (0.5%) 1	1 (0.2%) 1
体位性めまい	1 (0.2%) 1	0	1 (0.2%) 1
構語障害	1 (0.2%) 1	0	1 (0.2%) 1
頭痛	1 (0.2%) 1	0	1 (0.2%) 1
不全片麻痺	0	1 (0.5%) 1	1 (0.2%) 1
肝性脳症	0	1 (0.5%) 1	1 (0.2%) 1
末梢性ニューロパチー	1 (0.2%) 1	0	1 (0.2%) 1
一過性脳虚血発作	1 (0.2%) 1	0	1 (0.2%) 1
腎および尿路障害	30 (7.1%) 37	11 (5.2%) 11	41 (6.5%) 48
急性腎障害	21 (5.0%) 21	8 (3.8%) 8	29 (4.6%) 29
血尿	3 (0.7%) 5	0	3 (0.5%) 5
中毒性腎症	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
腎機能障害	3 (0.7%) 3	0	3 (0.5%) 3
慢性腎臓病	2 (0.5%) 2	0	2 (0.3%) 2
末期腎疾患	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
膀胱結石	1 (0.2%) 1	0	1 (0.2%) 1
腎結石症	1 (0.2%) 1	0	1 (0.2%) 1
腎前性腎不全	1 (0.2%) 1	0	1 (0.2%) 1
尿閉	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
呼吸器、胸郭および縦隔障害	18 (4.3%) 25	9 (4.3%) 10	27 (4.3%) 35
胸水	2 (0.5%) 2	4 (1.9%) 4	6 (0.9%) 6
呼吸困難	2 (0.5%) 2	3 (1.4%) 3	5 (0.8%) 5
労作性呼吸困難	3 (0.7%) 3	0	3 (0.5%) 3
呼吸不全	2 (0.5%) 3	0	2 (0.3%) 3
急性呼吸不全	2 (0.5%) 2	0	2 (0.3%) 2
慢性閉塞性肺疾患	2 (0.5%) 2	0	2 (0.3%) 2
胸膜炎	2 (0.5%) 2	0	2 (0.3%) 2
肺塞栓症	0	2 (0.9%) 2	2 (0.3%) 2
肺水腫	1 (0.2%) 3	0	1 (0.2%) 3
急性肺水腫	1 (0.2%) 1	0	1 (0.2%) 1
喘息	1 (0.2%) 1	0	1 (0.2%) 1
息詰まり	1 (0.2%) 1	0	1 (0.2%) 1
鼻出血	1 (0.2%) 1	0	1 (0.2%) 1
喀血	0	1 (0.5%) 1	1 (0.2%) 1
気胸	1 (0.2%) 1	0	1 (0.2%) 1
肺うっ血	1 (0.2%) 1	0	1 (0.2%) 1
一般・全身障害および投与部位の状態	15 (3.6%) 16	11 (5.2%) 13	26 (4.1%) 29

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
死亡	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
全身健康状態悪化	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
非心臓性胸痛	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
胸痛	1 (0.2%) 1	2 (0.9%) 3	3 (0.5%) 4
無力症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
多臓器機能不全症候群	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
発熱	2 (0.5%) 2	0	2 (0.3%) 2
医療機器関連合併症	1 (0.2%) 1	0	1 (0.2%) 1
嚢胞	0	1 (0.5%) 1	1 (0.2%) 1
疾患進行	0	1 (0.5%) 1	1 (0.2%) 1
疲労	1 (0.2%) 1	0	1 (0.2%) 1
粘膜の炎症	0	1 (0.5%) 1	1 (0.2%) 1
末梢腫脹	1 (0.2%) 1	0	1 (0.2%) 1
突然死	1 (0.2%) 1	0	1 (0.2%) 1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	16 (3.8%) 16	10 (4.7%) 13	26 (4.1%) 29
基底細胞癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
再発膀胱癌	2 (0.5%) 2	0	2 (0.3%) 2
慢性リンパ性白血病	0	2 (0.9%) 2	2 (0.3%) 2
遠隔転移を伴う前立腺癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
扁桃癌	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
移行上皮癌	2 (0.5%) 2	0	2 (0.3%) 2
遠隔転移を伴う扁桃癌	0	1 (0.5%) 2	1 (0.2%) 2
膵腺癌	0	1 (0.5%) 1	1 (0.2%) 1
膀胱癌	1 (0.2%) 1	0	1 (0.2%) 1
結腸直腸癌	1 (0.2%) 1	0	1 (0.2%) 1
びまん性大細胞型B細胞性リンパ腫	1 (0.2%) 1	0	1 (0.2%) 1
遠隔転移を伴う消化器癌	0	1 (0.5%) 1	1 (0.2%) 1
再発肺腺癌	0	1 (0.5%) 1	1 (0.2%) 1
遠隔転移を伴う肺癌	1 (0.2%) 1	0	1 (0.2%) 1
悪性黒色腫	0	1 (0.5%) 1	1 (0.2%) 1
悪性胸水	0	1 (0.5%) 1	1 (0.2%) 1
甲状腺髄様癌	1 (0.2%) 1	0	1 (0.2%) 1
肝転移	1 (0.2%) 1	0	1 (0.2%) 1
骨髄異形成症候群	0	1 (0.5%) 1	1 (0.2%) 1
前立腺癌	1 (0.2%) 1	0	1 (0.2%) 1
腎細胞癌	1 (0.2%) 1	0	1 (0.2%) 1
小腸腺癌	1 (0.2%) 1	0	1 (0.2%) 1
筋骨格系および結合組織障害	14 (3.3%) 15	12 (5.7%) 12	26 (4.1%) 27

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
変形性関節症	3 (0.7%) 3	4 (1.9%) 4	7 (1.1%) 7
筋骨格系胸痛	1 (0.2%) 1	3 (1.4%) 3	4 (0.6%) 4
関節痛	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
関節炎	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
背部痛	2 (0.5%) 2	0	2 (0.3%) 2
腰部脊柱管狭窄症	2 (0.5%) 2	0	2 (0.3%) 2
横紋筋融解症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
滑液包炎	0	1 (0.5%) 1	1 (0.2%) 1
椎間板突出	1 (0.2%) 1	0	1 (0.2%) 1
変形性脊椎症	1 (0.2%) 1	0	1 (0.2%) 1
脊柱管狭窄症	1 (0.2%) 1	0	1 (0.2%) 1
滑液嚢腫	1 (0.2%) 1	0	1 (0.2%) 1
腱鞘炎	0	1 (0.5%) 1	1 (0.2%) 1
血管障害	14 (3.3%) 14	8 (3.8%) 8	22 (3.5%) 22
起立性低血圧	3 (0.7%) 3	4 (1.9%) 4	7 (1.1%) 7
大動脈狭窄	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
低血圧	3 (0.7%) 3	0	3 (0.5%) 3
深部静脈血栓症	1 (0.2%) 1	0	1 (0.2%) 1
塞栓症	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
大腿動脈塞栓症	1 (0.2%) 1	0	1 (0.2%) 1
リンパ浮腫	1 (0.2%) 1	0	1 (0.2%) 1
末梢動脈閉塞性疾患	0	1 (0.5%) 1	1 (0.2%) 1
末梢血管障害	1 (0.2%) 1	0	1 (0.2%) 1
血栓症	0	1 (0.5%) 1	1 (0.2%) 1
静脈瘤破裂	0	1 (0.5%) 1	1 (0.2%) 1
代謝および栄養障害	11 (2.6%) 13	8 (3.8%) 10	19 (3.0%) 23
血液量増加症	3 (0.7%) 4	5 (2.4%) 7	8 (1.3%) 11
脱水	4 (1.0%) 4	1 (0.5%) 1	5 (0.8%) 5
低カリウム血症	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
悪液質	1 (0.2%) 1	0	1 (0.2%) 1
痛風	1 (0.2%) 1	0	1 (0.2%) 1
高カリウム血症	1 (0.2%) 1	0	1 (0.2%) 1
低カルシウム血症	1 (0.2%) 1	0	1 (0.2%) 1
低ナトリウム血症	0	1 (0.5%) 1	1 (0.2%) 1
血液およびリンパ系障害	9 (2.1%) 12	3 (1.4%) 7	12 (1.9%) 19
貧血	7 (1.7%) 9	2 (0.9%) 4	9 (1.4%) 13
鉄欠乏性貧血	1 (0.2%) 1	1 (0.5%) 3	2 (0.3%) 4

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
免疫性血小板減少症	1 (0.2%) 1	0	1 (0.2%) 1
正色素性正球性貧血	1 (0.2%) 1	0	1 (0.2%) 1
臨床検査	7 (1.7%) 7	3 (1.4%) 3	10 (1.6%) 10
血中クレアチニン増加	2 (0.5%) 2	0	2 (0.3%) 2
心拍出量低下	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
心電図QT延長	1 (0.2%) 1	0	1 (0.2%) 1
国際標準比増加	1 (0.2%) 1	0	1 (0.2%) 1
酸素飽和度低下	1 (0.2%) 1	0	1 (0.2%) 1
SARS-CoV-2検査陽性	0	1 (0.5%) 1	1 (0.2%) 1
トロポニンT増加	1 (0.2%) 1	0	1 (0.2%) 1
トロポニン増加	0	1 (0.5%) 1	1 (0.2%) 1
肝胆道系障害	4 (1.0%) 9	4 (1.9%) 4	8 (1.3%) 13
胆管炎	2 (0.5%) 6	0	2 (0.3%) 6
胆管結石	1 (0.2%) 1	0	1 (0.2%) 1
胆道仙痛	0	1 (0.5%) 1	1 (0.2%) 1
胆嚢炎	1 (0.2%) 1	0	1 (0.2%) 1
胆石症	0	1 (0.5%) 1	1 (0.2%) 1
肝不全	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
肝機能異常	1 (0.2%) 1	0	1 (0.2%) 1
虚血性肝炎	0	1 (0.5%) 1	1 (0.2%) 1
皮膚および皮下組織障害	5 (1.2%) 6	0	5 (0.8%) 6
血管浮腫	1 (0.2%) 1	0	1 (0.2%) 1
薬疹	1 (0.2%) 1	0	1 (0.2%) 1
皮脂欠乏性湿疹	1 (0.2%) 1	0	1 (0.2%) 1
老人性紫斑	1 (0.2%) 1	0	1 (0.2%) 1
皮膚潰瘍	1 (0.2%) 1	0	1 (0.2%) 1
毛細血管拡張症	1 (0.2%) 1	0	1 (0.2%) 1
製品の問題	3 (0.7%) 3	2 (0.9%) 2	5 (0.8%) 5
医療機器位置異常	0	1 (0.5%) 1	1 (0.2%) 1
医療機器不具合	1 (0.2%) 1	0	1 (0.2%) 1
医療機器のゆるみ	1 (0.2%) 1	0	1 (0.2%) 1
医療機器機能不良	0	1 (0.5%) 1	1 (0.2%) 1
リードの位置ずれ	1 (0.2%) 1	0	1 (0.2%) 1
精神障害	1 (0.2%) 1	2 (0.9%) 3	3 (0.5%) 4
双極性障害	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
錯乱状態	0	1 (0.5%) 1	1 (0.2%) 1
譫妄	0	1 (0.5%) 1	1 (0.2%) 1
不眠症	0	1 (0.5%) 1	1 (0.2%) 1
眼障害	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
結膜出血	0	1 (0.5%) 1	1 (0.2%) 1
黄斑円孔	1 (0.2%) 1	0	1 (0.2%) 1
網膜動脈閉塞	0	1 (0.5%) 1	1 (0.2%) 1
生殖系および乳房障害	1 (0.2%) 1	2 (0.9%) 2	3 (0.5%) 3
良性前立腺肥大症	0	2 (0.9%) 2	2 (0.3%) 2
前立腺炎	1 (0.2%) 1	0	1 (0.2%) 1
内分泌障害	1 (0.2%) 1	0	1 (0.2%) 1
甲状腺機能低下症	1 (0.2%) 1	0	1 (0.2%) 1
免疫系障害	0	1 (0.5%) 1	1 (0.2%) 1
アミロイドーシス	0	1 (0.5%) 1	1 (0.2%) 1
外科および内科処置	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.9
Treatment Emergent Serious Adverse Events by System Organ Class and Preferred Term[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
安楽死	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent serious adverse event (the subject is counted only once for each serious AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Serious Adverse events (SAEs) reported on the "Adverse Events" or "CV Hospitalizations and Events of Clinical Interest" eCRF occurring during the treatment period are considered treatment emergent serious adverse event (TESAE), if they were not present before the first dose of study drug or if they were present before the first dose of study drug but increased in severity during the treatment period. An SAE that occurs more than 30 days after the last dose of IMP will not be counted as a TESAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically.

Table 14.3.1.16
Treatment Emergent Adverse Events Leading to Discontinuation of IMP[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
Any treatment emergent adverse event leading to IMP discontinuation	39 (9.3%) 46	18 (8.5%) 22	57 (9.0%) 68
心臓障害	11 (2.6%) 11	7 (3.3%) 7	18 (2.8%) 18
心不全	5 (1.2%) 5	2 (0.9%) 2	7 (1.1%) 7
急性心不全	2 (0.5%) 2	0	2 (0.3%) 2
慢性心不全	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
心腎症候群	0	2 (0.9%) 2	2 (0.3%) 2
徐脈	1 (0.2%) 1	0	1 (0.2%) 1
心アミロイドーシス	0	1 (0.5%) 1	1 (0.2%) 1
うっ血性心不全	0	1 (0.5%) 1	1 (0.2%) 1
動悸	1 (0.2%) 1	0	1 (0.2%) 1
右室不全	1 (0.2%) 1	0	1 (0.2%) 1
胃腸障害	9 (2.1%) 9	0	9 (1.4%) 9
下痢	2 (0.5%) 2	0	2 (0.3%) 2
消化不良	2 (0.5%) 2	0	2 (0.3%) 2
悪心	2 (0.5%) 2	0	2 (0.3%) 2
腹部不快感	1 (0.2%) 1	0	1 (0.2%) 1
上腹部痛	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Percentage based on safety population for respective treatment. Discontinuation of IMP from action taken on “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF.

Table 14.3.1.16
Treatment Emergent Adverse Events Leading to Discontinuation of IMP[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
腸閉塞	1 (0.2%) 1	0	1 (0.2%) 1
神経系障害	5 (1.2%) 6	2 (0.9%) 2	7 (1.1%) 8
認知症	2 (0.5%) 2	0	2 (0.3%) 2
脳血管発作	0	1 (0.5%) 1	1 (0.2%) 1
舞踏病	1 (0.2%) 1	0	1 (0.2%) 1
浮動性めまい	1 (0.2%) 1	0	1 (0.2%) 1
パーキンソン病	0	1 (0.5%) 1	1 (0.2%) 1
くも膜下出血	1 (0.2%) 1	0	1 (0.2%) 1
振戦	1 (0.2%) 1	0	1 (0.2%) 1
感染症および寄生虫症	4 (1.0%) 4	0	4 (0.6%) 4
COVID-19	1 (0.2%) 1	0	1 (0.2%) 1
胃腸炎	1 (0.2%) 1	0	1 (0.2%) 1
敗血症性ショック	1 (0.2%) 1	0	1 (0.2%) 1
尿路感染	1 (0.2%) 1	0	1 (0.2%) 1
代謝および栄養障害	3 (0.7%) 3	1 (0.5%) 1	4 (0.6%) 4
食欲減退	2 (0.5%) 2	1 (0.5%) 1	3 (0.5%) 3

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Percentage based on safety population for respective treatment. Discontinuation of IMP from action taken on “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF.

Table 14.3.1.16
Treatment Emergent Adverse Events Leading to Discontinuation of IMP[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
低カルシウム血症	1 (0.2%) 1	0	1 (0.2%) 1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.5%) 2	2 (0.9%) 2	4 (0.6%) 4
遠隔転移を伴う消化器癌	0	1 (0.5%) 1	1 (0.2%) 1
遠隔転移を伴う肺癌	1 (0.2%) 1	0	1 (0.2%) 1
腎細胞癌	1 (0.2%) 1	0	1 (0.2%) 1
遠隔転移を伴う扁桃癌	0	1 (0.5%) 1	1 (0.2%) 1
腎および尿路障害	4 (1.0%) 4	0	4 (0.6%) 4
急性腎障害	2 (0.5%) 2	0	2 (0.3%) 2
慢性腎臓病	1 (0.2%) 1	0	1 (0.2%) 1
末期腎疾患	1 (0.2%) 1	0	1 (0.2%) 1
傷害、中毒および処置合併症	1 (0.2%) 3	1 (0.5%) 3	2 (0.3%) 6
転倒	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
頚椎骨折	0	1 (0.5%) 1	1 (0.2%) 1
鎖骨骨折	0	1 (0.5%) 1	1 (0.2%) 1
頭蓋脳損傷	1 (0.2%) 1	0	1 (0.2%) 1
硬膜下出血	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Percentage based on safety population for respective treatment. Discontinuation of IMP from action taken on “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF.

Table 14.3.1.16
Treatment Emergent Adverse Events Leading to Discontinuation of IMP[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
一般・全身障害および投与部位の状態	1 (0.2%) 1	1 (0.5%) 1	2 (0.3%) 2
無力症	1 (0.2%) 1	0	1 (0.2%) 1
疾患進行	0	1 (0.5%) 1	1 (0.2%) 1
精神障害	0	2 (0.9%) 2	2 (0.3%) 2
錯乱状態	0	1 (0.5%) 1	1 (0.2%) 1
うつ病	0	1 (0.5%) 1	1 (0.2%) 1
呼吸器、胸郭および縦隔障害	2 (0.5%) 2	0	2 (0.3%) 2
呼吸困難	1 (0.2%) 1	0	1 (0.2%) 1
咽頭出血	1 (0.2%) 1	0	1 (0.2%) 1
免疫系障害	0	1 (0.5%) 1	1 (0.2%) 1
アミロイドーシス	0	1 (0.5%) 1	1 (0.2%) 1
臨床検査	0	1 (0.5%) 1	1 (0.2%) 1
心電図QT延長	0	1 (0.5%) 1	1 (0.2%) 1
皮膚および皮下組織障害	1 (0.2%) 1	0	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Percentage based on safety population for respective treatment. Discontinuation of IMP from action taken on “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF.

Table 14.3.1.16
Treatment Emergent Adverse Events Leading to Discontinuation of IMP[1]
Safety Population

System Organ Class Preferred Term	Acoramidis N=421 n (%) E	Placebo N=211 n (%) E	Overall N=632 n (%) E
紅斑性皮疹	1 (0.2%) 1	0	1 (0.2%) 1
外科および内科処置	0	1 (0.5%) 1	1 (0.2%) 1
安楽死	0	1 (0.5%) 1	1 (0.2%) 1
血管障害	0	1 (0.5%) 1	1 (0.2%) 1
血栓症	0	1 (0.5%) 1	1 (0.2%) 1

Note: n = number of subjects experiencing a treatment emergent adverse event (the subject is counted only once for each AE). % is of the column total. E is the number of events for System Organ Class or Preferred Term.
1: All Adverse events (AEs) reported on the “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF occurring during the treatment period are considered treatment emergent adverse event (TEAE), if they were not present before the first dose of IMP or if they were present before the first dose of IMP but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as a TEAE. System organ class (SOC) and preferred term coded using Medical Dictionary for Regulatory Activities (MedDRA) version 24.1. Sorted by SOC in descending frequency based on all subjects then by preferred term within SOC in descending frequency based on all subjects. If two SOCs or preferred terms within SOC have the same frequency, then the SOC or preferred term will be sorted by descending number of events and if the same frequency and number of events, then the SOCs or preferred terms within SOC will be sorted alphabetically. Percentage based on safety population for respective treatment. Discontinuation of IMP from action taken on “Adverse Events” or “CV Hospitalizations and Events of Clinical Interest” eCRF.

9.3.1. 死亡に至った有害事象の詳細

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]	
Medical History [1]: Prostate cancer, Cardiac failure congestive, Oedema, Hypercholesterolaemia, Anxiety, Vitamin D decreased, Insomnia, Chronic kidney disease, Pleural effusion, Cardiac amyloidosis, Atrial flutter, Cataract, Gout, Vitamin B12 decreased, Thrombocytopenia					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 500			
Concomitant Medication [3]: COLECALCIFEROL, ATORVASTATIN, CYANOCOBALAMIN, TORASEMIDE, WARFARIN, ALLOPURINOL, EPLERENONE, AMIODARONE, TRAZODONE, TORASEMIDE, TRAZODONE, METOLAZONE, LORAZEPAM, FERUMOXYTOL, POTASSIUM CHLORIDE, HYDROMORPHONE HYDROCHLORIDE, TORASEMIDE, ZOLPIDEM TARTRATE					
Non-Serious Adverse Event [4]: Skin abrasion, International normalised ratio increased, Atrial flutter, Cardiac failure congestive, Blood iron decreased, Hypokalaemia, Fall, Fall					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	PROGRESSIVE HEART FAILURE	Day 500 / Day 533	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。						

F = female; IMP = Investigational Medicinal Product; M = male; MedDRA = Medical Dictionary for Regulatory Activities; NA = Not Available/Not Applicable; UK = United Kingdom; US = United States; WHO = World Health Organization.

[1] Medical conditions coded using MedDRA version 24.1.

[2] Day of first dose of study drug is Day 1. Study days to last dose of IMP are calculated as (date of last dose of IMP- date of first dose of IMP) +1.

[3] Concomitant medications are those taken on or after the day of initiation of IMP, including those started prior to IMP and continued past initiation of IMP. Medications coded using WHO Drug Dictionary 2022SEP01. Medication is preferred name.

[4] Preferred term coded using MedDRA version 24.1.

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Osteoarthritis, Neuropathy peripheral, Benign prostatic hyperplasia, Asthma, Sleep apnoea syndrome, Migraine, Strabismus, Pulmonary sarcoidosis, Thoracotomy, Arthroscopy, Tinnitus, Vasectomy, Carpal tunnel decompression, Tendon sheath incision, Neck pain, Pain in extremity, Anxiety, Atrial septal defect repair, Coronary artery disease, Acquired oesophageal web, Chronic obstructive pulmonary disease, Insomnia, Bicuspid aortic valve, Diabetes mellitus, Pleural effusion, Atrial fibrillation, Bundle branch block left, Cholecystectomy, Hypertension, Cardiac ablation, Cardiac ablation, Cardiac resynchronisation therapy, Deafness, Dizziness, Gait disturbance, Depression, Cardiac amyloidosis, Cardiac failure congestive, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 540		
Concomitant Medication [3]: NAPROXEN SODIUM, FUROSEMIDE, WARFARIN SODIUM, LACTOBACILLUS NOS, PANTOPRAZOLE SODIUM SESQUIHYDRATE, MAGNESIUM CITRATE, MULTIVITAMINS (PLAIN), LISINOPRIL, COLECALCIFEROL, CHONDROITIN SULFATE, BISOPROLOL FUMARATE, ALLOPURINOL, ALLOPURINOL, CYCLOBENZAPRINE, TROLAMINE SALICYLATE, VITAMIN K NOS, WARFARIN, DEXTROMETHORPHAN HYDROBROMIDE/ETHANOL/GUAIFENESIN, CEFALEXIN, CEFALEXIN, METHYLPREDNISOLONE, PARACETAMOL, MAGNESIUM CITRATE, PARAFFIN, DOCUSATE SODIUM, INSULIN ASPART, NAFCILLIN, PIPERACILLIN/TAZOBACTAM, PIPERACILLIN/TAZOBACTAM, VANCOMYCIN, SODIUM CHLORIDE, SODIUM CHLORIDE, MORPHINE, LIDOCAINE, QUETIAPINE				
Non-Serious Adverse Event [4]: Hypotension, Fall, Muscle spasms, Abdominal pain, Diarrhoea, Acute kidney injury, International normalised ratio increased, Haematuria, Upper respiratory tract infection, Urinary tract infection, Cellulitis, Gout, Tendon rupture, Back pain, Dysphonia, Dysphonia, Flatulence, Diarrhoea, Lymphocytic infiltration, Constipation, Influenza like illness, Leukocytosis, Normocytic anaemia, Thrombocytopenia, Cardiac failure acute, Gaze palsy, Gait disturbance, Sepsis, C-reactive protein increased, Red blood cell sedimentation rate increased, Diabetes mellitus, Hyperammonaemia, Hypoalbuminaemia, Back pain, Muscular weakness, Encephalopathy, Acute kidney injury, Pneumonitis, Supraventricular tachycardia				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ブドウ球菌性菌血症	BACTEREMIA DUE TO STAPHYLOCOCCUS	Day 540 / Day 547	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「ブドウ球菌性菌血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperlipidaemia, Ameloblastoma, Hip arthroplasty, Atrial fibrillation, Aortic valve incompetence, Inguinal hernia, Rotator cuff syndrome, Stress, Cardiac failure congestive, Orthopnoea, Palpitations, Cardioversion, Generalised oedema, Thyroid mass, Hepatic cyst, Insomnia, Mitral valve incompetence, Tricuspid valve incompetence, Ventricular extrasystoles, Atrioventricular block first degree, Myocardial infarction, Unevaluable event, Dizziness postural, Bundle branch block left, Sinus bradycardia, Aortic stenosis, Cardiac amyloidosis, Abdominal distension, Decreased appetite, Paraesthesia, Peripheral coldness, Supraventricular tachycardia, Neuropathy peripheral, Atrial flutter, Pericardial effusion, Functional residual capacity decreased, Cellulitis, Muscle injury, Dyspepsia, Eructation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 422		
Concomitant Medication [3]: ASCORBIC ACID/BETACAROTENE/BIOTIN/CALCIUM CARBONATE/CALCIUM PHOSPHATE/CHLORINE/COLECALCIFEROL/CUPRIC OXIDE/FERROUS FUMARATE/FOLIC ACID/IODINE/MAGNESIUM OXIDE/MANGANESE SULFATE/MOLYBDENUM/NICKEL SULFAT, METOPROLOL SUCCINATE, APIXABAN, TORASEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, CEFAZOLIN, HEPARIN, SODIUM CHLORIDE, LIDOCAINE, MIDAZOLAM, PROTAMINE, IOHEXOL, AMOXICILLIN, APIXABAN, ACETYLSALICYLIC ACID, DIGOXIN, METOPROLOL TARTRATE				
Non-Serious Adverse Event [4]: Dizziness, Ventricular arrhythmia, Aortic stenosis, Eructation, Thyroid mass, Epistaxis, Throat tightness, Atrial flutter, Headache				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大動脈弁狭窄	STENOSIS AORTIC VALVE ACQUIRED	Day 322 / Day 323	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心室細動	CARDIAC ARREST DUE TO VENTRICULAR FIBRILLATION	Day 422 / Day 422	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「大動脈弁狭窄」及び「心室細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Intervertebral disc protrusion, Basal cell carcinoma, Actinic keratosis, Congenital hearing disorder, Hearing aid user, Coronary artery bypass, Coronary artery disease, Hyperlipidaemia, Paraesthesia, Paraesthesia, Drug hypersensitivity, Chronic kidney disease, Rotator cuff syndrome, Rotator cuff repair, Ear pain, Age-related macular degeneration, Arthralgia, Neuropathy peripheral, Benign prostatic hyperplasia, Prostatitis, Essential hypertension, Aortic valve stenosis, Varicose vein operation, Carpal tunnel syndrome, Dry eye, Oedema peripheral, Neurogenic bladder, Carpal tunnel syndrome, Vertigo, Atrial fibrillation, Sinus node dysfunction, Varicose vein, Cataract, Cataract operation, Cataract operation, Tendon rupture, Muscle fatigue, Cardiac pacemaker insertion, Cardiac failure, Cardiac amyloidosis, Cholelithiasis, Bladder dilatation, Hydronephrosis, Prostatic operation				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 679			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, CYANOCOBALAMIN, UBIDECARENONE, COLECALCIFEROL, CALCIUM/MAGNESIUM/ZINC, ASCORBIC ACID/BETACAROTENE/CUPRIC OXIDE/TOCOPHERYL ACETATE/ZINC OXIDE, SIMVASTATIN, FLUOROURACIL, CALCIPOTRIOL, MULTIVITAMINS WITH MINERALS [UMBRELLA TERM], DEXTRAN 70/HYPROMELLOSE, POTASSIUM CHLORIDE, FUROSEMIDE, LEVOFLOXACIN, TAMSULOSIN, LINEZOLID, BUPIVACAINE, ROPIVACAINE, TRIAMCINOLONE ACETONIDE, FLUOROURACIL, DESONIDE, IBUPROFEN, POTASSIUM CHLORIDE, FUROSEMIDE, BEVACIZUMAB, INFLUENZA VACCINE, BEVACIZUMAB, TRIAMCINOLONE, TRIAMCINOLONE, BEVACIZUMAB, FLUOROURACIL, POTASSIUM CHLORIDE, FUROSEMIDE, PARACETAMOL, BEVACIZUMAB, TRIAMCINOLONE, VARICELLA ZOSTER VACCINES, BEVACIZUMAB, COVID-19 VACCINE, COVID-19 VACCINE, BEVACIZUMAB, FUROSEMIDE, APIXABAN, FUROSEMIDE, BEVACIZUMAB, FUROSEMIDE, FUROSEMIDE, AMIODARONE, AMIODARONE, LEVOTHYROXINE, LEVOTHYROXINE, AMIODARONE, AMIODARONE, MIDODRINE HYDROCHLORIDE, MIDODRINE HYDROCHLORIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Rotator cuff syndrome, Diverticulum, Inguinal hernia, Platelet count decreased, Basal cell carcinoma, Squamous cell carcinoma, Stress fracture, Neovascular age-related macular degeneration, Stasis dermatitis, Actinic keratosis, Squamous cell carcinoma, Leukopenia, Platelet count decreased, Osteoarthritis, Limb injury, Subretinal fibrosis, Prostatic specific antigen increased, Hypothyroidism, Orthostatic hypotension, Dyspnoea				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	HEART FAILURE DECOMPENSATION	Day 665 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
心不全（2）	HF EXACERBATION	Day 670 / Day 688	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Birth mark, Appendicectomy, Hyperlipidaemia, Limb operation, Prostatic specific antigen increased, Benign prostatic hyperplasia, Atrial fibrillation, Shoulder operation, Coronary artery disease, Atrial septal defect, Chronic left ventricular failure, Oedema, Hypotension, Atrioventricular block, Cardiac ventricular thrombosis, Pulmonary hypertension, Cardiac resynchronisation therapy, Sleep apnoea syndrome, Cardiomyopathy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 342		
Concomitant Medication [3]: CALCIUM CARBONATE, MULTIVITAMINS WITH MINERALS [UMBRELLA TERM], LISINOPRIL, SPIRONOLACTONE, APIXABAN, ALANINE/COPPER/CUCURBITA SPP/GLUTAMIC ACID/GLYCINE/SERENOA REPENS FRUIT/URTICA DIOICA LEAF/ZINC, CARVEDILOL, FUROSEMIDE, TORASEMIDE, TORASEMIDE, GLYCERYL TRINITRATE, SELENOMETHIONINE, CYANOCOBALAMIN, GLUCOSAMINE, POTASSIUM CHLORIDE, TORASEMIDE, TORASEMIDE, COVID-19 VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Oedema peripheral, Chest pain, Hypoglycaemia, Asthenia, Dyspnoea, Abdominal pain, Vomiting				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	Day 335 / Day 423	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Percutaneous coronary intervention, Coronary artery disease, Prostate cancer, Prostatectomy, Percutaneous coronary intervention, Atrial fibrillation, Atrial flutter, Cardiac failure congestive, Hypertension, Cardiac ablation, Drug hypersensitivity, Hypergammaglobulinaemia benign monoclonal, Neuropathy peripheral, Insomnia, Biopsy peripheral nerve, Foot deformity, Foot operation, Tenoplasty, Toe operation, Carpal tunnel syndrome, Cardiac amyloidosis, Carpal tunnel decompression, Hypercalcaemia, Sinus node dysfunction, Cardiac pacemaker insertion, Systemic inflammatory response syndrome				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 504		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN CALCIUM, FUROSEMIDE, DOCUSATE SODIUM, IRBESARTAN, WARFARIN, WARFARIN, GABAPENTIN, DULOXETINE HYDROCHLORIDE, CANDESARTAN CILEXETIL, AMIODARONE, AMIODARONE, ATORVASTATIN CALCIUM, AMIODARONE, VITAMIN K NOS, WARFARIN, WARFARIN, ATORVASTATIN, SPIRONOLACTONE, BUMETANIDE, DULOXETINE HYDROCHLORIDE, GABAPENTIN				
Non-Serious Adverse Event [4]: Dizziness, Hypotension, Limb injury, International normalised ratio increased, Acute kidney injury				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING OF ATRIAL FIBRILLATION	Day 349 / Day 363	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肝機能異常	LIVER DYSFUNCTION	Day 505 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Moderate
横紋筋融解症	RHABDOMYOLYSIS	Day 505 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Moderate
心不全	WORSENING HEART FAILURE	Day 505 / Day 510	Not Related	Drug Interrupted	Fatal	Moderate
治験責任医師の見解：「心房細動」、「肝機能異常」、「横紋筋融解症」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Other	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Knee arthroplasty, Hypertension, Carpal tunnel syndrome, Aortic aneurysm, Coronary artery disease, Hyperlipidaemia, Benign prostatic hyperplasia, Chronic obstructive pulmonary disease, Asthma, Constipation, Cardiac pacemaker insertion, Atrial fibrillation, Hypokalaemia, Cardiac resynchronisation therapy, Cardiac failure congestive, Trigger finger, Glucose tolerance impaired, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 270		
Concomitant Medication [3]: LISINOPRIL, METOPROLOL, SALBUTAMOL, LACTULOSE, APIXABAN, ROSUVASTATIN, TAMSULOSIN, TORASEMIDE, AMIODARONE HYDROCHLORIDE TORASEMIDE, TORASEMIDE, FUROSEMIDE, TORASEMIDE, LINACLOTIDE, FUROSEMIDE, TORASEMIDE, ATORVASTATIN, TORASEMIDE, TORASEMIDE, TORASEMIDE, METOLAZONE, IBUPROFEN, PARACETAMOL, DIPHTHERIA VACCINE TOXOID/PERTUSSIS VACCINE ACELLULAR/TETANUS VACCINE TOXOID, TORASEMIDE, MUPIROCIN, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, TORASEMIDE, SENNA ALEXANDRINA, PARACETAMOL, MACROGOL 3350, SACCHARATED IRON OXIDE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS)				
Non-Serious Adverse Event [4]: Hypotension, Acute kidney injury, Blood creatine phosphokinase increased, Cardiac failure, Arthralgia, Hypokalaemia, Cardiac failure, Oedema peripheral, Hypokalaemia, Hypothermia, Gastrointestinal haemorrhage, Acute kidney injury, Cellulitis, Transaminases increased, Shock, Dysphagia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全（1）	ACUTE HEART FAILURE	Day 146 / Day 166	Not Related	Dose Not Changed	Recovered /Resolved	Mild
ＣＯＶＩＤ－１９	ASYMPTOMATIC COVID19	Day 154 / Day 163	Not Related	Dose Not Changed	Recovered /Resolved	Mild
甲状腺機能低下症	HYPOTHYROIDISM	Day 180 / Day 304	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
皮膚裂傷	LEFT FOOT LACERATION	Day 201 / Day 203	Not Related	Dose Not Changed	Recovered /Resolved	Mild
急性心不全（2）	ACUTE HEART FAILURE	Day 259 / Day 280	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
急性心不全（3）	CHF EXACERBATION	Day 289 / Day 308	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「急性心不全（1）」、「ＣＯＶＩＤ－１９」、「甲状腺機能低下症」、「皮膚裂傷」、「急性心不全（2）」及び「急性心不全（3）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Adenoidectomy, Tonsillectomy, Appendicectomy, Benign prostatic hyperplasia, Hyperlipidaemia, Arthritis, Hypertension, Coronary artery disease, Rotator cuff repair, Sleep apnoea syndrome, Bradycardia, Aortic stenosis, Coronary artery disease, Ecchymosis, Atrioventricular block, Carpal tunnel syndrome, Tendon sheath incision, Normochromic normocytic anaemia, Gastrooesophageal reflux disease, Cardiac amyloidosis, Cardiac failure chronic, Bundle branch block right, Aortic valve replacement, Haematochezia, Leukopenia, Gastric ulcer, Haemorrhoids, Large intestinal ulcer, Diverticulitis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 433		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, CLOPIDOGREL, OMEGA-3 FATTY ACIDS, MULTIVITAMINS (PLAIN), FERROUS SULFATE, PANTOPRAZOLE, RANITIDINE, GLYCERYL TRINITRATE, VITAMIN B12 NOS, DIPHENHYDRAMINE/PARACETAMOL, FUROSEMIDE, FOLIC ACID, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, MUSCLE RELAXANTS, FUROSEMIDE, FUROSEMIDE, EPOETIN ALFA, TRIAMCINOLONE, ENOXAPARIN, PIPERACILLIN/TAZOBACTAM, VANCOMYCIN, CEFEPIME, HEPARIN, CEFTRIAXONE, MILRINONE, LOSARTAN, TAMSULOSIN, HEPARIN, ACETYLSALICYLIC ACID, FUROSEMIDE, PARACETAMOL, LIDOCAINE, RED BLOOD CELLS (CONCENTRATED), AMPICILLIN/SULBACTAM, PARACETAMOL, HYDROMORPHONE, HYDROCODONE/PARACETAMOL, PARACETAMOL, CEFAZOLIN, FENTANYL, CEFTRIAXONE				
Non-Serious Adverse Event [4]: Back pain, Ecchymosis, Anaemia, Abdominal pain upper, Flatulence, Subclavian vein occlusion, Superior vena cava occlusion, Nasopharyngitis, Venous pressure jugular increased, Urine albumin/creatinine ratio increased, Oedema peripheral, Asthenia, Acute kidney injury, Leukocytosis, Abnormal loss of weight				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
皮脂欠乏性湿疹	XEROTIC ECZEMA	Day 220 / Day 300	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
老人性紫斑	SENILE PURPURA	Day 220 / Day 300	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心筋梗塞（1）	TYPE II NSTEMI	Day 241 / Day 254	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
多臓器機能不全症候群	MULTI-ORGAN FAILURE	Day 241 / Day 254	Not Related	Drug Interrupted	Recovered /Resolved	Severe
菌血症	HIGH GRADE GPC BACTEREMIA	Day 241 / Day 254	Not Related	Drug Interrupted	Recovered /Resolved	Severe
細菌性敗血症	SEVERE SEPSIS (SECONDARY BACTEREMIA)	Day 241 / Day 254	Not Related	Drug Interrupted	Recovered /Resolved	Severe
急性心筋梗塞（2）	NSTEMI	Day 327 / Day 328	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

急性心不全	ACUTE CONGESTIVE HEART FAILURE EXACERBATION REQUIRING HOSPITALIZATION	Day 327 / Day 331	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
骨挫傷	RIGHT-SIDED RIB CONTUSION	Day 327 / Day 371	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
血腫感染	RIGHT UPPER EXTREMITY INFECTED HEMATOMA	Day 397 / NA	Not Related	Dose Not Changed	Recovering/Resolving	Moderate
焼痂	RIGHT UPPER EXTREMITY ESCHAR	Day 397 / Day 400	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
うっ血性心不全	CONGESTIVE HEART FAILURE	Day 397 / Day 435	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「皮脂欠乏性湿疹」、「老人性紫斑」、「急性心筋梗塞（1）」、「多臓器機能不全症候群」、「菌血症」、「細菌性敗血症」、「急性心筋梗塞（2）」、「急性心不全」、「骨挫傷」、「血腫感染」、「焼痂」及び「うっ血性心不全」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7■
Medical History [1]: Spinal laminectomy, Lumbar spinal stenosis, Carpal tunnel decompression, Coronary artery disease, Cervical radiculopathy, Atrial fibrillation, Spinal laminectomy, Coronary artery bypass, Hypertension, Hyperlipidaemia, Fatigue, Depression, Chronic kidney disease, Hypothyroidism, Gastrooesophageal reflux disease, Seasonal allergy, Deafness, Cardiac amyloidosis, Insomnia, Urinary retention, Cardiac failure, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 422		
Concomitant Medication [3]: ATORVASTATIN, WARFARIN, LEVOTHYROXINE, FAMOTIDINE, ESCITALOPRAM OXALATE, MELATONIN, TAMSULOSIN, FUROSEMIDE, LORATADINE, WARFARIN, FUROSEMIDE, ACETYLSALICYLIC ACID, FUROSEMIDE, PHYTOMENADIONE, PHYTOMENADIONE				
Non-Serious Adverse Event [4]: Lower respiratory tract infection, International normalised ratio increased, Venous pressure jugular increased, Depression, Acute kidney injury, Dyspnoea, Pleural effusion, International normalised ratio increased				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE DECOMPENSATED HEART FAILURE REQUIRING HOSPITALIZATION	Day 153 / Day 155	Not Related	Dose Not Changed	Recovered /Resolved	Severe
胸水	CHRONIC LEFT PLEURAL EFFUSION	Day 153 / Day 155	Not Related	Dose Not Changed	Recovered /Resolved	Severe
うっ血性心不全	CONGESTIVE CARDIAC FAILURE	Day 409 / Day 414	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	WORSENING HEART FAILURE	Day 420 / Day 423	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「急性心不全」、「胸水」、「うっ血性心不全」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]	
Medical History [1]: Cartilage operation, Tinnitus, Arthroscopy, Knee arthroplasty, Hyperlipidaemia, Osteoarthritis, Osteoarthritis, Carpal tunnel syndrome, Shoulder arthroplasty, Tenodesis, Carpal tunnel decompression, Restrictive cardiomyopathy, Dyspnoea exertional, Shoulder arthroplasty, Rash, Shoulder arthroplasty, Tenodesis, Dry eye, Oedema peripheral, Chronic kidney disease, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 344			
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), ATORVASTATIN, AMOXICILLIN, CLOBETASOL, PROPYLENE GLYCOL, TORASEMIDE					
Non-Serious Adverse Event [4]: No event					

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性左室不全	CHRONIC DIASTOLIC HEART FAILURE (CARDIAC DEATH)	Day 344 / Day 344	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「慢性左室不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]	
Medical History [1]: Intraocular lens implant, Cataract operation, Cataract operation, Bladder cancer, Epiretinal membrane, Vitreous detachment, Myopia, Atrial flutter, Chronic left ventricular failure, Essential hypertension, Cardiac amyloidosis, Hypersensitivity					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 243				
Concomitant Medication [3]: CHONDROITIN/GLUCOSAMINE, COLECALCIFEROL, APIXABAN, FUROSEMIDE, FUROSEMIDE, APIXABAN, APIXABAN, SPIRONOLACTONE, FUROSEMIDE, EPLERENONE, PEMBROLIZUMAB, PROCHLORPERAZINE, ONDANSETRON, FAMOTIDINE, TAMSULOSIN HYDROCHLORIDE, TRIAMCINOLONE, PREDNISONE, ATROPINE SULFATE/DIPHENOXYLATE HYDROCHLORIDE, PREDNISONE, PREDNISONE, PREDNISONE, TRAMADOL, PARACETAMOL, ATROPINE SULFATE/DIPHENOXYLATE HYDROCHLORIDE					
Non-Serious Adverse Event [4]: Diverticulum, Haemorrhoids					

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性腎臓病	WORSENING CHRONIC RENAL DISEASE	Day 29 / Day 144	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
房室ブロック（1）	AV BLOCK	Day 51 / Day 56	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
房室ブロック（2）	AV BLOCK	Day 64 / Day 65	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
再発膀胱癌	RECURRENCE OF BLADDER CANCER	Day 170 / Day 263	Not Related	Dose Not Changed	Fatal	Severe
腹痛	ACUTE ABDOMINAL PAIN	Day 193 / NA	Not Related	Dose Not Changed	Unknown	Moderate
下痢	DIARRHEA	Day 197 / NA	Not Related	Drug Withdrawn	Not Recovered /Not Resolved	Moderate

治験責任医師の見解：「慢性腎臓病」、「房室ブロック（1）」、「房室ブロック（2）」、「再発膀胱癌」、「腹痛」及び「下痢」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Syncope, Osteoarthritis, Carpal tunnel syndrome, Vascular device user, Carpal tunnel decompression, Atrial fibrillation, Atrial flutter, Coronary artery disease, Dyslipidaemia, Knee arthroplasty, Immune thrombocytopenia, Glaucoma, Hip arthroplasty, Aortic valve stenosis, Mitral valve incompetence, Cardiac amyloidosis, Anaemia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 398			
Concomitant Medication [3]: ATORVASTATIN, EZETIMIBE, TRAVOPROST, APIXABAN, CANDESARTAN, SPIRONOLACTONE, FUROSEMIDE, GLYCERYL TRINITRATE, FUROSEMIDE, FUROSEMIDE, VALSARTAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, APIXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, METFORMIN, DOCUSATE SODIUM, MACROGOL 3350, VALACICLOVIR				
Non-Serious Adverse Event [4]: Acute kidney injury, Cardiac failure chronic, Type 2 diabetes mellitus, Constipation, Herpes zoster				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
頭蓋脳損傷	TRAUMATIC BRAIN INJURY	Day 398 / Day 401	Not Related	Drug Withdrawn	Fatal	Severe
転倒	ACCIDENTAL FALL	Day 398 / Day 401	Not Related	Drug Withdrawn	Fatal	Severe
硬膜下出血	SUBDURAL HEMORRHAGE	Day 398 / Day 401	Not Related	Drug Withdrawn	Fatal	Severe
くも膜下出血	SUBARACHNOID HEMORRHAGE	Day 398 / Day 401	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「頭蓋脳損傷」、「転倒」、「硬膜下出血」及び「くも膜下出血」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8■
Medical History [1]: Hypertension, Cholecystectomy, Vitrectomy, Prostate cancer, Atrial fibrillation, Arthralgia, Back pain, Left ventricular hypertrophy, Cystitis radiation, Cardiac failure, Oedema peripheral, Renal failure, Cardiac amyloidosis, Dyspnoea exertional				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 709		
Concomitant Medication [3]: EDOXABAN, FUROSEMIDE, PARACETAMOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FEBUXOSTAT, INFLUENZA VACCINE, COVID-19 VACCINE, OMEPRAZOLE, CLARITHROMYCIN, CEFTRIAXONE, IRON SUCCINYL-PROTEIN COMPLEX, TIOTROPIUM, PIPERACILLIN/TAZOBACTAM, FUROSEMIDE, ZOPICLONE				
Non-Serious Adverse Event [4]: Cardiac failure, Haemorrhage urinary tract, Hyperuricaemia, Asthenia, Iron deficiency anaemia, Ear pain, Pyrexia, Fall, Multiple injuries				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
呼吸不全（1）	RESPIRATORY INSUFFICIENCY	Day 512 / Day 540	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
貧血	ANEMIA	Day 670 / Day 684	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
放射線性膀胱炎	CYSTITIS RADIATION	Day 670 / Day 684	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
呼吸不全（2）	RESPIRATORY INSUFFICIENCY	Day 686 / Day 709	Not Related	Dose Not Changed	Fatal	Severe
心不全	HEART INSUFFICIENCY	Day 702 / Day 709	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「呼吸不全（1）」、「貧血」、「放射線性膀胱炎」、「呼吸不全（2）」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Atrial fibrillation, Cardiac failure, Cardiac amyloidosis, Gout, Chronic kidney disease					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 113				
Concomitant Medication [3]: SPIRONOLACTONE, BUMETANIDE, BUMETANIDE, ALLOPURINOL, COLCHICINE, OMEPRAZOLE, PREDNISOLONE, ALLOPURINOL					
Non-Serious Adverse Event [4]: Blood bilirubin increased, Chest pain					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心アミロイドーシス	EXACERBATED CARDIAC ATTR AMYLOIDOSIS	Day 113 / Day 113	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心アミロイドーシス」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 6[redacted]
Medical History [1]: Gout, Myocardial ischaemia, Cardiac failure, Hypercholesterolaemia, Pruritus, Implantable cardiac monitor insertion, Hypertension, Angioplasty, Cardiac amyloidosis, Chronic kidney disease, Atrial fibrillation, Diabetes mellitus				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 660		
Concomitant Medication [3]: ALLOPURINOL, LANSOPRAZOLE, APIXABAN, BUMETANIDE, GLYCERYL TRINITRATE, ATORVASTATIN, CALCIUM CARBONATE/COLECALCIFEROL, PARAFFIN, AMIODARONE, LOSARTAN, SPIRONOLACTONE, AMOXICILLIN, BUMETANIDE, AMOXICILLIN, BISOPROLOL, LOSARTAN, BUMETANIDE, OTHER EMOLLIENTS AND PROTECTIVES, POTASSIUM CHLORIDE, APIXABAN, AMILORIDE, FUROSEMIDE, METOLAZONE, ALLOPURINOL, ZOPICLONE, FUROSEMIDE, AMITRIPTYLINE, PIVMECILLINAM, AMIODARONE, BUMETANIDE, POTASSIUM CHLORIDE, BUMETANIDE, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, POTASSIUM CHLORIDE, METOLAZONE, COVID-19 VACCINE, BUMETANIDE, CHLORPHENAMINE, COVID-19 VACCINE, NITROFURANTOIN, MACROGOL, AMIODARONE, ATORVASTATIN, AMILORIDE				
Non-Serious Adverse Event [4]: Nasopharyngitis, Cough, Dry skin, Influenza like illness, Dyspnoea, Fatigue, Lower respiratory tract infection, Insomnia, Urinary tract infection, Cardiac failure, Cardiac failure, Cardiac failure, Urinary tract infection, Constipation, Lower respiratory tract infection				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 361 / Day 375	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
心腎症候群	ACUTE DECOMPENSATED CARDIORENAL SYNDROME	Day 361 / Day 411	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 581 / NA	Not Related	Drug Interrupted	Recovering /Resolving	Moderate
心不全（3）	DECOMPENSATED CARDIAC FAILURE	Day 660 / Day 672	Not Related	Drug Interrupted	Fatal	Severe

治験責任医師の見解：「心不全（1）」、「心腎症候群」、「心不全（2）」及び「心不全（3）」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Carpal tunnel decompression, Asthma, Tendon sheath incision, Atrial fibrillation, Cerebrovascular accident, Pancreatitis, Gallbladder operation, Cardiac failure, Hepatic cirrhosis, Malignant melanoma, Skin neoplasm excision, Transient ischaemic attack, Implantable defibrillator insertion, Cardiac amyloidosis, Gout					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 777			
Concomitant Medication [3]: BECLOMETASONE DIPROPIONATE, WARFARIN, SALBUTAMOL, SPIRONOLACTONE, BUMETANIDE, ALLOPURINOL, BISOPROLOL, BUMETANIDE, COLECALCIFEROL, COVID-19 VACCINE, COVID-19 VACCINE, DOCUSATE SODIUM, BUMETANIDE					
Non-Serious Adverse Event [4]: Cough, Tachycardia, Constipation, Alopecia, Acute kidney injury					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳血管発作	LEFT TOTAL ANTERIOR CIRCULATION STROKE	Day 777 / Day 784	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「脳血管発作」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis	Race: Other	Country: UK	Sex: M	Age: 8[redacted]		
Medical History [1]: Appendicectomy, Hernia repair, Type 2 diabetes mellitus, Pain, Cardiac failure, Dry eye, Cardiac amyloidosis, Abdominal mass, Chronic kidney disease, Hepatic cirrhosis, Pruritus, Cardiac pacemaker insertion, Benign prostatic hyperplasia						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 198				
Concomitant Medication [3]: PARACETAMOL, CETIRIZINE, METFORMIN, FUROSEMIDE, IBUPROFEN/LEVOMENTHOL, CARMELLOSE SODIUM, BUMETANIDE, BUMETANIDE, FERRIC CARBOXYMALTOSE, SPIRONOLACTONE, FUROSEMIDE, METFORMIN, SENNA ALEXANDRINA, LACTULOSE, CHLORPHENAMINE, BUMETANIDE, METOLAZONE						
Non-Serious Adverse Event [4]: Rash pruritic, Fatigue, Dizziness						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	DECOMPENSATED HEART FAILURE	Day 55 / Day 67	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
偶発的過量投与	SPIRONOLACTONE OVERDOSE (PATIENT DRUG ERROR)	Day 71 / Day 86	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
高カリウム血症	HYPERKALEMIA	Day 71 / Day 89	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
頭痛	HEADACHE	Day 71 / Day 89	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
腸管虚血	ISCHAEMIC BOWEL	Day 198 / NA	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「心不全」、「偶発的過量投与」、「高カリウム血症」、「頭痛」及び「腸管虚血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Type 2 diabetes mellitus, Hypertension, Atrial fibrillation, Cardiac failure chronic, Chronic kidney disease, Amyloidosis, Anxiety, Carpal tunnel decompression, Carpal tunnel decompression, Cardiac pacemaker insertion, Osteoarthritis, Constipation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 421		
Concomitant Medication [3]: ACENOCOUMAROL, LORAZEPAM, LINAGLIPTIN, ESCITALOPRAM, CANDESARTAN, GLUCOSAMINE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, LACTULOSE, DABIGATRAN, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, INSULIN, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, OMEPRAZOLE, LINAGLIPTIN, FERROUS SULFATE, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, FUROSEMIDE, PARACETAMOL, METAMIZOLE, INSULIN, GLUCOSE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, CITALOPRAM, FUROSEMIDE, POTASSIUM CHLORIDE, LINAGLIPTIN, FERROUS SULFATE, FUROSEMIDE, DIAZEPAM, PARACETAMOL, PARACETAMOL, SPIRONOLACTONE, FUROSEMIDE, CITALOPRAM, RIVAROXABAN				
Non-Serious Adverse Event [4]: Constipation, Iron deficiency anaemia, Urinary incontinence, Rib fracture, Headache, Tension headache				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 226 / Day 232	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	DECOMPENSATED HEART FAILURE	Day 301 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe
息詰まり	EXITUS DUE TO CHOKE	Day 421/ Day 421	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全（1）」、「心不全（2）」及び「息詰まり」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Anal fistula repair, Catheterisation cardiac, Hypertension, Hyperlipidaemia, Benign prostatic hyperplasia, Prostate cancer, Atrial fibrillation, Herpes zoster, Cardiac failure chronic, Amyloidosis, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 411		
Concomitant Medication [3]: ATORVASTATIN, SILODOSIN, ACENOCOUMAROL, OMEPRAZOLE, FUROSEMIDE, LEUPRORELIN, SPIRONOLACTONE, BISOPROLOL, BISOPROLOL, VITAMIN K NOS, EDOXABAN, EPLERENONE, ABIRATERONE, PREDNISONE, FUROSEMIDE, FUSIDIC ACID, SILODOSIN, SODIUM CHLORIDE, POTASSIUM CHLORIDE, SODIUM CITRATE, GLUCOSE, MUPIROCIN, CEFUROXIME, SERENOA REPENS, COVID-19 VACCINE, COVID-19 VACCINE, FERROUS SULFATE, AMOXICILLIN, OLAPARIB, ALL OTHER THERAPEUTIC PRODUCTS, CEFTRIAXONE, SODIUM CHLORIDE, SODIUM CHLORIDE, GLUCOSE, DIGOXIN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Adenocarcinoma of colon, Asthenia, Decreased appetite, Syncope, Hypotension, Limb injury, Skin laceration, Iron deficiency anaemia, Buttock injury, Urinary tract infection, Diarrhoea, Skin laceration				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
全身健康状態悪化	MULTIFACTORIAL DETERIORATION OF GENERAL CONDITION	Day 181 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
心不全	DECOMPENSATED HEART FAILURE	Day 397 / Day 418	Not Related	Drug Interrupted	Fatal	Severe
尿路感染	URINARY INFECTION	Day 411 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
急性腎障害	ACUTE KIDNEY FAILURE	Day 411 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「全身健康状態悪化」、「心不全」、「尿路感染」及び「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]	
Medical History [1]: Dyslipidaemia, Cognitive disorder, Hiatus hernia, Trigeminal neuralgia, Amyloidosis, Benign prostatic hyperplasia					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 736				
Concomitant Medication [3]: SILODOSIN, MIRABEGRON, OMEPRAZOLE, ATORVASTATIN, PREGABALIN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PREGABALIN, PARACETAMOL, COVID-19 VACCINE, PARACETAMOL, PREGABALIN, METAMIZOLE MAGNESIUM, IRON SUCCINYL-PROTEIN COMPLEX, TRAZODONE, HALOPERIDOL					
Non-Serious Adverse Event [4]: Renal impairment, Back pain, COVID-19, Trigeminal neuralgia, Seborrhoeic keratosis, Anaemia, Insomnia, Arthralgia					

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
外傷性頭蓋内出血	POSTRAUMATIC BRAIN HEMORRHAGE	Day 736 / Day 744	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「外傷性頭蓋内出血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Carpal tunnel decompression, Type 2 diabetes mellitus, Joint prosthesis user, Hearing aid user, Atrial fibrillation, Knee arthroplasty, Lumbar hernia, Cardiac failure, Cardiac amyloidosis, Nephrolithiasis, Renal cyst, Depression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 116		
Concomitant Medication [3]: GLIMEPIRIDE, PANTOPRAZOLE, RIVAROXABAN, CANRENONE, FUROSEMIDE, CITALOPRAM, CARBIDOPA MONOHYDRATE/LEVODOPA, PLANTAGO OVATA SEED HUSK, DICLOFENAC, DEXAMETHASONE SODIUM PHOSPHATE, TRAMADOL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, POTASSIUM CHLORIDE, SODIUM CHLORIDE, MORPHINE, PARACETAMOL, PREGABALIN				
Non-Serious Adverse Event [4]: Diarrhoea, Intervertebral disc disorder, Liver injury, Spinal compression fracture, Hypernatraemia, Hypokalaemia, Osteoporosis				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼠径ヘルニア	LEFT INGUINAL HERNIA	Day 43 / Day 43	Not Related	Dose Not Changed	Recovered /Resolved	Mild
腸閉塞	INTESTINAL BLOCKAGE	Day 109 / Day 117	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「鼠径ヘルニア」及び「腸閉塞」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 6[redacted]
Medical History [1]: Dupuytren's contracture, Meniscus operation, Carpal tunnel decompression, Baker's cyst excision, Carpal tunnel decompression, Fibula fracture, Tibia fracture, Carpal tunnel syndrome, Implantable defibrillator insertion, Arthritis, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis, Ventricular fibrillation, Brachial artery entrapment syndrome				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 606		
Concomitant Medication [3]: BISOPROLOL, FEBUXOSTAT, APIXABAN, FUROSEMIDE, POTASSIUM CANRENOATE, FUROSEMIDE, FUROSEMIDE, ANTIDIARRHEAL MICROORGANISMS, FUROSEMIDE, INFLUENZA VACCINE, FUROSEMIDE, ALLOPURINOL, EPLERENONE, COVID-19 VACCINE, COVID-19 VACCINE, DICLOFENAC, METHYLPREDNISOLONE ACETATE, METOLAZONE, INFLUENZA VACCINE, COVID-19 VACCINE, PARACETAMOL, PAROXETINE				
Non-Serious Adverse Event [4]: Cardiac failure, Diarrhoea, Cough, Dry mouth, Abdominal pain, Cardiac failure, Depression				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	DEATH FOR HEART FAILURE	Day 607 / Day 607	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Osteoarthritis, Inguinal hernia, Inguinal hernia, Tendon operation, Carotid arteriosclerosis, Hypertension, Atrial fibrillation, Carpal tunnel decompression, Ischaemic stroke, Cardiac pacemaker insertion, Cholelithiasis, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 696		
Concomitant Medication [3]: RIVAROXABAN, PANTOPRAZOLE, OLMESARTAN MEDOXOMIL, FUROSEMIDE, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, DEXAMETHASONE, BISOPROLOL FUMARATE, SERTRALINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, HYALURONIC ACID, PNEUMOCOCCAL VACCINES, INFLUENZA VACCINE, FUROSEMIDE, HYALURONIC ACID, RIFAMPICIN, LEVOFLOXACIN, AMPICILLIN/SULBACTAM, AMOXICILLIN, FERROUS SULFATE, PALMIDROL, AMOXICILLIN, DAPAGLIFLOZIN, BISOPROLOL, NALOXONE/OXYCODONE, PARACETAMOL, PARACETAMOL, POTASSIUM CHLORIDE, ENOXAPARIN, POTASSIUM CHLORIDE, FUROSEMIDE, AMITRIPTYLINE HYDROCHLORIDE, DELORAZEPAM, FUROSEMIDE, RIVAROXABAN				
Non-Serious Adverse Event [4]: Cardiac failure, Proteinuria, Depression, Ventricular tachycardia, Ventricular tachycardia, Arthralgia, Anaemia, Syncope, Presyncope, COVID-19, Blood potassium decreased, Fall				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
レンサ球菌性化膿性関節炎	STREPTOCOCCUS GALLOLYTICUS SEPTIC ARTHRITIS	Day 501 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Mild
仙骨骨折	DISPLACED SACRAL FRACTURE	Day 587 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Mild
腰椎骨折	THE TRASVERSE PROCESS L5 FRACTURE	Day 587 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Mild
大腿骨骨折	LEFT FEMURE FRACTURE	Day 665 / Day 674	Not Related	Dose Not Changed	Recovered/ Resolved With Sequelae	Mild
死亡	DEATH IN SLEEP (NO FURTHER INFORMATION)	Day 697 / Day 697	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「レンサ球菌性化膿性関節炎」、「仙骨骨折」、「腰椎骨折」、「大腿骨骨折」及び「死亡」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 8[redacted]	
Medical History [1]: Hypercholesterolaemia, Benign prostatic hyperplasia, Angioplasty, Myocardial infarction, Carpal tunnel decompression, Dyslipidaemia, Atrial fibrillation, Cardioversion, Atrial fibrillation, Cardiac failure chronic, Cardiac amyloidosis, Myelodysplastic syndrome					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 193			
Concomitant Medication [3]: EDOXABAN, ATENOLOL, FUROSEMIDE, ATORVASTATIN, FUROSEMIDE					
Non-Serious Adverse Event [4]: Oedema peripheral, Hypokalaemia					
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
悪液質	ORGANIC CACHEXIA	NA / Start Day + 55 Days	Not Related	Drug Interrupted	Fatal	Severe
胃腸出血	ACUTE GASTROINTESTINAL BLEEDING	Day 193 / Day 200	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「悪液質」及び「胃腸出血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]
Medical History [1]: Asthma, Gouty arthritis, Osteoarthritis, Renal failure, Hypertension, Atrial fibrillation, Cardiac failure, Benign prostatic hyperplasia, Dyspnoea, Amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 775			
Concomitant Medication [3]: DESLORATADINE, ALLOPURINOL, METOPROLOL, APIXABAN, FUROSEMIDE, CANDESARTAN, SALBUTAMOL, VILANTEROL, UMECLIDINIUM BROMIDE, GABAPENTIN, PARACETAMOL, TAZOBACTAM, PIPERACILLIN, CLARITHROMYCIN, METHYLPREDNISOLONE SODIUM SUCCINATE, PREDNISOLONE, PANTOPRAZOLE, AMIODARONE, MICONAZOLE, BISACODYL, PANTOPRAZOLE, PREDNISOLONE, SODIUM PICOSULFATE, LACTULOSE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, ALFACALCIDOL, CEFUROXIME, CLOXACILLIN				
Non-Serious Adverse Event [4]: Renal impairment, Neuralgia, Spondylolisthesis, Renal failure, Myocardial ischaemia, Oral candidiasis, Constipation, Iron deficiency anaemia, Gastric ulcer haemorrhage, Hypocalcaemia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
細菌性肺炎	BILATERAL BACTERIAL PNEUMONIA	Day 476 / Day 486	Not Related	Dose Not Changed	Recovered /Resolved	Severe
椎間板炎	SPONDYLODISCITIS	Day 568 / Day 607	Not Related	Dose Not Changed	Recovered /Resolved	Severe
皮膚潰瘍	ULCERATION RIGHT FOOT	Day 710 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
ブドウ球菌性菌血症	BACTEREMIA: STAPHYLOCOCCUS AUREUS INFECTION	Day 773 / Day 775	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「細菌性肺炎」、「椎間板炎」、「皮膚潰瘍」及び「ブドウ球菌性菌血症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel decompression, Polyneuropathy, Cardiac failure, Myocardial ischaemia, Atrial fibrillation, Diabetic neuropathy, Type 2 diabetes mellitus, Atrioventricular block complete, Cardiac pacemaker insertion, Oedema peripheral, Hip arthroplasty, Proteinuria, Renal impairment, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 755		
Concomitant Medication [3]: ATORVASTATIN, GLYCERYL TRINITRATE, ENALAPRIL MALEATE, APIXABAN, BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, SODIUM CHLORIDE, FUROSEMIDE, EMPAGLIFLOZIN, POTASSIUM CHLORIDE, PARACETAMOL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, SODIUM CHLORIDE, SODIUM PICOSULFATE, DICLOXACILLIN, FUROSEMIDE, CODEINE PHOSPHATE, AMITRIPTYLINE HYDROCHLORIDE, BENZYLPENICILLIN, MORPHINE SULFATE, POTASSIUM CHLORIDE, BENZYLPENICILLIN SODIUM/PROCAINE BENZYLPENICILLIN, PARACETAMOL, PHENOXYMETHYLPENICILLIN, BISOPROLOL, AMIODARONE, SODIUM PICOSULFATE, MORPHINE, CLOXACILLIN, ERYTHROMYCIN, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, INSULIN, DALTEPARIN SODIUM, METOCLOPRAMIDE, APIXABAN, BUMETANIDE				
Non-Serious Adverse Event [4]: Diarrhoea, Renal impairment, Pyrexia, Diarrhoea, Diverticulum intestinal, Skin depigmentation, Cardiac failure, Wound infection, Hypokalaemia, Fall, Syncope, Medical device site haematoma, Constipation, Neuropathic ulcer, Pruritus, Weight decreased				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脱水	DEHYDRATION	Day 28 / Day 36	Not Related	Dose Not Changed	Recovered /Resolved	Severe
便秘	CONSTIPATION	Day 310 / Day 311	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
丹毒	ERYSIPELAS INTERMITTANT ACUTE OUTBREAKS	Day 574 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
体位性めまい	ORTHOSTATIC DIZZINESS	Day 630 / Day 631	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心室性頻脈	VENTRICULAR TACHYCARDIA	Day 658 / Day 664	Not Related	Dose Not Changed	Recovered /Resolved	Severe
埋込み部位感染	INFECTION PACEMAKER POCKET SITE	Day 678 / Day 702	Not Related	Dose Not Changed	Recovered /Resolved	Severe
慢性心不全	END STAGE HEART FAILURE	Day 754 / Day 755	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「脱水」、「便秘」、「丹毒」、「体位性めまい」、「心室性頻脈」、「埋込み部位感染」及び「慢性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel decompression, Cardiac failure, Hypertension, Type 2 diabetes mellitus, Atrial fibrillation, Vitamin B12 deficiency, Implantable defibrillator insertion, Hypercholesterolaemia, Urticaria, Atrioventricular block complete, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 239		
Concomitant Medication [3]: LOSARTAN POTASSIUM, WARFARIN, METOPROLOL, ATORVASTATIN, POTASSIUM CHLORIDE, METFORMIN, DAPAGLIFLOZIN, FUROSEMIDE, SPIRONOLACTONE, HYDROXOCOBALAMIN, METOLAZONE, METOPROLOL, FUROSEMIDE, METOPROLOL, BUMETANIDE, BUMETANIDE, BUMETANIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, BUMETANIDE, POTASSIUM CHLORIDE, METOLAZONE, DOBUTAMINE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM				
Non-Serious Adverse Event [4]: Blood potassium decreased, Pleural effusion, Pleural effusion, Urinary tract infection				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	HEART FAILURE WORSENING	Day 136 / Day 144	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	HEART FAILURE WORSENING	Day 151 / Day 157	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（3）	HEART FAILURE WORSENING	Day 182 / Day 196	Not Related	Dose Not Changed	Recovered /Resolved	Severe
低カリウム血症	HYPOKALEMIA	Day 226 / Day 232	Not Related	Dose Not Changed	Recovered /Resolved	Severe
慢性心不全	END STAGE HEART FAILURE	Day 236 / Day 239	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」、「低カリウム血症」及び「慢性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]
Medical History [1]: Hip arthroplasty, Intervertebral disc protrusion, Vitamin B12 deficiency, Atrial fibrillation, Asthma, Cardiac failure, Amyloidosis, Cerebrovascular accident, Chronic obstructive pulmonary disease, Constipation, Type 2 diabetes mellitus, Ocular hypertension, Neuralgia, Colon cancer				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 463		
Concomitant Medication [3]: CYANOCOBALAMIN, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, TERBUTALINE, CARVEDILOL, CARVEDILOL, FORMOTEROL, GLYCOPYRRONIUM BROMIDE, BECLOMETASONE DIPROPIONATE, MAGNESIUM HYDROXIDE, BRINZOLAMIDE, PARACETAMOL, CALCIUM, CALCIUM/VITAMIN D NOS, VITAMIN D NOS, SEMAGLUTIDE, LINAGLIPTIN, FUROSEMIDE, INSULIN, RIVAROXABAN, POTASSIUM CHLORIDE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, GABAPENTIN, POTASSIUM CHLORIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, PHENOXYMETHYLPENICILLIN, SODIUM PICOSULFATE, PIVMECILLINAM HYDROCHLORIDE, NYSTATIN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Haematuria, Renal impairment, Hypervolaemia, Sinus bradycardia, Erysipelas, Anaemia, Weight decreased, Urinary tract infection, Oral candidiasis, Limb injury, Dizziness				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心室性頻脈	VENTRICULAR TACHYCARDIA	Day 58 / Day 72	Not Related	Dose Not Changed	Recovered /Resolved	Severe
脱水	DEHYDRATION	Day 78 / Day 85	Not Related	Dose Not Changed	Recovered /Resolved	Severe
胸水	WORSENING OF DYSPNOE DUE TO PLEURAL EFFUSION RIGHT LUNG	Day 350 / Day 358	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
転倒	ACCIDENTAL FALL	Day 380 / Day 381	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	WORSENING OF HEART FAILURE	Day 448 / Day 464	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心室性頻脈」、「脱水」、「胸水」、「転倒」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Denmark	Sex: M	Age: 8[redacted]
Medical History [1]: Anaemia, Atrial fibrillation, Conjunctivitis allergic, Amyloidosis						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 337				
Concomitant Medication [3]: RIVAROXABAN, METOPROLOL SUCCINATE, POTASSIUM, POTASSIUM CHLORIDE, FUROSEMIDE, KETOTIFEN, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), PANTOPRAZOLE, AMOXICILLIN, CLARITHROMYCIN, FERROUS SULFATE, METOPROLOL, BENDROFLUMETHIAZIDE/POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, METOCLOPRAMIDE, FUROSEMIDE, FUROSEMIDE, DALTEPARIN SODIUM, METOLAZONE, METOPROLOL, FUROSEMIDE						
Non-Serious Adverse Event [4]: Anaemia, Gastric ulcer, Gastric ulcer, Dry mouth, Atrial fibrillation, Nausea, Oedema peripheral, Decreased appetite, Renal impairment						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING OF HEARTFAILURE	Day 295 / Day 297	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
慢性心不全	END STAGE HEART FAILURE	Day 324 / Day 338	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全」及び「慢性心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 7[redacted]
Medical History [1]: Benign prostatic hyperplasia, Constipation, Muscle spasms, Cardiac failure chronic, Cardiac amyloidosis, Depression, Insomnia, Malignant melanoma, Hypothyroidism, Gout, Hyponatraemia, Iron deficiency, Chronic kidney disease, Hypertension, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 831		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), TAMSULOSIN, CHLORDIAZEPOXIDE/CLIDINIUM BROMIDE, MACROGOL 3350, ESOMEPRAZOLE SODIUM, MAGNESIUM AMINO ACID CHELATE, SPIRONOLACTONE, FUROSEMIDE, SERTRALINE, ZOLPIDEM, LEVOTHYROXINE SODIUM, RIVAROXABAN, BECLOMETASONE, AMIODARONE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, DOPAMINE HYDROCHLORIDE, AMIODARONE, FUROSEMIDE, BROTIZOLAM, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, INFLUENZA VACCINE INACT SAG 4V, FUROSEMIDE, COLECALCIFEROL, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, COVID-19 VACCINE, COVID-19 VACCINE, METAMIZOLE SODIUM, RIVAROXABAN, ZOLPIDEM TARTRATE, FUROSEMIDE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS, SPIRONOLACTONE, COVID-19 VACCINE, COLECALCIFEROL, LEVOTHYROXINE SODIUM, RIVAROXABAN, SPIRONOLACTONE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, SPIRONOLACTONE, COVID-19 VACCINE, PNEUMOCOCCAL VACCINE POLYSACCH 23V				
Non-Serious Adverse Event [4]: Pleural effusion, Upper limb fracture, Hypothyroidism, Contusion, Weight decreased, Atrioventricular block first degree, Cholelithiasis, Renal cyst, Hypothyroidism, Balance disorder, Haemarthrosis, Urinary tract obstruction, Hyperkalaemia, Arthralgia, Hypothyroidism, Hyponatraemia, Anaemia, Cognitive disorder, Increased tendency to bruise, Cardiac failure chronic, General physical health deterioration				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
うっ血性心不全	WORSENING OF CONGESTIVE HEART FAILURE	Day 49 / Day 55	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
転倒	FALL	Day 729 / Day 729	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	WORSENING OF HEART FAILURE	Day 831 / Day 831	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「うっ血性心不全」、「転倒」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Greece	Sex: M	Age: 8[redacted]	
Medical History [1]: Tonsillectomy, Benign prostatic hyperplasia, Hypothyroidism, Inguinal hernia repair, Diabetes mellitus, Acute myocardial infarction, Cardiac pacemaker insertion, Hyperuricaemia, Hypoacusis, Atrial fibrillation, Amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 441			
Concomitant Medication [3]: TAMSULOSIN HYDROCHLORIDE, LEVOTHYROXINE SODIUM, ESOMEPRAZOLE, GLICLAZIDE, FUROSEMIDE, ALLOPURINOL, DABIGATRAN ETEXILATE MESILATE, CARVEDILOL, EPLERENONE, AMIODARONE HYDROCHLORIDE, OMEPRAZOLE, EPLERENONE, ALLOPURINOL, FUROSEMIDE, FUROSEMIDE, ASCORBIC ACID/FERROUS SULFATE/FOLIC ACID					
Non-Serious Adverse Event [4]: Atrial fibrillation, Oedema peripheral, Fatigue, Arthralgia, Dyspnoea, Anaemia					

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	CARDIAC FAILURE DUE TO ATTR AMYLOIDOSIS	Day 442 / Day 442	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK		Sex: M	Age: 6[redacted]
Medical History [1]: Prostate cancer, Hip arthroplasty, Cardiac amyloidosis, Atrial fibrillation					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 858				
Concomitant Medication [3]: CLOBAZAM, STEROIDS, TAMSULOSIN, BISOPROLOL, FUROSEMIDE, SPIRONOLACTONE, APIXABAN, VITAMIN B NOS, CYANOCOBALAMIN, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, FUROSEMIDE, FERROUS FUMARATE, TROPICAMIDE, PHENYLEPHRINE, COVID-19 VACCINE, BENZALKONIUM CHLORIDE/DEXAMETHASONE/PHENYLMERCURIC NITRATE, FLUCLOXACILLIN, PHENOXYMETHYLPENICILLIN, FUROSEMIDE, DIURETICS, FUROSEMIDE, DIURETICS, FUROSEMIDE					
Non-Serious Adverse Event [4]: Cardiac failure, Vitamin B12 deficiency, Hepatic mass, Iron deficiency anaemia, Lens dislocation, Retinal detachment, Cellulitis, Lens dislocation, Cardiac failure, Melaena					

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
舞踏病（1）	UNDIAGNOSED CHORELFORM DISORDER (WORSENING OF)	NA / NA	Not Related	Drug Withdrawn	Recovering /Resolving	Moderate
舞踏病（2）	UNDIAGNOSED CHOREIFORM DISORDER (WORSENING OF)	NA / Start Day + 64 Days	Not Related	Drug Interrupted	Recovered/ Resolved With Sequelae	Moderate
鼻出血	EPISTAXIS	Day 692 / Day 693	Not Related	Dose Not Changed	Recovered/ Resolved	Mild
心不全（1）	DECOMPENSATED HEART FAILURE	NA / Start Day + 68 Days	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
転倒	FALL	Day 821 / Day 822	Not Related	Dose Not Changed	Recovered/ Resolved	Mild
心不全（2）	DECOMPENSATED HEART FAILURE (NOT CONFIRMED)	NA / Start Day + 44 Days	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「舞踏病（1）」、「舞踏病（2）」、「鼻出血」、「心不全（1）」、「転倒」及び「心不全（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Seasonal allergy, Osteoarthritis, Chronic kidney disease, Type 2 diabetes mellitus, Hypertension, Rotator cuff syndrome, Knee arthroplasty, Carpal tunnel syndrome, Giant cell arteritis, Cardiac amyloidosis, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 883		
Concomitant Medication [3]: METFORMIN, ROSUVASTATIN, APIXABAN, BISOPROLOL, SACUBITRIL/VALSARTAN, BUMETANIDE, CALCIUM CARBONATE/MAGNESIUM CARBONATE, ANTIBIOTICS, BUMETANIDE, VITAMIN B12 NOS, BUMETANIDE, IBUPROFEN, CEFALEXIN, EPLERENONE, PLANTAGO OVATA, COVID-19 VACCINE, EPLERENONE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, INFLUENZA VACCINE, EPLERENONE, DOXYCYCLINE, DOXYCYCLINE, COVID-19 VACCINE, METFORMIN, BUMETANIDE, BUMETANIDE, ZOPICLONE, CETIRIZINE HYDROCHLORIDE, HERBAL NOS/MINERALS NOS/VITAMINS NOS, NUTRIENTS NOS, BUMETANIDE, BETAMETHASONE VALERATE/FUSIDIC ACID, MIRTAZAPINE				
Non-Serious Adverse Event [4]: Muscle spasms, Flatulence, Gastrooesophageal reflux disease, Fall, Urinary tract infection, Depressed mood, Constipation, Angina pectoris, Lower respiratory tract infection, Insomnia, Pruritus, Diabetic neuropathy				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	NA / Start Day + 722 Days	Not Related	Drug Withdrawn	Fatal	Severe
徐脈	BRADYCARDIA	Day 804 / Day 811	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
治験責任医師の見解：「心不全」及び「徐脈」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Drug hypersensitivity, Hypertension, Hip arthroplasty, Dermatitis contact, Gastrointestinal carcinoma, Chemotherapy, Cancer surgery, Carpal tunnel decompression, Gastrooesophageal reflux disease, Osteopenia, Arthralgia, Cardiac pacemaker insertion, Hip arthroplasty, Seasonal allergy, Benign prostatic hyperplasia, Eczema nummular, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: CLOBETASOL PROPIONATE, SIMVASTATIN, RAMIPRIL, LANSOPRAZOLE, CALCIUM CARBONATE/COLECALCIFEROL, ALENDRONIC ACID, PARACETAMOL, TAMSULOSIN, FEXOFENADINE, BISOPROLOL, AMITRIPTYLINE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, IBUPROFEN, BISOPROLOL, BUMETANIDE, FUROSEMIDE, CLOPIDOGREL, ATORVASTATIN, COVID-19 VACCINE, EMOLLIENTS AND PROTECTIVES, COVID-19 VACCINE, RIVAROXABAN, PARAFFIN, COVID-19 VACCINE, BISOPROLOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE, FUROSEMIDE, BUMETANIDE, BUMETANIDE, ERYTHROMYCIN, AMOXICILLIN, OXYCODONE				
Non-Serious Adverse Event [4]: Gastrointestinal disorder, Bursitis, Skin mass, Eczema, Speech disorder, Atrial fibrillation, Rash, Cardiac failure, Lower respiratory tract infection				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳梗塞	LEFT MCA INFARCT	Day 434 / Day 436	Not Related	Dose Not Changed	Recovered/ Resolved With Sequelae	Moderate
慢性心不全	END STAGE HEART FAILURE	NA / Start Day + 15 Days	Not Related	Dose Not Changed	Fatal	Severe
企図的過量投与	DELIBERATE DRUG OVERDOSE	Day 908 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate

治験責任医師の見解：「脳梗塞」、「慢性心不全」及び「企図的過量投与」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Cholelithiasis, Drug hypersensitivity, Carpal tunnel syndrome, Hip arthroplasty, Type 2 diabetes mellitus, Deafness, Hearing aid user, Acute myocardial infarction, Coronary arterial stent insertion, Myocardial ischaemia, Asbestosis, Cardiac amyloidosis, Constipation, Cardiac resynchronisation therapy, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 158		
Concomitant Medication [3]: RAMIPRIL, GLYCERYL TRINITRATE, ROSUVASTATIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, EPLERENONE, BUMETANIDE, APIXABAN, BUMETANIDE, APIXABAN, ALL OTHER THERAPEUTIC PRODUCTS, APIXABAN, RAMIPRIL, EPLERENONE, BUMETANIDE, BUMETANIDE, ROSUVASTATIN, FLUCONAZOLE, NYSTATIN				
Non-Serious Adverse Event [4]: Gastroenteritis viral, Abdominal discomfort, Oral candidiasis				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY	Day 79 / Day 84	Not Related	Drug Interrupted	Recovered /Resolved	Severe
慢性心不全	HEART FAILURE (CHRONIC) RESULTING IN SUBJECT DEATH	Day 158 / Day 158	Not Related	Unknown	Fatal	Severe

治験責任医師の見解：「急性腎障害」及び「慢性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Bundle branch block left, Sleep disorder, Cerebrovascular accident, Headache, Atrial fibrillation, Cardiac failure, Hyperlipidaemia, Coronary artery disease, Cardiac amyloidosis, Bundle branch block right, Stress				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 623		
Concomitant Medication [3]: PANTOPRAZOLE, APIXABAN, PERINDOPRIL, BUMETANIDE, ESCITALOPRAM, LORMETAZEPAM, ATORVASTATIN, PARACETAMOL, SULPIRIDE, SERENOA REPENS, TAMSULOSIN, PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, DICLOFENAC, PARACETAMOL, KETOPROFEN, COVID-19 VACCINE, DICLOFENAC, LORMETAZEPAM, DAPAGLIFLOZIN, AMOXICILLIN, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Urinary retention, Rotator cuff syndrome, Haematoma, Hypotension, Arthralgia, Arthralgia, Malaise, Cardiac failure, Iron deficiency anaemia, Ventricular tachycardia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	BRADYCARDIA	Day 165 / Day 168	Not Related	Dose Not Changed	Recovered /Resolved	Severe
起立性低血圧	SYNCOPE DUE TO ORTHOSTATIC HYPOTENSION	Day 165 / Day 168	Not Related	Dose Not Changed	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９	COVID19-INFECTION	Day 590 / Day 601	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心停止	SUDDEN CARDIAC ARREST	Day 623 / Day 624	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「徐脈」、「起立性低血圧」、「ＣＯＶＩＤ－１９」及び「心停止」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]	
Medical History [1]: Cataract, Cataract, Acute myocardial infarction, Pulmonary oedema, Cardiac failure, Electrocardiogram repolarisation abnormality, Cardiac amyloidosis, Coronary artery bypass, Cardioversion, Gastrointestinal haemorrhage, Chronic kidney disease, Metabolic acidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 547			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, AMIODARONE, PERINDOPRIL, BUMETANIDE, SODIUM BICARBONATE, LERCANIDIPINE, AMIODARONE, DEXAMETHASONE/TOBRAMYCIN, INDOMETACIN, DEXAMETHASONE/TOBRAMYCIN, DEXAMETHASONE/TOBRAMYCIN, COVID-19 VACCINE, COVID-19 VACCINE, EDOXABAN, AMIODARONE, VITAMIN D NOS, PARACETAMOL					
Non-Serious Adverse Event [4]: Hyperkalaemia, Hyperphosphataemia, Atrial fibrillation, Aphasia					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
遠隔転移を伴う肺癌	METASTATIC LUNG CANCER	Day 504 / Day 582	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「遠隔転移を伴う肺癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Gouty arthritis, Coronary artery disease, Cardiac failure, Hyperlipidaemia, Hypertension, Cardiac amyloidosis, Chronic kidney disease, Bundle branch block right, Atrial fibrillation, Arthralgia, Cough, Coronary artery disease, Sleep disorder				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 434		
Concomitant Medication [3]: BUMETANIDE, FEBUXOSTAT, APIXABAN, SPIRONOLACTONE, CHLORTALIDONE, PANTOPRAZOLE, CLOPIDOGREL, BUDESONIDE/FORMOTEROL, MAGNESIUM, LORMETAZEPAM, MAGNESIUM, SPIRONOLACTONE, PAPAVERINE, QUININE SULFATE, DICLOFENAC, CALCIUM, VITAMIN D NOS, ACETAZOLAMIDE, MACROGOL, PARACETAMOL, POTASSIUM, PENICILLIN NOS, SALICYLIC ACID, CHLORHEXIDINE, FLUCLOXACILLIN, CLAVULANIC ACID, AMOXICILLIN, PENICILLIN NOS, TAZOBACTAM, PIPERACILLIN, CIPROFLOXACIN, CINACALCET, DICLOFENAC, AMOXICILLIN, ALGINIC ACID/GLUCOSE/GLUCOSE OXIDASE/GUAIACOL/LACTOPEROXIDASE/MACROGOL, SPIRONOLACTONE, ACETAZOLAMIDE, DEXTROMETHORPHAN HYDROBROMIDE, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Oedema peripheral, Atrial tachycardia, Arthralgia, Balance disorder, Renal failure, Muscle spasms, Muscle injury, Osteoporosis, Cardiac failure chronic, Hypokalaemia, Blood parathyroid hormone increased, Skin abrasion, Venous pressure jugular increased, Wound, Blood potassium decreased, Blood sodium decreased, N-terminal prohormone brain natriuretic peptide increased, Skin abrasion, Back pain, Skin abrasion				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
丹毒（1）	ERYSIPELAS LEFT LOWER LEG	Day 229 / Day 248	Not Related	Dose Not Changed	Recovered /Resolved	Severe
丹毒（2）	ERYSIPELAS LOWER LEGS	Day 282 / Day 309	Not Related	Dose Not Changed	Recovered /Resolved	Severe
ブドウ球菌性肺炎	STAPHYLOCOCCAL PNEUMONIA	Day 406 / Day 416	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全	ACUTE EPISODE HEART FAILURE	Day 406 / Day 428	Not Related	Dose Not Changed	Recovered /Resolved	Severe
気胸	PNEUMOTHORAX RIGHT LUNG	Day 417 / Day 428	Not Related	Dose Not Changed	Recovered /Resolved	Severe
完全房室ブロック	THIRD DEGREE AV-BLOCK	Day 434 / Day 435	Not Related	Dose Not Changed	Fatal	Severe
心拍出量低下	LOW CARDIAC OUTPUT	Day 434 / Day 435	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「丹毒（1）」、「丹毒（2）」、「ブドウ球菌性肺炎」、「急性心不全」、「気胸」、「完全房室ブロック」及び「心拍出量低下」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: Not reported	Country: Netherlands	Sex: M	Age: 7[redacted]	
Medical History [1]: Spinal operation, Gout, Hypertension, Atrial flutter, Spinal stenosis, Polyneuropathy, Bladder calculus removal, Prostatectomy, Cardiac failure, Syncope, Cardiac amyloidosis, Peripheral arterial occlusive disease					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 427			
Concomitant Medication [3]: COLCHICINE, ACENOCOUMAROL, BUMETANIDE, EPLERENONE, PREDNISONE, POTASSIUM CHLORIDE, HYDROCHLOROTHIAZIDE, ALLOPURINOL, PREDNISONE, AMOXICILLIN, POTASSIUM CHLORIDE					
Non-Serious Adverse Event [4]: Atrial flutter, Dizziness, Peripheral arterial occlusive disease, Abnormal loss of weight					

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腹痛	ABDOMINAL PAIN	Day 337 / Day 343	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
全身健康状態悪化	GENERAL PHYSICAL HEALTH DETERIORATION	Day 433 / Day 433	Not Related	Unknown	Fatal	Severe
治験責任医師の見解：「腹痛」及び「全身健康状態悪化」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Not reported	Country: Netherlands	Sex: M	Age: 7[redacted]
Medical History [1]: Angina pectoris, Hypertension, Renal impairment, Benign prostatic hyperplasia, Carpal tunnel syndrome, Carpal tunnel syndrome, Cardiac failure, Atrial fibrillation, Psoriatic arthropathy, Spondylitis, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 397		
Concomitant Medication [3]: SIMVASTATIN, DUTASTERIDE, EPLERENONE, APIXABAN, CANDESARTAN, BISOPROLOL, SILODOSIN, PANTOPRAZOLE, METHOTREXATE, FOLIC ACID, BUMETANIDE, HYDROCHLOROTHIAZIDE, BISOPROLOL, HYDROCHLOROTHIAZIDE, PREDNISONE, PREDNISONE, PREDNISONE, PREDNISONE, PREDNISONE, HYDROCHLOROTHIAZIDE, PREDNISONE, COLCHICINE, PREDNISONE, ALLOPURINOL, PREDNISONE, PREDNISONE, POTASSIUM CHLORIDE, ANAKINRA, LIDOCAINE, METHYLPREDNISOLONE ACETATE, POTASSIUM CHLORIDE, CLOPIDOGREL, PREDNISONE, APIXABAN, APIXABAN, BISOPROLOL, ANAKINRA, EPLERENONE, APIXABAN, PREDNISONE				
Non-Serious Adverse Event [4]: Psoriatic arthropathy, Spondylitis, Osteoarthritis, Gout, Renal impairment, Hypotension, Dyspnoea exertional, Psoriatic arthropathy				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心筋梗塞	SUBACUTE NON STEMI	Day 326 / Day 330	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	WORSENING OF DECOMPENSATIO CORDIS	Day 382 / Day 391	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９	COVID INFECTOIN	Day 393 / Day 398	Not Related	Dose Not Changed	Fatal	Moderate

治験責任医師の見解：「急性心筋梗塞」、「心不全」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Hyperuricaemia, Arthralgia, Gouty arthritis, Radical prostatectomy, Cerebral infarction, Cardiac amyloidosis, Aortic valve incompetence, Cardiac failure, Benign prostatic hyperplasia, Dyspnoea exertional, Head injury, Bradycardia, Hypotension, Cardiac pacemaker insertion, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 840		
Concomitant Medication [3]: LANSOPRAZOLE, BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, SIMVASTATIN, ALLOPURINOL, COLCHICINE, EDOXABAN TOSILATE, RAMIPRIL, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, GABAPENTIN, TRAZODONE, UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE, FUROSEMIDE, LANSOPRAZOLE, SIMVASTATIN, LEVOFLOXACIN, FUROSEMIDE, BECLOMETASONE, OXYGEN, SALBUTAMOL, BECLOMETASONE				
Non-Serious Adverse Event [4]: Somnolence, Headache, Glomerular filtration rate decreased, Cognitive disorder, Atrial flutter, Blood creatinine increased, Blood urea increased, Glomerular filtration rate increased, N-terminal prohormone brain natriuretic peptide increased				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE HEART FAILURE	Day 772 / Day 780	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
慢性閉塞性肺疾患	COPD EXACERBATION	Day 772 / Day 780	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全	WORSENING HEART FAILURE	Day 844 / Day 844	Not Related	NA	Fatal	Severe

治験責任医師の見解：「急性心不全」、「慢性閉塞性肺疾患」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Hypothyroidism, Cataract, Hyperuricaemia, Osteoarthritis, Pleural effusion, Joint prosthesis user, Chronic kidney disease, Depression, Pituitary tumour benign, Parkinson's disease, Chronic obstructive pulmonary disease, Atrial fibrillation, Cardiac failure, Dyslipidaemia, Hypertension, Cardiac amyloidosis, Gastrointestinal haemorrhage				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 377		
Concomitant Medication [3]: LEVOTHYROXINE, OMEPRAZOLE, SIMVASTATIN, PARACETAMOL, CARBIDOPA, LEVODOPA, BISOPROLOL, FUROSEMIDE, CHLORTALIDONE, APIXABAN, POTASSIUM, EPLERENONE, VORTIOXETINE, TRAZODONE, PENTOXIFYLLINE, SERTRALINE HYDROCHLORIDE, LORAZEPAM, ALLOPURINOL, CEFUROXIME, EPLERENONE, MEGESTROL, ATORVASTATIN, DARBEPOETIN ALFA, DARBEPOETIN ALFA, CHLORTALIDONE, NUTRIENTS NOS, MEGESTROL, FUROSEMIDE, CHLORTALIDONE, ZINC OXIDE, POTASSIUM, BISOPROLOL, DARBEPOETIN ALFA, CHLORTALIDONE, CIPROFLOXACIN				
Non-Serious Adverse Event [4]: Urinary tract infection, Hypokalaemia, Arthralgia, Decreased appetite, Cognitive disorder, Depression, Anaemia, Anaemia, Cardiac failure, Skin ulcer, Chronic kidney disease, Hypokalaemia, Hypotension				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性腎臓病	WORSENING CHRONIC KIDNEY DISEASE	Day 377 / Day 501	Not Related	Drug Withdrawn	Fatal	Moderate
治験責任医師の見解：「慢性腎臓病」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Goitre, Decreased appetite, Musculoskeletal pain, Amnesia, Depression, Pleural effusion, Tonsillectomy, Prostatectomy, Benign prostatic hyperplasia, Cataract, Hypertension, Primary hyperthyroidism, Chronic obstructive pulmonary disease, Sleep apnoea syndrome, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis, Hernia repair, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 665		
Concomitant Medication [3]: FUROSEMIDE, CHLORTALIDONE, PARACETAMOL, METAMIZOLE, CHLORTALIDONE, CHLORTALIDONE, SERTRALINE, THIAMAZOLE, CITICOLINE, POTASSIUM, GLYCOPYRRONIUM/INDACATEROL, MEGESTROL, APIXABAN, POTASSIUM, FUROSEMIDE, MEPIPHYLLINE, BUDESONIDE, FUROSEMIDE, OMEPRAZOLE, CLAVULANIC ACID, CEFTRIAXONE, DEXAMETHASONE, FAMOTIDINE, CEFDITOREN, FUROSEMIDE, METAMIZOLE, THIAMAZOLE, PREDNISONE, PREDNISONE, PREDNISONE, CLAVULANIC ACID, AMOXICILLIN, PREDNISONE, FUROSEMIDE, CHLORTALIDONE, COLCHICINE, BUDESONIDE, ALLOPURINOL, CHLORTALIDONE, CHLORTALIDONE, CHLORTALIDONE, IPRATROPIUM/SALBUTAMOL, HYOSCINE BUTYLBROMIDE, DOXAZOSIN, DEXCHLORPHENIRAMINE, CLAVULANIC ACID, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN, AMOXICILLIN, LEVOFLOXACIN, BEMIPARIN, FUROSEMIDE, CHLORTALIDONE, PARACETAMOL, METAMIZOLE, CITICOLINE, SALBUTAMOL, IPRATROPIUM BROMIDE, LEVOFLOXACIN				
Non-Serious Adverse Event [4]: Syncope, Productive cough, Dyspnoea, Arthralgia, Gouty arthritis, Fall, Head injury, Syncope, Dyspnoea				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	COVID-19 PNEUMONIA	Day 173 / Day 194	Not Related	Drug Interrupted	Recovered /Resolved	Severe
脳神経麻痺	INCOMPLETE PARALYSIS OF THE RIGHT THIRD CRANIAL NERVE	Day 541 / Day 556	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肺炎	RIGHT PNEUMONIA	Day 552 / Day 600	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE HEART FAILURE	Day 660 / Day 665	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」、「脳神経麻痺」、「肺炎」及び「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Vertigo, Sciatica, Transient ischaemic attack, Benign prostatic hyperplasia, Dyslipidaemia, Type 2 diabetes mellitus, Dyspepsia, Cataract, Cardiac failure, Chronic obstructive pulmonary disease, Cardiac amyloidosis, Insomnia, Urinary incontinence, Cardiac pacemaker insertion, Hyperuricaemia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 277		
Concomitant Medication [3]: BUDESONIDE, IPRATROPIUM BROMIDE, OMEPRAZOLE, POTASSIUM ASCORBATE, EMPAGLIFLOZIN, SIMVASTATIN, THEOPHYLLINE, SILODOSIN, PARACETAMOL, OLODATEROL, TIOTROPIUM BROMIDE, SALBUTAMOL, FUROSEMIDE, CHLORTALIDONE, BISOPROLOL, ALLOPURINOL, EPLERENONE, QUETIAPINE, CLOPIDOGREL, FUROSEMIDE, FUROSEMIDE, INDAPAMIDE, ATORVASTATIN, CARBOCISTEINE, IPRATROPIUM BROMIDE, TIOTROPIUM BROMIDE				
Non-Serious Adverse Event [4]: Cardiac failure, Chronic obstructive pulmonary disease				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
敗血症性ショック	SEPCTIC SHOCK	Day 277 / Day 278	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「敗血症性ショック」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Multiple	Country: Brazil	Sex: M	Age: 8[redacted]
Medical History [1]: Affective disorder, Metabolic surgery, Orthopaedic procedure, Squamous cell carcinoma of skin, Diabetes mellitus, Intervertebral disc protrusion, Benign prostatic hyperplasia, Cardiac ablation, Atrial fibrillation, Atrial flutter, Sleep apnoea syndrome, Amyloidosis, Penile prosthesis user				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 175		
Concomitant Medication [3]: METFORMIN, EMPAGLIFLOZIN/LINAGLIPTIN, MULTIVITAMINS (PLAIN), VITAMIN D NOS, FERRIC PYROPHOSPHATE, SPIRONOLACTONE, FUROSEMIDE, MIRABEGRON, DONEPEZIL HYDROCHLORIDE, CITALOPRAM, AMIODARONE HYDROCHLORIDE, ACETYLSALICYLIC ACID/ALUMINIUM GLYCINATE/MAGNESIUM CARBONATE, CYANOCOBALAMIN, NUTRIENTS NOS, VITAMIN B COMPLEX, NUTRIENTS NOS, METFORMIN, GLICLAZIDE, LINAGLIPTIN, QUETIAPINE, ONDANSETRON HYDROCHLORIDE, PANTOPRAZOLE, INSULIN HUMAN, CEFAZOLIN SODIUM, AMIODARONE, METAMIZOLE SODIUM, ENOXAPARIN, ISOSORBIDE DINITRATE, MORPHINE SULFATE, MORPHINE SULFATE				
Non-Serious Adverse Event [4]: Pruritus, Asthenia, Haematuria, Haematuria, Hypertension				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
移行上皮癌	UROTHELIAL CARCINOMA	Day 76 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe
肺炎	PNEUMONIA	Day 177 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe
敗血症性ショック	SEPTIC SHOCK	Day 177 / Day 206	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「移行上皮癌」、「肺炎」及び「敗血症性ショック」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: Brazil	Sex: F	Age: 7[redacted]
Medical History [1]: Menopause, Hypertension, Spinal operation, Cataract operation, Depression, Cardiac failure, Electrocardiogram QT prolonged, Dyslipidaemia, Dyspepsia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 598		
Concomitant Medication [3]: ESCITALOPRAM OXALATE, SACUBITRIL/VALSARTAN, BISOPROLOL, FUROSEMIDE, ATORVASTATIN, PANTOPRAZOLE, CEFTRIAXONE SODIUM, DOBUTAMINE, LEVOSIMENDAN, COVID-19 VACCINE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, FLUOXETINE, COVID-19 VACCINE, APIXABAN, AMIODARONE, FUROSEMIDE, QUETIAPINE FUMARATE, FUROSEMIDE, QUETIAPINE FUMARATE, FUROSEMIDE, NITROFURANTOIN, QUETIAPINE FUMARATE, CEFTRIAXONE SODIUM				
Non-Serious Adverse Event [4]: Hypotension, Oedema peripheral, Blood creatinine increased, Hallucination, Presyncope, Dysphagia, Fall, Joint injury, Respiratory tract infection, Dyspepsia, Dyspepsia, Urinary tract infection, Abdominal pain upper, Decreased appetite, Drooling, Respiratory tract infection				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 439 / Day 461	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全（2）	DECOMPENSATED HEART FAILURE	Day 493 / Day 503	Not Related	Unknown	Recovered /Resolved	Severe
心電図ＱＴ延長	WORSENING QTC INTERVAL WIDENING	Day 573 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe
心不全（3）	DECOMPENSATED HEART FAILURE	Day 598 / Day 620	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心電図ＱＴ延長」及び「心不全（3）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Exostosis, Eyelid thickening, Haemarthrosis, Osteochondrosis, Haemorrhoids, Hypercholesterolaemia, Hypertension, Intervertebral disc protrusion, Carpal tunnel decompression, Dupuytren's contracture, Psoriasis, Gouty arthritis, Asthma, Atrial fibrillation, Annuloplasty, Annuloplasty, Aortic valve replacement, Cardiac failure, Transient ischaemic attack, Diarrhoea, Dysphonia, Biopsy heart, Cardiac amyloidosis, Magnetic resonance imaging heart, Osteoarthritis, Atrial flutter				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 699		
Concomitant Medication [3]: FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, APIXABAN, FUROSEMIDE, ROSUVASTATIN CALCIUM, PERINDOPRIL, BISOPROLOL, VITAMIN D NOS, PARACETAMOL, SILVER NITRATE, SODIUM CHLORIDE, PARACETAMOL, RABEPRAZOLE, COVID-19 VACCINE, RABEPRAZOLE, INFLUENZA VACCINE INACT SPLIT 4V, ALLOPURINOL, COVID-19 VACCINE, ALLOPURINOL, ALLOPURINOL, PREDNISOLONE, PREDNISOLONE, CHLORAMPHENICOL, DEXAMETHASONE, ALLOPURINOL, AMOXICILLIN, ROXITHROMYCIN, COVID-19 VACCINE, MESALAZINE, MESALAZINE, BUDESONIDE, SODIUM BICARBONATE, ALLOPURINOL, FUROSEMIDE, MESALAZINE, AMIODARONE, POTASSIUM CHLORIDE, ALLOPURINOL, AMIODARONE, FUROSEMIDE, IVABRADINE, FENTANYL, PARACETAMOL				
Non-Serious Adverse Event [4]: Blood creatinine increased, Vomiting, Lethargy, Chills, Pain in extremity, Dyspnoea, Epistaxis, Chills, Cataract, Anaemia, Barrett's oesophagus, Diverticulitis, Epistaxis, Nasopharyngitis, Upper respiratory tract infection, C-reactive protein increased, Colitis ulcerative, Glomerular filtration rate decreased, Atrial fibrillation, Nausea, Vomiting, Hypokalaemia, Atrial flutter				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脱水	DEHYDRATION (FORMERLY ACUTE KIDNEY INJURY)	Day 651 / Day 655	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全	WORSENED CARDIAC FAILURE	Day 697 / Day 701	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「脱水」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Chronic kidney disease, Hypertension, Dizziness, Carpal tunnel decompression, Gastrooesophageal reflux disease, Knee arthroplasty, Prostatectomy, Arthralgia, Atrial fibrillation, Biopsy heart, Cardiac amyloidosis, Cardiac failure, Cardiac pacemaker insertion, Echocardiogram, Hypothyroidism, Oedema peripheral, Joint swelling, Blood creatinine increased				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 402			
Concomitant Medication [3]: ENALAPRIL, PROCHLORPERAZINE, PANTOPRAZOLE, RIVAROXABAN, METOPROLOL, FUROSEMIDE, CODEINE PHOSPHATE/PARACETAMOL, LEVOTHYROXINE SODIUM, SODIUM POLYSTYRENE SULFONATE, FUROSEMIDE, PARACETAMOL, BISACODYL/DOCUSATE SODIUM, SENNA ALEXANDRINA, CALCIUM CARBONATE, TAPENTADOL, CEFALEXIN, TRANEXAMIC ACID, ENOXAPARIN SODIUM, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, APIXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, METOPROLOL, FUROSEMIDE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, FLUCLOXACILLIN, MOXIFLOXACIN, HEPARIN, FUROSEMIDE, SALBUTAMOL, FUROSEMIDE, FUROSEMIDE, HYDROCORTISONE, POTASSIUM CHLORIDE, GLUCOSE OXIDASE/LACTOFERRIN/LACTOPEROXIDASE/LYSOZYME, POTASSIUM CHLORIDE, COVID-19 VACCINE, FUROSEMIDE, RIVAROXABAN, INFLUENZA VACCINE INACT SPLIT 4V, CALCIUM, VANCOMYCIN, FUROSEMIDE, MAGNESIUM, CEFAZOLIN, CEFAZOLIN, POTASSIUM CHLORIDE, CEFTRIAXONE, FUROSEMIDE, NEBIVOLOL HYDROCHLORIDE, POTASSIUM CHLORIDE, SPIRONOLACTONE, PARACETAMOL, CEFALEXIN, CLOTRIMAZOLE, PARACETAMOL, SODIUM POLYSTYRENE SULFONATE				
Non-Serious Adverse Event [4]: Blood creatinine increased, Mouth ulceration, Hyperkalaemia, Fall, Epistaxis, Haemorrhagic diathesis, Systemic scleroderma, Hypoglycaemia, Fall, Cardiac failure, Hypokalaemia, Blood creatinine increased, Iron deficiency, Pleural effusion, Staphylococcal infection, Dry mouth, Arthralgia, Pain in extremity, Benign neoplasm of skin, Cellulitis, Renal failure, Pleural effusion, Anal candidiasis, Hyperkalaemia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血中クレアチニン増加	ELEVATED CREATININE WORSENED DUE TO ENALOPRIL	Day 29 / Day 34	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
大腿骨頚部骨折	FRACTURED NECK OF FEMUR LEFT	Day 71 / Day 84	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	DECOMPENSATED HEART FAILURE	Day 222 / Day 248	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肺炎	PNEUMONIA	Day 230 / Day 245	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
右室不全	SEVERE RIGHT HEART FAILURE	Day 393 / Day 405	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「血中クレアチニン増加」、「大腿骨頚部骨折」、「心不全」、「肺炎」及び「右室不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Other	Country: Australia	Sex: F	Age: 6[redacted]
Medical History [1]: Osteoarthritis, Osteoporosis, Chronic kidney disease, Hypertension, Benign breast lump removal, Vaginal haemorrhage, Vaginal haemorrhage, Atrial fibrillation, Cardiac failure, Gastrooesophageal reflux disease, Nausea, Hyperlipidaemia, Cardiac amyloidosis, Seasonal allergy, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 176		
Concomitant Medication [3]: DOMPERIDONE, PANTOPRAZOLE, COLECALCIFEROL, APIXABAN, NEBIVOLOL, ROSUVASTATIN CALCIUM, FUROSEMIDE, MOMETASONE FUROATE, SPIRONOLACTONE, DOCUSATE SODIUM/SENNOSIDE A+B, ONDANSETRON, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/SIMETICONE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, TEMAZEPAM, PARACETAMOL, HYDROCHLOROTHIAZIDE, FUROSEMIDE, ENOXAPARIN, LEVOTHYROXINE, ENOXAPARIN, ALBUMIN HUMAN, OTHER DRUGS FOR CONSTIPATION, ACETYLSALICYLIC ACID, MELATONIN, SODIUM CHLORIDE, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, PARACETAMOL, ENOXAPARIN, LACTULOSE, CEFTRIAXONE, DOXYCYCLINE, VANCOMYCIN, NYSTATIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, AMPICILLIN, ONDANSETRON, CONTACT LAXATIVES, PARACETAMOL, BUDESONIDE, SODIUM CHLORIDE, PROCHLORPERAZINE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/MAGNESIUM TRISILICATE, ONDANSETRON, MIDODRINE, CLOTRIMAZOLE, CEFTRIAXONE, FUROSEMIDE, OXYCODONE, FUROSEMIDE, PARACETAMOL, CEFEPIME, SODIUM CHLORIDE, SODIUM CHLORIDE, NOREPINEPHRINE, FUROSEMIDE, OXYGEN				
Non-Serious Adverse Event [4]: Dyspepsia, Nausea, Constipation, Joint injury, Fall, Hyponatraemia, Pleural effusion, Oedema peripheral, Muscle contractions involuntary, Nervous system disorder, Hyponatraemia, Dyspnoea, Synovial cyst, Muscle contractions involuntary, Fall, Delirium, Bacteraemia, Oral candidiasis, Hypokalaemia, Oropharyngeal pain, Ascites, Non-cardiac chest pain, Fungal skin infection, Peripheral swelling, Hypotension, Urosepsis, Vomiting, Blister, Rash				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE ON CHRONIC KIDNEY DISEASE	Day 88 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
骨盤骨折	LEFT PUBIC BONE FRACTURE	Day 117 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
血液量増加症（1）	FLUID OVERLOAD	Day 152 / Day 165	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
血液量増加症（2）	FLUID OVERLOAD	Day 167 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe
心原性ショック	CARDIOGENIC SHOCK	Day 176 / Day 185	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「急性腎障害」、「骨盤骨折」、「血液量増加症（1）」、「血液量増加症（2）」及び「心原性ショック」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Urge incontinence, Asthma, Bronchial hyperreactivity, Dyslipidaemia, Hypertension, Knee arthroplasty, Arthrodesis, Irritable bowel syndrome, Gastrooesophageal reflux disease, Prostate cancer, Rotator cuff syndrome, Neuralgia, Carpal tunnel syndrome, Carpal tunnel syndrome, Large intestine polyp, Knee arthroplasty, Osteomyelitis, Muscle spasms, Cardiac ablation, Coronary artery bypass, Atrial fibrillation, Bundle branch block right, Myocardial ischaemia, Insomnia, Sleep apnoea syndrome, Cardiac failure congestive, Cardiomyopathy, Chronic kidney disease, Obesity, Oedema peripheral, Oedema peripheral, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 292		
Concomitant Medication [3]: EZETIMIBE/SIMVASTATIN, SACUBITRIL/VALSARTAN, OXYBUTYNIN HYDROCHLORIDE, MULTIVITAMINS (PLAIN), LOPERAMIDE HYDROCHLORIDE, CHROMIUM, GABAPENTIN, MAGNESIUM, UBIDECARENONE, IVABRADINE HYDROCHLORIDE, FUROSEMIDE, FUROSEMIDE, MELATONIN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, APIXABAN, ZOPICLONE, KRILL OIL, FERROUS SULFATE EXSICCATED/SODIUM ASCORBATE, APIXABAN, DOCUSATE SODIUM/SENNOSIDE A+B, LACTULOSE, IBUPROFEN, OXYCODONE HYDROCHLORIDE, PARACETAMOL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, OXYCODONE, ONDANSETRON, PIPERACILLIN/TAZOBACTAM, VANCOMYCIN, PANTOPRAZOLE, PARACETAMOL, PIPERACILLIN/TAZOBACTAM, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, DIAZEPAM, FUROSEMIDE, TEMAZEPAM				
Non-Serious Adverse Event [4]: Anaemia, Anaemia, Constipation, Nausea, Acute kidney injury, Somnolence, Melaena, Osteomyelitis				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
背部痛	LUMBAR BACK PAIN	Day 278 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
敗血症	SEPSIS [SECONDARY TO SPINAL OSTEOMYELITIS]	Day 287/ Day 293	Not Related	Dose Not Changed	Fatal	Severe
心不全	WORSENING HEART FAILURE	Day 290 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
心停止	CARDIAC ARREST	Day 293 / Day 293	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「背部痛」、「敗血症」、「心不全」及び「心停止」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Ex-tobacco user, Carpal tunnel syndrome, Inguinal hernia repair, Gastrooesophageal reflux disease, Dyslipidaemia, Osteoarthritis, Carpal tunnel decompression, Inguinal hernia repair, Benign prostatic hyperplasia, Dysphagia, Atrial fibrillation, Constipation, Cardiac failure, Dilatation atrial, Eyelid ptosis, Muscle spasms, Vertebral osteophyte, Cardiac amyloidosis, Cataract, Cataract, Bundle branch block left, Electrocardiogram QT prolonged, Chronic kidney disease, Nephrosclerosis, Gastritis, Cataract operation, Intraocular lens implant, Diabetes mellitus				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 834		
Concomitant Medication [3]: OXYBUTYNIN, PARACETAMOL, PANTOPRAZOLE, ROSUVASTATIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FENOFIBRATE, MAGNESIUM, RAMIPRIL, WARFARIN, FUROSEMIDE, PROCHLORPERAZINE, POTASSIUM CHLORIDE, AMLODIPINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, ISOPRENALINE, PARACETAMOL, PANTOPRAZOLE, ACETYLSALICYLIC ACID, ISOPRENALINE, FUROSEMIDE, OXYBUTYNIN, PARACETAMOL, MAGNESIUM ASPARTATE, RAMIPRIL, FUROSEMIDE, FUROSEMIDE, TEICOPLANIN, LIDOCAINE, FENTANYL, MIDAZOLAM, PREDNISOLONE ACETATE, CHLORAMPHENICOL, FUROSEMIDE, CLOTRIMAZOLE/HYDROCORTISONE ACETATE, AMOXICILLIN TRIHYDRATE, CIPROFLOXACIN, WARFARIN, CHLORAMPHENICOL, CEFALEXIN, CHLORAMPHENICOL, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE, COVID-19 VACCINE, PARACETAMOL, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, GENTAMICIN, AMPICILLIN, FUROSEMIDE, RAMIPRIL, FUROSEMIDE, AMOXICILLIN, COVID-19 VACCINE, LOPERAMIDE, FUROSEMIDE, FUROSEMIDE, CETIRIZINE HYDROCHLORIDE, INFLUENZA VACCINE, DICLOXACILLIN				
Non-Serious Adverse Event [4]: Gout, Ear injury, Post procedural infection, Eye infection, Hypervolaemia, Renal impairment, Diarrhoea, Cardiac failure, Arthropod bite, Limb injury				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
完全房室ブロック	COMPLETE HEART BLOCK	Day 119 / Day 143	Not Related	Drug Interrupted	Recovered /Resolved	Severe
尿路感染	URINARY TRACT INFECTION	Day 675 / Day 679	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
脳梗塞	ACUTE RIGHT MIDDLE CEREBRAL ARTERY INFARCTION	Day 835 / Day 839	Not Related	Drug Interrupted	Fatal	Severe
誤嚥性肺炎	ASPIRATION PNEUMONIA	Day 836 / Day 838	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「完全房室ブロック」、「尿路感染」、「脳梗塞」及び「誤嚥性肺炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Gastrooesophageal reflux disease, Gout, Muscle spasms, Benign prostatic hyperplasia, Atrioventricular block complete, Escherichia urinary tract infection, Cardiac pacemaker insertion, Chronic kidney disease, Lower respiratory tract infection, Acute myocardial infarction, Left ventricular dysfunction, Pneumothorax, Coronary artery bypass, Pancreatic cyst, Seroma, Pleural effusion, Cardiac failure, Cellulitis, Localised infection, Deep vein thrombosis, Skin ulcer, Iron deficiency anaemia, Bursitis, Cardiac amyloidosis, Arthropathy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 737		
Concomitant Medication [3]: BISOPROLOL, OMEPRAZOLE, ACETYLSALICYLIC ACID, ATORVASTATIN, FUROSEMIDE, POTASSIUM CHLORIDE, EPLERENONE, RAMIPRIL, PNEUMOCOCCAL VACCINES, CEFALEXIN, TETANUS VACCINE, CEFALEXIN, CEFALEXIN, DICLOXACILLIN, INFLUENZA VACCINE, ROXITHROMYCIN, SULFAMETHOXAZOLE, TRIMETHOPRIM, COVID-19 VACCINE, CORTISONE, COVID-19 VACCINE, AMOXICILLIN, SALBUTAMOL, CORTISONE, RIVAROXABAN, COVID-19 VACCINE, SULFAMETHOXAZOLE/TRIMETHOPRIM, DIPHTHERIA VACCINE TOXOID/TETANUS VACCINE TOXOID, CEFAZOLIN, FUROSEMIDE, PANTOPRAZOLE, RIVAROXABAN, EPLERENONE, FUROSEMIDE, IRON, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE, COVID-19 VACCINE, CEFALEXIN, FLUCLOXACILLIN, CEFALEXIN, CEFALEXIN, SALBUTAMOL, DOCUSATE SODIUM/SENNOSIDE A+B, LINCOMYCIN, MEROPENEM, OXYCODONE HYDROCHLORIDE, PARACETAMOL, VANCOMYCIN, MEROPENEM, POTASSIUM CHLORIDE, CLINDAMYCIN, VITAMIN K NOS, PANTOPRAZOLE, PANTOPRAZOLE, CEFTRIAXONE, FOLIC ACID, EPHEDRINE, METARAMINOL, PROPOFOL, LIDOCAINE, PANTOPRAZOLE, PANTOPRAZOLE, FLUCONAZOLE, ALBUMIN HUMAN, ALBUMIN HUMAN, BISOPROLOL, PANTOPRAZOLE, PANTOPRAZOLE, MICONAZOLE				
Non-Serious Adverse Event [4]: Wound infection, Limb injury, Cellulitis, Contusion, Atrial fibrillation, Limb injury, Orthopnoea, Haematoma, Skin abrasion, Limb injury, Wound infection, Skin laceration, Skin ulcer, Blister, Inguinal hernia, Fall, Oesophageal candidiasis, Musculoskeletal chest pain, Diarrhoea, Dyspnoea, International normalised ratio increased, Enterococcal infection, Vitamin B12 deficiency, Hypotension, Groin infection, Metabolic acidosis				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血液量増加症	FLUID OVERLOADED	Day 500 / Day 516	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
急性腎障害	ACUTE KIDNEY INJURY	Day 513 / Day 518	Not Related	Drug Interrupted	Recovered /Resolved	Severe
転倒	MECHANICAL FALL	Day 514 / Day 514	Not Related	Drug Interrupted	Recovered /Resolved	Severe
腸上皮化生	GASTRIC INTESTINAL METAPLASIA	Day 722 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
蜂巣炎	WORSENING CELLULITIS LEFT LEG	Day 722 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Severe

末期腎疾患	ENDSTAGE RENAL FAILURE	Day 734 / Day 743	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「血液量増加症」、「急性腎障害」、「転倒」、「腸上皮化生」、「蜂巣炎」及び「末期腎疾患」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Basal cell carcinoma, Carpal tunnel syndrome, Carpal tunnel syndrome, Hypercholesterolaemia, Atrial fibrillation, Transurethral prostatectomy, Hypertension, Cardiac amyloidosis, Cardiac failure, Osteoporosis, Ventricular fibrillation, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 531		
Concomitant Medication [3]: SPIRONOLACTONE, AMITRIPTYLINE, COLECALCIFEROL, ASCORBIC ACID/VACCINIUM MACROCARPON, AMIODARONE, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, APIXABAN, MAGNESIUM, POTASSIUM CHLORIDE, FUROSEMIDE, ATORVASTATIN, LEVOTHYROXINE SODIUM, WARFARIN, LEVOTHYROXINE SODIUM, POTASSIUM CHLORIDE, FUROSEMIDE, TRIMETHOPRIM, PARACETAMOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, AMOXICILLIN/CLAVULANIC ACID, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, SODIUM CHLORIDE				
Non-Serious Adverse Event [4]: Skin lesion, Skin laceration, Haematuria, Fall, Skin laceration, Hypervolaemia, Fall				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
くも膜下出血	SUB ARAHCNOID HAEMORRHAGE	Day 433 / Day 451	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
血尿	HAEMATURIA	Day 531 / NA	Not Related	Drug Interrupted	Not Recovered /Not Resolved	Moderate
敗血症性ショック	SEPTIC SHOCK FROM ESCHERICHIA COLI	Day 537 / Day 541	Not Related	Drug Interrupted	Fatal	Severe

治験責任医師の見解：「くも膜下出血」、「血尿」及び「敗血症性ショック」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 6[redacted]
Medical History [1]: Hyperlipidaemia, Atrial fibrillation, Embolic stroke, Constipation, Cardiac amyloidosis, Cardiac failure, Muscle spasms, Gout				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 434			
Concomitant Medication [3]: WARFARIN, DOCUSATE SODIUM/SENNOSIDE A+B, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, CELECOXIB, PREDNISONE, COLECALCIFEROL/MAGNESIUM CITRATE/PYRIDOXINE HYDROCHLORIDE/VIBURNUM OPULUS, MULTIVITAMINS (PLAIN), PREDNISONE, ALLOPURINOL, MAGNESIUM, ALLOPURINOL, BENDROFLUMETHIAZIDE, ALLOPURINOL, LORATADINE, FUROSEMIDE, FUROSEMIDE, DOMPERIDONE, ALLOPURINOL, GABAPENTIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, ALLOPURINOL, PREDNISONE, BUMETANIDE, MORPHINE, METOLAZONE, PREDNISONE, ALLOPURINOL				
Non-Serious Adverse Event [4]: Fatigue, Drug eruption, Inguinal hernia, Gout, Dehydration, Skin laceration, Fall, Loss of consciousness				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心アミロイドーシス	WORSENING OF FAMILIAL CARDIAC AMYLOIDOSIS CARDIOMYOPATHY	Day 434 / Day 434	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心アミロイドーシス」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Anaemia, Hypertension, Helicobacter infection, Peptic ulcer, Bacterial sepsis, Pneumonia, Venous thrombosis, Osteoarthritis, Hypoacusis, Hip arthroplasty, Spinal pain, Carpal tunnel decompression, Atrial flutter, Rib fracture, Hypercholesterolaemia, Type 2 diabetes mellitus, Diabetic neuropathy, Atrial tachycardia, Prostatic operation, Cataract operation, Gout, Hyperuricaemia, Shoulder arthroplasty, Chronic kidney disease, Appendicectomy, Acute myocardial infarction, Percutaneous coronary intervention, Cardiac amyloidosis, Cardiac ablation, Cardiac ablation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 677		
Concomitant Medication [3]: FERROUS SULFATE, NITRENDIPINE, NITRENDIPINE, WARFARIN, WARFARIN, URAPIDIL, ATORVASTATIN CALCIUM, INSULIN ASPART, INSULIN ASPART, INSULIN DETEMIR, METOPROLOL SUCCINATE, ALLOPURINOL, GABAPENTIN, FUROSEMIDE, CLOPIDOGREL BISULFATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, CALCITRIOL, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, FUROSEMIDE, RIVAROXABAN, FUROSEMIDE, COVID-19 VACCINE, RIVAROXABAN, COVID-19 VACCINE, URAPIDIL, URAPIDIL, METOPROLOL SUCCINATE, METOPROLOL SUCCINATE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, MORPHINE, LEVOFLOXACIN, AMIODARONE HYDROCHLORIDE				
Non-Serious Adverse Event [4]: Albumin urine present, Urine albumin/creatinine ratio increased, Limb injury, Diverticulum intestinal, Cardiac failure, Cardiac failure, Cardiac failure, Dizziness, Chest discomfort, Dyspnoea, Heart rate increased, Chronic kidney disease, Atrial flutter, COVID-19				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
洞結節機能不全	SICK SINUS SYNDROME	Day 571 / Day 591	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
うっ血性心不全	CONGESTIVE HEART FAILURE	Day 659 / Day 678	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「洞結節機能不全」及び「うっ血性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]	
Medical History [1]: Microcytic anaemia, Abdominal hernia repair, Appendicectomy, Atrial fibrillation, Hypertension, Benign prostatic hyperplasia, Chronic kidney disease, Varicose vein operation, Carpal tunnel decompression, Carpal tunnel decompression, Myocardial ischaemia, Percutaneous coronary intervention, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 124			
Concomitant Medication [3]: BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, ACETYLSALICYLIC ACID/GLYCINE, SACUBITRIL/VALSARTAN, SACUBITRIL/VALSARTAN, ATORVASTATIN CALCIUM, FINASTERIDE, BISOPROLOL, SPIRONOLACTONE					
Non-Serious Adverse Event [4]: Bradycardia					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
突然死	SUDDEN DEATH OF UNKNOWN CAUSE	Day 125 / Day 125	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「突然死」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Colorectal cancer, Colectomy, Type 2 diabetes mellitus, Chronic obstructive pulmonary disease, Hyperuricaemia, Benign prostatic hyperplasia, Cataract, Cardiac amyloidosis, Pneumonia, Urosepsis, Pulmonary calcification, Skin ulcer, Peripheral venous disease, Cardiac failure acute, Urinary tract infection bacterial, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 182		
Concomitant Medication [3]: LINAGLIPTIN, TAMSULOSIN HYDROCHLORIDE, AMIODARONE HYDROCHLORIDE, FENOTEROL HYDROBROMIDE/IPRATROPIUM BROMIDE, APIXABAN, BISOPROLOL FUMARATE, SPIRONOLACTONE, FUROSEMIDE, BISULEPIN HYDROCHLORIDE, LORATADINE, EPLERENONE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CANRENOATE, FUROSEMIDE, POTASSIUM CANRENOATE, FUROSEMIDE, FUROSEMIDE, NADROPARIN CALCIUM, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, MORPHINE, PARACETAMOL				
Non-Serious Adverse Event [4]: Peripheral swelling, Joint swelling, Fall				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	CARDIAL DECOMPENSATION MOSTLY RIGHT SIDED BASED ON ATTR-CM	Day 105 / Day 183	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	CARDIAL DECOMPESATION BASED ON ATTR CM	Day 163 / Day 183	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 8[redacted]	
Medical History [1]: Meniere's disease, Carpal tunnel decompression, Atrial fibrillation, Carpal tunnel decompression, Chronic obstructive pulmonary disease, Hyperacusis, Hyperlipidaemia, Prostate cancer, Osteoarthritis, Cardiac failure chronic, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 117			
Concomitant Medication [3]: BETAHISTINE, WARFARIN, ROSUVASTATIN CALCIUM, SPIRONOLACTONE, FUROSEMIDE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM					
Non-Serious Adverse Event [4]: Bronchitis					
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
失神	SYNCOPE	Day 100 / Day 100	Not Related	Dose Not Changed	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９	COVID 19 INFECTION	Day 117 / Day 121	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「失神」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White	Country: Poland		Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Cardiac failure, Osteoporosis, Benign prostatic hyperplasia, Cholecystectomy, Cardiac ablation, Cardiac pacemaker insertion, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 621			
Concomitant Medication [3]: PANTOPRAZOLE, RIVAROXABAN, METOPROLOL, FUROSEMIDE						
Non-Serious Adverse Event [4]: No event						
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
死亡	DEATH OF UNKNOWN REASON	Day 621 / Day 621	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「死亡」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Poland	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Coronary artery disease, Cardiac failure, Coronary angioplasty, Cardiac tamponade						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 439			
Concomitant Medication [3]: PANTOPRAZOLE, POTASSIUM CHLORIDE, CARVEDILOL, EPLERENONE, FUROSEMIDE, ATORVASTATIN, RIVAROXABAN, RAMIPRIL, FUROSEMIDE						
Non-Serious Adverse Event [4]: Fatigue						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING OF HEART FAILURE	Day 344 / Day 350	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
死亡	DEATH [NO FURTHER INFORMATION]	Day 440 / Day 440	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全」及び「死亡」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Congenital renal disorder, Nephrectomy, Transient ischaemic attack, Prostate cancer, Prostatic operation, Tendon sheath incision, Hyperlipidaemia, Ptosis repair, Neuropathy peripheral, Tenosynovitis stenosans, Carpal tunnel decompression, Hypertension, Pericardial effusion, Pericardial drainage, Cardiac amyloidosis, Atrial fibrillation, Diastolic dysfunction, Pleural effusion, Chronic kidney disease, Cerebrovascular accident, Insomnia, Pericardial excision, Cardiac pacemaker insertion, Orthostatic hypotension				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 722		
Concomitant Medication [3]: ATORVASTATIN, GABAPENTIN, APIXABAN, TORASEMIDE, DIPHENHYDRAMINE, MIDODRINE HYDROCHLORIDE, ROPINIROLE HYDROCHLORIDE, TRAMADOL, COLCHICINE, SULFAMETHOXAZOLE/TRIMETHOPRIM, LEVOTHYROXINE, MECLOZINE, MIDODRINE HYDROCHLORIDE, Not coded: Tafamidis, TAFAMIDIS, TORASEMIDE, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE, VANCOMYCIN, METRONIDAZOLE, CEFEPIME, PARACETAMOL, PHYTOMENADIONE, HEPARIN, HEPARIN, CEFEPIME, CYCLOBENZAPRINE, OXYCODONE, OXYCODONE, LIDOCAINE, SODIUM ZIRCONIUM CYCLOSILICATE, CEFTRIAXONE SODIUM, FUROSEMIDE, HYDROMORPHONE, ALTEPLASE, DORNASE ALFA, FUROSEMIDE, ALTEPLASE, DORNASE ALFA, HEPARIN, ATORVASTATIN, SODIUM ZIRCONIUM CYCLOSILICATE, DOCUSATE/SENNA ALEXANDRINA, MACROGOL, NALOXEGOL, FUROSEMIDE, METOLAZONE, CEFDINIR, APIXABAN, ACETYLSALICYLIC ACID, FUROSEMIDE, FLUOXETIN, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, BUMETANIDE, RAMELTEON, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, BUMETANIDE, COLECALCIFEROL				
Non-Serious Adverse Event [4]: Insomnia, Joint dislocation, Arthralgia, Gout, Fall, Limb injury, Hypothyroidism, Balance disorder, Vertigo, Dyspnoea, Pleural effusion, Pleural effusion, Dyspnoea, Squamous cell carcinoma, Pneumonia, Depressed mood, Procedural pain, Acute kidney injury, International normalised ratio increased, Muscle spasms, Hyperkalaemia, Constipation				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胸水	WORSENING PLEURAL EFFUSION	Day 682 / NA	Not Related	Drug Interrupted	Recovering /Resolving	Severe
アミロイドーシス	END STAGE AMYLOIDOSIS	Day 722 / Day 734	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「胸水」及び「アミロイドーシス」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Benign prostatic hyperplasia, Transurethral prostatectomy, Hypotonic urinary bladder, Arthritis, Carpal tunnel decompression, Carpal tunnel syndrome, Deafness, Malignant melanoma, Cardiac failure, Insomnia, Haemorrhoids, Orthostatic hypotension, Coronary artery disease, Dyslipidaemia, Atrial fibrillation, Mitral valve incompetence, Tricuspid valve incompetence, Sleep apnoea syndrome, Cataract, Cardiac amyloidosis, Hypothyroidism				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 293		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, MELATONIN, ATORVASTATIN, FUROSEMIDE, RIVAROXABAN, SACUBITRIL/VALSARTAN, METOPROLOL, MULTIVITAMINS (PLAIN), SACUBITRIL/VALSARTAN, LEVOTHYROXINE, FUROSEMIDE, LEVOTHYROXINE, CIPROFLOXACIN, FUROSEMIDE, CIPROFLOXACIN, MUPIROCIN, NYSTATIN, GLYCERYL TRINITRATE, GLUCOSAMINE SULFATE, RIVAROXABAN, GLYCERYL TRINITRATE, SACUBITRIL/VALSARTAN, METHYLSULFONYLMETHANE, FUROSEMIDE, RIVAROXABAN, ALLOPURINOL, POTASSIUM CHLORIDE, BISACODYL, TORASEMIDE, ALLOPURINOL, ALLOPURINOL, POTASSIUM CHLORIDE, LORAZEPAM, POTASSIUM CHLORIDE, BUMETANIDE, LORAZEPAM, POTASSIUM CHLORIDE, BUMETANIDE, LORAZEPAM, TAFAMIDIS, BUMETANIDE, SENNA ALEXANDRINA, HYOSCYAMINE, POTASSIUM, MORPHINE				
Non-Serious Adverse Event [4]: Flatulence, Haematuria, Hypotension, Urinary tract infection, Cardiac failure, Basal cell carcinoma, Skin infection, Cardiac failure, Hyperbilirubinaemia, Hyperuricaemia, Constipation, Anxiety				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
狭心症	ANGINA PECTORIS	Day 165 / Day 166	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全（1）	ACUTE CONGESTIVE HEART FAILURE EXACERBATION	Day 236 / Day 242	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（2）	ACUTE CONGESTIVE HEART FAILURE EXACERBATION	Day 244 / Day 250	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心アミロイドーシス	END STAGE CARDIAC AMYLOIDOSIS	Day 291 / Day 299	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「狭心症」、「急性心不全（1）」、「急性心不全（2）」及び「心アミロイドーシス」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]	
Medical History [1]: Ischaemic cardiomyopathy, Dyslipidaemia, Hypertension, Cardiac failure congestive, Palpitations, Chronic kidney disease, Cough, Cardiac amyloidosis, Hypokalaemia, Vitamin D deficiency					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 211			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, BENZONATATE, BUMETANIDE, ISOSORBIDE MONONITRATE, POTASSIUM CHLORIDE, METOLAZONE, COLECALCIFEROL, LEVOFLOXACIN, BUMETANIDE, BUMETANIDE, TORASEMIDE, TORASEMIDE, CLAVULANATE POTASSIUM, AMOXICILLIN, AZITHROMYCIN, BUMETANIDE, VANCOMYCIN, FUROSEMIDE, CHLOROTHIAZIDE, PIPERACILLIN/TAZOBACTAM					
Non-Serious Adverse Event [4]: Varicocele, Epididymitis, Epididymal cyst, Cardiac failure, Diarrhoea, Pneumonia					

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	CONGESTIVE HEART FAILURE EXACERBATION	Day 196 / Day 198	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
心不全	WORSENING HEART FAILURE	Day 211 / Day 231	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「急性心不全」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Tonsillectomy, Arthralgia, Knee arthroplasty, Transient ischaemic attack, Dyslipidaemia, Hypertension, Cataract, Pain, Arthritis, Intervertebral disc degeneration, Spinal osteoarthritis, Sleep apnoea syndrome, Cataract operation, Squamous cell carcinoma, Ventricular tachycardia, Atrial fibrillation, Gastrooesophageal reflux disease, Acute myocardial infarction, Biopsy lung, Pulmonary mass, Large intestine polyp, Large intestinal polypectomy, Cardiac resynchronisation therapy, Carpal tunnel syndrome, Cardiac amyloidosis, Hydrocele, Chronic kidney disease, Left ventricular failure, Lymphoedema, Dental caries				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 882		
Concomitant Medication [3]: HYDROCODONE, PARACETAMOL, PANTOPRAZOLE, METOPROLOL, AMIODARONE, RIVAROXABAN, TORASEMIDE, DOCUSATE SODIUM, AMIODARONE, NYSTATIN, FLUOROURACIL, METHYLPREDNISOLONE ACETATE, METHYLPREDNISOLONE ACETATE, HYDROCODONE, CELECOXIB, PNEUMOCOCCAL VACCINE POLYSACCH 23V, VARICELLA ZOSTER VACCINE RGE (CHO), DICLOFENAC, DICLOFENAC, METHYLPREDNISOLONE ACETATE, INFLUENZA VACCINE, VARICELLA ZOSTER VACCINE RGE (CHO), COVID-19 VACCINE, COVID-19 VACCINE, ONDANSETRON HYDROCHLORIDE, AZITHROMYCIN, CEFTRIAXONE SODIUM, SODIUM CHLORIDE, FUROSEMIDE, AZITHROMYCIN, CEFALEXIN, OXYMETAZOLINE HYDROCHLORIDE, APIXABAN, APIXABAN, TORASEMIDE, TORASEMIDE, TORASEMIDE, METOPROLOL, TORASEMIDE				
Non-Serious Adverse Event [4]: Oral candidiasis, Arthralgia, Arthralgia, Back pain, Arthralgia, Solar lentigo, Neurofibroma, Seborrhoeic keratosis, Actinic keratosis, Osteoarthritis, Acute kidney injury, Epistaxis, Constipation, Cardiac failure, Acute kidney injury				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	COMMUNITY ACQUIRED PNEUMONIA	Day 546 / Day 558	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
変形性関節症	WORSENING OSTEOARTHRITIS OF RIGHT HIP JOINT	Day 749 / Day 749	Not Related	Dose Not Changed	Recovered /Resolved	Severe
慢性心不全	END STAGE HEART FAILURE	Day 878 / NA	Not Related	Drug Withdrawn	Not Recovered /Not Resolved	Severe
遠隔転移を伴う消化器癌	METASTATIC GI CANCER WITH UNKNOWN PRIMARY	Day 881 / Day 891	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「肺炎」、「変形性関節症」、「慢性心不全」及び「遠隔転移を伴う消化器癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Non-Hodgkin's lymphoma, Atrial fibrillation, Hyperlipidaemia, Type 2 diabetes mellitus, Hypertension, Arthritis, Hip arthroplasty, Knee arthroplasty, Aortic stenosis, Carpal tunnel syndrome, Nephrolithiasis, Cardiac amyloidosis, Cardiac failure, Pulmonary hypertension, Pancytopenia, Eye irritation, Insomnia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 112		
Concomitant Medication [3]: WARFARIN, PRAVASTATIN, PARACETAMOL, TORASEMIDE, MELATONIN, TOBRAMYCIN, METOLAZONE, POTASSIUM CHLORIDE, TRIAMCINOLONE, POTASSIUM, POTASSIUM CHLORIDE, CEFTRIAXONE SODIUM, SPIRONOLACTONE, TORASEMIDE, MUPIROCIN, AMMONIUM LACTATE				
Non-Serious Adverse Event [4]: Hypervolaemia, Limb injury, Cellulitis, Acute kidney injury, Fall, Dehydration				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路感染	URINARY TRACT INFECTION	Day 50 / Day 59	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
失神	SYNCOPE (ONCE DUE TO DEHYDRATION, SEPARATELY REPORTED)	Day 113 / Day 113	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心アミロイドーシス	WORSENED CARDIAC AMYLOIDOSIS	Day 121 / Day 124	Not Related	NA	Fatal	Severe
治験責任医師の見解：「尿路感染」、「失神」及び「心アミロイドーシス」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]	
Medical History [1]: Prostatomegaly, Atrial fibrillation, Hypertension, Cardiac failure, Amyloidosis					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 753				
Concomitant Medication [3]: ACETYLSALICYLIC ACID, TAMSULOSIN, FINASTERIDE, FUROSEMIDE, LISINOPRIL, APIXABAN, ATORVASTATIN, FUROSEMIDE, FUROSEMIDE, TORASEMIDE, FUROSEMIDE, METOLAZONE, APIXABAN, APIXABAN, Not coded: Tafamidis, TAFAMIDIS, DONEPEZIL, QUETIAPINE, METOLAZONE, METOLAZONE, TORASEMIDE					
Non-Serious Adverse Event [4]: Dementia, Head injury, Fall, Peripheral swelling, Peripheral swelling					
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE DECOMPENSATED HEART FAILURE	Day 64 / Day 68	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
起立性低血圧	ORTHOSTATIC HYPOTENSION	Day 260 / Day 273	Not Related	Drug Interrupted	Recovered /Resolved	Mild
呼吸困難	SHORTNESS OF BREATH	Day 434 / Day 435	Not Related	Drug Interrupted	Recovered /Resolved	Mild
転倒	MECHANICAL FALL	Day 492 / Day 492	Not Related	Drug Interrupted	Recovered /Resolved	Mild
多臓器機能不全症候群	MULTI ORGAN FAILURE	Day 750 / Day 753	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「急性心不全」、「起立性低血圧」、「呼吸困難」、「転倒」及び「多臓器機能不全症候群」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]	
Medical History [1]: Dyslipidaemia, Type 2 diabetes mellitus, Hypertension, Hypothyroidism, Neuralgia, Atrial fibrillation, Non-cardiac chest pain, Oedema, Insomnia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 537				
Concomitant Medication [3]: METFORMIN, APIXABAN, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, ATORVASTATIN, ZOLPIDEM, LEVOTHYROXINE, FUROSEMIDE, GABAPENTIN, LOSARTAN, METOPROLOL, PREGABALIN, GABAPENTIN, CALCIUM GLUCONATE, SODIUM CHLORIDE, EPINEPHRINE					
Non-Serious Adverse Event [4]: Neuropathy peripheral, Ecchymosis, N-terminal prohormone brain natriuretic peptide increased, Telangiectasia					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心停止	CARDIAC ARREST	Day 537 / Day 537	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心停止」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Abnormal loss of weight, Gastrooesophageal reflux disease, Constipation, Benign prostatic hyperplasia, Haematuria, Essential hypertension, Squamous cell carcinoma, Atrial fibrillation, Cardiac failure congestive, Cardiac pacemaker insertion, Irritable bowel syndrome, Depression, Oedema, Nasal dryness, Amyloidosis senile				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 607			
Concomitant Medication [3]: FINASTERIDE, APIXABAN, LISINOPRIL, LISINOPRIL, TAMSULOSIN, COLECALCIFEROL, METOPROLOL, FUROSEMIDE, VARICELLA ZOSTER VACCINE RGE (CHO), SODIUM CHLORIDE, SACUBITRIL/VALSARTAN, SPIRONOLACTONE, TORASEMIDE				
Non-Serious Adverse Event [4]: N-terminal prohormone brain natriuretic peptide increased, Urine albumin/creatinine ratio increased, Oedema peripheral				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
死亡	DEATH-NO FURTHER INFORMATION	Day 607 / Day 607	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「死亡」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: F	Age: 8[redacted]
Medical History [1]: Secondary hyperthyroidism, Intestinal obstruction, Spinal osteoarthritis, Parkinsonism, Postmenopause, Hypertension, Peripheral venous disease, Vertigo, Chronic gastritis, Hip arthroplasty, Hip arthroplasty, Atrial fibrillation, Type 2 diabetes mellitus, Urinary tract infection, Renal failure, Transurethral bladder resection, Cardiac amyloidosis, Hypertonic bladder				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 700		
Concomitant Medication [3]: OMEPRAZOLE, FUROSEMIDE, APIXABAN, BISOPROLOL, FOSFOMYCIN, SOLIFENACIN, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, CLAVULANIC ACID, CIPROFLOXACIN, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMOXICILLIN, LACTULOSE, FOSFOMYCIN, CARBOHYDRATES NOS/MINERALS NOS/PROTEINS NOS/VITAMINS NOS, CIPROFLOXACIN, FUROSEMIDE, FUROSEMIDE, MIRTAZAPINE, PANTOPRAZOLE, ALBUMIN HUMAN, FUROSEMIDE, FUROSEMIDE, NYSTATIN, BEMIPARIN SODIUM, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, POTASSIUM CHLORIDE, FUROSEMIDE, MIDAZOLAM, NYSTATIN, BETAINE/CALCIUM LACTATE/CARBOMER/DEXPANTHENOL/GLYCEROL/OLEA EUROPAEA OIL/PETROSELINUM CRISPUM OIL/TOCOPHERYL ACID SUCCINATE/XYLITOL, NYSTATIN, APIXABAN, MIRTAZAPINE, OMEPRAZOLE, ASCORBIC ACID/POTASSIUM BICARBONATE, BISOPROLOL, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, MIRTAZAPINE, COLCHICINE, ALLOPURINOL, COLCHICINE, FUROSEMIDE, BROMAZEPAM, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, MIRTAZAPINE, PANTOPRAZOLE, GENTAMICIN, CEPHALOSPORIN NOS, FUROSEMIDE, OMEPRAZOLE, POTASSIUM CHLORIDE, BISOPROLOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, FUROSEMIDE, OMEPRAZOLE, FUROSEMIDE, METOCLOPRAMIDE, FUROSEMIDE, PANTOPRAZOLE, ALLOPURINOL, COLCHICINE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, OMEPRAZOLE, CEPHALOSPORIN NOS, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, METAMIZOLE, CEPHALOSPORIN NOS, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, ASPARTIC ACID/POTASSIUM ASCORBATE, BROMAZEPAM, POTASSIUM CHLORIDE, NYSTATIN, HYDROCORTISONE/MICONAZOLE, MIRTAZAPINE, HYDROCORTISONE/MICONAZOLE, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE				
Non-Serious Adverse Event [4]: Anal fissure, Oedema peripheral, Cardiac failure chronic, Cardiac failure chronic, Urethral syndrome, Weight decreased, Constipation, Cardiac failure, Restless legs syndrome, Nervousness, Gout, Gout, Gout, Urinary tract infection, Haemorrhoids, Arthralgia, Oral candidiasis, Vulvovaginal erythema, Dysphagia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 182 / Day 189	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	DESCOMPENSATED HEART FAILURE	Day 419 / Day 424	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（3）	DESCOMPENSATED HEART FAILURE	Day 453 / Day 459	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

心不全（4）	DESCOMPENSATED HEART FAILURE	Day 495 / Day 498	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（5）	CARDIAC INSUFFICIENCY	Day 691 / Day 735	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」、「心不全（4）」及び「心不全（5）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Cholecystectomy, Vertigo, Skin lesion removal, Blood cholesterol increased, Coronary artery bypass, Myocardial ischaemia, Gastrooesophageal reflux disease, Rheumatoid arthritis, Cardiac failure, Cardiac amyloidosis, Chronic kidney disease, Decreased appetite				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 567		
Concomitant Medication [3]: BETAHISTINE, LANSOPRAZOLE, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, SIMVASTATIN, METHOTREXATE, FOLIC ACID, BUMETANIDE, DOXYCYCLINE, BUMETANIDE, BUMETANIDE, MORPHINE SULFATE, ISOSORBIDE MONONITRATE, EDOXABAN, COVID-19 VACCINE, SPIRONOLACTONE, RANOLAZINE, SIMVASTATIN, PARAFFIN SOFT/PARAFFIN (LIQUID)				
Non-Serious Adverse Event [4]: Decreased appetite, Lower respiratory tract infection, Dyspnoea, Weight decreased, Headache, Atrial fibrillation, Angina pectoris, Angina pectoris, Urticaria, Cardiac failure, Fall				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性心不全	END STAGE HEART FAILURE	Day 567 / Day 577	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「慢性心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Prostatic operation, Inguinal hernia repair, Cardiac failure, Myocardial ischaemia, Hypercholesterolaemia, Hypertension, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 819		
Concomitant Medication [3]: LANSOPRAZOLE, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, ATORVASTATIN, BISOPROLOL, BUMETANIDE, COPPER SULFATE/FERROUS FUMARATE/FOLIC ACID/PYRIDOXINE HYDROCHLORIDE/VITAMIN B12 NOS/ZINC SULFATE, BUMETANIDE, RAMIPRIL, CANDESARTAN, BISOPROLOL, SPIRONOLACTONE, VITAMIN B COMPLEX, OTHER LIPID MODIFYING AGENTS, ANTIMALARIALS, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, GABAPENTIN, APIXABAN				
Non-Serious Adverse Event [4]: Dyspnoea, Cardiac failure, Pain in extremity, Abdominal distension, Constipation, Erectile dysfunction, Dizziness postural, Non-cardiac chest pain, Pain in extremity, Atrial fibrillation, Blood creatine phosphokinase increased				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	COVID-19 PNEUMONIA	Day 734 / Day 769	Not Related	Drug Interrupted	Recovered /Resolved	Severe
血栓症	EXTENSIVE SYSTEMIC THROMBUS	Day 820 / Day 844	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」及び「血栓症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]	
Medical History [1]: Intervertebral disc operation, Dyslipidaemia, Hypertension, Benign prostatic hyperplasia, Pulmonary embolism, Intervertebral disc degeneration, Carpal tunnel syndrome, Atrial fibrillation, Parkinson's disease, Cardiac failure chronic, Amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 468			
Concomitant Medication [3]: ENALAPRIL, SIMVASTATIN, ACENOCOUMAROL, TAMSULOSIN, SOLIFENACIN SUCCINATE, CARBIDOPA, LEVODOPA, GABAPENTIN, EPLERENONE, FUROSEMIDE, FOSFOMYCIN, ENALAPRIL, ENALAPRIL, ALLOPURINOL, COVID-19 VACCINE, FUROSEMIDE, COVID-19 VACCINE, ENALAPRIL, FUROSEMIDE, CETIRIZINE, PREDNISONE, PREDNISONE, ENALAPRIL					
Non-Serious Adverse Event [4]: Cardiac failure, Urticaria					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心停止	CARDIAC ARREST	Day 469 / Day 469	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心停止」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Prostatectomy, Hypertension, Hypogammaglobulinaemia, Selective IgA immunodeficiency, Lumbar spinal stenosis, Spondylolisthesis, Sleep apnoea syndrome, Haemochromatosis, Cardiac ablation, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis, Polymyalgia rheumatica				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 713		
Concomitant Medication [3]: ACENOCOUMAROL, BISOPROLOL, FUROSEMIDE, PREDNISONE, DISOPYRAMIDE, POTASSIUM CHLORIDE, SIMVASTATIN, ALLOPURINOL, LEVOFLOXACIN, PIROXICAM, FLUTICASONE FUROATE/VILANTEROL TRIFENATATE, CEFTRIAXONE, CHLORTALIDONE, PREDNISONE, PREDNISONE, EDOXABAN, PREDNISONE, FERRIC CARBOXYMALTOSE, AMIODARONE, BUDESONIDE/FORMOTEROL, BUDESONIDE, AMIODARONE, POTASSIUM, TRAZODONE, IPRATROPIUM BROMIDE/SALBUTAMOL SULFATE, DAPAGLIFLOZIN, INSULIN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Tooth infection, Post procedural infection, Large intestine polyp, Interstitial lung disease, Diabetes mellitus, Cardiac failure, Anaemia, Lymphopenia, Electrocardiogram QT prolonged, Urinary tract infection, Hiatus hernia, Type 2 diabetes mellitus				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING HEART FAILURE	Day 238 / Day 247	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	HEART FAILURE DECOMPENSATION	Day 475 / Day 479	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（3）	WORSENING HEART FAILURE	Day 565 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
メレナ	MALAENA	Day 571 / Day 578	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９肺炎	COVID-19 PNEUMONIA	Day 598 / Day 618	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（4）	REFRACTORY HEART FAILURE	Day 638 / Day 644	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」、「メレナ」、「ＣＯＶＩＤ－１９肺炎」及び「心不全（4）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]		
Medical History [1]: Barrett's oesophagus, Thalassaemia, Sleep apnoea syndrome, Retinopathy, Type 2 diabetes mellitus, Hypertension, Carotid endarterectomy, Basal cell carcinoma, Diarrhoea, Dizziness, Cardiac failure, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 810				
Concomitant Medication [3]: LINAGLIPTIN, RIVAROXABAN, ATORVASTATIN, ALLOPURINOL, ESOMEPRAZOLE, FUROSEMIDE, EPOETIN ALFA, GLYCERYL TRINITRATE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, LATANOPROST, FUROSEMIDE, EMPAGLIFLOZIN, TAMSULOSIN HYDROCHLORIDE, TAMSULOSIN, LORMETAZEPAM, IRON, TORASEMIDE, HYDROCHLOROTHIAZIDE						
Non-Serious Adverse Event [4]: Cataract, Glaucoma, Back pain, Benign prostatic hyperplasia, Insomnia, Renal impairment, Cardiac failure, Iron deficiency						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	HEART FAILURE	Day 722 / Day 729	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（2）	WORSENING HEART FAILURE	Day 811 / Day 811	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Glaucoma, Joint prosthesis user, Cardiac failure, Renal cyst, Pericarditis, Cardiac amyloidosis, Atrial fibrillation, Pleural effusion, Hyperuricaemia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 690			
Concomitant Medication [3]: LATANOPROST, ENALAPRIL, TORASEMIDE, OMEPRAZOLE, RIVAROXABAN, EPLERENONE, ALLOPURINOL, ENALAPRIL, FUROSEMIDE, TORASEMIDE, TORASEMIDE, VALSARTAN, SACUBITRIL, VALSARTAN, SACUBITRIL, VALSARTAN, SACUBITRIL, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, ENOXAPARIN, POTASSIUM CHLORIDE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, APIXABAN, DOBUTAMINE, ACETAZOLAMIDE, CALCIUM GLUCONATE, MAGNESIUM SULFATE, CALCIUM GLUCONATE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, SODIUM CHLORIDE, FUROSEMIDE, SPIRONOLACTONE, HYOSCINE BUTYLBROMIDE				
Non-Serious Adverse Event [4]: Cardiac failure, Decreased appetite, Pleural effusion, Ventricular tachycardia, Ascites, Hepatomegaly				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	HF DECOMPENSATION	Day 183 / Day 211	Not Related	Dose Not Changed	Recovered /Resolved	Severe
起立性低血圧	ORTHOSTATIC HYPOTENSION	Day 660 / Day 661	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
右室不全	RIGHT HEART FAILURE	Day 660 / Day 691	Not Related	Dose Not Changed	Fatal	Severe
心拍出量低下	LOW CARDIAC OUTPUT	Day 671 / Day 691	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全」、「起立性低血圧」、「右室不全」及び「心拍出量低下」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: F	Age: 7[redacted]
Medical History [1]: Bicuspid aortic valve, Drug hypersensitivity, Drug hypersensitivity, Drug hypersensitivity, Drug hypersensitivity, Hypercholesterolaemia, Obesity, Bronchostenosis, Angioedema, Menopause, Tonsillectomy, Encephalomyelitis rubella, Depression, Asthma, Thyroid operation, Carpal tunnel syndrome, Cholecystectomy, Lumbar spinal stenosis, Hypertension, Cardiac failure, Transient ischaemic attack, Cardiac amyloidosis, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 351		
Concomitant Medication [3]: LORAZEPAM, AMITRIPTYLINE, SALBUTAMOL, LEVOTHYROXINE, MONTELUKAST, TIOTROPIUM BROMIDE, FUROSEMIDE, FUROSEMIDE, RAMIPRIL, APIXABAN, AMIODARONE, FLUTICASONE/SALMETEROL, FUROSEMIDE, CETIRIZINE HYDROCHLORIDE, PARACETAMOL, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, MELATONIN, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Dyspnoea, Erythema, Osteoarthritis, Joint swelling, Dyspnoea, Insomnia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
房室ブロック	SYNPTOMATIC ATRIAL VENTRICULAR BLOCK	Day 169 / Day 173	Not Related	Dose Not Changed	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９肺炎	PNEUMONIA COVID 19	Day 342 / Day 352	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「房室ブロック」及び「ＣＯＶＩＤ－１９肺炎」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7■
Medical History [1]: Chronic kidney disease, Carpal tunnel syndrome, Inguinal hernia, Appendicectomy, Hypertension, Dyslipidaemia, Insomnia, Cataract, Spinal operation, Hypoacusis, Maculopathy, Sciatica, Rotator cuff repair, Cardiac failure, Benign prostatic hyperplasia, Pulmonary mass, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 671		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, OTHER OPHTHALMOLOGICALS, IVABRADINE, SPIRONOLACTONE, FUROSEMIDE, TAMSULOSIN, ALPROSTADIL, BEVACIZUMAB, SPIRONOLACTONE, FUROSEMIDE, MELATONIN/MELISSA OFFICINALIS/PASSIFLORA INCARNATA, DICLOFENAC, THIOCOLCHICOSIDE, FLUCONAZOLE, FENTICONAZOLE, BEVACIZUMAB, INFLUENZA VACCINE, BEVACIZUMAB, BEVACIZUMAB, ASCORBIC ACID/ERGOCALCIFEROL/FERRIC SODIUM PYROPHOSPHATE/MILK (FAT FREE)/NICOTINAMIDE/RETINOL PALMITATE/RIBOFLAVIN/THIAMINE HYDROCHLORIDE, PARACETAMOL, ACETYLCYSTEINE, COVID-19 VACCINE, DICLOFENAC, POTASSIUM CANRENOATE, FUROSEMIDE, LEVOFLOXACIN, SULFAMETHOXAZOLE/TRIMETHOPRIM, APIXABAN, ENOXAPARIN SODIUM, BISOPROLOL, APIXABAN, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, OXYGEN, FUROSEMIDE, METOLAZONE, METOLAZONE, INSULIN LISPRO				
Non-Serious Adverse Event [4]: Cardiac failure, Back pain, Fungal infection, Erectile dysfunction, Cardiac failure, Influenza, Cough, Back pain, Urinary tract infection, Atrial flutter, Anaemia, Cholelithiasis, Pulmonary mass, Diabetes mellitus, Hepatitis B				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
良性前立腺肥大症	WORSENING PROSTATIC HYPERTROPHY	Day 467 / Day 472	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（1）	WORSENING HEART FAILURE	Day 528 / Day 540	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Mild
心不全（2）	WORSENING HEART FAILURE	Day 540 / Day 678	Not Related	Dose Not Changed	Recovered /Resolved	Mild
肝不全	LIVER FAILURE	Day 669 / Day 678	Not Related	Drug Interrupted	Fatal	Severe

治験責任医師の見解：「良性前立腺肥大症」、「心不全（1）」、「心不全（2）」及び「肝不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Israel	Sex: M	Age: 8[redacted]
Medical History [1]: Inguinal hernia repair, Hypertension, Prostatectomy, Atrial fibrillation, Inguinal hernia repair, Retinal detachment, Hypercholesterolaemia, Abscess drainage, Appendicectomy, Diabetes mellitus, Varicose vein, Cataract operation, Cardiomyopathy, Pulmonary hypertension, Cardiac amyloidosis, Left ventricular failure, Atrial thrombosis, Adrenal disorder, Sleep disorder, Limb injury, Thoracic cavity drainage				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 79		
Concomitant Medication [3]: SPIRONOLACTONE, BISOPROLOL FUMARATE, APIXABAN, BROTIZOLAM, DOPAMINE, FUROSEMIDE, FUROSEMIDE, SODIUM POLYSTYRENE SULFONATE, SPIRONOLACTONE, GRAMICIDIN/NEOMYCIN SULFATE/NYSTATIN/TRIAMCINOLONE ACETONIDE				
Non-Serious Adverse Event [4]: Blood potassium increased				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心肺停止	CARDIAC AND RESPIRATORY ARREST	Day 80 / Day 80	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心肺停止」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■						
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 7■		
Medical History [1]: Carpal tunnel syndrome, Hypertension, Atrial fibrillation, Cardiac failure, Amyloidosis, Dyspnoea, Renal failure, Constipation						
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 568					
Concomitant Medication [3]: EPLERENONE, PARACETAMOL, FUROSEMIDE, WARFARIN, POTASSIUM, BENDROFLUMETHIAZIDE, POTASSIUM, FUROSEMIDE, MIRTAZAPINE, POTASSIUM, BENDROFLUMETHIAZIDE, MOMETASONE, METOLAZONE, HYDROXYZINE, CLOBETASOL, FEXOFENADINE HYDROCHLORIDE, AMIODARONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, CARVEDILOL, AMIODARONE, AMIODARONE, FUROSEMIDE, METOLAZONE, FUROSEMIDE						
Non-Serious Adverse Event [4]: Fatigue, Oedema peripheral, Cough, Depression, Hypervolaemia, Rash, Erysipelas, Ventricular tachycardia, Rash, Blood potassium increased						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性心不全（1）	HEART FAILURE END STAGE	Day 141 / Day 269	Not Related	Dose Not Changed	Recovered /Resolved	Severe
血液量増加症（1）	FLUID OVERLOAD	Day 251 / Day 257	Not Related	Dose Not Changed	Recovered /Resolved	Severe
血液量増加症（2）	FLUID OVERLOAD	Day 523 / Day 527	Not Related	Dose Not Changed	Recovered /Resolved	Severe
血液量増加症（3）	FLUID OVERLOAD	Day 538 / Day 543	Not Related	Dose Not Changed	Recovered /Resolved	Severe
慢性心不全（2）	WORSENING OF END STAGE HEARTFAILURE	Day 578 / Day 583	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「慢性心不全（1）」、「血液量増加症（1）」、「血液量増加症（2）」、「血液量増加症（3）」及び「慢性心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertension, Pleural effusion, Vitamin D deficiency, Gouty arthritis, Amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 611			
Concomitant Medication [3]: POTASSIUM CHLORIDE, FUROSEMIDE, ENALAPRIL MALEATE, PARACETAMOL, VITAMIN D NOS, SPIRONOLACTONE, RIVAROXABAN, METOPROLOL, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, BENDROFLUMETHIAZIDE, SODIUM BICARBONATE, PROBENECID, AMIODARONE HYDROCHLORIDE, COLCHICINE, AMIODARONE, ATORVASTATIN, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, LIDOCAINE, MEXILETINE, AMIODARONE HYDROCHLORIDE, AMIODARONE, METOPROLOL, AMIODARONE HYDROCHLORIDE, AMIODARONE HYDROCHLORIDE				
Non-Serious Adverse Event [4]: Atrial fibrillation, Renal impairment, Hypervolaemia, Ascites, Gout, Coronary artery disease, Blood potassium decreased, Hypotension, Ventricular tachycardia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胸水	PLEURAL EXUDATE	Day 274 / Day 277	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心室性頻脈（1）	VENTRICULAR TACHYCARDIA	Day 312 / Day 319	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心室性頻脈（2）	VENTRICULAR TACHYCARDIA	Day 493 / Day 497	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心室性頻脈（3）	VENTRICULAR TACHYCARDIA	Day 499 / Day 512	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房細動	RAPID ATRIAL FIBRILLATION	Day 542 / Day 547	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心停止	CARDIAC ARREST	Day 611 / Day 611	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「胸水」、「心室性頻脈（1）」、「心室性頻脈（2）」、「心室性頻脈（3）」、「心房細動」及び「心停止」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Placebo		Race: Not reported		Country: Netherlands	Sex: M	Age: 8[redacted]
Medical History [1]: Trifascicular block, Hip arthroplasty, Cardiac failure, Cardiac amyloidosis, Pulmonary embolism						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 277			
Concomitant Medication [3]: SPIRONOLACTONE, CANDESARTAN, BISOPROLOL, RIVAROXABAN, BUPRENORPHINE						
Non-Serious Adverse Event [4]: Daydreaming, COVID-19, Fall						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
頭部損傷	TRAUMA CAPITIS	Day 206 / Day 213	Not Related	Dose Not Changed	Recovered /Resolved	Severe
安楽死	EUTHANASIA	Day 277 / Day 277	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「頭部損傷」及び「安楽死」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: Not reported	Country: Netherlands	Sex: M	Age: 8[redacted]	
Medical History [1]: Atrial fibrillation, Fibromyalgia, Parkinsonism, Transurethral prostatectomy, Cardiac failure, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 666				
Concomitant Medication [3]: APIXABAN, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, CARBIDOPA MONOHYDRATE/LEVODOPA, BUMETANIDE, OMEPRAZOLE, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, COVID-19 VACCINE, COVID-19 VACCINE, MELOXICAM, LIDOCAINE HYDROCHLORIDE/METHYLPREDNISOLONE ACETATE, Not coded: Tafamidis, TAFAMIDIS, BUMETANIDE, OXYCODONE					
Non-Serious Adverse Event [4]: Arthralgia, Pain in extremity					

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
疾患進行	DECEASED AFTER PALLIATIVE CARE FOR DISEASE PROGRESSION	Day 666 / Day 675	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「疾患進行」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Hypercholesterolaemia, Osteoarthritis, Ex-tobacco user, Meniscus removal, Carpal tunnel decompression, Cardioversion, Atrial fibrillation, Knee arthroplasty, Cryotherapy, Carpal tunnel syndrome, Carpal tunnel decompression, Cardiac amyloidosis, Depression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 836		
Concomitant Medication [3]: RAMIPRIL, ATORVASTATIN, APIXABAN, CITALOPRAM, FUROSEMIDE, SERTRALINE, LEVOTHYROXINE, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, TAMSULOSIN, BUMETANIDE, FLUCLOXACILLIN, ANESTHETICS (LOCAL), APIXABAN, EPLERENONE, LEVOTHYROXINE, EPLERENONE, POTASSIUM, IRON, APIXABAN, EPLERENONE, EPLERENONE, BUMETANIDE, BUMETANIDE, BUMETANIDE, METOLAZONE, DOCUSATE SODIUM, DAPAGLIFLOZIN, BUMETANIDE, FUROSEMIDE, METOLAZONE, POTASSIUM, POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Hypothyroidism, Atrial fibrillation, Cardiac failure, Benign prostatic hyperplasia, Hypokalaemia, Iron deficiency, Acute kidney injury, Constipation, Fall, Eosinophilia, Blood glucose increased, Hypokalaemia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
三束ブロック	TRIFASCICULAR BLOCK	Day 649 / Day 655	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（1）	WORSENING HEART FAILURE	NA / Start Day + 19 Days	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
心不全（2）	WORSENING HEART FAILURE	Day 741 / Day 794	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全（3）	HEART FAILURE	Day 836 / Day 836	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「三束ブロック」、「心不全（1）」、「心不全（2）」及び「心不全（3）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: UK	Sex: M	Age: 6[redacted]
Medical History [1]: Anaemia, Hypercholesterolaemia, Umbilical hernia repair, Type 2 diabetes mellitus, Angina pectoris, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 875		
Concomitant Medication [3]: LANSOPRAZOLE, FERROUS SULFATE, ACETYLSALICYLIC ACID, ATORVASTATIN, LOSARTAN, BISOPROLOL, EPLERENONE, FUROSEMIDE, APIXABAN, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, COVID-19 VACCINE, ANESTHETICS (LOCAL), EPLERENONE, DAPAGLIFLOZIN, RAMIPRIL, BISOPROLOL, SACUBITRIL, BUMETANIDE, FUROSEMIDE, ANESTHETICS (LOCAL), BUMETANIDE, CHLORTALIDONE, METARAMINOL, BUMETANIDE, COLECALCIFEROL, AMOXICILLIN				
Non-Serious Adverse Event [4]: Syncope, Atrial fibrillation, Syncope, Dysphagia, Gastritis, Arthralgia, Cardiac failure congestive, COVID-19, Gout, Vitamin D deficiency, Renal impairment, Cardiac failure, Urinary tract infection, Syncope				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 72 / Day 73	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 348 / Day 388	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心腎症候群	CARDIORENAL SYNDROME	NA / Start Day + 51 Days	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」及び「心腎症候群」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 8■
Medical History [1]: Vertigo, Hypothyroidism, Hypercholesterolaemia, Restless legs syndrome, Chronic kidney disease, Dry skin, Hypertension, Atrial fibrillation, Haemochromatosis, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 339		
Concomitant Medication [3]: PROCHLORPERAZINE, LANSOPRAZOLE, RAMIPRIL, RAMIPRIL, SPIRONOLACTONE, BUMETANIDE, PARAFFIN SOFT/PARAFFIN (LIQUID), QUININE SULFATE, BECLOMETASONE DIPROPIONATE, LEVOTHYROXINE, WARFARIN, ATORVASTATIN, BUMETANIDE, BUMETANIDE, BENDROFLUMETHIAZIDE, CYCLIZINE, BUMETANIDE, FUROSEMIDE, ANESTHETICS (LOCAL), FUROSEMIDE, METOLAZONE, METOLAZONE, I.V. SOLUTIONS				
Non-Serious Adverse Event [4]: Nausea, Arrhythmia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 241 / Day 264	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全（2）	WORSENING HEART FAILURE	Day 273 / Day 280	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全（3）	WORSENING HEART FAILURE	Day 299 / Day 308	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
うっ血性心不全	CONGESTIVE HEART FAILURE	Day 339 / Day 339	Not Related	Drug Interrupted	Fatal	Severe

治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」及び「うっ血性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Placebo		Race: White		Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Drug hypersensitivity, Hypercholesterolaemia, Chronic kidney disease, Hypertension, Knee arthroplasty, Type 2 diabetes mellitus, Knee arthroplasty, Cardiac pacemaker removal, Carpal tunnel syndrome, Gout, Carpal tunnel decompression, Deep vein thrombosis, Cardiac pacemaker removal, Implantable defibrillator insertion, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 273			
Concomitant Medication [3]: PRAVASTATIN, EPLERENONE, FUROSEMIDE, COLCHICINE, METFORMIN, WARFARIN, SACUBITRIL/VALSARTAN, SACUBITRIL/VALSARTAN, BUMETANIDE, BUMETANIDE, FUROSEMIDE						
Non-Serious Adverse Event [4]: No event						
Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心腎症候群（1）	CARDIORENAL SYNDROME	Day 252 / Day 259	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
心腎症候群（2）	CARDIORENAL SYNDROME	Day 273 / Day 282	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「心腎症候群（1）」及び「心腎症候群（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Chronic kidney disease, Parotitis, Carpal tunnel decompression, Carpal tunnel decompression, Benign prostatic hyperplasia, Spinal decompression, Acute myocardial infarction, Atrial fibrillation, Cardiac amyloidosis, Myalgia					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 739			
Concomitant Medication [3]: FUROSEMIDE, ALFUZOSIN, FINASTERIDE, LANSOPRAZOLE, APIXABAN, BISOPROLOL, EPLERENONE, ATORVASTATIN, PARACETAMOL, COLECALCIFEROL, ATORVASTATIN, COVID-19 VACCINE, COVID-19 VACCINE, FOLIC ACID					
Non-Serious Adverse Event [4]: Muscle atrophy, Folate deficiency, Vitreous haemorrhage					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心筋梗塞	MYOCARDIAL INFARCTION	Day 739 / Day 739	Not Related	Dose Not Changed	Fatal	Severe
治験責任医師の見解：「心筋梗塞」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: F	Age: 9[redacted]
Medical History [1]: Menopause, Sinus node dysfunction, Cardiac pacemaker insertion, Hyperlipidaemia, Hypertension, Cardiac failure, Cardiac amyloidosis, Diabetes mellitus, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 579		
Concomitant Medication [3]: SPIRONOLACTONE, PERINDOPRIL, TORASEMIDE, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN, COVID-19 VACCINE, INFLUENZA VACCINE, Not coded: Tafamidis, TAFAMIDIS, FLUCLOXACILLIN, PARACETAMOL, DAPAGLIFLOZIN, METHYLPREDNISOLONE, COLCHICINE, ALIZAPRIDE HYDROCHLORIDE, AMIKACIN, AMOXICILLIN, PARACETAMOL				
Non-Serious Adverse Event [4]: Hyperkalaemia, Cardiac failure, Erysipelas, Blood bicarbonate increased, Hyperkalaemia, Varicose vein, Erysipelas, COVID-19, Peripheral venous disease, Gout, Troponin increased				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腹部敗血症	ABDOMINAL SEPSIS	Day 579 / Day 580	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「腹部敗血症」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 8[redacted]	
Medical History [1]: Hyperuricaemia, Iron deficiency, Benign prostatic hyperplasia, Pleural effusion, Dyslipidaemia, Type 2 diabetes mellitus, Hypertension, Chronic kidney disease, Glaucoma, Pulmonary mass, Cardiac amyloidosis, Cardiac failure, Atrial fibrillation					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 148			
Concomitant Medication [3]: LATANOPROST, FEBUXOSTAT, POTASSIUM, LINAGLIPTIN, INSULIN GLARGINE, CHLORTALIDONE, INSULIN LISPRO, EDOXABAN, IVABRADINE, AMIODARONE, FUROSEMIDE, CHLORTALIDONE, EPLERENONE, LORAZEPAM, CHLORTALIDONE, LORAZEPAM, INSULIN GLARGINE, INSULIN ASPART, INSULIN GLARGINE, MAGNESIUM, POTASSIUM, POTASSIUM, EPLERENONE, FUROSEMIDE, FUROSEMIDE, CHLORTALIDONE					
Non-Serious Adverse Event [4]: Insomnia					
Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENINF HEART FAILURE	Day 147 / Day 150	Not Related	Drug Interrupted	Fatal	Severe
治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Atrial fibrillation, Dyspepsia, Aortic stenosis, Gastrooesophageal reflux disease, Dyslipidaemia, Gout, Haemothorax, Type 2 diabetes mellitus, Pleural effusion, Benign prostatic hyperplasia, Knee arthroplasty, Normocytic anaemia, Osteoarthritis, Dyspnoea, Cardiac failure, Tracheostomy, Amyloidosis senile, Insomnia, Chronic kidney disease, Anxiety, Chronic obstructive pulmonary disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 222		
Concomitant Medication [3]: HALOPERIDOL, QUETIAPINE, BISOPROLOL, PANTOPRAZOLE, CALCIFEDIOL, FUROSEMIDE, FENTANYL, INDACATEROL, GLYCOPYRRONIUM, ACETYLSALICYLIC ACID, DIAZEPAM, PARACETAMOL, METAMIZOLE, AMLODIPINE, VALSARTAN, IRON, VALSARTAN, FUROSEMIDE, CHLORTALIDONE, CHLORTALIDONE, OMEPRAZOLE, ENOXAPARIN SODIUM, FUROSEMIDE				
Non-Serious Adverse Event [4]: Post procedural haemorrhage, Post procedural haemorrhage, COVID-19, Hypertensive crisis, Post procedural haemorrhage, Cardiac failure, Nephropathy, Device related infection, Asthenia, Urinary tract infection, Confusional state				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	PNEUMONIA DUE TO COVID 19 INFECTION	Day 90 / Day 91	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心腎症候群	CARDIORENAL	Day 222 / Day 225	Not Related	Drug Withdrawn	Fatal	Severe

治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」及び「心腎症候群」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]	
Medical History [1]: Osteoarthritis, Diabetes mellitus, Dyslipidaemia, Hypertension, Atrial fibrillation, Nausea, Cardiac failure, Arthralgia, Cardiac amyloidosis, Vertigo					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 162				
Concomitant Medication [3]: METFORMIN, VILDAGLIPTIN, VALSARTAN, SACUBITRIL, FUROSEMIDE, ATORVASTATIN, BETAHISTINE HYDROCHLORIDE, RIVAROXABAN, BISOPROLOL, BISOPROLOL, PANTOPRAZOLE, INSULIN, INSULIN GLARGINE, AZITHROMYCIN, CEFTRIAXONE, ENOXAPARIN SODIUM, BISOPROLOL, PARACETAMOL, DEXAMETHASONE					
Non-Serious Adverse Event [4]: No event					

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	PNEUMONIA DUE TO COVID-19	Day 162 / Day 169	Not Related	Drug Interrupted	Fatal	Severe

治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Angiopathy, Type 2 diabetes mellitus, Carpal tunnel decompression, Carpal tunnel decompression, Sciatica, Coronary angioplasty, Coronary arterial stent insertion, Hypercholesterolaemia, Myocardial ischaemia, Hypertension, Herpes zoster, Post herpetic neuralgia, Restless legs syndrome, Renal impairment, Knee arthroplasty, Herpes zoster, Gastrooesophageal reflux disease, Chronic obstructive pulmonary disease, Cardiac amyloidosis, Intraocular lens implant, Cataract, Cardiac failure, Cataract, Intraocular lens implant, Pleural effusion				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 599			
Concomitant Medication [3]: LINAGLIPTIN, LORATADINE, ACETYLSALICYLIC ACID, EZETIMIBE, GLYCERYL TRINITRATE, BUDESONIDE/FORMOTEROL FUMARATE, TIOTROPIUM BROMIDE, ESOMEPRAZOLE SODIUM, INSULIN ASPART/INSULIN DEGLUDEC, CHLORAMPHENICOL, SPIRONOLACTONE, FUROSEMIDE, PREGABALIN, SPIRONOLACTONE, SPIRONOLACTONE, INSULIN ASPART, INSULIN ASPART, INSULIN ASPART/INSULIN DEGLUDEC, INSULIN ASPART/INSULIN DEGLUDEC, SPIRONOLACTONE, FUROSEMIDE, ISOSORBIDE MONONITRATE, INSULIN ASPART, INSULIN ASPART/INSULIN DEGLUDEC, PREGABALIN, INFLUENZA VACCINE, CLONAZEPAM, CLONAZEPAM, ENOXAPARIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, MAGNESIUM ASPARTATE, PRAMIPEXOLE, LACTULOSE, FUROSEMIDE, ALLOPURINOL, TEMAZEPAM, CLONAZEPAM, PRAMIPEXOLE, CARBIDOPA/LEVODOPA, MAGNESIUM, CLONAZEPAM, LACTITOL/PLANTAGO INDICA, LACTULOSE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, DOMPERIDONE, CLONAZEPAM, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, ALLOPURINOL, EMPAGLIFLOZIN, FUROSEMIDE, FUROSEMIDE, CARBIDOPA/LEVODOPA, PRAMIPEXOLE, MIRTAZAPINE				
Non-Serious Adverse Event [4]: Hypervolaemia, Neuralgia, Restless legs syndrome, Constipation, Blood uric acid increased, Insomnia, Parkinson's disease, Parkinson's disease, Vibration test abnormal, Areflexia, Restless legs syndrome				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
下肢静止不能症候群（1）	WORSENING OF RESTLESS LEG SYNDROME	Day 155 / Day 159	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
パーキンソン病（1）	WORSENING OF PARKINSONS DISEASE WITH INCREASING BRADYKINESIA	Day 165 / Day 192	Not Related	Dose Not Changed	Recovered /Resolved	Mild
便秘	CONSTIPATION (MILD FAECAL LOADING)	Day 313 / Day 328	Not Related	Dose Not Changed	Recovered /Resolved	Mild
血液量増加症	FLUID OVERLOAD	Day 370 / Day 375	Not Related	Dose Not Changed	Recovered /Resolved	Mild

下肢静止不能症候群（2）	WORSENING OF RESTLESS LEG SYNDROME	Day 454 / Day 460	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
パーキンソン病（2）	WORSENING PARKINSON'S DISEASE	Day 587 / Day 606	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「下肢静止不能症候群（1）」、「パーキンソン病（1）」、「便秘」、「血液量増加症」、「下肢静止不能症候群（2）」及び「パーキンソン病（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Neuropathy peripheral, Epistaxis, Limb injury, Atrial fibrillation, Gastritis, Insomnia, Liver function test abnormal, Atrial enlargement, Coronary artery stenosis, Pericardial effusion, Pleural effusion, Iron deficiency anaemia, Proteinuria, Electrocardiogram abnormal, Left ventricular dysfunction, Cardiac amyloidosis, Osteoarthritis, Scoliosis, Nausea				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 722		
Concomitant Medication [3]: ESOMEPRAZOLE, VALSARTAN, BISOPROLOL, SACUBITRIL, ROSUVASTATIN, APIXABAN, DOMPERIDONE, FUROSEMIDE, BISOPROLOL, VALSARTAN, VALSARTAN, SACUBITRIL, SACUBITRIL, ESOMEPRAZOLE, MOMETASONE FUROATE, PROBIOTICS NOS, ESOMEPRAZOLE, APIXABAN, BISOPROLOL, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE, FUROSEMIDE, DOCUSATE SODIUM/SENNOSIDE B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, ESOMEPRAZOLE, MAGNESIUM, COVID-19 VACCINE, MAGNESIUM SULFATE, FUROSEMIDE, TEMAZEPAM, POTASSIUM CHLORIDE, FUROSEMIDE, PARACETAMOL, ONDANSETRON, METOCLOPRAMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, POTASSIUM CHLORIDE, METOLAZONE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, COVID-19 VACCINE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, COVID-19 VACCINE, POTASSIUM, FUROSEMIDE, OXYCODONE, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, OXYCODONE, OXYCODONE, NALOXONE				
Non-Serious Adverse Event [4]: Renal impairment, Gastritis, Dysphagia, Cough, Constipation, Fluid retention, Hypokalaemia				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 428 / Day 453	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	DECOMPENSATED HEART FAILURE	Day 529 / Day 537	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
心不全（3）	DECOMPENSATED HEART FAILURE	Day 706 / Day 784	Not Related	Drug Withdrawn	Fatal	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」及び「心不全（3）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: New Zealand	Sex: M	Age: 6[redacted]
Medical History [1]: Hodgkin's disease, Gastrooesophageal reflux disease, Back pain, Insomnia, Hypothyroidism, Cardiac failure congestive, Aortic valve replacement, Anxiety, Depression, Dyslipidaemia, Gout, Rectal haemorrhage, Vitamin D deficiency, Type 2 diabetes mellitus, Acute myocardial infarction, Atrial flutter, Coronary artery disease, Constipation, Lip injury, Oropharyngeal pain, Cardiac ablation, Hypertension, Cardiac resynchronisation therapy, Cardiac amyloidosis, Orthostatic hypotension				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 782			
Concomitant Medication [3]: OMEPRAZOLE, PARACETAMOL, ZOPICLONE, LEVOTHYROXINE, FUROSEMIDE, QUETIAPINE, ROSUVASTATIN, ALLOPURINOL, VENLAFAXINE, LACTULOSE, COLECALCIFEROL, RIVAROXABAN, EZETIMIBE, FUROSEMIDE, MORPHINE, MIRTAZAPINE, VENLAFAXINE, ERYTHROMYCIN, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, MIRTAZAPINE, DOCUSATE SODIUM/SENNOSIDE A+B, SERTRALINE, LORAZEPAM, QUETIAPINE, SERTRALINE, ATORVASTATIN, SERTRALINE, MORPHINE, NYSTATIN, MORPHINE, LIDOCAINE HYDROCHLORIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, STOMATOLOGICAL PREPARATIONS, AMOXICILLIN/CLAVULANATE POTASSIUM, MORPHINE SULFATE, AMITRIPTYLINE, FUROSEMIDE, INFLUENZA VACCINE, ZOPICLONE, COVID-19 VACCINE, NYSTATIN, COVID-19 VACCINE, MAGNESIUM, MELATONIN, BUDESONIDE, FAMOTIDINE, ALLOPURINOL, MULTIVITAMINS (PLAIN), PENTOXIFYLLINE, MIRTAZAPINE, TEMAZEPAM, FERRIC CARBOXYMALTOSE, LEVOTHYROXINE, AMOXICILLIN, FUROSEMIDE, CALCIUM CARBONATE, MIRTAZAPINE, MORPHINE SULFATE, OMEPRAZOLE, MORPHINE, LEVOTHYROXINE				
Non-Serious Adverse Event [4]: Basal cell carcinoma, Anaemia, Fatigue, Stomatitis radiation, Nasopharyngitis, Oral candidiasis, Ventricular tachycardia, Dehydration, Blood magnesium decreased, Serum ferritin decreased, COVID-19, Lower respiratory tract infection, Nausea, Dehydration, Acute kidney injury, Oral candidiasis, Blood magnesium decreased, Pneumonia, COVID-19				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
扁桃癌	SQUARMOUS CELL CARCINOMA OF LEFT TONSIL	Day 37 / Day 157	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺炎	RIGHT LOWER LOBE PNEUMONIA REQUIRING HOSPITALISATION	Day 41 / Day 49	Not Related	Dose Not Changed	Recovered /Resolved	Severe
粘膜の炎症	MUCOCITIS THROAT PAIN	Day 212 / Day 218	Not Related	Dose Not Changed	Recovered /Resolved	Severe
浮動性めまい	DIZZINESS CAUSING HOSPITALISATION	Day 420 / Day 421	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Mild
不眠症	WORSENING INSOMNIA	Day 550 / Day 555	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

悪性胸水	PLEURAL EFFUSION SECONDARY TO CANCER	Day 725 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
遠隔転移を伴う扁桃癌（1）	METASTATIC LUNG LESION FROM THE TONSILLAR PRIMARY TUMOR	Day 730 / Day 839	Not Related	Drug Withdrawn	Fatal	Severe
遠隔転移を伴う扁桃癌（2）	HOSPITALIZATION FOR PROGRESSIVE METASTATIC TONSILLAR SQUAMOUS CELL CANCER WITH LUNG METASTASES	Day 757 / Day 760	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
譫妄	DELIRIUM CAUSING HOSPITALISATION	Day 787 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「扁桃癌」、「肺炎」、「粘膜の炎症」、「浮動性めまい」、「不眠症」、「悪性胸水」、「遠隔転移を伴う扁桃癌（1）」、「遠隔転移を伴う扁桃癌（2）」及び「譫妄」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Atrial fibrillation, Dyslipidaemia, Gout, Hypertension, Transurethral prostatectomy, Obesity, Benign prostatic hyperplasia, Inguinal hernia repair, Diverticulum, Osteoarthritis, Cervical radiculopathy, Carpal tunnel decompression, Finger repair operation, Tonsillectomy, Gastrooesophageal reflux disease, Inguinal hernia, Varicose vein, Type 2 diabetes mellitus, Pulmonary embolism, Right ventricular failure, Haemoglobin decreased, Cardiac amyloidosis, Skin ulcer				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 671		
Concomitant Medication [3]: ALLOPURINOL, WARFARIN, OMEPRAZOLE, PARACETAMOL, PREGABALIN, PREGABALIN, DIGOXIN, SPIRONOLACTONE, ROSUVASTATIN, FUROSEMIDE, METFORMIN, CANDESARTAN, BISOPROLOL, ONDANSETRON, OXYCODONE, PARACETAMOL, FENTANYL, CEFAZOLIN, FACTOR II (PROTHROMBIN)/FACTOR IX COMPLEX HUMAN/FACTOR VII (PROCONVERTIN)/FACTOR X (STUART PROWER FACTOR), VITAMIN K NOS, ENOXAPARIN SODIUM, ENOXAPARIN SODIUM, METARAMINOL, SUXAMETHONIUM, ROCURONIUM, FENTANYL, PROPOFOL, LIDOCAINE, ENOXAPARIN SODIUM, WARFARIN, FUROSEMIDE, DOCUSATE SODIUM/SENNOSIDE A+B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, LACTULOSE, TRAMADOL, ENOXAPARIN SODIUM, SODIUM PHOSPHATE DIBASIC/SODIUM PHOSPHATE MONOBASIC, CANDESARTAN, VITAMIN D NOS, FERROUS FUMARATE, RICINUS COMMUNIS OIL, MAGNESIUM, FUROSEMIDE, FUROSEMIDE, CEFALEXIN, FLUTICASONE PROPIONATE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, OXYCODONE HYDROCHLORIDE, CEFALEXIN, CORTISONE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, SALBUTAMOL, FERRIC CARBOXYMALTOSE				
Non-Serious Adverse Event [4]: Skin ulcer, Nausea, Hypotension, Constipation, Musculoskeletal discomfort, Muscle spasms, Pollakiuria, Oedema, Proteinuria, Hypoaesthesia, Inguinal hernia, Abdominal pain lower, Skin laceration, Non-cardiac chest pain, Dyspnoea, Lower respiratory tract infection, Inguinal hernia, Arthralgia, Headache, Arthralgia, Constipation, Localised infection, Wound, Syncope, Dyspnoea exertional, Neck pain, Scrotal swelling, Venous pressure jugular increased, Amnesia, Dizziness, COVID-19, Dyspnoea, Constipation, Blood iron decreased, Skin abrasion, Skin ulcer, Chest pain				

Adverse Event Leading to Fatal Outcome/Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼠径ヘルニア	WORSENING OF RIGHT INGUINAL HERNIA.	Day 20 / Day 29	Not Related	Drug Interrupted	Recovered /Resolved	Severe
処置後血腫	POST PROCEDURAL HAEMATOMA RIGHT GROIN	Day 23 / Day 93	Not Related	Dose Not Changed	Recovered /Resolved	Severe
静脈瘤破裂	RUPTURED VARICOSE VEIN L) LEG	Day 431 / Day 431	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
右室不全	WORSENING RIGHT SIDED HEART FAILURE	Day 672 / Day 672	Not Related	NA	Fatal	Severe

治験責任医師の見解：「鼠径ヘルニア」、「処置後血腫」、「静脈瘤破裂」及び「右室不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: F	Age: 8[redacted]
Medical History [1]: Amenorrhoea, Hysterectomy, Intestinal obstruction, Intestinal operation, Anaemia, Gastrooesophageal reflux disease, Vitamin D deficiency, Corneal oedema, Vitamin B12 deficiency, Dyspnoea, Cardiac amyloidosis, Decreased appetite, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 352		
Concomitant Medication [3]: PANTOPRAZOLE, VITAMIN B12 NOS, COLECALCIFEROL, SODIUM CHLORIDE, FUROSEMIDE, APIXABAN, AMIODARONE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, AMIODARONE, PANTOPRAZOLE, SPIRONOLACTONE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, LEVOTHYROXINE SODIUM, FUROSEMIDE, ENOXAPARIN, WARFARIN, POTASSIUM CHLORIDE, VITAMIN K NOS, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, HYDROCHLOROTHIAZIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, PARACETAMOL, HYDROMORPHONE				
Non-Serious Adverse Event [4]: Ear pain, Swelling, Cognitive disorder, Anxiety, Dyspnoea, Localised oedema, Oedema peripheral, Abdominal tenderness, Oedema peripheral, Blood thyroid stimulating hormone increased, Transferrin saturation decreased, Venous pressure jugular increased, Renal function test abnormal, Taste disorder, Skin discolouration, Renal impairment, Fatigue, Oedema peripheral, Dyspnoea, Dyspnoea, N-terminal prohormone brain natriuretic peptide increased, Fall, Skin laceration				

Adverse Event Leading to Fatal Outcome (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	Day 303 / Day 356	Not Related	Drug Interrupted	Fatal	Severe
末期腎疾患	END STAGE RENAL FAILURE	Day 348 / Day 356	Not Related	Dose Not Changed	Fatal	Severe

治験責任医師の見解：「心不全」及び「末期腎疾患」は治験薬と関連なしと判断した。

9.3.2. その他の重篤な有害事象の詳細

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Shoulder arthroplasty, Hypertension, Squamous cell carcinoma, Neoplasm skin, Neck pain, Atrial fibrillation, Chronic kidney disease, Insomnia, Palpitations, Gastrooesophageal reflux disease, Chronic left ventricular failure, Benign prostatic hyperplasia, Pulmonary embolism, Angiocardiogram, Biopsy heart, Catheterisation cardiac, Catheterisation cardiac, Cardiac amyloidosis, Polymyalgia rheumatica, Implantable defibrillator insertion, Neuropathy peripheral, Cataract				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 893		
Concomitant Medication [3]: OMEPRAZOLE, DIPHENHYDRAMINE, PREDNISONE, APIXABAN, PREDNISONE, POTASSIUM CHLORIDE, TORASEMIDE, SODIUM CHLORIDE, CARVEDILOL, AMIODARONE, CARVEDILOL, AMIODARONE, AMIODARONE, ONDANSETRON, SENNA ALEXANDRINA, BISACODYL, OXYCODONE, PARACETAMOL, LIDOCAINE, MELATONIN, APIXABAN, APIXABAN, DICLOFENAC, HYDROMORPHONE, MAGNESIUM HYDROXIDE, HYDROMORPHONE, PARACETAMOL, OMEPRAZOLE, PREDNISONE, PREDNISONE, APIXABAN, TORASEMIDE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, ADENOSINE, ADENOSINE, TERBINAFINE HYDROCHLORIDE, MINERAL OIL LIGHT/PARAFFIN/PETROLATUM/WOOL ALCOHOLS, PREDNISONE, PREDNISONE, PREDNISONE, POTASSIUM CHLORIDE, TORASEMIDE, PREDNISONE, PREDNISONE, FUROSEMIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, CEFALEXIN, PREDNISONE, SPIRONOLACTONE, ALLOPURINOL, TORASEMIDE, TORASEMIDE, PREDNISONE, ALLOPURINOL, SPIRONOLACTONE, PROPOFOL, TORASEMIDE, COVID-19 VACCINE, TORASEMIDE, COVID-19 VACCINE, TORASEMIDE, TORASEMIDE, METOLAZONE, TORASEMIDE, IRON DEXTRAN, LEVOTHYROXINE, TORASEMIDE, AMIODARONE, HEPARIN, FUROSEMIDE, LIDOCAINE, PROTAMINE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, SPIRONOLACTONE, CEFALEXIN, VANCOMYCIN HYDROCHLORIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, VANCOMYCIN HYDROCHLORIDE, AMOXICILLIN, DOXYCYCLINE MONOHYDRATE, LEVOTHYROXINE, OMEPRAZOLE, POTASSIUM CHLORIDE, TORASEMIDE, LEVOTHYROXINE				
Non-Serious Adverse Event [4]: Liver function test increased, Fall, Musculoskeletal chest pain, Skin ulcer, Oedema peripheral, Gout, Leukocytosis, Atrial tachycardia, Acute kidney injury, Skin ulcer, Pain in extremity, Atrial tachycardia, Tachycardia, Atrial tachycardia, Hypothyroidism, Acute kidney injury, Iron deficiency anaemia, Atrial tachycardia, Cardiac ablation, Acute kidney injury, Peripheral arterial occlusive disease, Peripheral artery occlusion				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING PAROXYSMAL ATRIAL FIBRILLATION	Day 84 / Day 86	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肋骨骨折	BROKEN RIBS	Day 171 / Day 357	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	DECOMPENSATED HEART FAILURE	Day 418 / Day 421	Not Related	Drug Interrupted	Recovered /Resolved	Severe
急性心不全	ACUTE CONGESTIVE HEART FAILURE	Day 425 / Day 434	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心腎症候群	CARDIORENAL SYNDROME	Day 475 / Day 476	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

心房頻脈	ATRIAL TACHYCARDIA	Day 671 / Day 673	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
蜂巣炎	CELLULITIS OF LEFT ANTERIOR LOWER LEG	Day 804 / Day 813	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房細動」、「肋骨骨折」、「心不全」、「急性心不全」、「心腎症候群」、「心房頻脈」及び「蜂巣炎」は治験薬と関連なしと判断した。						

F = female; IMP = Investigational Medicinal Product; M = male; MedDRA = Medical Dictionary for Regulatory Activities; NA = Not Available/Not Applicable; UK = United Kingdom; US = United States; WHO = World Health Organization.

[1] Medical conditions coded using MedDRA version 24.1.

[2] Day of first dose of study drug is Day 1. Study days to last dose of IMP are calculated as (date of last dose of IMP- date of first dose of IMP) +1.

[3] Concomitant medications are those taken on or after the day of initiation of IMP, including those started prior to IMP and continued past initiation of IMP. Medications coded using WHO Drug Dictionary 2022SEP01. Medication is preferred name.

[4] Preferred term coded using MedDRA version 24.1.

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Pilonidal sinus repair, Myelodysplastic syndrome, Hypercholesterolaemia, Hypertension, Ventricular tachycardia, Arthralgia, Myocardial infarction, Percutaneous coronary intervention, Thrombocytopenia, Gastrooesophageal reflux disease, Cardiac failure congestive, Cardiomyopathy, Aortic stenosis, Cardiac amyloidosis, Cardiac murmur				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: LOSARTAN, SIMVASTATIN, ACETYLSALICYLIC ACID, FUROSEMIDE, SPIRONOLACTONE, SPIRONOLACTONE, CEFALEXIN, VANCOMYCIN, ENOXAPARIN SODIUM, CEFTRIAXONE, SULFAMETHOXAZOLE/TRIMETHOPRIM, ACETYLSALICYLIC ACID, TRAMADOL, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, DEXAMETHASONE/TOBRAMYCIN, APIXABAN, APIXABAN, AMOXICILLIN, METOPROLOL, FUROSEMIDE				
Non-Serious Adverse Event [4]: Hypotension, Renal impairment, Atrial fibrillation, Hypervolaemia, Eye infection, Cellulitis, Chronic kidney disease, COVID-19, Post procedural haematoma, Hypervolaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
足関節部骨折	FRACTURED ANKLE	Day 62 / Day 122	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
蜂巣炎	CELLULITIS	Day 68 / Day 87	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「足関節部骨折」及び「蜂巣炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Not reported	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Tuberculosis, Gout, Hyperlipidaemia, Anxiety, Rotator cuff repair, Hypertension, Cardiac failure congestive, Helicobacter infection, Glucose tolerance impaired, Abdominal distension, Nocturia, Pollakiuria, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 747		
Concomitant Medication [3]: POTASSIUM CHLORIDE, ACETYLSALICYLIC ACID, BISOPROLOL, ALLOPURINOL, CITALOPRAM, METFORMIN HYDROCHLORIDE, TORASEMIDE, METFORMIN HYDROCHLORIDE, ALLOPURINOL, TORASEMIDE, TORASEMIDE, DAPAGLIFLOZIN, ZINC, ASCORBIC ACID, ACETYLCYSTEINE, MONTELUKAST, OMEPRAZOLE, VALSARTAN, FUROSEMIDE, PANTOPRAZOLE, MACROGOL, INSULIN, BENZOCAINE/MENTHOL, FUROSEMIDE, OXYCODONE, IPRATROPIUM, SENNA ALEXANDRINA, INSULIN, OTHER AGENTS FOR LOCAL ORAL TREATMENT, VANCOMYCIN, VALSARTAN, PARACETAMOL, LIDOCAINE, SALBUTAMOL, ACETYLSALICYLIC ACID, DOCUSATE SODIUM, LEVOFLOXACIN, HEPARIN, HYDROCORTISONE, INSULIN, TORASEMIDE, CAMPHOR/MENTHOL, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE				
Non-Serious Adverse Event [4]: Diarrhoea, Abdominal discomfort, Nausea, Fatigue, Dyspnoea, Muscle spasms, Chest injury, Fall, Hiatus hernia, Non-cardiac chest pain, Asthenia, Oedema peripheral, Atelectasis, Cough, Fall, Hypervolaemia, Oedema peripheral, Dyspnoea, SARS-CoV-2 test positive, Leukocytosis, Decreased appetite, Hypervolaemia, Pruritus, Aortic valve thickening, Mitral valve incompetence, Mitral valve thickening, Pulmonary valve incompetence, Tricuspid valve incompetence, Lung opacity, Pleural effusion, Pain, Weight decreased, Malnutrition, Lung disorder, Pneumothorax, Abdominal distension, Type 2 diabetes mellitus, Lymphadenopathy, Lymphadenopathy mediastinal, Aortic valve calcification, Arteriosclerosis coronary artery, Intra-abdominal fluid collection, Granulomatous liver disease, Pleural thickening, Pneumothorax, Pulmonary mass, Subcutaneous emphysema, Arteriosclerosis, Pulmonary oedema, Hyperkalaemia, Pain in extremity, Asthenia, Mobility decreased, Balance disorder, Rash, Respiratory failure, Respiratory failure, Cachexia, Facial wasting				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全（1）	ACUTE DECOMPENSATED HEART FAILURE	Day 619 / Day 622	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（2）	ACUTE DECOMPENSATED HEART FAILURE	Day 633 / Day 649	Not Related	Dose Not Changed	Recovered /Resolved	Severe
びまん性大細胞型Ｂ細胞性リンパ腫	HHV8-POSITIVE LARGE CELL LYMPHOMA	Day 635 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
胸膜炎	PLEURISY DUE TO PLEURAL DISEASE (NO FURTHER INFORMATION)	Day 675 / Day 678	Not Related	Dose Not Changed	Recovered /Resolved	Severe
酸素飽和度低下	LOW BLOOD OXYGEN SATURATION	Day 733 / NA	Not Related	Dose Not Changed	Unknown	Severe

治験責任医師の見解：「急性心不全（1）」、「急性心不全（2）」、「びまん性大細胞型Ｂ細胞性リンパ腫」、「胸膜炎」及び「酸素飽和度低下」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Appendicectomy, Hepatitis, Arthroscopy, Arthroscopy, Meniscus operation, Osteoarthritis, Knee arthroplasty, Carpal tunnel syndrome, Carpal tunnel decompression, Knee arthroplasty, Prostate cancer, Carpal tunnel syndrome, Carpal tunnel decompression, Atrioventricular block first degree, Obesity, Incisional hernia, Coronary artery disease, Dyslipidaemia, Hypertension, Rosacea, Erectile dysfunction, Trigger finger, Thrombocytopenia, Atrial fibrillation, Gilbert's syndrome, Memory impairment, Muscle spasms, Eructation, Amyloidosis senile, Bronchial hyperreactivity, Bundle branch block left, Ventricular extrasystoles, Cardiac failure congestive, Sleep apnoea syndrome				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 905		
Concomitant Medication [3]: VARDENAFIL HYDROCHLORIDE, MULTIVITAMINS (PLAIN), BUMETANIDE, ATORVASTATIN CALCIUM, LOSARTAN POTASSIUM, CARVEDILOL, SPIRONOLACTONE, IVERMECTIN, RIVAROXABAN, MAGNESIUM, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, SALBUTAMOL, AMOXICILLIN, RIVAROXABAN, SALBUTAMOL, AZITHROMYCIN, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, PREDNISONE, AZITHROMYCIN, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, SODIUM CHLORIDE, SODIUM CHLORIDE, METOPROLOL TARTRATE, LIDOCAINE, AMIODARONE, PROPOFOL, CARVEDILOL, AMIODARONE, AMIODARONE, SODIUM CHLORIDE, CEFAZOLIN, RIVAROXABAN, SODIUM CHLORIDE, PARACETAMOL, FENTANYL, BUPIVACAINE HYDROCHLORIDE, LIDOCAINE, CARVEDILOL, APIXABAN, CYCLOBENZAPRINE HYDROCHLORIDE, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN/CLAVULANATE POTASSIUM, CODEINE PHOSPHATE/GUAIFENESIN, BISACODYL, MACROGOL, MACROGOL 3350, CEFALEXIN, CEFAZOLIN, SODIUM CHLORIDE, GLUCOSE, SODIUM CHLORIDE, LIDOCAINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Eructation, Sleep apnoea syndrome, Chest discomfort, Tooth infection, Tooth fracture, Hypotension, Tooth socket haemorrhage, Cough, Upper respiratory tract infection, Haematuria, Muscle spasms, Atrial flutter, Chronic left ventricular failure, Burning sensation, Bradycardia, Sinus bradycardia, Chronic kidney disease, Fatigue, Muscle spasms, Acute sinusitis, Constipation, Cellulitis, Ventricular tachycardia, Chest discomfort, Dizziness, Headache				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
洞結節機能不全	SINUS NODE DYSFUNCTION	Day 359 / Day 360	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「洞結節機能不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Hyperlipidaemia, Obesity, Spinal stenosis, Otitis media chronic, Erectile dysfunction, Testicular mass, Sleep apnoea syndrome, Snoring, Colon adenoma, Deafness, Osteoarthritis, Seborrhoeic keratosis, Actinic keratosis, Photodermatosis, Hypertension, Carpal tunnel syndrome, Intervertebral disc protrusion, Cardiac amyloidosis, Cardiac failure congestive, Spinal laminectomy, Chronic kidney disease, Squamous cell carcinoma, Hypotension, Hyperglycaemia, Hyperuricaemia, Transient ischaemic attack, Atrial fibrillation, Constipation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, MENTHOL, WARFARIN SODIUM, AMIODARONE, ATORVASTATIN CALCIUM, FUROSEMIDE, FUROSEMIDE, LYSINE, AZITHROMYCIN, AZITHROMYCIN, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, LIDOCAINE, EPINEPHRINE, PARAFFIN, TRIAMCINOLONE, EPINEPHRINE, VORHYALURONIDASE ALFA, LIDOCAINE, BUPIVACAINE, MOXIFLOXACIN, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, VORHYALURONIDASE ALFA, FENTANYL, ROPIVACAINE, MIDAZOLAM, TIMOLOL, APRACLONIDINE HYDROCHLORIDE, EPINEPHRINE, CEFUROXIME, POVIDONE-IODINE, POVIDONE-IODINE, PREDNISOLONE ACETATE, DEXAMETHASONE/NEOMYCIN SULFATE/POLYMYXIN B SULFATE, BUPIVACAINE, LIDOCAINE, CYCLOPENTOLATE/PHENYLEPHRINE, CALCIUM CHLORIDE/MAGNESIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM ACETATE/SODIUM CHLORIDE/SODIUM CITRATE, MOXIFLOXACIN, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, FENTANYL, ROPIVACAINE, MIDAZOLAM, EPINEPHRINE, CEFUROXIME, POVIDONE-IODINE, POVIDONE-IODINE, DEXAMETHASONE/NEOMYCIN SULFATE/POLYMYXIN B SULFATE, LIDOCAINE, CYCLOPENTOLATE/PHENYLEPHRINE, CALCIUM CHLORIDE/MAGNESIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM ACETATE/SODIUM CHLORIDE/SODIUM CITRATE, TIMOLOL, APRACLONIDINE HYDROCHLORIDE, AMIODARONE, BUPIVACAINE, EPINEPHRINE, LIDOCAINE, MALUS SPP. VINEGAR EXTRACT, TORASEMIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, GUAIFENESIN, PARACETAMOL, PARACETAMOL, LIDOCAINE, IOHEXOL, MACROGOL 3350, COVID-19 VACCINE, COVID-19 VACCINE, PARACETAMOL, ACETYLSALICYLIC ACID, COVID-19 VACCINE, AZITHROMYCIN, VARICELLA ZOSTER VACCINE RGE (CHO), LOPERAMIDE HYDROCHLORIDE, PROXYMETACAINE, INFLUENZA VACCINE				
Non-Serious Adverse Event [4]: Actinic keratosis, Bowen's disease, Chronic kidney disease, International normalised ratio increased, Nocturia, Blood loss anaemia, Skin abrasion, Epistaxis, Fall, Herpes simplex, Viral upper respiratory tract infection, Musculoskeletal chest pain, Hair disorder, Squamous cell carcinoma, Squamous cell carcinoma, Asthenia, Bowen's disease, Weight decreased, Cardiac failure, Skin ulcer, Squamous cell carcinoma, Age-related macular degeneration, Cataract, Fall, Atrioventricular block first degree, Bradycardia, Conduction disorder, Limb injury, Bronchitis, Constipation, Haemoptysis, Bowen's disease, Haemangioma of skin, Melanocytic naevus, Actinic keratosis, Skin haemorrhage, Solar lentigo, Pain in extremity, Fall, Posterior capsule opacification, Cough				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胸痛	CHEST PAIN, UNSPECIFIED	Day 202 / Day 203	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「胸痛」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Vasectomy, Deep vein thrombosis, Osteoarthritis, Pulmonary mass, Vertigo positional, Bradycardia, Hyperglycaemia, Dry age-related macular degeneration, Macular degeneration, Ventricular extrasystoles, Hyperlipidaemia, Carpal tunnel decompression, Osteoarthritis, Sleep apnoea syndrome, Positive airway pressure therapy, Talipes, Gastritis, Atrial fibrillation, Hypertension, Tinea pedis, Back pain, Seborrhoeic keratosis, Constipation, Bundle branch block right, Neuropathy peripheral, Coronary artery disease, Obesity, Seasonal allergy, Cardiac amyloidosis, Cardiac failure congestive, Chronic kidney disease, Urticaria, Osteoarthritis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 893		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, PARACETAMOL, ATORVASTATIN CALCIUM, DOCOSAHEXAENOIC ACID/EICOSAPENTAENOIC ACID, ASCORBIC ACID/BETACAROTENE/CUPRIC OXIDE/TOCOPHERYL ACETATE/ZINC OXIDE, WARFARIN SODIUM, GLYCERYL TRINITRATE, TORASEMIDE, POTASSIUM CHLORIDE, BRIMONIDINE, LIDOCAINE, ROPIVACAINE, CORTICOSTEROIDS, WARFARIN, DOCUSATE SODIUM, CEFAZOLIN, INFLUENZA VACCINE, SODIUM CHLORIDE, SODIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, PARACETAMOL, FENTANYL, PROPOFOL, LIDOCAINE, MIDAZOLAM, WARFARIN, IRRIGATING SOLUTIONS, ANTIBIOTICS FOR TOPICAL USE, MEDICATED DRESSINGS WITH ANTIINFECTIVES, SULFADIAZINE SILVER, TRAMADOL HYDROCHLORIDE, POLYMYXIN B SULFATE/TRIMETHOPRIM, DEXAMETHASONE/TOBRAMYCIN, OLOPATADINE HYDROCHLORIDE, MUPIROCIN, PREDNISONE, TRIAMCINOLONE ACETONIDE, DOCUSATE/SENNOSIDE A+B, CEFAZOLIN, TRANEXAMIC ACID, WARFARIN, SODIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, PHENYLEPHRINE, OXYCODONE, PARACETAMOL, EPINEPHRINE/ROPIVACAINE, FAMOTIDINE, OXYCODONE HYDROCHLORIDE, ACETYLSALICYLIC ACID, HYDROCORTISONE, MACROGOL/PROPYLENE GLYCOL/SIMETICONE/SORBIC ACID/SORBITOL/WHITE SOFT PARAFFIN, GABAPENTIN, PREDNISONE, ALLOPURINOL, COLCHICINE, ALLOPURINOL, DOCUSATE SODIUM, BENZYLPENICILLIN, COVID-19 VACCINE, LIDOCAINE, COVID-19 VACCINE, MACROGOL, GLYCEROL, SENNOSIDE A+B, COLCHICINE, PREDNISONE				
Non-Serious Adverse Event [4]: Abdominal pain upper, Incision site cellulitis, Fall, Conjunctivitis, Arthralgia, Gout, Skin abrasion, Pain in extremity, Pain in extremity, Pain in extremity, Myalgia, Eczema, Pain in extremity, Musculoskeletal stiffness, Scrotal dermatitis, Dactylitis, Hyperaesthesia, Fluid retention, Chest discomfort, Arthralgia, Peripheral swelling, Pain in extremity, Ventricular tachycardia, Gout, Ventricular extrasystoles, Fall, Humerus fracture, Arthralgia, Tooth infection, Ulnar nerve injury, Dysaesthesia, Constipation, Nerve compression, Neuropathy peripheral, Neuropathy peripheral, Pain in extremity				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	BRADYCARDIA (INFRA-HISIAN CONDUCTION DISEASE) SYMPTOMATIC	Day 49 / Day 50	Not Related	Dose Not Changed	Recovered /Resolved	Severe
脚ブロック	ALTERNATING BUNDLE BRANCH BLOCK	Day 49 / Day 50	Not Related	Dose Not Changed	Recovered /Resolved	Severe
関節炎	WORSENING ARTHRITIS HIP	Day 188 / Day 190	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「徐脈」、「脚ブロック」及び「関節炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Hepatitis, Bell's palsy, Hypertension, Headache, Hyperlipidaemia, Restless legs syndrome, Polymyalgia rheumatica, Spinal operation, Diabetes mellitus, Organic erectile dysfunction, Sleep apnoea syndrome, Retinal injury, Diabetic neuropathy, Spinal osteoarthritis, Myelopathy, Cervix operation, Spinal laminectomy, Retinal vein occlusion, Cataract, Glaucoma, Chronic kidney disease, Medical induction of coma, Rhinitis allergic, Atrial fibrillation, Cardiac failure congestive, Neuropathy peripheral, Leukocytosis, Joint arthroplasty, Intervertebral disc displacement, Spinal stenosis, Ventricular extrasystoles, Cardiac assistance device user, Atrial flutter, Anaemia, Arterial therapeutic procedure, Hypertrophic cardiomyopathy, Syncope, Cardiac resynchronisation therapy, Peripheral arterial occlusive disease, Angioplasty, Coronary artery disease, Implantable cardiac monitor insertion, Cardiac amyloidosis, Benign prostatic hyperplasia, Peripheral venous disease, Hypothyroidism, Ultrasound thyroid abnormal, Gastrooesophageal reflux disease, Carpal tunnel syndrome, Arthritis, Gouty tophus, Gout, Deafness, Balance disorder, Depression, Hyperkeratosis, Lumbosacral radiculopathy, Spinal osteoarthritis, Blood uric acid increased, Chronic lymphocytic leukaemia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 895			
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), ROSUVASTATIN CALCIUM, COLECALCIFEROL, ACETYLSALICYLIC ACID, PARACETAMOL, GABAPENTIN, GABAPENTIN, BRIMONIDINE TARTRATE/TIMOLOL MALEATE, CARVEDILOL, FLUTICASONE PROPIONATE, HYDRALAZINE HYDROCHLORIDE, RIVAROXABAN, TORASEMIDE, DOCUSATE SODIUM, LIRAGLUTIDE, METOLAZONE, TESTS FOR DIABETES, OMEPRAZOLE, INSULIN DEGLUDEC, ISOSORBIDE DINITRATE, LEVOTHYROXINE SODIUM, ALLOPURINOL, FEXOFENADINE HYDROCHLORIDE, OLOPATADINE HYDROCHLORIDE, BRINZOLAMIDE, ALL OTHER NON-THERAPEUTIC PRODUCTS, POTASSIUM CHLORIDE, PREDNISONE, CYCLOBENZAPRINE HYDROCHLORIDE, CYCLOBENZAPRINE HYDROCHLORIDE, HYDRALAZINE HYDROCHLORIDE, SODIUM BICARBONATE/SODIUM CHLORIDE, HYDROCORTISONE ACETATE, TESTS FOR DIABETES, INSULIN ASPART, FUROSEMIDE, HEPARIN, SODIUM CHLORIDE, FENTANYL, LIDOCAINE, MIDAZOLAM HYDROCHLORIDE, APIXABAN, ASCORBIC ACID/FERROUS FUMARATE, FERROUS SULFATE, CETIRIZINE, METHOCARBAMOL, TIZANIDINE, TRAMADOL, COVID-19 VACCINE, COVID-19 VACCINE, FACTOR II (PROTHROMBIN)/FACTOR IX/FACTOR VII (PROCONVERTIN)/FACTOR X (STUART PROWER FACTOR)/PROTEIN C (COAGULATION INHIBITOR)/PROTEIN S, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, VANCOMYCIN, ERTAPENEM, APIXABAN, ACETYLSALICYLIC ACID, SODIUM CHLORIDE, VANCOMYCIN, AMOXICILLIN/CLAVULANATE POTASSIUM, MENTHOL, VANCOMYCIN HYDROCHLORIDE, CEFTRIAXONE, SODIUM CHLORIDE, SULFADIAZINE SILVER, CEFALEXIN, DOXYCYCLINE, NYSTATIN, TRIAMCINOLONE ACETONIDE, CEFALEXIN				
Non-Serious Adverse Event [4]: Gout, Sciatica, Orthostatic hypotension, Upper respiratory tract infection, Haemorrhoids, Type 2 diabetes mellitus, Headache, Restless legs syndrome, Deafness neurosensory, Diplopia, Arthralgia, Urinary retention, Eustachian tube dysfunction, Otitis media, Back pain, Fall, Ecchymosis, Arthralgia, Arthralgia, Nocturia, Dysphagia, Cough, Fall, Skin laceration, Hypokalaemia, Cardiac failure, Sepsis, Lactic acidosis, Fall, Contusion, Oral disorder, Somnolence, Paraesthesia, Oral pigmentation, Skin ulcer, Skin candida, Cellulitis, Wound, Head injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性心不全	CHRONIC MIXED SYSTOLIC/DIASTOLIC HEART FAILURE	Day 272 / Day 276	Not Related	Dose Not Changed	Recovered /Resolved	Severe
硬膜下血腫	ACUTE PARAFALCINE SUBDURAL HEMATOMA	Day 546 / Day 556	Not Related	Dose Not Changed	Recovered /Resolved	Severe

誤嚥性肺炎	ACUTE ASPIRATION PNEUMONIA	Day 556 / Day 565	Not Related	Dose Not Changed	Recovered /Resolved	Severe
蜂巣炎	CELLULITIS OF RIGHT LOWER EXTREMITY	Day 819 / Day 821	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「慢性心不全」、「硬膜下血腫」、「誤嚥性肺炎」及び「蜂巣炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 6[redacted]	
Medical History [1]: Knee arthroplasty, Carpal tunnel decompression, Coronary artery disease, Atrial fibrillation, Chronic left ventricular failure, Hyperlipidaemia, Cardiac amyloidosis, Chronic kidney disease, Cardioversion					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900			
Concomitant Medication [3]: POTASSIUM, COLECALCIFEROL, VITAMIN B COMPLEX, ROSUVASTATIN, AMIODARONE, TORASEMIDE, TORASEMIDE, COVID-19 VACCINE					
Non-Serious Adverse Event [4]: Dehydration					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE ON CHRONIC RENAL INSUFFICIENCY	Day 274 / Day 458	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Sleep apnoea syndrome, Hypertension, Hyperlipidaemia, Stent placement, Knee arthroplasty, Coronary artery bypass, Cardiac operation, Diverticulum, Cardioversion, Chronic kidney disease, Cardiac failure congestive, Syncope, Atrial fibrillation, Coronary artery disease, Hypotension, Implantable cardiac monitor insertion, Gastrooesophageal reflux disease, Cardiac amyloidosis, Asthenia, Gait disturbance, Fall, Neuropathy peripheral				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: PRAVASTATIN, ACETYLSALICYLIC ACID, MAGNESIUM, ERGOCALCIFEROL, RIVAROXABAN, POTASSIUM CHLORIDE, MIDODRINE HYDROCHLORIDE, BUMETANIDE, COLECALCIFEROL, MIDODRINE HYDROCHLORIDE, MACROGOL/POTASSIUM CHLORIDE/SODIUM BICARBONATE, COLECALCIFEROL, HEPARIN, PERFLUTREN, FENTANYL, MIDAZOLAM, PANTOPRAZOLE, FERROUS SULFATE, SACCHARATED IRON OXIDE, BUMETANIDE, LIDOCAINE, MIDODRINE HYDROCHLORIDE, UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE, IBUPROFEN, COVID-19 VACCINE, COVID-19 VACCINE, POTASSIUM CHLORIDE, APIXABAN, SPIRONOLACTONE, BUMETANIDE				
Non-Serious Adverse Event [4]: Anaemia, Gastritis, Presyncope, Gastrointestinal disorder, Nausea, Hypoaesthesia, Fatigue, Fall, Hypokalaemia, Pruritus				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胃腸出血（1）	GI BLEED	Day 35 / Day 36	Not Related	Dose Not Changed	Recovered /Resolved	Severe
胃腸出血（2）	GI BLEED	Day 50 / Day 53	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「胃腸出血（1）」及び「胃腸出血（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Osteoarthritis, Hypertension, Gout, Prostatectomy, Prostate cancer, Erectile dysfunction, Knee arthroplasty, Nocturia, Hyperlipidaemia, Atrial fibrillation, Mixed incontinence, Corneal dystrophy, Cataract, Vitreous detachment, Eye operation, Intraocular lens implant, Radicular pain, Gastrooesophageal reflux disease, Hip arthroplasty, Neuropathy peripheral, Bladder neck obstruction, Pulmonary oedema, Cardiac failure congestive, Oedema peripheral, Coronary artery disease, Cardiomyopathy, Back pain, Haematuria, Vitamin D deficiency, Hereditary neuropathic amyloidosis, Left ventricular hypertrophy, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 922		
Concomitant Medication [3]: ALLOPURINOL, AMLODIPINE, LOSARTAN, PRAVASTATIN, OMEPRAZOLE, GABAPENTIN, APIXABAN, ACETYLSALICYLIC ACID, COLECALCIFEROL, SPIRONOLACTONE, POTASSIUM CHLORIDE, BUMETANIDE, FUROSEMIDE, CIPROFLOXACIN, DICLOFENAC SODIUM, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, HALOPERIDOL, HALOPERIDOL, CIPROFLOXACIN, LOSARTAN, BUMETANIDE, BACLOFEN				
Non-Serious Adverse Event [4]: Urinary tract infection, Fall, Blood creatinine increased, Gingival bleeding, Fatigue, Hiccups, Acute kidney injury, Anaemia, Fall				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胃腸出血	GASTROINTESTINAL HEMORRHAGE	Day 821 / Day 826	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「胃腸出血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: Asian	Country: US	Sex: M	Age: 6[redacted]	
Medical History [1]: Gastrooesophageal reflux disease, Cardiac amyloidosis, Cardiovascular disorder, Dyslipidaemia, Alopecia, Essential hypertension					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, FUROSEMIDE, PRAVASTATIN, FINASTERIDE, LISINOPRIL, METOPROLOL, TADALAFIL, FINASTERIDE, TADALAFIL, LOSARTAN, PHENOXYMETHYLPENICILLIN POTASSIUM, SACUBITRIL/VALSARTAN, APIXABAN, CLAVULANATE POTASSIUM, AMOXICILLIN, AMIODARONE, AMIODARONE, EMPAGLIFLOZIN, SPIRONOLACTONE, PANTOPRAZOLE, METOPROLOL					
Non-Serious Adverse Event [4]: Erectile dysfunction, Tooth abscess, Haemorrhoids, Heart rate decreased					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	NEW ONSET ATRIAL FIBRILLATION	Day 449 / Day 493	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Hypothyroidism, Depression, Meniscus operation, Ankle fracture, Knee arthroplasty, Rotator cuff repair, Tendon sheath incision, Dyslipidaemia, Prostatectomy, Sleep apnoea syndrome, Bradycardia, Cardiac amyloidosis, Atrial flutter, Shoulder operation, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), COLECALCIFEROL, CYANOCOBALAMIN, LEVOTHYROXINE, LIOTHYRONINE, FUROSEMIDE, ALLOPURINOL, APIXABAN, SACUBITRIL/VALSARTAN, FUROSEMIDE, LEVOTHYROXINE, ENOXAPARIN, WARFARIN SODIUM, Not coded: Tafamidis, TAFAMIDIS, PARACETAMOL, TRIAMCINOLONE, HEPARIN, WARFARIN SODIUM, CEFAZOLIN SODIUM, CEFAZOLIN SODIUM, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, EPHEDRINE, PHENYLEPHRINE, PHENYLEPHRINE, PARACETAMOL, FENTANYL, PROPOFOL, LIDOCAINE, WARFARIN, WARFARIN, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Dermatitis contact, Ligament sprain, Oedema peripheral, Cellulitis, Bursitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脱水	DEHYDRATION	Day 656 / Day 657	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
徐脈	WORSENING BRADYCARDIA	Day 827 / Day 854	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
治験責任医師の見解：「脱水」及び「徐脈」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Ulcer haemorrhage, Paraesthesia, Carpal tunnel syndrome, Arthralgia, Type V hyperlipidaemia, Hypertension, Diabetes mellitus, Prostate cancer, Brachytherapy, Gastrooesophageal reflux disease, Coronary artery disease, Gout, Chronic left ventricular failure, Spinal stenosis, Hip arthroplasty, Cardiac amyloidosis, Carpal tunnel decompression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 617		
Concomitant Medication [3]: PANTOPRAZOLE, GLIPIZIDE, VITAMIN B12 NOS, ACETYLSALICYLIC ACID, LISINOPRIL, PRAVASTATIN SODIUM, PRAVASTATIN SODIUM, COLCHICINE/PROBENECID, TORASEMIDE, SPIRONOLACTONE, CARVEDILOL, CARVEDILOL, LISINOPRIL, INFLUENZA VACCINE, ALLOPURINOL, CARVEDILOL, TORASEMIDE, COLECALCIFEROL, OMEPRAZOLE, Not coded: Tafamidis, TAFAMIDIS, OMEPRAZOLE, SENNA ALEXANDRINA, POTASSIUM CHLORIDE, HEPARIN, FUROSEMIDE, CHLOROTHIAZIDE SODIUM, PARACETAMOL, INSULIN LISPRO, COVID-19 VACCINE, POTASSIUM CHLORIDE, BUMETANIDE, FUROSEMIDE, CHLOROTHIAZIDE SODIUM, HYDROCHLOROTHIAZIDE, DOBUTAMINE				
Non-Serious Adverse Event [4]: Hypoglycaemia, Arthralgia, Nausea, Chronic kidney disease, Diarrhoea, Gastric ulcer, N-terminal prohormone brain natriuretic peptide increased, Urine albumin/creatinine ratio increased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全（1）	ACUTE DECOMPENSATED HEART FAILURE	Day 517 / Day 520	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全（2）	ACUTE DECOMPENSATED HEART FAILURE	Day 587 / Day 589	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性左室不全	ACUTE DECOMPENSATED HEART SYSTOLIC FAILURE	Day 602 / Day 608	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性心不全（1）」、「急性心不全（2）」及び「急性左室不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Carpal tunnel decompression, Cardiac pacemaker insertion, Sinus node dysfunction, Arthritis reactive, Sleep apnoea syndrome, Hypertension, Chronic lymphocytic leukaemia, Acute kidney injury, Proteinuria, Cardiac amyloidosis, Chronic left ventricular failure, Prostate cancer, Restless legs syndrome, Coronary artery disease, Insomnia, Dyspepsia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 64		
Concomitant Medication [3]: DIPHENHYDRAMINE HYDROCHLORIDE/PARACETAMOL, TRAZODONE HYDROCHLORIDE, POTASSIUM CHLORIDE, OMEPRAZOLE, SUCRALFATE, GABAPENTIN, OXYCODONE HYDROCHLORIDE, VALACICLOVIR HYDROCHLORIDE, METOPROLOL SUCCINATE, GLYCERYL TRINITRATE, ZOLPIDEM TARTRATE, FERROUS SULFATE, DIGESTIVES (INCL. ENZYMES), ASCORBIC ACID, FERROUS SULFATE, FUROSEMIDE, SPIRONOLACTONE, LEVETIRACETAM				
Non-Serious Adverse Event [4]: Weight decreased, Constipation, Craniocerebral injury, Essential hypertension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
硬膜下血腫	BILATERAL SUBDURAL HEMATOMA DUE TO CLOSED HEAD INJURY	Day 63 / Day 225	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「硬膜下血腫」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]	
Medical History [1]: Ventricular tachycardia, Benign prostatic hyperplasia, Knee arthroplasty, Joint resurfacing surgery, Post procedural hypothyroidism, Dyspnoea, Thyroid cancer, Anomalous pulmonary venous connection, Dyslipidaemia, Hypertension, Rash, Atrial fibrillation, Chronotropic incompetence, Amyloidosis, Chronic left ventricular failure					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896			
Concomitant Medication [3]: ATORVASTATIN CALCIUM, LEVOTHYROXINE SODIUM, OXYGEN, FINASTERIDE, APIXABAN, TRIAMCINOLONE ACETONIDE, HYDROCHLOROTHIAZIDE, AMOXICILLIN, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, METOPROLOL SUCCINATE, FUROSEMIDE					
Non-Serious Adverse Event [4]: Neuropathy peripheral, Myalgia, Pneumonia bacterial, COVID-19, Syncope					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	PNEUMONIA	Day 746 / Day 749	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「肺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Nasal dryness, Spinal stenosis, Spinal operation, Carpal tunnel decompression, Angina unstable, Angina pectoris, Coronary artery disease, Body tinea, Hypertension, Gout, Osteoarthritis, Hip arthroplasty, Arthritis, Hyperlipidaemia, Hypercholesterolaemia, Myalgia, Spinal stenosis, Spinal operation, Left ventricular hypertrophy, Facet joint syndrome, Lumbar spinal stenosis, Spinal claudication, Dizziness, Atrial fibrillation, Dyspnoea, Atrial fibrillation, Cardiac failure congestive, Ischaemic cardiomyopathy, Troponin I increased, Acute pulmonary oedema, Dyspnoea exertional, Orthopnoea, Sleep apnoea syndrome, Benign prostatic hyperplasia, Oesophageal spasm, Restrictive cardiomyopathy, Vascular device user, Angioplasty, Chronic left ventricular failure, Cardiac amyloidosis, Amyloidosis senile, Erectile dysfunction				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: MULTIVITAMINS WITH MINERALS [UMBRELLA TERM], MELATONIN, SIMVASTATIN, SODIUM CHLORIDE, TAMSULOSIN HYDROCHLORIDE, OMEPRAZOLE, NORTRIPTYLINE, OXYGEN, APIXABAN, CLOPIDOGREL BISULFATE, ALLOPURINOL, FUROSEMIDE, LOSARTAN POTASSIUM, SILDENAFIL CITRATE, ACETYLSALICYLIC ACID, TADALAFIL, COVID-19 VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, ATORVASTATIN CALCIUM, VANCOMYCIN, CEFTRIAXONE, DOXYCYCLINE HYCLATE, CLOPIDOGREL BISULFATE, COVID-19 VACCINE, ACETYLSALICYLIC ACID, SILDENAFIL CITRATE, ATORVASTATIN CALCIUM, EZETIMIBE				
Non-Serious Adverse Event [4]: Back pain, Tinnitus, Pruritus, Contusion, Deafness bilateral				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
末梢血管障害	PERIPHERAL VASCULAR DISEASE	Day 484 / Day 500	Not Related	Dose Not Changed	Recovered /Resolved	Severe
蜂巣炎	CELLULITIS OF LEFT FOOT	Day 487 / Day 501	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全	WORSENING ACUTE CONGESTIVE HEART FAILURE UNSPECIFIED HEART FAILURE TYPE	Day 910 / Day 916	Related	NA	Recovered /Resolved	Mild

治験責任医師の見解：「末梢血管障害」及び「蜂巣炎」は治験薬と関連なしと判断した。「急性心不全」は治験薬と関連ありと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Dental care, Allergy to animal, Carpal tunnel decompression, Carpal tunnel decompression, Hairy cell leukaemia, Hypercholesterolaemia, Pollakiuria, Benign prostatic hyperplasia, Essential hypertension, Rhinitis perennial, Atrial fibrillation, Osteoarthritis, Chronic kidney disease, Dermatitis contact, Mitral valve repair, Tricuspid valve repair, Tricuspid valve repair, Drug hypersensitivity, Dermatitis contact, Left ventricular hypertrophy, Cardiac amyloidosis, Chronic left ventricular failure, Anticoagulant therapy, Amyloidosis senile, Hyperlipidaemia, Muscle spasms				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 251		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), ATORVASTATIN CALCIUM, ALL OTHER THERAPEUTIC PRODUCTS, SALBUTAMOL, TAMSULOSIN HYDROCHLORIDE, WARFARIN, TORASEMIDE, POTASSIUM, SPIRONOLACTONE, TORASEMIDE, FLUTICASONE PROPIONATE, COVID-19 VACCINE, COVID-19 VACCINE, LEVOTHYROXINE				
Non-Serious Adverse Event [4]: Hypothyroidism				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
滑液嚢腫	LEFT LEG EDEMA DUE TO BAKER'S CYST	Day 29 / Day 83	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
低血圧	HYPOTENSION	Day 280 / Day 283	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「滑液嚢腫」及び「低血圧」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Hypertension, Deep vein thrombosis, Coronary artery disease, Hyperlipidaemia, Cardiac failure, Cardiac amyloidosis, Prostate cancer, Radical prostatectomy, Stress urinary incontinence, Chronic kidney disease, Hypergammaglobulinaemia benign monoclonal, Arthralgia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: CARVEDILOL, HYDRALAZINE, PRAVASTATIN, FUROSEMIDE, ISOSORBIDE DINITRATE, DICLOFENAC SODIUM, FUROSEMIDE, VARICELLA ZOSTER VACCINE RGE (CHO), PREDNISONE, ACETYLSALICYLIC ACID, ALLOPURINOL, PREDNISONE, COLECALCIFEROL, METOPROLOL, AMIODARONE, TORASEMIDE, CLINDAMYCIN, CLINDAMYCIN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Pain in extremity, Vitamin D deficiency, Gout, Gout, Atrial flutter, Acute kidney injury, Urinary retention, Deep vein thrombosis, Cellulitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼡径ヘルニア	RIGHT INGUINAL HERNIA	Day 428 / Day 429	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全（1）	ACUTE HEART FAILURE	Day 631 / Day 641	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（2）	CHF EXACERBATION	Day 697 / Day 707	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（3）	CHF EXACERBATION	Day 781 / Day 788	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「鼡径ヘルニア」、「急性心不全（1）」、「急性心不全（2）」及び「急性心不全（3）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Hernia repair, Prostate cancer, Radical prostatectomy, Hip arthroplasty, Knee arthroplasty, Tinea cruris, Hip arthroplasty, Dental operation, Neuropathy peripheral, Dyspnoea exertional, Barrett's oesophagus, Orthostatic hypotension, Cataract operation, Atrial fibrillation, Atrial flutter, Cataract operation, Cataract operation, Rotator cuff repair, Pulmonary embolism, Fatigue, Hypertension, Left ventricular failure, Sleep apnoea syndrome, Cardiac amyloidosis, Varicose vein, Bundle branch block left				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: OMEPRAZOLE, VITAMINS NOS, COLECALCIFEROL, VITAMIN B12 NOS, FISH OIL, RIVAROXABAN, FUROSEMIDE, CYCLOBENZAPRINE, KETOCONAZOLE, HEPARIN, FUROSEMIDE, AMIODARONE, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Urine albumin/creatinine ratio increased, Central venous pressure increased, Fatigue, Urine albumin/creatinine ratio increased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	SYMPTOMATIC BRADYCARDIA	Day 560 / Day 564	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性左室不全	ACUTE DIASTOLIC HEART FAILURE	Day 560 / Day 566	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「徐脈」及び「急性左室不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]	
Medical History [1]: Spinal operation, Spinal laminectomy, Carpal tunnel syndrome, Carpal tunnel decompression, Seasonal allergy, Atrial fibrillation, Bundle branch block right, Cardiac failure, Pollakiuria, Benign prostatic hyperplasia, Hypertension, Bradycardia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 916			
Concomitant Medication [3]: COLECALCIFEROL, TAMSULOSIN, FEXOFENADINE HYDROCHLORIDE, OXYBUTYNIN, APIXABAN, LISINOPRIL, METOPROLOL, BUMETANIDE, ASCORBIC ACID, OXYBUTYNIN HYDROCHLORIDE, BUMETANIDE, COVID-19 VACCINE, COVID-19 VACCINE, CEFALEXIN, APIXABAN, CIPROFLOXACIN, FINASTERIDE, ACETYLSALICYLIC ACID, METOPROLOL, DILTIAZEM, DILTIAZEM, ATORVASTATIN, METOPROLOL SUCCINATE					
Non-Serious Adverse Event [4]: Haematuria, Urinary retention					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心筋梗塞	NSTEMI	Day 756 / Day 761	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心房細動	RAPID ATRIAL FIBRILLATION	Day 756 / Day 761	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「急性心筋梗塞」及び「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Rheumatic fever, Cardiac murmur, Prostate cancer, Dust allergy, Erectile dysfunction, Sleep apnoea syndrome, Hypertension, Glucose tolerance impaired, Back pain, Carpal tunnel syndrome, Carpal tunnel decompression, Knee arthroplasty, Gastrooesophageal reflux disease, Muscle rupture, Hyperlipidaemia, Osteoarthritis, Gout, Pneumonia, Aortic stenosis, Cardiac failure congestive, Cardiac amyloidosis, Type 2 diabetes mellitus				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: COLECALCIFEROL, SILDENAFIL CITRATE, MENTHOL/METHYL SALICYLATE, LIDOCAINE, LORATADINE, KETOTIFEN, OMEPRAZOLE, ROSUVASTATIN, ALLOPURINOL, METHYLPREDNISOLONE, LOSARTAN, METOPROLOL SUCCINATE, FUROSEMIDE, GLIPIZIDE, FLUOROMETHOLONE, ACETYLSALICYLIC ACID, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, PROPOFOL, LIDOCAINE, DOCUSATE, HEPARIN, HEPARIN, CLOPIDOGREL, SODIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, MAGNESIUM SULFATE, EPINEPHRINE/LIDOCAINE, LIDOCAINE, DEXMEDETOMIDINE, CLOPIDOGREL, METHYLPREDNISOLONE, APIXABAN, TORASEMIDE, TORASEMIDE, AMLODIPINE, AMIODARONE, AMLODIPINE, AMIODARONE, FENTANYL, MIDAZOLAM, AMLODIPINE, TORASEMIDE, TORASEMIDE, COVID-19 VACCINE, LOSARTAN, COVID-19 VACCINE, EPLERENONE, TORASEMIDE, GABAPENTIN, TORASEMIDE, TORASEMIDE				
Non-Serious Adverse Event [4]: Gout, Dizziness, Oedema peripheral, Hypertension, Sinus bradycardia, Muscle spasms, Back pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大動脈狭窄	WORSENING AORTIC STENOSIS	Day 30 / Day 58	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	ATRIAL FIBRILLATION	Day 66 / Day 477	Not Related	Dose Not Changed	Recovered /Resolved	Mild
医療機器不具合	PRIOR LEFT KNEE ARTHROPLASTY FAILURE	NA / NA	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
治験責任医師の見解：「大動脈狭窄」、「心房細動」及び「医療機器不具合」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Acne, Spinal stenosis, Haemorrhoids, Spinal laminectomy, Carpal tunnel syndrome, Carpal tunnel decompression, Coronary artery disease, Pulmonary hypertension, Sleep apnoea syndrome, Cardiac failure, Mitral valve incompetence, Cardiac amyloidosis, Atrial fibrillation, Implantable defibrillator insertion, Carpal tunnel syndrome, Rash				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 115		
Concomitant Medication [3]: CARVEDILOL, SACUBITRIL/VALSARTAN, APIXABAN, SPIRONOLACTONE, DOXEPIN HYDROCHLORIDE, AMPICILLIN, HYDROCORTISONE, FUROSEMIDE, DABIGATRAN ETEXILATE MESILATE, NALTREXONE, SODIUM CHLORIDE, SODIUM CHLORIDE, DIPHENHYDRAMINE/ZINC ACETATE, SODIUM CHLORIDE, VALSARTAN, APIXABAN, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Cardiac failure, Polyuria				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY [SECONDARY TO OVERDIURESIS]	Day 14 / Day 19	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「急性腎障害」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: F	Age: 7■
Medical History [1]: Hysterectomy, Atrial fibrillation, Hypertension, Dyslipidaemia, Palpitations, Iron deficiency anaemia, Exostosis, Haematuria, Gastric polyps, Vitamin D deficiency, Transurethral bladder resection, Dry eye, Glaucoma, Cardiac amyloidosis, Oedema peripheral, Osteoarthritis, Arthralgia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 537		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, FERROUS SULFATE, COLECALCIFEROL, WARFARIN, WARFARIN, VALSARTAN, AMIODARONE, LATANOPROST, BRIMONIDINE, METOPROLOL, AMLODIPINE, PARACETAMOL, CEFALEXIN, INFLUENZA VACCINE, METOPROLOL, METOPROLOL, AMIODARONE, ADENOSINE, ADENOSINE, METOPROLOL, METOPROLOL, METOPROLOL, ADENOSINE, ADENOSINE, ADENOSINE, METOPROLOL, PROPOFOL, AMIODARONE, METOPROLOL, DICLOFENAC, MAGNESIUM, HEPARIN, SODIUM CHLORIDE, METOPROLOL, DILTIAZEM, ONDANSETRON, PANTOPRAZOLE, PNEUMOCOCCAL VACCINE, APIXABAN, SODIUM CHLORIDE, PROPOFOL, GLUCOSE, LOSARTAN, AMIODARONE, METOPROLOL, AMIODARONE				
Non-Serious Adverse Event [4]: Urinary tract infection, Ventricular extrasystoles, Palpitations, Atrial flutter, Osteoarthritis, Faeces hard, Insomnia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
上室性頻脈	SUPRAVENTRICULAR TACHYCARDIA	Day 331 / Day 335	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
心房細動	SYMPTOMATIC ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 492 / NA	Not Related	Drug Interrupted	Recovering/ Resolving	Moderate

治験責任医師の見解：「上室性頻脈」及び「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Cataract, Cataract, Prostatic specific antigen increased, Gastrooesophageal reflux disease, Benign prostatic hyperplasia, Cataract operation, Glaucoma, Neuralgia, Restless legs syndrome, Sciatica, Sleep apnoea syndrome, Percutaneous coronary intervention, Coronary artery disease, Dyslipidaemia, Hypertension, Cardiac failure congestive, Pulmonary mass, Colonoscopy, Dyspnoea, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: LATANOPROST, TAMSULOSIN, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, ATORVASTATIN, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, REGADENOSON, FUROSEMIDE, DOCUSATE, VANCOMYCIN, VANCOMYCIN, CEFAZOLIN, HEPARIN SODIUM, LIDOCAINE, MUPIROCIN, CHLORHEXIDINE, PARACETAMOL, FENTANYL, PROPOFOL, BUPIVACAINE HYDROCHLORIDE, BUPIVACAINE HYDROCHLORIDE, BUPIVACAINE HYDROCHLORIDE, IOHEXOL, IOHEXOL, IOHEXOL, APIXABAN, METOPROLOL, ONDANSETRON, DOCUSATE, VANCOMYCIN, CEFAZOLIN, CEFAZOLIN SODIUM, HEPARIN SODIUM, MUPIROCIN, CHLORHEXIDINE, PARACETAMOL, FENTANYL, PROPOFOL, BUPIVACAINE HYDROCHLORIDE, BUPIVACAINE HYDROCHLORIDE, LIDOCAINE, MAGNESIUM, METOPROLOL, AMIODARONE, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Abnormal dreams, Irritability, Nausea, Dizziness, Dyspnoea, Atrial fibrillation, Pericardial effusion, Hypomagnesaemia, Conduction disorder				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心室性頻脈	INTERMITTENT NONSUSTAINED VENTRICULAR TACHYCARDIA	Day 337 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
医療機器関連合併症	MECHANICAL COMPLICATION OF CARDIAC ELECTRODE	Day 490 / Day 504	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 570 / Day 571	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心室性頻脈」、「医療機器関連合併症」及び「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: F	Age: 7[redacted]
Medical History [1]: Hysterectomy, Cholecystectomy, Elbow operation, Angioplasty, Dyslipidaemia, Hypertension, Coronary artery bypass, Coronary artery disease, Left ventricular failure, Spinal stenosis, Pulmonary hypertension, Knee operation, Rotator cuff repair, Hiatus hernia, Carpal tunnel syndrome, Vertigo, Hypocalcaemia, Osteoarthritis, Carpal tunnel syndrome, Knee arthroplasty, Skin cancer, Cataract, Irritable bowel syndrome, Hypomagnesaemia, Vitamin D deficiency, Hypoxia, Carpal tunnel decompression, Sinus node dysfunction, Hypokalaemia, Atrial fibrillation, Atrial flutter, Syncope, Cardiac pacemaker insertion, Cardiac ablation, Hernia hiatus repair, Neuropathy peripheral, Cataract operation, Cardiac amyloidosis, Blood uric acid increased				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 892		
Concomitant Medication [3]: POLYCARBOPHIL CALCIUM, CURCUMA LONGA, LOSARTAN, GLYCERYL TRINITRATE, ATORVASTATIN, FISH OIL, CALCIUM CITRATE, MULTIVITAMINS (PLAIN), GLUCOSAMINE, LOPERAMIDE HYDROCHLORIDE, DICYCLOVERINE, MAGNESIUM OXIDE, PROBIOTICS [UMBRELLA TERM], ASCORBIC ACID, VITAMIN B NOS, COLECALCIFEROL, POTASSIUM CHLORIDE, RIVAROXABAN, BISOPROLOL, DOFETILIDE, TORASEMIDE, ISOSORBIDE MONONITRATE, GABAPENTIN, OXYGEN, CYCLOBENZAPRINE, HYDROCODONE, HYDROCODONE BITARTRATE/PARACETAMOL, PARACETAMOL, NALOXONE, MORPHINE, VALSARTAN, GABAPENTIN, TORASEMIDE, TORASEMIDE, ALLOPURINOL, COVID-19 VACCINE, COVID-19 VACCINE, ALLOPURINOL, GABAPENTIN, VALSARTAN, METOPROLOL, BENAZEPRIL HYDROCHLORIDE, AMIODARONE				
Non-Serious Adverse Event [4]: Muscle spasms, Lumbar radiculopathy, Dyspnoea, Foot fracture, Cardiac failure, Urinary tract infection, Rib fracture, Irritable bowel syndrome				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腰部脊柱管狭窄症	WORSENING LUMBAR SPINAL STENOSIS	Day 25 / Day 124	Not Related	Dose Not Changed	Recovered /Resolved	Mild
動悸	PALPITATIONS	Day 515 / Day 516	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心房細動	ATRIAL FIBRILLATION	Day 616 / Day 617	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「腰部脊柱管狭窄症」、「動悸」及び「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Ventricular tachycardia, Essential hypertension, Diabetes mellitus, Gout, Coronary artery bypass, Coronary artery disease, Aortic dilatation, Benign prostatic hyperplasia, Obesity, Type V hyperlipidaemia, Deep vein thrombosis, Myasthenia gravis, Sleep apnoea syndrome, Diabetic neuropathy, Cervical spinal stenosis, Deafness neurosensory, Psoriasis, Polyneuropathy idiopathic progressive, Cholecystectomy, Chronic kidney disease, Percutaneous coronary intervention, Lumbar spinal stenosis, Respiratory failure, Epistaxis, Carpal tunnel syndrome, Peripheral venous disease, Tendon rupture, Lymphoedema, Cardiac amyloidosis, Acute myocardial infarction, Cardiac failure chronic, Atrial fibrillation, Atrial thrombosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ALLOPURINOL, ATORVASTATIN, METOPROLOL, TAMSULOSIN HYDROCHLORIDE, APIXABAN, DULAGLUTIDE, TORASEMIDE, TRAMADOL, TORASEMIDE, DULAGLUTIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, DILTIAZEM, DILTIAZEM, DILTIAZEM, TORASEMIDE, METOPROLOL TARTRATE, METOPROLOL TARTRATE, DULAGLUTIDE, SEMAGLUTIDE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, Not coded: Tafamidis, TAFAMIDIS, INSULIN DEGLUDEC				
Non-Serious Adverse Event [4]: Cardiac failure, Dysphagia, Proteinuria, Arthralgia, Non-cardiac chest pain, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大腸炎	ACUTE COLITIS	Day 154 / Day 159	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性左室不全	ACUTE ON CHRONIC DIASTOLIC HEART FAILURE	Day 713 / Day 724	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「大腸炎」及び「急性左室不全」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■						
Treatment Arm: Acoramidis		Race: Black or African American	Country: US		Sex: M	Age: 8■
Medical History [1]: Carpal tunnel decompression, Carpal tunnel decompression, Atrial fibrillation, Chronic left ventricular failure, Hypertension, Glaucoma, Oedema peripheral, Lumbar spinal stenosis, Chronic kidney disease, Hyperlipidaemia, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 905			
Concomitant Medication [3]: SPIRONOLACTONE, FUROSEMIDE, BISOPROLOL FUMARATE, BRIMONIDINE, VALSARTAN, SACUBITRIL, FUROSEMIDE, RIVAROXABAN, FUROSEMIDE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, BISOPROLOL						
Non-Serious Adverse Event [4]: Chronic kidney disease, Chronic kidney disease						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY	Day 757 / Day 759	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
ＣＯＶＩＤ－１９	COVID-19	Day 757 / Day 765	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
治験責任医師の見解：「急性腎障害」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: Not reported	Country: US	Sex: M	Age: 9[redacted]	
Medical History [1]: Myocardial infarction, Diabetes mellitus, Cardiac pacemaker insertion, Hypothyroidism, Essential hypertension, Coronary arterial stent insertion, Chronic kidney disease, Atrial appendage closure, Benign prostatic hyperplasia, Cardiac amyloidosis, Cardiac failure congestive, Hyperlipidaemia					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 23			
Concomitant Medication [3]: LOSARTAN, ACETYLSALICYLIC ACID, ROSUVASTATIN, TAMSULOSIN, FUROSEMIDE, LEVOTHYROXINE					
Non-Serious Adverse Event [4]: Abdominal discomfort, Dyspepsia, Chest discomfort					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
転倒	MECHANICAL FALL	Day 27 / Day 27	Not Related	NA	Recovered /Resolved	Severe
失神寸前の状態	NEAR SYNCOPE	Day 27 / Day 27	Not Related	NA	Recovered /Resolved	Severe
治験責任医師の見解：「転倒」及び「失神寸前の状態」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Hydrocephalus, Ventriculo-peritoneal shunt, Coronary artery disease, Deafness bilateral, Carpal tunnel syndrome, Dyslipidaemia, Osteoarthritis, Coronary artery bypass, Carpal tunnel decompression, Urinary tract infection, Neurogenic bladder, Erectile dysfunction, Meniscus removal, Transient ischaemic attack, Cardiac failure, Spinal osteoarthritis, Atrial fibrillation, Amyloidosis senile				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: FUROSEMIDE, APIXABAN, CANDESARTAN, EZETIMIBE, ACETYLSALICYLIC ACID, ATORVASTATIN CALCIUM, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, GABAPENTIN, FUROSEMIDE, PREGABALIN				
Non-Serious Adverse Event [4]: Aphasia, Gait disturbance, Muscle spasms, Functional gastrointestinal disorder, Vertigo, Pain in extremity, Cerebrovascular accident, Vertigo, Myelopathy, Platelet count decreased, Fall, Haematuria, Varicose vein ruptured, Petechiae, Diarrhoea, Gastrointestinal pain, Bladder spasm				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
膀胱癌	URINARY BLADDER CARCINOMA	Day 767 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「膀胱癌」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 8■
Medical History [1]: Nephrolithiasis, Appendicectomy, Hypertension, Hiatus hernia, Transient ischaemic attack, Dyslipidaemia, Endarterectomy, Atrial fibrillation, Fall, Sleep apnoea syndrome, Pneumonia, Carpal tunnel decompression, Glaucoma, Polycythaemia, Cardiac failure congestive, Amyloidosis senile				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ATORVASTATIN CALCIUM, RIVAROXABAN, VITAMIN D NOS, TRAVOPROST, SPIRONOLACTONE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, VARICELLA ZOSTER VACCINE RGE (CHO), Not coded: Tafamidis, TAFAMIDIS, PANTOPRAZOLE SODIUM SESQUIHYDRATE, COVID-19 VACCINE, DIMENHYDRINATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, FUROSEMIDE, VITAMIN B12 NOS, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE				
Non-Serious Adverse Event [4]: Fatigue, Musculoskeletal chest pain, Venous pressure jugular increased, Abdominal pain, Pulmonary fibrosis, Glomerular filtration rate decreased, Hyponatraemia, Gynaecomastia, Hypokalaemia, Rectal polyp, Coeliac disease, Diverticulum, Blood creatinine increased, N-terminal prohormone brain natriuretic peptide increased, COVID-19, Peripheral artery stenosis, Peripheral artery stenosis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
裂孔ヘルニア	WORSENED HIATUS HERNIA	Day 424 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe
無力症	WORSENED GENERALIZED WEAKNESS	Day 424 / Day 533	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
疲労	WORSENED FATIQUE	Day 424 / Day 533	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
治験責任医師の見解：「裂孔ヘルニア」、「無力症」及び「疲労」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Intervertebral disc operation, Diabetes mellitus, Hyperlipidaemia, Hypertension, Carpal tunnel syndrome, Atrial fibrillation, Cardiac failure congestive, Benign prostatic hyperplasia, Chronic obstructive pulmonary disease, Amyloidosis senile, Chronic kidney disease, Nephrolithiasis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: METFORMIN, RAMIPRIL, APIXABAN, AMIODARONE, AMIODARONE, METOCLOPRAMIDE HYDROCHLORIDE, LABETALOL, HYDROMORPHONE HYDROCHLORIDE, ATORVASTATIN, ISOPRENALINE, ACETYLSALICYLIC ACID, FOSFOMYCIN, MIRABEGRON, RAMIPRIL, COVID-19 VACCINE, COVID-19 VACCINE, SALBUTAMOL, AMIODARONE, IPRATROPIUM BROMIDE, INSULIN LISPRO, LIDOCAINE, EPINEPHRINE, ATROPINE, CLOTRIMAZOLE, ROCURONIUM, PARACETAMOL, PROPOFOL, OXYGEN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, CEFAZOLIN SODIUM, SENNOSIDE A+B, RAMIPRIL, AMIODARONE, COVID-19 VACCINE, FUROSEMIDE, AMLODIPINE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, CEFAZOLIN, FUROSEMIDE, FUROSEMIDE, EMPAGLIFLOZIN, FUROSEMIDE, EMPAGLIFLOZIN				
Non-Serious Adverse Event [4]: Nephrolithiasis, Facet joint syndrome, Spinal osteoarthritis, Bradycardia, Fatigue, Depressed mood, Chronic kidney disease, Orthostatic hypotension, Haematochezia, Diverticulum, Large intestine polyp, Bronchial hyperreactivity, Fungal skin infection, Anaemia, Rotator cuff syndrome, Cardiac failure congestive, Heart rate increased, Blood creatinine increased, N-terminal prohormone brain natriuretic peptide increased, Blood thyroid stimulating hormone decreased, Blood glucose increased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
虚血性脳卒中	ISCHEMIC STROKE	Day 115 / Day 120	Not Related	Dose Not Changed	Recovered /Resolved	Severe
完全房室ブロック	COMPLETE HEART BLOCK	Day 499 / Day 504	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「虚血性脳卒中」及び「完全房室ブロック」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 9[redacted]	
Medical History [1]: Atrial fibrillation, Glucose tolerance impaired, Chronic kidney disease, Benign prostatic hyperplasia, Sleep apnoea syndrome, Hypertension, Cardiac failure, Peripheral arterial occlusive disease, Cardiac amyloidosis, Atrioventricular block, Cardiac pacemaker insertion					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 26			
Concomitant Medication [3]: SIMVASTATIN, VITAMIN D NOS, LOSARTAN, TAMSULOSIN HYDROCHLORIDE, APIXABAN, FUROSEMIDE					
Non-Serious Adverse Event [4]: Diarrhoea, Hypomagnesaemia					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY	Day 27 / Day 33	Not Related	Drug Withdrawn	Recovered /Resolved	Severe
治験責任医師の見解：「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: Canada	Sex: F	Age: 7[redacted]
Medical History [1]: Iron deficiency anaemia, Dyslipidaemia, Cataract operation, Hypertension, Foot deformity, Hysterectomy, Tenosynovitis stenosans, Thyroid operation, Ear pain, Odynophagia, Dysphagia, Synovial cyst, Haematoma, Tendonitis, Type 2 diabetes mellitus, Carpal tunnel decompression, Epicondylitis, Rotator cuff syndrome, Arthritis, Epistaxis, Breast cancer, Breast conserving surgery, Radiotherapy to breast, Rotator cuff syndrome, Cardiac failure, Cerebrovascular accident, Cardiac amyloidosis, Neuropathy peripheral, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 5		
Concomitant Medication [3]: METFORMIN, LINAGLIPTIN, FERROUS FUMARATE, ACETYLSALICYLIC ACID, IRBESARTAN, FUROSEMIDE, SIMVASTATIN, SPIRONOLACTONE, METOLAZONE				
Non-Serious Adverse Event [4]: Atrial tachycardia, Rash, Rash, Rash				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE ON CHRONIC KIDNEY DISEASE	Day 4 / Day 50	Not Related	Drug Withdrawn	Recovered /Resolved	Severe
治験責任医師の見解：「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Prostate cancer, Carpal tunnel syndrome, Dyslipidaemia, Osteoarthritis, Insomnia, Chronic obstructive pulmonary disease, Carpal tunnel decompression, Knee arthroplasty, Atrioventricular block first degree, Gastric ulcer, Ventricular tachycardia, Atrial fibrillation, Mitral valve incompetence, Dysarthria, Restless legs syndrome, Constipation, Gynaecomastia, Cardiac amyloidosis, Tricuspid valve incompetence, Blood bilirubin increased, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 908		
Concomitant Medication [3]: ATORVASTATIN, LORAZEPAM, PERINDOPRIL, INDAPAMIDE, AMLODIPINE, PANTOPRAZOLE, APIXABAN, NADOLOL, FUROSEMIDE, SPIRONOLACTONE, PERINDOPRIL, SPIRONOLACTONE, FUROSEMIDE, COLCHICINE, COVID-19 VACCINE, FERROUS SULFATE, NADOLOL, EPLERENONE, NADOLOL, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, APIXABAN, FUROSEMIDE, COVID-19 VACCINE, COLCHICINE, FUROSEMIDE, FUROSEMIDE, AMLODIPINE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Acute kidney injury, Fall, VIIth nerve injury, Gout, Anaemia, Polyneuropathy				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
嚥下障害	DYSPHAGIA OF UNKNOWN ETIOLOGY	Day 368 / Day 369	Not Related	Dose Not Changed	Recovered /Resolved	Mild
構語障害	WORSENING OF DYSARTHRIA	Day 368 / Day 369	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「嚥下障害」及び「構語障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Dyslipidaemia, Type 2 diabetes mellitus, Hypertension, Carpal tunnel syndrome, Carpal tunnel decompression, Osteoarthritis, Constipation, Gastrooesophageal reflux disease, Insomnia, Dyspnoea exertional, Ventricular tachycardia, Lung neoplasm malignant, Lung lobectomy, Anaemia, Coronary artery disease, Ventricular extrasystoles, Cardiac amyloidosis, Tendonitis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: GLICLAZIDE, METFORMIN, BISOPROLOL, ACETYLSALICYLIC ACID, ROSUVASTATIN, PANTOPRAZOLE, FERROUS SULFATE, LORAZEPAM, SEMAGLUTIDE, ROSUVASTATIN, AMOXICILLIN, DIPHENHYDRAMINE HYDROCHLORIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, ISOPRENALINE HYDROCHLORIDE, BISOPROLOL, CITALOPRAM, BISOPROLOL, AMIODARONE, MACROGOL				
Non-Serious Adverse Event [4]: Drug hypersensitivity, Tooth infection, Pulmonary mass, Hypervolaemia, Depression, Ventricular tachycardia, Ventricular tachycardia, Constipation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
完全房室ブロック	THIRD-DEGREE ATRIOVENTRICULAR BLOCK	Day 642 / Day 645	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「完全房室ブロック」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Dyslipidaemia, Type 2 diabetes mellitus, Diverticulum, Aortic valve replacement, Coronary artery bypass, Aortic stenosis, Atrial fibrillation, Coronary artery disease, Dry skin, Urinary incontinence, Glaucoma, Constipation, Basal cell carcinoma, Anaemia, Chronic kidney disease, Mitral valve incompetence, Tricuspid valve incompetence, Pancytopenia, Bradycardia, Cardiac pacemaker insertion, Cardiac amyloidosis, Osteoporosis, Pelvic fracture, Fracture treatment				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 234		
Concomitant Medication [3]: APIXABAN, METOPROLOL, FUROSEMIDE, DORZOLAMIDE HYDROCHLORIDE/TIMOLOL MALEATE, MACROGOL, ROSUVASTATIN, METFORMIN, ALENDRONATE SODIUM, VITAMIN D NOS, FERROUS SULFATE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE, APIXABAN, FUROSEMIDE, POTASSIUM CHLORIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), BLOOD TRANSFUSION (AUXILIARY PRODUCTS), POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, CEFTRIAXONE, AMOXICILLIN/CLAVULANIC ACID, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FERROUS SULFATE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), BLOOD TRANSFUSION (AUXILIARY PRODUCTS), FUROSEMIDE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Hyperkalaemia, Acute kidney injury, Anaemia, Cardiac failure chronic, Cardiac failure chronic, Cardiac failure chronic, Delirium, Dehydration, Hypervolaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
敗血症	SEPSIS	Day 123 / Day 127	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
トロポニンT増加	POSSIBLE TYPE 2 NSTEMI (INCREASE IN TROPONIN T HS)	Day 123 / Day 127	Not Related	Dose Not Changed	Recovered /Resolved	Mild
蜂巣炎	CELLULITIS	Day 123 / Day 141	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
貧血	WORSENING OF ANEMIA	Day 201 / Day 207	Not Related	Dose Not Changed	Recovered /Resolved	Mild
創傷出血	LOWER LEFT LEG WOUND BLEEDING	Day 201 / Day 207	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「敗血症」、「トロポニンT増加」、「蜂巣炎」、「貧血」及び「創傷出血」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Cardiac failure, Hypoacusis, Hypothyroidism, Drug hypersensitivity, Carpal tunnel decompression, Dyslipidaemia, Dyspnoea, Orthostatic hypotension, Cardiac amyloidosis, Dyspepsia, Insomnia, Benign prostatic hyperplasia, Erectile dysfunction, Nasal congestion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: TRIAMCINOLONE, ACETYLSALICYLIC ACID, PANTOPRAZOLE, RANITIDINE, ATORVASTATIN, OXAZEPAM, SILODOSIN, DUTASTERIDE, TADALAFIL, FUROSEMIDE, POLYMYXIN B, ALFUZOSIN, TRIAMCINOLONE ACETONIDE, INFLUENZA VACCINE INACT SPLIT 4V, VARICELLA ZOSTER VACCINE RGE (CHO), PNEUMOCOCCAL VACCINE CONJ 13V (CRM197), PREGABALIN, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, MORPHINE SULFATE, INFLUENZA VACCINE INACT SPLIT 4V, COVID-19 VACCINE, FERROUS SULFATE				
Non-Serious Adverse Event [4]: Ear infection, Urinary incontinence, Arthralgia, Loss of consciousness, Neck mass, Dry mouth, Musculoskeletal stiffness				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
扁桃癌	RIGHT TONSIL CANCER	Day 456 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe

治験責任医師の見解：「扁桃癌」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 6[redacted]
Medical History [1]: Chronic obstructive pulmonary disease, Hypertension, Tobacco user, Sleep apnoea syndrome, Dyslipidaemia, Acute myocardial infarction, Percutaneous coronary intervention, Coronary artery disease, Atrial fibrillation, Obesity, Cardiac failure chronic, Endocarditis, Tachycardia induced cardiomyopathy, Endocarditis, Liver disorder, Acute kidney injury, Anaemia, Chronic kidney disease, Bladder transitional cell carcinoma, Cardiac amyloidosis, Dizziness, Umbilical hernia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 916		
Concomitant Medication [3]: ATORVASTATIN, OXYGEN, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, VITAMIN D NOS, CYANOCOBALAMIN, WARFARIN, BISOPROLOL, SALBUTAMOL, DIGOXIN, FUROSEMIDE, COLCHICINE, COVID-19 VACCINE, COVID-19 VACCINE, APIXABAN, ARNICA MONTANA FLOWER, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, TRANEXAMIC ACID, BISOPROLOL, AMOXICILLIN, DILTIAZEM, FUROSEMIDE, BETAMETHASONE DIPROPIONATE/CLOTRIMAZOLE, APIXABAN, AMIODARONE, DIGOXIN, AMIODARONE, DIGOXIN				
Non-Serious Adverse Event [4]: Gout, Rash, Skin lesion				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
歯肉出血	BLEEDING GUM	Day 642 / Day 644	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心房細動	ATRIAL FIBRILLATION WITH FAST VENTRICULAR RESPONSE	Day 643 / Day 659	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「歯肉出血」及び「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Canada	Sex: F	Age: 8[redacted]
Medical History [1]: Hypertension, Colectomy, Rectal haemorrhage, Colon cancer, Osteoarthritis, Intervertebral disc disorder, Diffuse idiopathic skeletal hyperostosis, Wrist fracture, Osteopenia, Gout, Atrial fibrillation, Chronic kidney disease, Cardiac failure, Avulsion fracture, Cardiac amyloidosis, Hypergammaglobulinaemia benign monoclonal				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 924		
Concomitant Medication [3]: TRIAMTERENE, HYDROCHLOROTHIAZIDE, RIVAROXABAN, POTASSIUM, CANDESARTAN, FUROSEMIDE, SENNOSIDE A+B, MACROGOL, RIVAROXABAN, RIVAROXABAN, DALTEPARIN, SENNOSIDE A+B, MACROGOL, APIXABAN, FUROSEMIDE, COLCHICINE, PREDNISONE, POTASSIUM, LOSARTAN, COLCHICINE, MACROGOL, CALCIUM, ASCORBIC ACID, VITAMIN E NOS, VITAMIN D NOS, FISH OIL, GLUCOSAMINE, PANAX GINSENG, GINKGO BILOBA, CURCUMA LONGA/ZINGIBER OFFICINALE, FUROSEMIDE, FUROSEMIDE, COLCHICINE, ALLOPURINOL, PREDNISONE, FUROSEMIDE, SPIRONOLACTONE, COVID-19 VACCINE, SPIRONOLACTONE, ALLOPURINOL, COVID-19 VACCINE, ALLOPURINOL, SPIRONOLACTONE, SPIRONOLACTONE, ALLOPURINOL, COLCHICINE, FUROSEMIDE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Fatigue, Dehydration, Urinary retention, Constipation, Foot deformity, Gout, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY	Day 29 / Day 34	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Sleep apnoea syndrome, Bipolar I disorder, Glucose tolerance impaired, Dyslipidaemia, Hypertension, Hypothyroidism, Carpal tunnel decompression, Deafness, Chronic kidney disease, Prostate cancer, Upper gastrointestinal haemorrhage, Cerebrovascular accident, Cardiac amyloidosis, Bipolar II disorder				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: LEVOTHYROXINE SODIUM, LITHIUM CARBONATE, APIXABAN, IRBESARTAN, PANTOPRAZOLE, METOPROLOL, COVID-19 VACCINE, LITHIUM CARBONATE, COVID-19 VACCINE, COVID-19 VACCINE, APIXABAN, TOBRAMYCIN, CIPROFLOXACIN, AMIODARONE, AMIODARONE, AMIODARONE, AMLODIPINE				
Non-Serious Adverse Event [4]: Musculoskeletal stiffness, Pruritus, Abdominal pain, Vertigo, Diarrhoea, Arthralgia, Rectal haemorrhage, Pyrexia, Pyelonephritis acute, Pain in extremity, COVID-19, Ejection fraction decreased, Dyspnoea, Hypertension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
交通事故	CAR ACCIDENT	Day 779 / Day 779	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心室性頻脈	VENTRICULAR ARRHYTHMIA (TACHYCARDIA)	Day 779 / Day 786	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「交通事故」及び「心室性頻脈」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Bundle branch block left, Deafness, Pneumonia, Benign prostatic hyperplasia, Hypertension, Cataract, Carpal tunnel syndrome, Anxiety, Deep vein thrombosis, Chronic kidney disease, Pulmonary hypertension, Atrial flutter, Cardiac failure, Osteoarthritis, Atrial fibrillation, Mitral valve incompetence, Tricuspid valve incompetence, Hypokalaemia, Cystitis, Cardiac amyloidosis, Influenza, Cystitis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 720		
Concomitant Medication [3]: OXAZEPAM, FOSINOPRIL, TAMSULOSIN, APIXABAN, BISOPROLOL, FELODIPINE, POTASSIUM CHLORIDE, FUROSEMIDE, PANTOPRAZOLE, FUROSEMIDE, COLECALCIFEROL, COVID-19 VACCINE, APIXABAN, COVID-19 VACCINE, COLCHICINE, COLCHICINE, FUROSEMIDE, ALLOPURINOL, AMOXICILLIN/CLAVULANATE POTASSIUM, CEFTRIAXONE, DOXYCYCLINE, FUROSEMIDE, PARACETAMOL, SALBUTAMOL, DEXAMETHASONE, PREDNISONE, CLOPIDOGREL, GLYCERYL TRINITRATE, ROSUVASTATIN, DUTASTERIDE				
Non-Serious Adverse Event [4]: Oedema peripheral, Gout, Urinary retention, Bronchospasm				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	PNEUMONIA	Day 659 / Day 665	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「肺炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Benign prostatic hyperplasia, Dyspnoea paroxysmal nocturnal, Appendicectomy, Hypertension, Hyperuricaemia, Osteoarthritis, Cardiac amyloidosis, Cardiac failure, Depression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 909		
Concomitant Medication [3]: TAMSULOSIN, ALLOPURINOL, SPIRONOLACTONE, FUROSEMIDE, APIXABAN, VENLAFAXINE, FUROSEMIDE, FUROSEMIDE, MEPIVACAINE, PARACETAMOL, METAMIZOLE, GABAPENTIN, VENLAFAXINE, FUROSEMIDE, TRAMADOL, PARACETAMOL, PARACETAMOL, CLONAZEPAM, PIPERACILLIN/TAZOBACTAM, FERRIC CARBOXYMALTOSE, METAMIZOLE, IPRATROPIUM BROMIDE, AMOXICILLIN/CLAVULANIC ACID, ALBUMIN HUMAN, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, TRAMADOL, QUETIAPINE, FUROSEMIDE, ACETAZOLAMIDE, FUROSEMIDE, PANTOPRAZOLE, AMOXICILLIN/CLAVULANIC ACID, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, ASCORBIC ACID/POTASSIUM BICARBONATE, FUROSEMIDE, POTASSIUM CHLORIDE, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, MIRTAZAPINE, ESCITALOPRAM, LORAZEPAM, ALPRAZOLAM, ESCITALOPRAM, ASCORBIC ACID/POTASSIUM BICARBONATE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, FUROSEMIDE, ALLOPURINOL, QUETIAPINE, ESCITALOPRAM				
Non-Serious Adverse Event [4]: Generalised oedema, Dyspnoea, Increased appetite, Arthralgia, Dysphagia, Squamous cell carcinoma of skin, Back pain, Respiratory tract infection, Cognitive disorder, Acute kidney injury, Iron deficiency anaemia, Cardiac failure, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	EXACERBATION OF HEART FAILURE	Day 482 / Day 487	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Hyperparathyroidism, Cataract, Diverticulum, Hyperuricaemia, Myalgia, Chronic kidney disease, Hypertension, Hemiplegia, Benign prostatic hyperplasia, Gastritis, Lentigo maligna, Cardiac amyloidosis, Seborrhoeic keratosis, Osteoarthritis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: VITAMINS NOS, TORASEMIDE, CANDESARTAN, OMEPRAZOLE, APIXABAN, METHYLPREDNISOLONE, PARACETAMOL, PARACETAMOL/TRAMADOL HYDROCHLORIDE, METAMIZOLE, METAMIZOLE, LEVOSULPIRIDE, CALCIFEDIOL, CALCIFEDIOL, COLECALCIFEROL, OMEPRAZOLE, OMEPRAZOLE, RANITIDINE, CEFAZOLIN, METAMIZOLE, FENTANYL, PROPOFOL, LORAZEPAM, MIDAZOLAM, OMEPRAZOLE, PANTOPRAZOLE, LEVOSULPIRIDE, APIXABAN, PARACETAMOL, TORASEMIDE, CARBOHYDRATES NOS/MINERALS NOS/PROTEINS NOS/VITAMINS NOS, COLCHICINE, DEFLAZACORT, MUPIROCIN, MYROXYLON BALSAMUM BALSAM/RICINUS COMMUNIS OIL, MICONAZOLE, HYDROCORTISONE, COLCHICINE, DEFLAZACORT, EZETIMIBE/ROSUVASTATIN				
Non-Serious Adverse Event [4]: Dyspepsia, Dyspepsia, Atrial fibrillation, Nodal rhythm, Lichenification, Neck pain, Weight decreased, Gouty arthritis, Body tinea, COVID-19, Oedema peripheral, Choroidal effusion				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳血管発作	STROKE	Day 683 / Day 689	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「脳血管発作」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Hernia repair, Carpal tunnel decompression, Intention tremor, Carpal tunnel decompression, Bladder transitional cell carcinoma, Hernia repair, Knee arthroplasty, Cardiac failure, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 895			
Concomitant Medication [3]: FUROSEMIDE, PRIMIDONE, PRIMIDONE, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN/CLAVULANATE POTASSIUM, TAMSULOSIN, FUROSEMIDE, COVID-19 VACCINE						
Non-Serious Adverse Event [4]: Hypoaesthesia						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
再発膀胱癌	RECURRENCE OF BLADDER CANCER	Day 734 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe
治験責任医師の見解：「再発膀胱癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Hypertension, Hip arthroplasty, Osteoarthritis, Benign prostatic hyperplasia, Rhinitis, Catarrh, Carpal tunnel syndrome, Cardiac failure, Swollen tongue, Insomnia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902			
Concomitant Medication [3]: TAMSULOSIN, RAMIPRIL, BUMETANIDE, EPLERENONE, APIXABAN, BUMETANIDE, APIXABAN, PREDNISOLONE, COLCHICINE, ALLOPURINOL, COLCHICINE, COVID-19 VACCINE, ALLOPURINOL, COVID-19 VACCINE, CETIRIZINE, FLUTICASONE, PREDNISOLONE, FERROUS SULFATE, OMEPRAZOLE, FERROUS FUMARATE, FERROUS FUMARATE, BUMETANIDE, ALFACALCIDOL					
Non-Serious Adverse Event [4]: Atrial flutter, Dyspnoea, Melaena, Lip swelling, Melaena, Conjunctivitis, Fatigue, Gout, Abdominal pain upper, Pruritus, Dyspnoea, Anaemia					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
小腸腺癌	DUODENAL INTRAMUCOSAL ADENOCARCINOMA	Day 792 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「小腸腺癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Tuberculosis, Carpal tunnel decompression, Spinal operation, Cardioversion, Cardiac ablation, Cardioversion, Cataract, Macular fibrosis, Atrial fibrillation, Inguinal hernia repair, Cardiac failure, Cardiac amyloidosis, Dizziness postural, Spinal stenosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902			
Concomitant Medication [3]: DABIGATRAN, SPIRONOLACTONE, INFLUENZA VACCINE, COVID-19 VACCINE, PARACETAMOL, COVID-19 VACCINE, INFLUENZA VACCINE, COVID-19 VACCINE					
Non-Serious Adverse Event [4]: Nasopharyngitis, Conjunctival haemorrhage					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
房室ブロック	2:1 HEART BLOCK REQUIRING PACEMAKER INSERTION	Day 169 / Day 171	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「房室ブロック」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Limb injury, Internal fixation of fracture, Hypothyroidism, Arthroscopy, Asthma, Benign prostatic hyperplasia, Hip arthroplasty, Ventricular extrasystoles, Carpal tunnel decompression, Aortic aneurysm, Cardiac failure, Cardiac amyloidosis, Osteoarthritis, Lumbar spinal stenosis, Dry eye, Abdominal pain, Diverticulum				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: LEVOTHYROXINE SODIUM, ACETYLSALICYLIC ACID, FISH OIL, ASCORBIC ACID, UBIDECARENONE, VITAMIN D NOS, VITAMIN B COMPLEX, PARACETAMOL, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, HYDROCORTISONE SODIUM PHOSPHATE, TREHALOSE, CURCUMA LONGA, ATORVASTATIN, CALCIUM/COLECALCIFEROL, OMEPRAZOLE, CLARITHROMYCIN, METRONIDAZOLE, MORPHINE SULFATE, AMITRIPTYLINE, TAMSULOSIN, FINASTERIDE, ATORVASTATIN, CODEINE PHOSPHATE, SERTRALINE, TRIAMCINOLONE ACETONIDE, HYALURONIC ACID, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, COLLAGEN, GLUCOSAMINE, LANSOPRAZOLE, GABAPENTIN, SERTRALINE, UBIDECARENONE, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, LANSOPRAZOLE, COVID-19 VACCINE, HYALURONIC ACID, HYALURONIC ACID, TESTOSTERONE, COVID-19 VACCINE, TESTOSTERONE, TOLTERODINE, LANSOPRAZOLE, AMOXICILLIN, METRONIDAZOLE, LANSOPRAZOLE, CLARITHROMYCIN, METRONIDAZOLE, FONDAPARINUX, ACETYLSALICYLIC ACID, CLOPIDOGREL, BETAMETHASONE, LIDOCAINE, METHYLPREDNISOLONE ACETATE, COVID-19 VACCINE, SENNA ALEXANDRINA, DOCUSATE SODIUM, CODEINE, ACETYLSALICYLIC ACID, FERROUS SULFATE				
Non-Serious Adverse Event [4]: Abdominal pain, Trigger finger, Myalgia, Ligament rupture, Diarrhoea, Dizziness, Depression, Dupuytren's contracture, Rotator cuff syndrome, Arthralgia, Bradycardia, Gastrooesophageal reflux disease, Helicobacter gastritis, Anaemia, Tooth infection, Palpitations, Dermatitis, Productive cough, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胆嚢炎	CHOLECYSTITIS	Day 24 / Day 29	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胃食道逆流性疾患	GASTROESOPHAGEAL REFLUX DISEASE	Day 195 / Day 196	Not Related	Dose Not Changed	Recovered /Resolved	Mild
失神寸前の状態	VASOVAGAL EPISODE	Day 195 / Day 196	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「胆嚢炎」、「胃食道逆流性疾患」及び「失神寸前の状態」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Pneumonia, Weil's disease, Cardiac failure, Chronic kidney disease, Asthma, Cardiac amyloidosis, Carpal tunnel decompression, Tenotomy, Trigger finger, Gout					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911			
Concomitant Medication [3]: BUMETANIDE, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, MOMETASONE, STEROIDS, APIXABAN, APIXABAN, AMIODARONE, AMOXICILLIN, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, APIXABAN, BUMETANIDE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, INFLUENZA VACCINE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, AMOXICILLIN					
Non-Serious Adverse Event [4]: Muscle spasms, Tachycardia, Lower respiratory tract infection, Renal impairment, Muscle twitching, Neck pain, Oedema peripheral, Dyspnoea, COVID-19, Lower respiratory tract infection					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	ATRIAL FIBRILLATION	Day 311 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel decompression, Aortic stenosis, Spinal stenosis, Cardiac failure, Transient acantholytic dermatosis, Angina pectoris, Palpitations, Cardiac amyloidosis, Benign prostatic hyperplasia, Dizziness postural, Transcatheter aortic valve implantation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: OMEPRAZOLE, ACETYLSALICYLIC ACID, BISOPROLOL, FUROSEMIDE, TAMSULOSIN, BISOPROLOL, AMOXICILLIN, PARAFFIN, NITROFURANTOIN, BISOPROLOL, FUROSEMIDE, DEGARELIX, RAMIPRIL, FLUCLOXACILLIN, CLOBETASOL PROPIONATE, COVID-19 VACCINE, ATORVASTATIN, COVID-19 VACCINE, GLYCERYL TRINITRATE, MOMETASONE, MOMETASONE FUROATE, MOMETASONE FUROATE, DIAZEPAM, BISOPROLOL, INFLUENZA VACCINE, ATORVASTATIN, COVID-19 VACCINE, TACROLIMUS MONOHYDRATE				
Non-Serious Adverse Event [4]: Supraventricular tachycardia, Postoperative wound infection, Rash pruritic, Urinary tract infection, Chest discomfort, Fatigue, Folliculitis, Myalgia, Fatigue, Dyspnoea				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
完全房室ブロック	COMPLETE HEART BLOCK	Day 237 / Day 243	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
前立腺癌	PROSTATE CANCER	Day 366 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe
治験責任医師の見解：「完全房室ブロック」及び「前立腺癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 6[redacted]	
Medical History [1]: Intervertebral disc protrusion, Spinal fusion surgery, Gout, Androgen deficiency, Carpal tunnel decompression, Cardiac failure congestive, Carcinoid tumour, Lung lobectomy, Atrioventricular block complete, Cardiac amyloidosis, Cardiac resynchronisation therapy, Chronic kidney disease					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897			
Concomitant Medication [3]: ROSUVASTATIN, ALLOPURINOL, TESTOSTERONE, APIXABAN, SPIRONOLACTONE, FUROSEMIDE, DAPAGLIFLOZIN, COVID-19 VACCINE, COVID-19 VACCINE, LANSOPRAZOLE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, COLCHICINE, FUROSEMIDE, PARACETAMOL, COVID-19 VACCINE					
Non-Serious Adverse Event [4]: Cough, Muscle spasms, Atrial fibrillation, Type 2 diabetes mellitus, Pericardial effusion, COVID-19					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
処置後感染	HOSPITAL ACQUIRED INFECTION	Day 669 / Day 678	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「処置後感染」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Hypothyroidism, Hypercholesterolaemia, Hypertension, Muscle spasms, Carpal tunnel decompression, Cardiac failure, Thrombocytopenia, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 896			
Concomitant Medication [3]: IRBESARTAN, SIMVASTATIN, WARFARIN SODIUM, QUININE SULFATE, BISOPROLOL, LEVOTHYROXINE, BUMETANIDE, CODEINE PHOSPHATE, AMITRIPTYLINE, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE						
Non-Serious Adverse Event [4]: Rash, Fatigue, Abdominal distension, Cataract, Cataract, Sciatica, Presyncope, Fatigue, Fall, Fall, COVID-19						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
失神	SYNCOPE	Day 668 / Day 669	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「失神」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Black or African American	Country: UK	Sex: M	Age: 6[redacted]
Medical History [1]: Carpal tunnel decompression, Cataract operation, Cardiac failure congestive, Cardiac amyloidosis, Cataract operation, Gout, Chronic kidney disease, Atrial fibrillation, Epistaxis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: BISOPROLOL, FUROSEMIDE, SPIRONOLACTONE, ALLOPURINOL, APIXABAN, INFLUENZA VACCINE, APIXABAN, INSULIN HUMAN, AMIODARONE, FUROSEMIDE, SODIUM BICARBONATE, SALBUTAMOL, PREDNISOLONE, OMEPRAZOLE, SENNA ALEXANDRINA, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, BUMETANIDE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, COLCHICINE, BUMETANIDE, ALLOPURINOL, COLCHICINE, ALLOPURINOL, INFLUENZA VACCINE, VITAMIN D NOS, COVID-19 VACCINE, CALCIUM CARBONATE/COLECALCIFEROL, COVID-19 VACCINE, EPLERENONE, FUROSEMIDE, ALLOPURINOL, BISOPROLOL, METOLAZONE, BUMETANIDE, DIGOXIN, METOLAZONE, METOLAZONE, METOLAZONE, METOLAZONE, METOLAZONE				
Non-Serious Adverse Event [4]: Dysgeusia, Acute kidney injury, Constipation, Gout, Gout, Gynaecomastia, Constipation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胃腸炎	GASTROENTERITIS	Day 122 / Day 137	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心房頻脈	ATRIAL TACHYCARDIA	Day 136 / Day 137	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
急性腎障害	ACUTE KIDNEY INJURY	Day 136 / Day 163	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全	DECOMPENSATED HEART FAILURE	Day 590 / Day 628	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「胃腸炎」、「心房頻脈」、「急性腎障害」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 6[redacted]	
Medical History [1]: Carpal tunnel syndrome, Atrial fibrillation, Osteoarthritis, Cardiac amyloidosis, Cardiac failure congestive, Cardiac pacemaker insertion					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895			
Concomitant Medication [3]: ATORVASTATIN, APIXABAN, BISOPROLOL, BISOPROLOL, APIXABAN, CHLORAMPHENICOL, COVID-19 VACCINE, COVID-19 VACCINE, FLUCLOXACILLIN, FLUCLOXACILLIN, VANCOMYCIN, CLOTRIMAZOLE, SULFAMETHOXAZOLE/TRIMETHOPRIM, HYDROCORTISONE, COVID-19 VACCINE, BISOPROLOL, FLUCLOXACILLIN					
Non-Serious Adverse Event [4]: Conjunctivitis, Diarrhoea, Vomiting, Dyspepsia, Oral candidiasis, Rash, Postoperative wound infection					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
医療機器関連感染	PACEMAKER INFECTION	Day 629 / Day 646	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「医療機器関連感染」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]		
Medical History [1]: Carpal tunnel decompression, Hernia hiatus repair, Bradyarrhythmia, Syncope, Cardiac failure, Hypertension, Cardiac pacemaker insertion, Cardiac amyloidosis, Chronic kidney disease, Inguinal hernia						
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 895					
Concomitant Medication [3]: OMEPRAZOLE, LOSARTAN, BISOPROLOL, ATORVASTATIN, CEFTRIAXONE SODIUM, FLUCLOXACILLIN, NITROFURANTOIN, TRIMETHOPRIM, TAMSULOSIN, COVID-19 VACCINE, COVID-19 VACCINE, TRIMETHOPRIM, APIXABAN, AMOXICILLIN/CLAVULANATE POTASSIUM, COVID-19 VACCINE, TADALAFIL, COVID-19 VACCINE						
Non-Serious Adverse Event [4]: Bursitis, Urinary tract infection, Urinary tract infection, Urinary tract infection, Atrial fibrillation						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
術後尿閉	POST-OPERATIVE URINARY RETENTION	Day 391 / Day 392	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「術後尿閉」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: Black or African American		Country: UK	Sex: M	Age: 5[redacted]
Medical History [1]: Asthma, Eyelid ptosis, Carpal tunnel decompression, Atrial fibrillation, Cardiac failure, Cardiac ablation, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 898			
Concomitant Medication [3]: BUDESONIDE/FORMOTEROL FUMARATE, SALBUTAMOL, RIVAROXABAN, SPIRONOLACTONE, FUROSEMIDE, TRIMETHOPRIM, NITROFURANTOIN, COVID-19 VACCINE, COVID-19 VACCINE, FEXOFENADINE, PREDNISOLONE, NAPROXEN, COVID-19 VACCINE, AMOXICILLIN, DOXYCYCLINE, PREDNISOLONE, CIPROFLOXACIN						
Non-Serious Adverse Event [4]: Hyperhidrosis, Night sweats, Dyspnoea, Inguinal hernia, Weight decreased, Fatigue, Hypoaesthesia, Urinary tract infection, Hypoglycaemia, Seasonal allergy, Ear haemorrhage, Back pain, Nasopharyngitis, Lower respiratory tract infection, Lower respiratory tract infection						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
精巣炎	EPIDIDYMO-ORCHITIS	Day 849 / Day 868	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「精巣炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Benign prostatic hyperplasia, Inguinal hernia, Type 2 diabetes mellitus, Dyslipidaemia, Atrioventricular block first degree, Cardiac pacemaker insertion, Large intestinal polypectomy, Iron deficiency anaemia, Cardiac failure chronic, Atrial fibrillation, Chronic kidney disease, Amyloidosis, Prostatectomy, Transurethral prostatectomy, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: ATORVASTATIN, METFORMIN, VILDAGLIPTIN, SPIRONOLACTONE, OMEPRAZOLE, DABIGATRAN, ALLOPURINOL, FERROUS GLYCINE SULFATE, FUROSEMIDE, METHYLPREDNISOLONE, RED BLOOD CELLS, SPIRONOLACTONE, FUROSEMIDE, METHYLPREDNISOLONE, FERRIC CARBOXYMALTOSE, FEBUXOSTAT, FERRIC CARBOXYMALTOSE, GLYCERYL TRINITRATE, RED BLOOD CELLS (LEUCOCYTE DEPLETED), FERRIC CARBOXYMALTOSE, FERRIC CARBOXYMALTOSE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, HYDROCHLOROTHIAZIDE, FUROSEMIDE, POTASSIUM BICARBONATE, ASCORBIC ACID, FUROSEMIDE, FUROSEMIDE, ASPARTIC ACID, FUROSEMIDE, FUROSEMIDE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, AZITHROMYCIN, ONDANSETRON, OMEPRAZOLE, INSULIN, CLAVULANIC ACID, AMOXICILLIN, SODIUM CHLORIDE, SODIUM CHLORIDE, GLUCOSE, GLUCOSE, DEXKETOPROFEN, TRAMADOL, PARACETAMOL, METAMIZOLE, DIAZEPAM, FUROSEMIDE, OMEPRAZOLE, GLUCOSE, PARACETAMOL, METAMIZOLE, METOCLOPRAMIDE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, OMEPRAZOLE, POTASSIUM BICARBONATE, ASCORBIC ACID, FUROSEMIDE, HYDROCHLOROTHIAZIDE, POTASSIUM BICARBONATE, ASCORBIC ACID, FUROSEMIDE, HYDROCHLOROTHIAZIDE, FERRIC CARBOXYMALTOSE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, AMOXICILLIN, FUROSEMIDE, TRAZODONE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, HYDROCHLOROTHIAZIDE, FUROSEMIDE, DARBEPOETIN ALFA, COVID-19 VACCINE, SULFADIAZINE SILVER, HYDROXYZINE, METHYLPREDNISOLONE, FUROSEMIDE, INSULIN GLULISINE, GLUCOSE MONOHYDRATE/SODIUM CHLORIDE				
Non-Serious Adverse Event [4]: Gout, Iron deficiency anaemia, Acute kidney injury, Angina pectoris, Iron deficiency anaemia, Acute kidney injury, Tooth infection, Cardiac failure, Cardiac failure, Cardiac failure, Tooth infection, Cardiac failure, Constipation, Tooth infection, Insomnia, Ascites, Iron deficiency, Skin ulcer, Conjunctival haemorrhage, Urticaria, Decreased appetite, Dizziness, Fall, Syncope				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
単径ヘルニア	LEFT INGUINOSCROTAL HERNIA	Day 341 / Day 346	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「単径ヘルニア」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Appendicectomy, Inguinal hernia repair, Hypertension, Prostate cancer, Radiation proctitis, Proctitis, Iron deficiency anaemia, Cardiac failure, Aortic stenosis, Colon adenoma, Ischaemic cardiomyopathy, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: TOCOPHERYL ACETATE, RETINOL PALMITATE, OMEPRAZOLE, AMLODIPINE, ATORVASTATIN, FERRIC CARBOXYMALTOSE, EPLERENONE, FUROSEMIDE, ARGININE ASPARTATE/CYPROHEPTADINE ALPHAKETOGLUTARATE, AZELASTINE, FLUTICASONE PROPIONATE, GLYCERYL TRINITRATE, GLYCERYL TRINITRATE, ISOSORBIDE MONONITRATE, BUTYLSCOPOLAMINE, ENOXAPARIN, SPIRONOLACTONE, FUROSEMIDE, PARACETAMOL, ENOXAPARIN, DEXKETOPROFEN, IPRATROPIUM BROMIDE, FUROSEMIDE, TAMSULOSIN HYDROCHLORIDE, MOMETASONE, FUROSEMIDE, FUROSEMIDE, CIPROFLOXACIN, MORPHINE HYDROCHLORIDE, OMEPRAZOLE, INSULIN HUMAN, AMIKACIN, TAZOBACTAM, TAZOBACTAM, PIPERACILLIN, PIPERACILLIN, ENOXAPARIN, ENOXAPARIN, POTASSIUM CHLORIDE, SODIUM CHLORIDE, GLUCOSE, NOREPINEPHRINE, EPLERENONE, PARACETAMOL, SODIUM CHLORIDE, POTASSIUM PHOSPHATE MONOBASIC, GLUCOSE, FUROSEMIDE, OMEPRAZOLE, CIPROFLOXACIN, CIPROFLOXACIN, PHYTOMENADIONE, RIVAROXABAN, RIVAROXABAN, POTASSIUM PHOSPHATE MONOBASIC, PANTOPRAZOLE, CIPROFLOXACIN, SODIUM CHLORIDE, ATORVASTATIN, MESALAZINE, FUROSEMIDE, INSULIN, IRON/SUCROSE, EPLERENONE, FUROSEMIDE, ALPRAZOLAM, OMEPRAZOLE, CIPROFLOXACIN, ENOXAPARIN, DOMPERIDONE, POTASSIUM CHLORIDE, FUROSEMIDE, LORAZEPAM, HYDROCORTISONE, MUPIROCIN, EPLERENONE, ATORVASTATIN, TAMSULOSIN HYDROCHLORIDE, BUTYLSCOPOLAMINE, FUROSEMIDE, METAMIZOLE, HALOPERIDOL, DIAZEPAM, RED BLOOD CELLS (CONCENTRATED), CEFTRIAXONE, LEVOFLOXACIN, LACTULOSE, FUROSEMIDE, MEROPENEM, SODIUM CHLORIDE, ALPRAZOLAM, LORAZEPAM, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, FLUOXETINE, METOCLOPRAMIDE, CEFTRIAXONE, CIPROFLOXACIN, ENOXAPARIN, GLUCOSE/SODIUM CHLORIDE, ISOSORBIDE MONONITRATE, PARACETAMOL, TIAPRIDE, ALPRAZOLAM, IPRATROPIUM BROMIDE, METHYLPREDNISOLONE, AMLODIPINE, SILODOSIN, LEVOFLOXACIN, FUROSEMIDE, FORMOTEROL, SALBUTAMOL, BECLOMETASONE, DEFLAZACORT, FUROSEMIDE, TAMSULOSIN, BISOPROLOL, COVID-19 VACCINE, COVID-19 VACCINE, RANOLAZINE, OMEPRAZOLE, RED BLOOD CELLS (CONCENTRATED), POTASSIUM CHLORIDE, FUROSEMIDE, GLUCOSE/SODIUM CHLORIDE, PARACETAMOL, CITRIC ACID, MAGNESIUM OXIDE, SODIUM PICOSULFATE, RANOLAZINE, OMEPRAZOLE, FUROSEMIDE, FERROUS GLYCINE SULFATE, ATORVASTATIN, SILODOSIN, FUROSEMIDE, FORMOTEROL, BECLOMETASONE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, ENOXAPARIN, FUROSEMIDE, SALBUTAMOL, IPRATROPIUM BROMIDE, METHYLPREDNISOLONE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, METHYLPREDNISOLONE, FUROSEMIDE, METHYLPREDNISOLONE, EBASTINE, PREDNISONE, METHYLPREDNISOLONE, DEXCHLORPHENIRAMINE, METHYLPREDNISOLONE, PREDNISONE, PREDNISONE, AZITHROMYCIN, CEFTRIAXONE, FUROSEMIDE, METOCLOPRAMIDE, ENOXAPARIN, PARACETAMOL, ACETYLCYSTEINE, FORMOTEROL, IPRATROPIUM BROMIDE, BUDESONIDE, METHYLPREDNISOLONE, FUROSEMIDE, TAMSULOSIN, FERROUS GLYCINE SULFATE, FORMOTEROL, SALBUTAMOL, BECLOMETASONE, EPLERENONE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, FERROUS GLYCINE SULFATE, FUROSEMIDE, PARACETAMOL, FORMOTEROL, BUDESONIDE, POTASSIUM CHLORIDE, SACCHARATED IRON OXIDE, ALPRAZOLAM, FUROSEMIDE, ENOXAPARIN, ACETYLCYSTEINE, FORMOTEROL, BUDESONIDE, FLUOXETINE, FUROSEMIDE, FUROSEMIDE, FOLIC ACID, FUROSEMIDE, ALPRAZOLAM, FORMOTEROL, BECLOMETASONE, FERROUS GLYCINE SULFATE, EPLERENONE, FUROSEMIDE, AMLODIPINE, ENOXAPARIN, AMLODIPINE, FUROSEMIDE, PARACETAMOL, ALPRAZOLAM, CLOMETHIAZOLE, FORMOTEROL, BUDESONIDE, FUROSEMIDE, MORPHINE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, IRON/SUCROSE, IRON/SUCROSE, DEXCHLORPHENIRAMINE, MOMETASONE, FOSFOMYCIN, FORMOTEROL, BECLOMETASONE, AMLODIPINE, FUROSEMIDE, SILODOSIN, ALPRAZOLAM, LORAZEPAM, AZITHROMYCIN, CEFIXIME, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE				

Non-Serious Adverse Event [4]: Asthenia, Rhinitis, Angina pectoris, Depression, Urinary tract infection bacterial, Chronic obstructive pulmonary disease, Non-cardiac chest pain, Constipation, Aortic stenosis, Non-cardiac chest pain, Neutropenia, Rectal haemorrhage, Angina pectoris, Eczema asteatotic, Back pain, Hypoaesthesia, Upper respiratory tract infection, Dysphonia, Angina pectoris, Rectal haemorrhage, Iron deficiency anaemia, Cardiac failure						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鉄欠乏性貧血	ACUTE EPISODE OF CHRONIC IRON DEFICIENCY ANEMIA	Day 176 / Day 198	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（1）	DECOMPENSATED HEART FAILURE	Day 176 / Day 198	Not Related	Dose Not Changed	Recovered /Resolved	Severe
処置後血尿	POST PROCEDURAL HAEMATURIA	Day 181 / Day 198	Not Related	Dose Not Changed	Recovered /Resolved	Severe
敗血症性ショック	URINARY SEPTIC SHOCK	Day 183 / Day 198	Not Related	Dose Not Changed	Recovered /Resolved	Severe
毛細血管拡張症	HEMORRHAGIC TELANGIECTASIAS	Day 203 / Day 220	Not Related	Dose Not Changed	Recovered /Resolved	Severe
細菌性尿路感染	URINARY TRACT INFECTION (E.COLI BACTEREMIA)	Day 255 / Day 262	Not Related	Drug Interrupted	Recovered /Resolved	Severe
外傷性血尿	HEMATURIA DUE TO ACCIDENTAL SELFREMOVE OF URINARY CATHETER	Day 255 / Day 262	Not Related	Drug Interrupted	Recovered /Resolved	Severe
貧血（1）	SEVERE ACUTE ANEMIA	Day 399 / Day 414	Not Related	Drug Interrupted	Recovered /Resolved	Severe
下部消化管出血	LOWER GASTROINTESTINAL BLEEDING	Day 399 / Day 414	Not Related	Drug Interrupted	Recovered /Resolved	Severe
慢性閉塞性肺疾患	WORSENING OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	Day 485 / Day 492	Not Related	Drug Interrupted	Recovered /Resolved	Severe

心不全（2）	DECOMPENSATED HEART FAILURE	Day 567 / Day 575	Not Related	Drug Interrupted	Recovered /Resolved	Severe
下気道感染	LOWER RESPIRATORY INFECTION	Day 567 / Day 575	Not Related	Drug Interrupted	Recovered /Resolved	Severe
急性呼吸不全	ACUTE RESPIRATORY FAILURE	Day 567 / Day 575	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全（3）	DECOMPENSATED HEART FAILURE	Day 596 / Day 609	Not Related	Drug Interrupted	Recovered /Resolved	Severe
急性肺水腫	ACUTE PULMONARY EDEMA	Day 596 / Day 609	Not Related	Drug Interrupted	Recovered /Resolved	Severe
呼吸不全	RESPIRATORY FAILURE	Day 596 / Day 609	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全（4）	DECOMPENSATED HEART FAILURE	Day 653 / Day 657	Not Related	Drug Interrupted	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９	SARS-COV-2 INFECTION	Day 653 / Day 671	Not Related	Drug Interrupted	Recovered /Resolved	Severe
狭心症	ANGINA PECTORIS	Day 655 / Day 665	Not Related	Drug Interrupted	Recovered /Resolved	Severe
貧血（2）	SEVERE ACUTE ANEMIA	Day 664 / Day 674	Not Related	Drug Interrupted	Recovered /Resolved	Severe
直腸出血	RECTAL BLEEDING	Day 664 / Day 812	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「鉄欠乏性貧血」、「心不全（1）」、「処置後血尿」、「敗血症性ショック」、「毛細血管拡張症」、「細菌性尿路感染」、「外傷性血尿」、「貧血（1）」、「下部消化管出血」、「慢性閉塞性肺疾患」、「心不全（2）」、「下気道感染」、「急性呼吸不全」、「心不全（3）」、「急性肺水腫」、「呼吸不全」、「心不全（4）」、「ＣＯＶＩＤ－１９」、「狭心症」、「貧血（2）」及び「直腸出血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]	
Medical History [1]: Hypertension, Atrial fibrillation, Cardiac failure, Hypothyroidism, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 897				
Concomitant Medication [3]: EDOXABAN TOSILATE, AMIODARONE HYDROCHLORIDE, TORASEMIDE, CANDESARTAN CILEXETIL, LEVOTHYROXINE SODIUM, COVID-19 VACCINE, COVID-19 VACCINE, EDOXABAN TOSILATE					
Non-Serious Adverse Event [4]: Epistaxis, Fall, Raynaud's phenomenon, Cataract, Cataract, Pain in extremity					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
転倒	FALL	Day 804 / Day 807	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「転倒」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: F	Age: 7[redacted]	
Medical History [1]: Appendicectomy, Tonsillectomy, Cholecystectomy, Atrial fibrillation, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 64				
Concomitant Medication [3]: BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, FUROSEMIDE, ACENOCOUMAROL, DIGOXIN, FUROSEMIDE, FUROSEMIDE, METHYLPREDNISOLONE					
Non-Serious Adverse Event [4]: Atrial tachycardia					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胃炎	GASTRITIS (PREVIOUSLY REPORTED AS ABDOMINAL PAIN)	Day 59 / Day 69	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９	SARS-COV2 INFECTION WITHOUT PNEUMONIA	Day 64 / Day 69	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「胃炎」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Peroneal nerve palsy, Cholecystectomy, Bladder neoplasm, Carpal tunnel syndrome, Catheterisation cardiac, Aortic injury, Oedema peripheral, Dyslipidaemia, Insomnia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, FUROSEMIDE, DIAZEPAM, ROSUVASTATIN, COVID-19 VACCINE, COVID-19 VACCINE, CEFTRIAXONE, CIPROFLOXACIN, PARACETAMOL, METAMIZOLE, PARACETAMOL, DICLOFENAC, LORAZEPAM				
Non-Serious Adverse Event [4]: Nerve injury, Clavicle fracture, Tachycardia, COVID-19, Arthralgia, Aortic injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
シュードモナス性尿路感染	URINARY TRACT INFECTION SECONDARY TO PSEUDOMONA AERUGINOSA	Day 296 / Day 302	Not Related	Dose Not Changed	Recovered /Resolved	Mild
絞扼性鼡径ヘルニア	STRANGLED INGUINAL HERNIA	Day 454 / Day 458	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「シュードモナス性尿路感染」及び「絞扼性鼡径ヘルニア」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White	Country: Spain		Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Deep vein thrombosis, Ocular hypertension, Hyperuricaemia, Hypertensive nephropathy, Atrial fibrillation, Amaurosis fugax, Rotator cuff syndrome, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 64			
Concomitant Medication [3]: TIMOLOL, OMEPRAZOLE, ALLOPURINOL, CHLORTALIDONE, ACENOCOUMAROL, CALCIFEDIOL, BISOPROLOL, FUROSEMIDE, OLMESARTAN						
Non-Serious Adverse Event [4]: Overdose, Prostatic disorder						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	BILATERAL PNEUMONIA DUE TO SARS-COV2	Day 1 / Day 12	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Stent placement, Prostate cancer, Acute myocardial infarction, Osteoarthritis, Cardiac failure, Hypercholesterolaemia, Spinal column injury, Intervertebral disc protrusion, Lumbar spinal stenosis, Insomnia, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 895			
Concomitant Medication [3]: DIAZEPAM, ROSUVASTATIN CALCIUM, RIVAROXABAN, SERTRALINE, FUROSEMIDE, CEFTRIAXONE, CEFIXIME, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, ROSUVASTATIN, EZETIMIBE, ZOLPIDEM						
Non-Serious Adverse Event [4]: Somnolence, Anaemia						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路感染	URINARY TRACT INFECTION	Day 94 / Day 101	Not Related	Drug Interrupted	Recovered /Resolved	Mild
大腿骨骨折	FEMUR FRACTURE	Day 608 / Day 622	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「尿路感染」及び「大腿骨骨折」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperuricaemia, Asthma, Dyslipidaemia, Hypertension, Sleep apnoea syndrome, Carpal tunnel syndrome, Aortic valve incompetence, Chronic kidney disease, Prophylaxis against gastrointestinal ulcer, Depression, Cardiac amyloidosis, Cardiac failure, Abdominal pain, Decreased appetite				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 231		
Concomitant Medication [3]: FORMOTEROL FUMARATE DIHYDRATE, BECLOMETASONE DIPROPIONATE, PANTOPRAZOLE, ACETYLSALICYLIC ACID, SERTRALINE, TRAZODONE, SPIRONOLACTONE, FUROSEMIDE, CARVEDILOL, MEGESTROL ACETATE, ALLOPURINOL, MIRTAZAPINE, SPIRONOLACTONE, TRAZODONE, SPIRONOLACTONE, GABAPENTIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, RIFAXIMIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, CHLORTALIDONE, CHLORTALIDONE				
Non-Serious Adverse Event [4]: Acute kidney injury, Cardiac failure, Cardiac failure, Cardiac failure, Cardiac failure, Cardiac failure, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心腎症候群	WORSENING CARDIORENAL SYNDROME	Day 54 / Day 84	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	HEART FAILURE HOSPITALIZATION	Day 231 / Day 243	Not Related	Drug Withdrawn	Recovered /Resolved With Sequelae	Severe
治験責任医師の見解：「心腎症候群」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Portugal	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel syndrome, Tonsillectomy, Intervertebral disc protrusion, Hypertension, Dyslipidaemia, Insomnia, Hyperuricaemia, Rib fracture, Renal stone removal, Carpal tunnel decompression, Ischaemic stroke, Myalgia, Cerebrovascular disorder, Atheroembolism, Gout, Ischaemic stroke, Cardiac failure, Hypotension, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 806		
Concomitant Medication [3]: BROMAZEPAM, ALLOPURINOL, CLOPIDOGREL, FUROSEMIDE, ROSUVASTATIN, GABAPENTIN, FUROSEMIDE, CLOPIDOGREL, COVID-19 VACCINE, CANDESARTAN, MIDODRINE, FUROSEMIDE, COVID-19 VACCINE, MIDODRINE, IPRATROPIUM BROMIDE, BUDESONIDE, BUDESONIDE/FORMOTEROL FUMARATE, FUROSEMIDE, MIDODRINE, FUROSEMIDE, MIDODRINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, MIDODRINE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE INACT SAG 4V, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, ENOXAPARIN SODIUM, FUROSEMIDE, POTASSIUM CHLORIDE, ENOXAPARIN SODIUM, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE				
Non-Serious Adverse Event [4]: Fatigue, Dizziness postural, Oedema peripheral, Urine albumin/creatinine ratio increased, Rales, Epistaxis, Upper respiratory tract infection, Bilirubin conjugated increased, Cardiac failure, Iron deficiency, Cardiac failure, Fall				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 373 / Day 395	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	WORSENING HEART FAILURE	Day 502 / Day 504	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（3）	WORSENING HEART FAILURE	Day 572 / Day 586	Not Related	Dose Not Changed	Recovered /Resolved	Severe
失神寸前の状態	PRE SYNCOPE	NA / Start Day + 6 Days	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」及び「失神寸前の状態」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]	
Medical History [1]: Carpal tunnel decompression, Hypertrophic cardiomyopathy, Cardiac amyloidosis, Cardiac failure, Palpitations, Implantable defibrillator insertion, Benign prostatic hyperplasia, Presyncope					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 578			
Concomitant Medication [3]: METOPROLOL SUCCINATE, CANRENONE, FUROSEMIDE, TAMSULOSIN HYDROCHLORIDE, DUTASTERIDE, LANSOPRAZOLE, RIVAROXABAN, MAGALDRATE					
Non-Serious Adverse Event [4]: Abdominal pain upper					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
狭心症	EFFORT ANGINA	Day 57 / Day 59	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「狭心症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Cardiac failure, Gilbert's syndrome, Hypercholesterolaemia, Osteoarthritis, Joint prosthesis user, Tonsillectomy, Myocardial infarction, Percutaneous coronary intervention, Carpal tunnel decompression, Carpal tunnel decompression, Percutaneous coronary intervention, Dyspnoea, Percutaneous coronary intervention, Hyperuricaemia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 551		
Concomitant Medication [3]: CANRENONE, FUROSEMIDE, ACETYLSALICYLIC ACID, ESOMEPRAZOLE, BISOPROLOL, EZETIMIBE/ROSUVASTATIN ZINC, ALLOPURINOL, FUROSEMIDE, ANTIBIOTICS, HEPARIN, CORTISONE, FUROSEMIDE, EZETIMIBE/ROSUVASTATIN ZINC, COVID-19 VACCINE, COVID-19 VACCINE, RIVAROXABAN, ACETYLSALICYLATE LYSINE				
Non-Serious Adverse Event [4]: Fatigue, Decreased appetite, Dizziness, Dysgeusia, Orthopnoea, Pyrexia, Asthenia, COVID-19, Haematuria, Nausea, Pruritus, Haematuria, Atrial fibrillation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
移行上皮癌	RIGHT UROTHELIAL CARCINOMA	Day 489 / Day 608	Not Related	Drug Interrupted	Recovered /Resolved	Severe
貧血	SEVERE ANEMIA	Day 552 / Day 571	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「移行上皮癌」及び「貧血」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Tendon rupture, Chronic kidney disease, Cardiac failure, Mitral valve incompetence, Mitral valve replacement, Carpal tunnel decompression, Atrial fibrillation, Hyperthyroidism, Carotid artery stenosis, Cardioversion, Embolic stroke, Atrioventricular block first degree, Cardiac amyloidosis, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: FUROSEMIDE, DABIGATRAN, OMEPRAZOLE SODIUM, FUROSEMIDE, ATORVASTATIN CALCIUM, DIGOXIN, BISOPROLOL FUMARATE, INFLUENZA VACCINE, OMEPRAZOLE, ATORVASTATIN CALCIUM, ACETYLSALICYLIC ACID, WARFARIN, ALLOPURINOL, AZITHROMYCIN, INFLUENZA VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS				
Non-Serious Adverse Event [4]: Gamma-glutamyltransferase increased, Hyperuricaemia, Benign prostatic hyperplasia, Oropharyngeal pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
一過性脳虚血発作	TRANSITOR ISCHEMI ATTACK	Day 432 / Day 433	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「一過性脳虚血発作」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperuricaemia, Tendon operation, Haemorrhoid operation, Inguinal hernia repair, Inguinal hernia repair, Hypertension, Chronic kidney disease, Hyperthyroidism, Hypothyroidism, Atrial fibrillation, Cardiac failure, Benign prostatic hyperplasia, Neoplasm skin, Chronic obstructive pulmonary disease, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 510		
Concomitant Medication [3]: BISOPROLOL, FINASTERIDE, FUROSEMIDE, FUROSEMIDE, ALFUZOSIN HYDROCHLORIDE, RIVAROXABAN, LEVOTHYROXINE SODIUM, ALLOPURINOL, CLARITHROMYCIN, BETAMETHASONE/GENTAMICIN, RIVAROXABAN, FUROSEMIDE, METOLAZONE, CODEINE/PARACETAMOL, TRIAZOLAM, FUROSEMIDE, METOLAZONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, LEVOTHYROXINE SODIUM, PANTOPRAZOLE, IRON, BISOPROLOL, ALFUZOSIN HYDROCHLORIDE, ALLOPURINOL, FUROSEMIDE, AMOXICILLIN TRIHYDRATE, ENOXAPARIN SODIUM, PARACETAMOL, TRIAZOLAM, POTASSIUM CHLORIDE, METOLAZONE, PROMAZINE HYDROCHLORIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PROMAZINE HYDROCHLORIDE, METOLAZONE, SACCHAROMYCES BOULARDII, VANCOMYCIN, FERROGLYCINE SULFATE COMPLEX, FUROSEMIDE, VANCOMYCIN, VANCOMYCIN, VANCOMYCIN, VANCOMYCIN, EPOETIN ALFA				
Non-Serious Adverse Event [4]: Dermatitis, Back pain, Insomnia, Cardiac failure, Anaemia, Seasonal allergy, Seasonal allergy, Renal failure, Urinary tract infection, Scrotal haematoma, Idiopathic interstitial pneumonia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING HEART FAILURE	Day 216 / Day 240	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（2）	WORSENING HEART FAILURE	Day 320 / Day 327	Not Related	Dose Not Changed	Recovered /Resolved	Mild
頭部損傷	HEAD INGIURY	Day 330 / Day 338	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（3）	WORSENING HEART FAILURE	Day 345 / Day 380	Not Related	Dose Reduced	Recovered /Resolved	Mild
直腸出血	RECTORRHAGIA	Day 428 / Day 455	Not Related	Dose Not Changed	Recovered /Resolved	Mild
クロストリジウム・ディフィシレ感染	CLOSTRIDIUM DIFFICILE INFECTION	Day 428 / Day 495	Not Related	Dose Not Changed	Recovered /Resolved	Mild
尿路感染	URINARY INFECTION	Day 520 / Day 533	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「心不全（1）」、「心不全（2）」、「頭部損傷」、「心不全（3）」、「直腸出血」、「クロストリジウム・ディフィシレ感染」及び「尿路感染」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Tonsillectomy, Arthralgia, Drug-induced liver injury, Tuberculosis, Abdominal operation, Inguinal hernia, Hypertension, Carpal tunnel decompression, Carpal tunnel decompression, Dyslipidaemia, Atrial flutter, Atrial flutter, Cardiac amyloidosis, Atrial fibrillation, Cardiac failure, Cyst removal				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: APIXABAN, BISOPROLOL, FUROSEMIDE, GLUCOSE, AMIODARONE, AMIODARONE, COVID-19 VACCINE, COVID-19 VACCINE, ROSUVASTATIN, LEVOTHYROXINE, FACTOR II (PROTHROMBIN)/FACTOR IX/FACTOR X (STUART PROWER FACTOR), APIXABAN, INFLUENZA VACCINE, COVID-19 VACCINE, AMIODARONE, LEVOTHYROXINE, LEVOTHYROXINE, PANTOPRAZOLE, COVID-19 VACCINE, NYSTATIN, METOCLOPRAMIDE, AZITHROMYCIN DIHYDRATE, CEFIXIME, BISOPROLOL, METHYLPREDNISOLONE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, METHYLPREDNISOLONE, METHYLPREDNISOLONE, FUROSEMIDE, UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE, BISOPROLOL FUMARATE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Hypothyroidism, Hypercholesterolaemia, Epistaxis, Dyspepsia, Hypertransaminasaemia, COVID-19, Atrial fibrillation, Hepatitis C, Syncope, Gastroenteritis, Heart rate increased, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING HIGH FREQUENCY ARTIAL FIBRILLATION	Day 87 / Day 92	Not Related	Dose Not Changed	Recovered /Resolved	Severe
胃腸炎	ACUTE GASTROENTERITIS	Day 778 / Day 784	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「心房細動」及び「胃腸炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Bundle branch block right, Abscess drainage, Phlebectomy, Appendicectomy, Inguinal hernia, Benign prostatic hyperplasia, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: SERENOA REPENS, EDOXABAN, POTASSIUM CANRENOATE, FUROSEMIDE, INFLUENZA VACCINE, CHLORPHENAMINE/PARACETAMOL, ASCORBIC ACID/BIOTIN/CALCIUM PANTOTHENATE/CYANOCOBALAMIN/ERGOCALCIFEROL/FOLIC ACID/NICOTINAMIDE/PYRIDOXINE HYDROCHLORIDE/RETINOL/RIBOFLAVIN/THIAMINE HYDROCHLORIDE/TOCOPHEROL, BISOPROLOL, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, METOLAZONE, SERTRALINE, AMOXICILLIN/CLAVULANIC ACID, BISOPROLOL, FUROSEMIDE, ACETYLSALICYLIC ACID, CLOPIDOGREL, ATORVASTATIN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, CEFIXIME, FUROSEMIDE, ALLOPURINOL, BISOPROLOL FUMARATE, FUROSEMIDE, EDOXABAN, WARFARIN SODIUM, EZETIMIBE/ROSUVASTATIN, FUROSEMIDE, BISOPROLOL, POTASSIUM CANRENOATE, FUROSEMIDE, PARACETAMOL, INFLUENZA VACCINE, COLECALCIFEROL, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Nasopharyngitis, Fatigue, Ventricular tachycardia, Depression, Diarrhoea, Dysuria, Pathological fracture, Atrial fibrillation, Thoracic spinal stenosis, Vomiting, Chronic kidney disease, Urinary tract infection, Alanine aminotransferase increased, Aspartate aminotransferase increased, Hyperuricaemia, Brachial artery entrapment syndrome, Cardiac failure, Blood potassium increased, COVID-19, Hyperparathyroidism, Arthralgia, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	NA / Start Day + 136 Days	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性腎障害	ACUTE RENAL FAILURE	Day 288 / Day 310	Not Related	Dose Reduced	Recovered /Resolved	Moderate
心房細動	ATRIAL FIBRILATION AND FLUTTER HIGH-FREQUENCY	Day 433 / Day 434	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「心不全」、「急性腎障害」及び「心房細動」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7■
Medical History [1]: Tonsillectomy, Limb injury, Hypertension, Joint prosthesis user, Chronic kidney disease, Respiratory failure, Cardiac failure chronic, Hypertrophic cardiomyopathy, Hyperuricaemia, Obesity, Chronic obstructive pulmonary disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 937		
Concomitant Medication [3]: PANTOPRAZOLE, ENALAPRIL, ATENOLOL, AMLODIPINE, SPIRONOLACTONE, ALLOPURINOL, GLYCOPYRRONIUM, POTASSIUM CANRENOATE, FUROSEMIDE, VALSARTAN, AMLODIPINE, FUROSEMIDE, ALLOPURINOL, DIURETICS, OXYGEN, ENOXAPARIN, RAMIPRIL, CANRENONE, FUROSEMIDE, LORAZEPAM, SERTRALINE, COVID-19 VACCINE, NEBIVOLOL HYDROCHLORIDE, VALSARTAN, FUROSEMIDE, ALLOPURINOL, FUROSEMIDE, OXYGEN, OXYGEN, VORTIOXETINE, POTASSIUM CANRENOATE, FUROSEMIDE, AZITHROMYCIN, CEFTRIAXONE, ENOXAPARIN, FUROSEMIDE, METHYLPREDNISOLONE, METHYLPREDNISOLONE, METHYLPREDNISOLONE, METHYLPREDNISOLONE, RIVAROXABAN, TAMSULOSIN, MIRTAZAPINE, OXYGEN, TAZOBACTAM, PIPERACILLIN, AZITHROMYCIN, RIVAROXABAN				
Non-Serious Adverse Event [4]: Oedema peripheral, Renal impairment, Anxiety, Hyperkalaemia, Benign prostatic hyperplasia, Asymptomatic COVID-19, Arthropathy				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性呼吸不全	HYPOXEMIC HYPERCAPNIC ACUTE RESPIRATORY FAILURE	Day 109 / Day 117	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全（1）	ACUTE HEART FAILURE	Day 833 / Day 839	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（2）	ACUTE HEART FAILURE	Day 864 / Day 876	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺炎	PNEUMONIA	Day 908 / Day 921	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「急性呼吸不全」、「急性心不全（1）」、「急性心不全（2）」及び「肺炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 7[redacted]
Medical History [1]: Ex-tobacco user, Hyperlipidaemia, Erosive duodenitis, Gastrointestinal haemorrhage, Myocardial infarction, Coronary angioplasty, Coronary arterial stent insertion, Rotator cuff repair, Benign prostatic hyperplasia, Myocardial ischaemia, Sigmoidectomy, Obesity, Colon cancer, Hydrocele operation, Abdominal hernia repair, Bronchiectasis, Osteoarthritis, Hypertension, Atrioventricular block complete, Cardiac pacemaker insertion, Cardioversion, Atrial fibrillation, Gout, Chronic obstructive pulmonary disease, Osteoarthritis, Knee arthroplasty, Cardiac failure congestive, Sleep apnoea syndrome, Coronary angioplasty, Stent placement, Coronary angioplasty, Stent placement, Thrombocytopenia, Cardiac ablation, Cataract, Hyperthyroidism, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: BISOPROLOL FUMARATE, ROSUVASTATIN, APIXABAN, ALFUZOSIN HYDROCHLORIDE, COLECALCIFEROL, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, METOLAZONE, MAGNESIUM, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, APIXABAN, FUROSEMIDE, FUROSEMIDE, DOPAMINE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, DOPAMINE, FUROSEMIDE, POTASSIUM CHLORIDE, APIXABAN, FUROSEMIDE, ALLOPURINOL, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, SPIRONOLACTONE, COLCHICINE, PREDNISONE, ALLOPURINOL, COLCHICINE, FUROSEMIDE, ALLOPURINOL, MAGNESIUM, POTASSIUM CHLORIDE, CEFALEXIN, EPLERENONE, FENTANYL CITRATE, MIDAZOLAM, LOSARTAN, PNEUMOCOCCAL VACCINES, FAMOTIDINE, LOSARTAN POTASSIUM, COVID-19 VACCINE, ALLOPURINOL, COVID-19 VACCINE, SACUBITRIL/VALSARTAN, EPLERENONE, ALLOPURINOL, PROPOFOL, SACUBITRIL/VALSARTAN, EPLERENONE, MIDODRINE HYDROCHLORIDE, COVID-19 VACCINE, PREDNISONE, Not coded: Tafamidis, SACUBITRIL/VALSARTAN, TAFAMIDIS, COLCHICINE, PREDNISONE, INFLUENZA VACCINE, ASCORBIC ACID, COLCHICINE, ALLOPURINOL, VITAMIN B12 NOS, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, DEXTRAN 70/HYPROMELLOSE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Gynaecomastia, Atrial fibrillation, Rales, Gout, Gastritis, Hypotension, Gout				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	CHF EXACERBATION	Day 104 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate

治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: F	Age: 7[redacted]
Medical History [1]: Carpal tunnel syndrome, Postmenopause, Diabetes mellitus, Spinal stenosis, Back pain, Age-related macular degeneration, Thrombocytopenia, Retinopathy, Breast cancer, Breast conserving surgery, Cholelithiasis, Chronic kidney disease, Cardiac amyloidosis, Cardiac failure congestive, Cardiomyopathy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: METFORMIN HYDROCHLORIDE, ROSUVASTATIN CALCIUM, VITAMIN D NOS, CLOPIDOGREL BISULFATE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE, CYANOCOBALAMIN/PYRIDOXINE HYDROCHLORIDE/THIAMINE HYDROCHLORIDE, FERROUS GLUCONATE/FOLIC ACID, LIRAGLUTIDE, FUROSEMIDE, SPIRONOLACTONE, LETROZOLE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE, METFORMIN HYDROCHLORIDE, COVID-19 VACCINE, SPIRONOLACTONE, COVID-19 VACCINE, LETROZOLE, FERROUS GLUCONATE/FOLIC ACID, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE/METFORMIN HYDROCHLORIDE, FEXOFENADINE HYDROCHLORIDE, DOXEPIN HYDROCHLORIDE, BILASTINE, AZITHROMYCIN, ENOXAPARIN SODIUM, WARFARIN SODIUM, PHYTOMENADIONE, WARFARIN SODIUM, APIXABAN, COVID-19 VACCINE, BILASTINE, AZITHROMYCIN, MACROGOL/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FENTANYL, PROPOFOL, MIDAZOLAM, COVID-19 VACCINE, DULOXETINE HYDROCHLORIDE, DULOXETINE HYDROCHLORIDE, Not coded: Tafamidis, TAFAMIDIS				
Non-Serious Adverse Event [4]: Decreased appetite, Weight decreased, Myelodysplastic syndrome, Pruritus, Campylobacter infection, Occult blood positive, Chronic kidney disease, Atrial thrombosis, Nasopharyngitis, Diverticulum, Large intestine polyp				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房血栓症	TROMBUS IN LEFT ATRIUM	Day 558 / NA	Not Related	Dose Not Changed	Unknown	Severe
国際標準比増加	INR ELEVATION	Day 568 / Day 569	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「心房血栓症」及び「国際標準比増加」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: F	Age: 8[redacted]	
Medical History [1]: Iron deficiency anaemia, Myocardial ischaemia, Postmenopause, Diabetes mellitus, Atrial fibrillation, Thyroidectomy, Carpal tunnel syndrome, Hypothyroidism, Cardiac ablation, Cardiac pacemaker insertion, Acute myocardial infarction, Cardiac failure congestive, Constipation, Cardiac amyloidosis, Dizziness					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 30			
Concomitant Medication [3]: LEVOTHYROXINE SODIUM, APIXABAN, LINAGLIPTIN, ATORVASTATIN CALCIUM, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, MEROPENEM, FLUCONAZOLE, FUROSEMIDE, SPIRONOLACTONE					
Non-Serious Adverse Event [4]: No event					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腸閉塞	BOWEL OBSTRUCTION	Day 31 / NA	Not Related	Drug Withdrawn	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「腸閉塞」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Not reported	Country: Ireland	Sex: M	Age: 6[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Hyperlipidaemia, Osteoarthritis, Spinal stenosis, Insomnia, Benign prostatic hyperplasia, Hypertension, Carpal tunnel syndrome, Knee arthroplasty, Spinal decompression, Epistaxis, Amyloidosis, Toothache				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: LANSOPRAZOLE, BISOPROLOL, ROSUVASTATIN, VALSARTAN, PREGABALIN, PARACETAMOL, PREGABALIN, DOMPERIDONE, AMOXICILLIN, PREGABALIN, TRAMADOL, PREGABALIN, TRAMADOL, PREGABALIN, STEROIDS, COVID-19 VACCINE, CORTISONE, HYDROCORTISONE, ESOMEPRAZOLE MAGNESIUM/NAPROXEN, VALSARTAN, COVID-19 VACCINE, ESOMEPRAZOLE, CAFFEINE/CODEINE PHOSPHATE HEMIHYDRATE/PARACETAMOL, MUPIROCIN, CHLORHEXIDINE, TEICOPLANIN, CEFUROXIME, TRANEXAMIC ACID, ENOXAPARIN SODIUM, IBUPROFEN, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, PARACETAMOL, PROPOFOL, ONDANSETRON, VANCOMYCIN, DICLOFENAC SODIUM, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE, ACETYLSALICYLIC ACID, PRAZEPAM, FISH OIL, STEROIDS, FISH OIL, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, ALL OTHER THERAPEUTIC PRODUCTS, COVID-19 VACCINE, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Back pain, Abdominal pain upper, Diarrhoea, Dizziness, Headache, Diarrhoea, Pain in extremity, Paraesthesia, Chills, Headache, Erythema, Influenza, Erythema, Staphylococcal infection, Nausea, Orthostatic hypotension, Palpitations, COVID-19, Depression, Blood creatine phosphokinase increased, Gastrointestinal motility disorder, Back pain, Carpal tunnel syndrome, Dizziness, Paraesthesia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性関節症	WORSENING OSTEOARTHRITIS	Day 538 / Day 539	Not Related	Dose Not Changed	Recovered /Resolved	Mild
脊柱管狭窄症	WORSENING SPINAL STENOSIS	NA / Start Day + 41 Days	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「変形性関節症」及び「脊柱管狭窄症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Ireland	Sex: M	Age: 6[redacted]	
Medical History [1]: Atrial fibrillation, Cardiomyopathy, Osteoarthritis, Hypertension, Blood creatinine increased, Hypercholesterolaemia, Amyloidosis, Atrioventricular block					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903			
Concomitant Medication [3]: OMEPRAZOLE, APIXABAN, OLMESARTAN, SOTALOL, COLECALCIFEROL, ROSUVASTATIN, OLMESARTAN, AMIODARONE, AMIODARONE, AMIODARONE, COVID-19 VACCINE, COVID-19 VACCINE, AMLODIPINE, OLMESARTAN, OLMESARTAN, ESOMEPRAZOLE MAGNESIUM, COVID-19 VACCINE, OLMESARTAN, Not coded: Tafamidis, TAFAMIDIS, BISOPROLOL, OLMESARTAN, ESOMEPRAZOLE, OLMESARTAN					
Non-Serious Adverse Event [4]: Hypertension, Joint swelling, Syncope, Atrioventricular block, N-terminal prohormone brain natriuretic peptide increased					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房粗動	UNRESOLVED ATRIAL AFLUTTER	Day 408 / Day 435	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房粗動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Cardiac failure, Arthritis, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 895			
Concomitant Medication [3]: RIVAROXABAN, POTASSIUM CHLORIDE, FUROSEMIDE, DICLOFENAC, RAMIPRIL, SPIRONOLACTONE, RIVAROXABAN, CETIRIZINE HYDROCHLORIDE, BENDROFLUMETHIAZIDE, METOLAZONE, ALLOPURINOL, ZOPICLONE, BUMETANIDE, BUMETANIDE, BUMETANIDE, COLCHICINE, POTASSIUM CHLORIDE, BUMETANIDE, ZOPICLONE, DICLOXACILLIN, FUROSEMIDE, ONDANSETRON, PARACETAMOL, TAMSULOSIN, FINASTERIDE, DICLOXACILLIN, SOLIFENACIN, METOLAZONE, PARACETAMOL, VALPROATE SODIUM, RISPERIDONE				
Non-Serious Adverse Event [4]: Rash, Dry throat, Renal impairment, Diarrhoea, Gout, Ascites, Intermittent claudication, Insomnia, Ascites, Gout, Oedema peripheral, Skin ulcer, Insomnia, Nausea, Nocturia, Hypokalaemia, Mania, Bleeding varicose vein				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	HEART FAILURE WORSENING	Day 684 / Day 692	Not Related	Dose Not Changed	Recovered /Resolved	Severe
失神	LIPOTYMI, CAUSE UNKNOWN	Day 824 / Day 826	Not Related	Dose Not Changed	Recovered /Resolved	Severe
双極性障害	BIPOLAR DISORDER	Day 826 / Day 858	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心不全」、「失神」及び「双極性障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Dupuytren's contracture, Nephropathy, Cardiac failure, Benign prostatic hyperplasia, Atrial fibrillation, Cardiac ablation, Amyloidosis, Hypothyroidism						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 895			
Concomitant Medication [3]: FINASTERIDE, WARFARIN, POTASSIUM CHLORIDE, FUROSEMIDE, LEVOTHYROXINE SODIUM, AMIODARONE, FUROSEMIDE, POTASSIUM CHLORIDE, LOSARTAN, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE						
Non-Serious Adverse Event [4]: Confusional state, Hypertension, Cardiac failure						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	ATRIAL FIBRILLATION	Day 754 / Day 754	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Cerebral arteriosclerosis, Dyslipidaemia, Constipation, Aortic valve stenosis, Benign prostatic hyperplasia, Prostatic operation, Amyloidosis, Cystitis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 900			
Concomitant Medication [3]: OMEPRAZOLE, ATORVASTATIN, POTASSIUM CHLORIDE, FUROSEMIDE, SPIRONOLACTONE, CLOPIDOGREL, CALCIUM/COLECALCIFEROL, MULTIVITAMINS (PLAIN), MIRABEGRON, CLAVULANIC ACID, AMOXICILLIN, FUROSEMIDE, POTASSIUM CHLORIDE, SPIRONOLACTONE, FUROSEMIDE, PARACETAMOL, AMLODIPINE, ISOSORBIDE MONONITRATE, APIXABAN, AMIODARONE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, AMIODARONE HYDROCHLORIDE, APIXABAN, PIVMECILLINAM, DALTEPARIN SODIUM, CEFUROXIME SODIUM, APIXABAN, AMOXICILLIN, POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Dyspnoea, Fall, Atrial fibrillation, Renal impairment, Urinary tract infection, Hyperkalaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路性敗血症	UROSEPSIS	Day 74 / Day 78	Not Related	Dose Not Changed	Recovered /Resolved	Mild
急性心筋梗塞（1）	NON STEMI	Day 418 / Day 418	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心筋梗塞（2）	STEMI	Day 428 / Day 428	Not Related	Dose Not Changed	Recovered /Resolved	Severe
大動脈狭窄	AORTASTENOSIS	Day 537 / Day 540	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「尿路性敗血症」、「急性心筋梗塞（1）」、「急性心筋梗塞（2）」及び「大動脈狭窄」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7■
Medical History [1]: Polyneuropathy, Type 2 diabetes mellitus, Hypertension, Prostate cancer, Polymyalgia rheumatica, Gastritis, Myocardial ischaemia, Depression, Dyslipidaemia, Amyloidosis, Insomnia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: FELODIPINE, METFORMIN, ACETYLSALICYLIC ACID, POTASSIUM CHLORIDE, BENDROFLUMETHIAZIDE, CALCIUM/COLECALCIFEROL, BICALUTAMIDE, PANTOPRAZOLE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, DULOXETINE, EZETIMIBE, PARACETAMOL, PREDNISOLONE, ROSUVASTATIN, OXYCODONE HYDROCHLORIDE, ZOLPIDEM TARTRATE, LEUPRORELIN, DENOSUMAB, OXAZEPAM, POTASSIUM CHLORIDE, LOSARTAN, CEFUROXIME, CEFUROXIME SODIUM, PHENOXYMETHYLPENICILLIN POTASSIUM, CYANOCOBALAMIN, RIVAROXABAN, MELATONIN, FUROSEMIDE, AMIODARONE, FUROSEMIDE, FUROSEMIDE, METFORMIN, MORPHINE SULFATE, RIVAROXABAN, AMLODIPINE, BENDROFLUMETHIAZIDE, LOSARTAN POTASSIUM, OXYCODONE HYDROCHLORIDE, METOPROLOL, PARACETAMOL, MAGNESIUM OXIDE, ZOLPIDEM, AMIODARONE, GLYCERYL TRINITRATE, ALPRAZOLAM, ENZALUTAMIDE, ISOSORBIDE MONONITRATE, POTASSIUM CHLORIDE, FUROSEMIDE, AMIODARONE, POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Cardiac failure, Electrocardiogram QT prolonged				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
気道感染	RESPIRATORY INFECTION	Day 208 / Day 217	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	PAROXYSMAL ATRIAL FIBRILLATION	Day 237 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
肺水腫（1）	PULMONARY OEDEMA	Day 257 / Day 259	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺水腫（2）	PULMONARY OEDEMA	Day 267 / Day 268	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺水腫（3）	PULMONARY OEDEMA	Day 412 / Day 414	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	WORSENING OF HEARTFAILURE	Day 873 / Day 876	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「気道感染」、「心房細動」、「肺水腫（1）」、「肺水腫（2）」、「肺水腫（3）」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 8■
Medical History [1]: Cardiac failure, Atrial fibrillation, Constipation, Amyloidosis, Chronic obstructive pulmonary disease, Renal impairment, Inguinal hernia, Gout, Conjunctivitis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: PLANTAGO OVATA, APIXABAN, RAMIPRIL, SPIRONOLACTONE, PARACETAMOL, ALLOPURINOL, POTASSIUM, BENDROFLUMETHIAZIDE, PIVMECILLINAM, METOPROLOL, APIXABAN, POTASSIUM CHLORIDE, FUROSEMIDE, ACICLOVIR, CARBOMER, TAZOBACTAM, PIPERACILLIN, METOPROLOL, MECILLINAM, FUROSEMIDE, CARBOMER, METOPROLOL, PARACETAMOL, MACROGOL, AMOXICILLIN, BETA-LACTAMASE INHIBITORS				
Non-Serious Adverse Event [4]: Cough, Renal impairment, Keratitis, Weight increased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路感染	URINARY TRACT INFECTION	Day 218 / Day 230	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房細動	EXACERBATION OF ATRIAL FIBRILLATION	Day 225 / Day 228	Not Related	Dose Not Changed	Recovered /Resolved	Severe
膀胱炎	CYSTITIS	Day 249 / Day 259	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	HEART FAILURE WORSENING	Day 611 / Day 642	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「尿路感染」、「心房細動」、「膀胱炎」及び「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Dizziness, Hypertension, Spinal stenosis, Dyslipidaemia, Atrial fibrillation, Inguinal hernia, Amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 895			
Concomitant Medication [3]: LOSARTAN, RIVAROXABAN, ATORVASTATIN, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, OXYCODONE HYDROCHLORIDE, FERROUS SULFATE						
Non-Serious Adverse Event [4]: Upper limb fracture, Hypergammaglobulinaemia benign monoclonal, Carpal tunnel syndrome, Dizziness, Musculoskeletal chest pain, Haemoglobin decreased, Epistaxis						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腰部脊柱管狭窄症	WORSENING LUMBAL STENOSIS	Day 470 / Day 471	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「腰部脊柱管狭窄症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]
Medical History [1]: Transient ischaemic attack, Spinal stenosis, Myocardial ischaemia, Hypertension, Carpal tunnel decompression, Hypercholesterolaemia, Atrial fibrillation, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: METOPROLOL, FOLIC ACID, ATORVASTATIN, GLYCERYL TRINITRATE, RIVAROXABAN, POTASSIUM CHLORIDE, ISOSORBIDE MONONITRATE, FUROSEMIDE, DIGOXIN, BISACODYL, OXYCODONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE, VITAMIN D NOS, FERROUS SULFATE, ZOLEDRONIC ACID, BENDROFLUMETHIAZIDE/POTASSIUM CHLORIDE, FUSIDIC ACID, PARACETAMOL				
Non-Serious Adverse Event [4]: Haemoglobin decreased, Osteoporosis, Contusion, Angina pectoris, Eye inflammation, Musculoskeletal chest pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大腿骨頚部骨折	FRACTURE COLLUM FEMORIS RIGHT SIDE	Day 87 / Day 91	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「大腿骨頚部骨折」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: Denmark	Sex: F	Age: 8[redacted]
Medical History [1]: Menopause, Dyslipidaemia, Atrial fibrillation, Amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 904			
Concomitant Medication [3]: POTASSIUM, SIMVASTATIN, METOPROLOL, APIXABAN, FUROSEMIDE, TRIAMCINOLONE ACETONIDE, DICLOFENAC, PARACETAMOL						
Non-Serious Adverse Event [4]: Rash, Fall, Paraesthesia, Back pain, Dizziness						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳振盪	CONCUSION	Day 286 / Day 287	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「脳振盪」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertensive nephropathy, Chronic kidney disease, Hypertension, Erectile dysfunction, Dyslipidaemia, Osteoporosis, Atrial fibrillation, Cardiac amyloidosis, Colon cancer, Constipation, Oral herpes, Dry eye, Dry mouth, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: MYCOPHENOLIC ACID, PREDNISOLONE, TACROLIMUS, ALPROSTADIL, TACROLIMUS, COLECALCIFEROL, EZETIMIBE, ZOLEDRONIC ACID, RIVAROXABAN, MAGNESIUM HYDROXIDE, DALTEPARIN, ACICLOVIR, OTHER AGENTS FOR LOCAL ORAL TREATMENT, KETOTIFEN FUMARATE, ALLOPURINOL, FUROSEMIDE, LOSARTAN, PIVMECILLINAM HYDROCHLORIDE, PARACETAMOL, MACROGOL, MAGNESIUM				
Non-Serious Adverse Event [4]: Hypertension, Cystitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
便秘	WORSENING OF OBSTIPATION	Day 455 / Day 462	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「便秘」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]	
Medical History [1]: Glaucoma, Eyelid ptosis, Intervertebral disc degeneration, Hypertension, Atrial fibrillation, Conjunctivitis allergic, Rhinitis, Amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 456			
Concomitant Medication [3]: LATANOPROST, LOSARTAN, APIXABAN, OLOPATADINE HYDROCHLORIDE, VERAPAMIL, PARACETAMOL, AZELASTINE, FLUTICASONE PROPIONATE, POTASSIUM, BENDROFLUMETHIAZIDE, METOPROLOL SUCCINATE, SIMVASTATIN, POTASSIUM CHLORIDE, FUROSEMIDE, PANTOPRAZOLE, BISACODYL, LACTULOSE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, PROMETHAZINE HYDROCHLORIDE					
Non-Serious Adverse Event [4]: Constipation, Haemoglobin decreased, Insomnia					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺うっ血	PULMONARY CONGESTION	Day 434 / Day 434	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「肺うっ血」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 7[redacted]
Medical History [1]: Spinal laminectomy, Scoliosis, Hypercholesterolaemia, Benign prostatic hyperplasia, Arthralgia, Atrial fibrillation, Cardiac failure congestive, Cardiac amyloidosis, Chronic kidney disease, Insomnia, Eczema				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 906		
Concomitant Medication [3]: DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, APIXABAN, AMIODARONE, SPIRONOLACTONE, OMEPRAZOLE, FUROSEMIDE, FUROSEMIDE, BROTIZOLAM, FEXOFENADINE, NEPIDERMIN, OMEPRAZOLE, FEXOFENADINE, LORAZEPAM, SPIRONOLACTONE, FEXOFENADINE, VITAMIN D NOS, COVID-19 VACCINE, COVID-19 VACCINE, BROTIZOLAM, SPIRONOLACTONE, AMIODARONE, AMIODARONE HYDROCHLORIDE, FUROSEMIDE, APIXABAN, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, AMIODARONE, MACROGOL 3350, SPIRONOLACTONE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, SACUBITRIL/VALSARTAN, APIXABAN, ENOXAPARIN SODIUM, APIXABAN, FUROSEMIDE, FUROSEMIDE, VITAMIN D NOS, FUROSEMIDE				
Non-Serious Adverse Event [4]: Blood creatinine increased, Eosinophil count increased, Anxiety, Blood thyroid stimulating hormone increased, Renal impairment, Sciatica, Constipation, Dyspnoea, Cardiac failure congestive, Arthralgia, Blood pressure increased, Hypoaesthesia, Blood thyroid stimulating hormone increased, Anaemia, Renal cyst, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE PRERENAL FAILURE	Day 796 / Day 810	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
急性心不全	CHF EXACERBATION	Day 929 / NA	Not Related	NA	Not Recovered /Not Resolved	Moderate

治験責任医師の見解：「急性腎障害」及び「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Ex-tobacco user, Benign prostatic hyperplasia, Cervical spinal stenosis, Hyperlipidaemia, Aortic valve replacement, Coronary artery bypass, Carpal tunnel syndrome, Osteoporosis, Erectile dysfunction, Cardiac failure congestive, Pulmonary hypertension, Anaemia, Chronic obstructive pulmonary disease, Inguinal hernia repair, Cardiac amyloidosis, Paravalvular regurgitation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: DOXAZOSIN, SIMVASTATIN, ENALAPRIL MALEATE, PARACETAMOL/TRAMADOL HYDROCHLORIDE, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, OMEPRAZOLE, FUROSEMIDE, FLUTICASONE/VILANTEROL, FUROSEMIDE, ENALAPRIL MALEATE, SILDENAFIL, UMECLIDINIUM BROMIDE, BETAMETHASONE DIPROPIONATE, TAMSULOSIN HYDROCHLORIDE, DICLOFENAC, DOXAZOSIN, METAMIZOLE SODIUM, SPIRONOLACTONE, RED BLOOD CELLS (CONCENTRATED), ENALAPRIL MALEATE, FUROSEMIDE, LACTULOSE, ACETYLSALICYLIC ACID, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, UMECLIDINIUM BROMIDE, TAMSULOSIN HYDROCHLORIDE, MACROGOL/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, SACCHARATED IRON OXIDE, FENTANYL, FENTANYL, LIDOCAINE HYDROCHLORIDE, MIDAZOLAM, MIDAZOLAM, UMECLIDINIUM, COVID-19 VACCINE, COVID-19 VACCINE, IBUPROFEN, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, SODIUM POLYSTYRENE SULFONATE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, CAFFEINE/CODEINE PHOSPHATE/PARACETAMOL, BETAMETHASONE DIPROPIONATE/BETAMETHASONE SODIUM PHOSPHATE, APIXABAN, DICLOFENAC, INFLUENZA VACCINE, CANNABIS SATIVA, SACCHARATED IRON OXIDE, OXYCODONE HYDROCHLORIDE/PARACETAMOL, LORATADINE, SACCHARATED IRON OXIDE, APIXABAN, FUROSEMIDE, OXYCODONE HYDROCHLORIDE/PARACETAMOL, OXYCODONE HYDROCHLORIDE/PARACETAMOL, IRON/SUCROSE				
Non-Serious Adverse Event [4]: Urinary tract infection, Blood creatine phosphokinase increased, Acute kidney injury, Dyspnoea, Constipation, Iron deficiency, Chronic gastritis, Diverticulum, Gastrointestinal angiodysplasia, Carpal tunnel syndrome, Contusion, Vomiting, Malignant melanoma, Atrial fibrillation, Asthenia, Anaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
貧血	WORSENING OF ANEMIA	Day 279 / Day 323	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
急性腎障害	ACUTE RENAL FAILURE	Day 543 / Day 551	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
呼吸困難	DYSPNEA	Day 573 / Day 581	Not Related	Dose Not Changed	Recovered /Resolved	Mild
労作性呼吸困難	EXERTIONAL DYSPNEA	Day 834 / Day 903	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「貧血」、「急性腎障害」、「呼吸困難」及び「労作性呼吸困難」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 8[redacted]
Medical History [1]: Ex-tobacco user, Prostatectomy, Cerebrovascular accident, Hypertension, Large intestine polyp, Neuroendocrine tumour, Pericardial effusion, Myocardial ischaemia, Percutaneous coronary intervention, Bradycardia, Atrioventricular block, Atrioventricular block second degree, Atrial flutter, Tendonitis, Cardiac amyloidosis, Cardiac failure congestive				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 900			
Concomitant Medication [3]: HYDROCHLOROTHIAZIDE/RAMIPRIL, APIXABAN, SPIRONOLACTONE, BETACAROTENE/BIOFLAVONOIDS NOS/MINERALS NOS/RUTOSIDE/VACCINIUM MYRTILLUS/VITAMINS NOS/XANTOFYL, COVID-19 VACCINE, COVID-19 VACCINE, ACICLOVIR, CALAMINE, BETAMETHASONE VALERATE, METAMIZOLE SODIUM, LORATADINE, RAMIPRIL, SPIRONOLACTONE, COVID-19 VACCINE, RAMIPRIL, RAMIPRIL, HYDROCHLOROTHIAZIDE, Not coded: Tafamidis, TAFAMIDIS, TAFAMIDIS, APIXABAN, TAFAMIDIS, RAMIPRIL, FUROSEMIDE, LORATADINE, LORATADINE, BILASTINE, METAMIZOLE SODIUM, HEPARIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, ACETYLSALICYLIC ACID, CLOPIDOGREL, TETRACOSACTIDE, COLCHICINE, CEFAZOLIN SODIUM, METAMIZOLE SODIUM, FENTANYL, MIDAZOLAM, APIXABAN, CLOPIDOGREL, METAMIZOLE SODIUM, FUROSEMIDE, CEFAZOLIN SODIUM, FENTANYL, MIDAZOLAM, APIXABAN, FUROSEMIDE, METAMIZOLE SODIUM, TAFAMIDIS, TAFAMIDIS, METAMIZOLE SODIUM, TAFAMIDIS				
Non-Serious Adverse Event [4]: Herpes zoster, Duodenal ulcer, Thrombocytopenia, Asthenia, Bleeding varicose vein, Pruritus, Oedema peripheral, Varicose vein, Pruritus, Renal impairment, Chondrocalcinosis pyrophosphate, COVID-19, Arthralgia, Cardiac failure congestive				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
労作性呼吸困難	EXERTIONAL DYSPNEA	Day 597 / Day 639	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
徐脈	EXCESSIVE BRADYCARDIA	Day 652 / Day 689	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
リードの位置ずれ	DISLODGMENT OF RV ELECTRODE	Day 716 / Day 719	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「労作性呼吸困難」、「徐脈」及び「リードの位置ずれ」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Israel	Sex: M	Age: 7[redacted]
Medical History [1]: Appendicectomy, Knee arthroplasty, Knee arthroplasty, Percutaneous coronary intervention, Myocardial ischaemia, Hyperlipidaemia, Atrial fibrillation, Cardiac failure congestive, Cardiac amyloidosis, Insomnia, Hypertension				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: ATORVASTATIN CALCIUM, APIXABAN, ZOLPIDEM, SPIRONOLACTONE, RAMIPRIL, PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, CEFAZOLIN SODIUM, FENTANYL, MIDAZOLAM, TAFAMIDIS, CHLORPHENAMINE MALEATE/DEXTROMETHORPHAN HYDROBROMIDE/PARACETAMOL/PSEUDOEPHEDRINE HYDROCHLORIDE, EPHEDRINE HYDROCHLORIDE/GLAUCINE HYDROBROMIDE, PROPOFOL, MIDAZOLAM				
Non-Serious Adverse Event [4]: Headache, Respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	BRADYCARDIA	Day 383 / Day 400	Not Related	Dose Not Change	Recovered /Resolved	Moderate

治験責任医師の見解：「徐脈」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Urethral operation, Hand fracture, Fracture treatment, Medical device removal, Intervertebral disc protrusion, Anxiety, Prostatitis, Clavicle fracture, Rib fracture, Upper limb fracture, Corneal degeneration, Corneal operation, Cataract, Cataract, Hypercholesterolaemia, Cataract operation, Cataract operation, Left ventricular hypertrophy, Aortic stenosis, Respiratory tract infection, Cardiac failure, Pyrexia, Haematuria, Atrial fibrillation, Atrial thrombosis, Cardiac amyloidosis, Epistaxis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: AMITRIPTYLINE HYDROCHLORIDE, ALPRAZOLAM, SIMVASTATIN, EZETIMIBE, SPIRONOLACTONE, BUMETANIDE, EDOXABAN TOSILATE, BISOPROLOL FUMARATE, SPIRONOLACTONE, BUMETANIDE, BISOPROLOL FUMARATE, INFLUENZA VACCINE, BUMETANIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, NYSTATIN, XYLOMETAZOLINE HYDROCHLORIDE, NYSTATIN, COVID-19 VACCINE, COVID-19 VACCINE, ALPRAZOLAM, EDOXABAN TOSILATE, XYLOMETAZOLINE HYDROCHLORIDE, ALPRAZOLAM, COVID-19 VACCINE, BUMETANIDE, BISOPROLOL, COLECALCIFEROL, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, OTHER COUGH SUPPRESSANTS, AMYLMETACRESOL/DICHLOROBENZYL ALCOHOL, AMOXICILLIN, METHYLPREDNISOLONE, SODIUM BICARBONATE, GLUCOSE, ALPRAZOLAM, BISOPROLOL, BUMETANIDE				
Non-Serious Adverse Event [4]: Contusion, Wound, Balance disorder, Acute kidney injury, Hypotension, Candida infection, Diarrhoea, Vomiting, Epistaxis, Apathy, Fall, Skin laceration, Fall, Head injury, Nasopharyngitis, Syncope, COVID-19, Cardiac failure, General physical health deterioration, Hyperkalaemia, Acute kidney injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
労作性呼吸困難	DYSPNOE D'EFFORT	Day 128 / Day 151	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
上気道感染	UPPER RESPIRATORY TRACT INFECTION	Day 859 / Day 879	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「労作性呼吸困難」及び「上気道感染」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Sciatica, Nephrolithiasis, Appendicectomy, Testicular swelling, Atrioventricular block first degree, Left ventricular hypertrophy, Meniscus injury, Arthroscopy, Osteoarthritis, Atrial fibrillation, Atrial fibrillation, Angiocardiogram, Bundle branch block right, Cardiac pacemaker insertion, Angiocardiogram, Orthostatic hypotension, Cystitis, Prostatitis, Arthritis, Hypertension, Cubital tunnel syndrome, Neurolysis, Angiocardiogram, Arteriosclerosis coronary artery, Cardiac pacemaker replacement, Atrial fibrillation, Knee arthroplasty, Benign prostatic hyperplasia, Parkinson's disease, Intervertebral disc degeneration, Ureterolithiasis, Renal stone removal, Scoliosis, Spinal osteoarthritis, Spinal claudication, Lumbar spinal stenosis, Spinal decompression, Patellofemoral pain syndrome, Aortic aneurysm, Carpal tunnel syndrome, Neurolysis, Rib fracture, Cataract, Cataract, Skin ulcer, Skin ulcer, Cataract operation, Cataract operation, Facet joint syndrome, Cardiac failure, Chronic kidney disease, Hydrocele operation, Carpal tunnel syndrome, Neurolysis, Cardiac amyloidosis, Rapid eye movement sleep behaviour disorder				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 446			
Concomitant Medication [3]: DABIGATRAN ETEXILATE MESILATE, SPIRONOLACTONE, AMITRIPTYLINE HYDROCHLORIDE, NEBIVOLOL, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, BUMETANIDE, PRAMIPEXOLE DIHYDROCHLORIDE, CLONAZEPAM, AMOXICILLIN/CLAVULANATE POTASSIUM, BUMETANIDE, BUMETANIDE, METHYLPREDNISOLONE SODIUM SUCCINATE, BUMETANIDE, BUMETANIDE, DABIGATRAN ETEXILATE MESILATE, NEBIVOLOL, BOTULINUM TOXIN TYPE A, BUMETANIDE, BUMETANIDE, BUMETANIDE, PIROXICAM, FLUCLOXACILLIN, BOTULINUM TOXIN TYPE A, FEBUXOSTAT, BUMETANIDE, BUMETANIDE, BOTULINUM TOXIN TYPE A, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, BENSERAZIDE HYDROCHLORIDE/LEVODOPA, CEFAZOLIN, BUMETANIDE, PIROXICAM, PIROXICAM BETADEX, COVID-19 VACCINE, DICLOFENAC				
Non-Serious Adverse Event [4]: Microalbuminuria, Blood uric acid increased, Wound infection, Liver function test abnormal, Acute kidney injury, Salivary hypersecretion, Cardiac failure, Gout, Cardiac failure, Salivary hypersecretion, Urinary retention, Hypotension, Microalbuminuria, Localised infection, Hypotension, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
基底細胞癌	BASOCELLULAR SKIN CARCINOMA	Day 52 / Day 288	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE CORDECOMPENSATION	Day 165 / Day 169	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「基底細胞癌」及び「急性心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Shoulder operation, Hydrocele, Cataract, Hydrocele operation, Biopsy prostate, Cataract operation, Cataract operation, Benign prostatic hyperplasia, Coronary angioplasty, Myocardial ischaemia, Calculus bladder, Urinary calculus removal, Hypertension, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 104		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, PERINDOPRIL, SPIRONOLACTONE, PARACETAMOL, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, PERINDOPRIL, SPIRONOLACTONE, PNEUMOCOCCAL VACCINE, COLECALCIFEROL, PERINDOPRIL, SPIRONOLACTONE, PERINDOPRIL, SPIRONOLACTONE, PANTOPRAZOLE SODIUM SESQUIHYDRATE				
Non-Serious Adverse Event [4]: Renal impairment, Thrombocytopenia, Haematuria, Melaena, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	BRADYCARDIA	Day 90 / Day 149	Not Related	Drug Withdrawn	Recovered /Resolved	Moderate

治験責任医師の見解：「徐脈」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: F	Age: 8[redacted]
Medical History [1]: Ventricular tachycardia, Gastritis, Oesophagitis, Hypercholesterolaemia, Hyperglycaemia, Ophthalmoplegic migraine, Cholecystectomy, Knee arthroplasty, Hypertension, Osteoarthritis, Varicose vein operation, Varicose vein operation, Colon adenoma, Large intestine polyp, Urinary tract infection, Adenocarcinoma, Colon adenoma, Gastrointestinal tract adenoma, Colectomy total, Intestinal anastomosis, Proctitis, Diverticulitis, Ileostomy, Sigmoidectomy, Stoma site abscess, Meniere's disease, Ventricular flutter, Ventricular hypertrophy, Chest pain, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: SIMVASTATIN, BETAHISTINE HYDROCHLORIDE, ESCITALOPRAM OXALATE, APIXABAN, PERINDOPRIL, BUMETANIDE, BISOPROLOL, BISOPROLOL, BUMETANIDE, INFLUENZA VACCINE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, MOMETASONE FUROATE, MOMETASONE FUROATE, COVID-19 VACCINE, COVID-19 VACCINE, PARACETAMOL, ESCITALOPRAM OXALATE, COVID-19 VACCINE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, LACTULOSE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, BUMETANIDE, DICLOFENAC, IBUPROFEN, PARACETAMOL, COLCHICINE, BUMETANIDE, IBUPROFEN, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, BUMETANIDE, IBUPROFEN, AMIODARONE HYDROCHLORIDE, IBUPROFEN, SPIRONOLACTONE, BUMETANIDE, ENOXAPARIN SODIUM, LORAZEPAM, EMPAGLIFLOZIN, APIXABAN, QUETIAPINE, ALPRAZOLAM, CEFAZOLIN, AMLODIPINE BESILATE, PARACETAMOL, LACTULOSE, FLUCLOXACILLIN, ENOXAPARIN SODIUM, BISOPROLOL, BETAHISTINE HYDROCHLORIDE, ALPRAZOLAM, APIXABAN, AMIODARONE HYDROCHLORIDE, ESCITALOPRAM, ALPRAZOLAM, SPIRONOLACTONE, BUMETANIDE, LACTULOSE, APIXABAN, Not coded: Tafamidis, TAFAMIDIS, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, ALPRAZOLAM, SACCHAROMYCES BOULARDII, LOPERAMIDE HYDROCHLORIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, APIXABAN, PARACETAMOL, TAFAMIDIS, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, ALPRAZOLAM, HYOSCINE BUTYLBROMIDE, DIAZEPAM, LIDOCAINE, ALPRAZOLAM, PERINDOPRIL, ACETYLCYSTEINE, SPIRONOLACTONE, BUMETANIDE, AZITHROMYCIN, BISOPROLOL FUMARATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, BUMETANIDE, LIDOCAINE, APIXABAN, TAFAMIDIS, SPIRONOLACTONE, MIRTAZAPINE, BUMETANIDE, ESCITALOPRAM OXALATE				
Non-Serious Adverse Event [4]: Pruritus, Muscle spasms, Dyspepsia, Alopecia, Chest pain, Pruritus, Muscle spasms, Emotional distress, Blood bilirubin increased, Acute kidney injury, Melaena, Acute kidney injury, Diarrhoea, Hypocalcaemia, Decreased appetite, Hyperglycaemia, Pulmonary congestion, Hyponatraemia, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	CARDIAC CORDECOMPENSATION	Day 499 / Day 503	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胸膜炎	PLEURITIS	Day 499 / Day 508	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
失神寸前の状態	PRE-SYNCOPE	Day 520 / Day 531	Not Related	Dose Not Changed	Recovered /Resolved	Mild
気道感染	RESPIRATORY INFECTION	Day 576 / Day 588	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心不全」、「胸膜炎」、「失神寸前の状態」及び「気道感染」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Colorectal cancer, Gastrointestinal anastomotic leak, Colectomy, Ileostomy, Central venous catheterisation, Intestinal anastomosis complication, Spinal osteoarthritis, Anastomotic stenosis, Intestinal anastomosis complication, Large intestine anastomosis, Cholecystitis chronic, Metastases to liver, Cholecystectomy, Hepatectomy, Cystitis, Intestinal anastomosis complication, Large intestine anastomosis, Ileostomy closure, Post procedural complication, Post procedural complication, Intervertebral disc protrusion, Carpal tunnel syndrome, Neurolysis, Sleep apnoea syndrome, Ventricular flutter, Bradycardia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: LOSARTAN POTASSIUM, ATORVASTATIN CALCIUM, APIXABAN, AMITRIPTYLINE HYDROCHLORIDE, MOMETASONE FUROATE, BUMETANIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, INFLUENZA VACCINE, CIPROFLOXACIN, AMITRIPTYLINE HYDROCHLORIDE, COVID-19 VACCINE, COVID-19 VACCINE, AMITRIPTYLINE HYDROCHLORIDE, COVID-19 VACCINE, CARBOCISTEINE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, INFLUENZA VACCINE, Not coded: Tafamidis, TAFAMIDIS, LOPERAMIDE HYDROCHLORIDE, APIXABAN, BUMETANIDE, AMITRIPTYLINE HYDROCHLORIDE, COLECALCIFEROL, BUMETANIDE, LOSARTAN, BUMETANIDE, BUPIVACAINE/METHYLPREDNISOLONE				
Non-Serious Adverse Event [4]: Constipation, Microalbuminuria, Urinary tract infection, Muscle spasms, Atrial fibrillation, Nasopharyngitis, Constipation, Atrial fibrillation, Diarrhoea, Acute kidney injury, Diarrhoea, Vitamin D deficiency, Arthropathy				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE HEART FAILURE	Day 795 / Day 811	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 6[redacted]
Medical History [1]: Colon cancer, Urinary bladder polyp, Pulmonary mass, Atrial fibrillation, Angiocardiogram, Biliary colic, Hypertrophic cardiomyopathy, Cardiac amyloidosis, Dental caries, Duodenitis, Gastric disorder, Urinary bladder polyp, Transurethral bladder resection				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: BISOPROLOL FUMARATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, RIVAROXABAN, BUMETANIDE, METFORMIN, METFORMIN, BUMETANIDE, METFORMIN, APIXABAN, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, COVID-19 VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, COVID-19 VACCINE, MAGNESIUM OXIDE, BUMETANIDE, BUMETANIDE, METFORMIN, POTASSIUM GLUCONATE, FERRIC CARBOXYMALTOSE, SPIRONOLACTONE, BUMETANIDE, FERRIC CARBOXYMALTOSE, DIPHTHERIA VACCINE TOXOID/PERTUSSIS VACCINE ACELLULAR 5-COMPONENT/TETANUS VACCINE TOXOID				
Non-Serious Adverse Event [4]: Type 2 diabetes mellitus, Abdominal pain, Back pain, Chest discomfort, Post procedural haemorrhage, Influenza like illness, Palpitations, Chest discomfort, Chest discomfort, Muscle spasms, Dyspnoea, Intestinal polyp, Wound haemorrhage, Blood iron decreased, Hypokalaemia, Rash, Palpitations, Hypertension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
膀胱結石	LARGE BLADDER STONE (URINARY)	Day 79 / Day 117	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
処置後出血	POST PROCEDURAL HEMORRHAGE	Day 575 / Day 578	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE HEART FAILURE EPISODE	Day 578 / Day 612	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「膀胱結石」、「処置後出血」及び「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Ireland	Sex: M	Age: 8[redacted]	
Medical History [1]: Diarrhoea, Gastrooesophageal reflux disease, Small intestinal obstruction, Insomnia, Rash pruritic, Transurethral prostatectomy, Hypertension, Amyloidosis senile, Atrial fibrillation, Cardiac failure, Chronic obstructive pulmonary disease					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 50			
Concomitant Medication [3]: LOPERAMIDE HYDROCHLORIDE, LANSOPRAZOLE, APIXABAN, BISOPROLOL, EPLERENONE, BUMETANIDE, FINASTERIDE, TRIAZOLAM, FEXOFENADINE HYDROCHLORIDE, FLUTICASONE/SALMETEROL, TIOTROPIUM BROMIDE MONOHYDRATE, MONTELUKAST, MIRTAZAPINE					
Non-Serious Adverse Event [4]: Asthenia, Fatigue, Dizziness, Fatigue					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腎細胞癌	LEFT CELL CARCINOMA - KIDNEY	Day 50 / NA	Not Related	Drug Withdrawn	Recovering/ Resolving	Moderate
転倒	FALL WITHOUT LOSS OF CONSCIOUSNESS AND WAS HOSPITALISED	Day 50 / Day 58	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
治験責任医師の見解：「腎細胞癌」及び「転倒」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■					
Treatment Arm: Acoramidis	Race: Not reported	Country: Netherlands	Sex: M	Age: 8■	
Medical History [1]: Asthma, Atrial fibrillation, Hypertension, Carpal tunnel syndrome, Gout, Cardiac failure, Hip arthroplasty, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901			
Concomitant Medication [3]: OMEPRAZOLE, COLECALCIFEROL, CANDESARTAN, BISOPROLOL, FUROSEMIDE, DABIGATRAN, MACROGOL/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, AMIODARONE, BUDESONIDE, COVID-19 VACCINE, COVID-19 VACCINE, LEVOTHYROXINE, LEVOTHYROXINE, LEVOTHYROXINE, LEVOTHYROXINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, NORTRIPTYLINE					
Non-Serious Adverse Event [4]: Constipation, Hypothyroidism, Pain, Plicated tongue, Tongue geographic, Neuropathy peripheral					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
機械的イレウス	MECHANICAL ILEUS, DUE TO ADHESIONS	Day 12 / Day 34	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「機械的イレウス」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]	
Medical History [1]: Atrial fibrillation, Atrial fibrillation, Atrial tachycardia, Hypercholesterolaemia, Hypertension, Cardiac amyloidosis, Nodal arrhythmia, Hernia repair					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 897				
Concomitant Medication [3]: APIXABAN, PERINDOPRIL, ATORVASTATIN CALCIUM/EZETIMIBE, AMIODARONE HYDROCHLORIDE, BUMETANIDE, PARACETAMOL, OMEPRAZOLE, BUMETANIDE, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, COVID-19 VACCINE, AMIODARONE HYDROCHLORIDE, COVID-19 VACCINE, BUMETANIDE, VITAMIN D NOS, PANTOPRAZOLE, CYANOCOBALAMIN/PYRIDOXINE HYDROCHLORIDE/RIBOFLAVIN/THIAMINE MONONITRATE, PERINDOPRIL, PARACETAMOL					
Non-Serious Adverse Event [4]: Memory impairment, Back pain					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
椎間板突出	RECURRENT HERNIATED DISC L4-5	Day 15 / Day 239	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
医療機器のゆるみ	LOOSENING OF CUP RIGHT TOTAL HIP PROSTHESIS	Day 43 / Day 239	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate

治験責任医師の見解：「椎間板突出」及び「医療機器のゆるみ」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Other	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Anaemia of chronic disease, Hypoparathyroidism secondary, Toxic nodular goitre, Raynaud's phenomenon, Amaurosis fugax, Atrial fibrillation, Coronary artery disease, Epistaxis, Cardiac ablation, Trifascicular block, Cardioversion, Macular degeneration, Gout, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: LEVOTHYROXINE, ATORVASTATIN, EDOXABAN, RAMIPRIL, SOTALOL, EPLERENONE, FUROSEMIDE, AFLIBERCEPT, ALLOPURINOL, AFLIBERCEPT, FERROUS FUMARATE, EDOXABAN, RAMIPRIL, ALLOPURINOL, ALLOPURINOL, COVID-19 VACCINE, AFLIBERCEPT, COVID-19 VACCINE, LOPERAMIDE, OMEPRAZOLE, ANTIBIOTICS, AMOXICILLIN/CLAVULANATE POTASSIUM, ENOXAPARIN, TAMSULOSIN, I.V. SOLUTIONS, AMOXICILLIN, METRONIDAZOLE, ENOXAPARIN, EDOXABAN, RED BLOOD CELLS, FUROSEMIDE, ANTIBIOTICS, AMOXICILLIN/CLAVULANATE POTASSIUM, MEGLUMINE AMIDOTRIZOATE/SODIUM AMIDOTRIZOATE, I.V. SOLUTIONS, OMEPRAZOLE, MAGNESIUM ASPARTATE, CODEINE PHOSPHATE, PARACETAMOL, TAMSULOSIN, SOTALOL, COVID-19 VACCINE, INFLUENZA VACCINE, LOPERAMIDE, LEVOTHYROXINE				
Non-Serious Adverse Event [4]: Sciatica, Iron deficiency anaemia, Macular oedema, Subclavian vein thrombosis, Gastritis, Benign prostatic hyperplasia, Urinary tract infection, Acute kidney injury, Anal incontinence, Duodenal ulcer, Mobility decreased, Acute kidney injury, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
結腸直腸癌	COLORECTAL CANCER	Day 336 / NA	Not Related	Drug Interrupted	Recovered /Resolved	Severe
尿路性敗血症	UROSEPSIS	Day 440 / Day 453	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
イレウス	SMALL BOWEL ILEUS	Day 445 / Day 453	Not Related	Drug Interrupted	Recovered /Resolved	Severe
小腸閉塞	SMALL BOWEL OBSTRUCTION	Day 664 / Day 673	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
上部消化管出血	UPPER GASTROINTESTINAL BLEED	Day 782 / Day 874	Not Related	Drug Interrupted	Recovered /Resolved	Severe
腸管穿孔	INTESTINAL PERFORATION	Day 783 / Day 817	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「結腸直腸癌」、「尿路性敗血症」、「イレウス」、「小腸閉塞」、「上部消化管出血」及び「腸管穿孔」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: Asian		Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Sciatica, Hypertension, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 623				
Concomitant Medication [3]: LISINOPRIL, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, FAMOTIDINE, EDOXABAN, ANTIBIOTICS						
Non-Serious Adverse Event [4]: Atrial fibrillation, Gastrooesophageal reflux disease, Cardiac failure, Urinary tract infection, Dementia, Dysphagia, Lower respiratory tract infection, Herpes zoster						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
敗血症	SEPSIS	Day 639 / NA	Not Related	NA	Recovering/Resolving	Moderate
治験責任医師の見解：「敗血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 8[redacted]	
Medical History [1]: Angina pectoris, Atrial fibrillation, Irritable bowel syndrome, Vitamin B complex deficiency, Vitamin D deficiency, Malignant melanoma, Carpal tunnel syndrome, Benign prostatic hyperplasia, Coronary arterial stent insertion, Appendicectomy, Myocardial infarction, Neuralgia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 256			
Concomitant Medication [3]: NICOTINAMIDE, RIVAROXABAN, BISOPROLOL, FUROSEMIDE, PRAVASTATIN, FINASTERIDE, NICOTINAMIDE, LORATADINE, NICOTINIC ACID, KAOLIN, OMEPRAZOLE, MEBEVERINE, FERRIC CARBOXYMALTOSE					
Non-Serious Adverse Event [4]: Malaise, Hot flush, Eyelid irritation					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
貧血	ANAEMIA	Day 176 / NA	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「貧血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Hypercholesterolaemia, Osteoarthritis, Alcohol abuse, Erectile dysfunction, Hypertension, Ex-tobacco user, Tenoplasty, Knee arthroplasty, Carpal tunnel syndrome, Limb injury, Carpal tunnel decompression, Inguinal hernia repair, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: OMEPRAZOLE, LOSARTAN, FUROSEMIDE, SIMVASTATIN, SILDENAFIL, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, GLUCOCORTICOIDS, FUROSEMIDE, PARACETAMOL, IBUPROFEN, CODEINE PHOSPHATE, ACETYLSALICYLIC ACID, GLUCOCORTICOIDS, COVID-19 VACCINE, APIXABAN, TINZAPARIN, BISOPROLOL, PARACETAMOL, POTASSIUM BICARBONATE/SODIUM ALGINATE, NUTRIENTS NOS, LOSARTAN, BISOPROLOL, COVID-19 VACCINE, COVID-19 VACCINE, BISOPROLOL, LOSARTAN				
Non-Serious Adverse Event [4]: Gastrooesophageal reflux disease, COVID-19, Atrial flutter, Physical deconditioning, Cardiac failure, Acute kidney injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
筋骨格系胸痛	MUSCULOSKELETAL CHEST PAIN	Day 643 / Day 645	Not Related	Dose Not Changed	Recovered /Resolved	Mild
小腸閉塞	SMALL BOWEL OBSTRUCTION	Day 787 / Day 810	Not Related	Drug Interrupted	Recovered /Resolved	Severe
塞栓症	CARDIAC EMBOLUS	Day 787 / Day 810	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
完全房室ブロック	COMPLETE HEART BLOCK	Day 838 / Day 842	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「筋骨格系胸痛」、「小腸閉塞」、「塞栓症」及び「完全房室ブロック」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Carpal tunnel decompression, Knee arthroplasty, Hypertension, Osteoarthritis, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 894			
Concomitant Medication [3]: PERINDOPRIL, BISOPROLOL, INDAPAMIDE, PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE						
Non-Serious Adverse Event [4]: Palpitations, COVID-19, Rhinorrhoea, Ligament sprain						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
甲状腺髄様癌	MEDULLARY THYROID CARCINOMA	NA / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
治験責任医師の見解：「甲状腺髄様癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Seasonal allergy, Hypercholesterolaemia, Osteoarthritis, Post stroke seizure, Erectile dysfunction, Corrective lens user, Carpal tunnel decompression, Tendon sheath incision, Hypertension, Ankle fracture, Upper limb fracture, Internal fixation of fracture, Colitis ulcerative, Cerebrovascular accident, Coronary artery stenosis, Cardiac amyloidosis, Ventricular tachycardia, Cardiac resynchronisation therapy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 893		
Concomitant Medication [3]: OMEPRAZOLE, ASCORBIC ACID, RAMIPRIL, BISOPROLOL, ATORVASTATIN, TADALAFIL, CARBAMAZEPINE, CARBAMAZEPINE, LORATADINE, BUDESONIDE, SULFASALAZINE, SPIRONOLACTONE, COVID-19 VACCINE, CLOPIDOGREL, LANSOPRAZOLE, SPIRONOLACTONE, SPIRONOLACTONE, ANTIBIOTICS, WARFARIN, FUROSEMIDE, SPIRONOLACTONE, COVID-19 VACCINE, RAMIPRIL, PARACETAMOL, VITAMIN D NOS, WARFARIN, SPIRONOLACTONE, CALCIUM CARBONATE/COLECALCIFEROL, VITAMIN D NOS, COVID-19 VACCINE, SPIRONOLACTONE, ALENDRONIC ACID, WARFARIN				
Non-Serious Adverse Event [4]: Amaurosis fugax, Musculoskeletal pain, Atrial fibrillation, Cardiac failure, Lower respiratory tract infection, Skin lesion, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳梗塞	RIGHT MCA TERRITORY INFRACT	Day 231 / Day 236	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
脳血管発作	CEREBROVASCULAR ACCIDENT	Day 373 / Day 383	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
大腿骨頚部骨折	RIGHT NECK OF FEMUR FRACTURE	Day 750 / Day 783	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「脳梗塞」、「脳血管発作」及び「大腿骨頚部骨折」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Cataract, Gastrooesophageal reflux disease, Drug hypersensitivity, Seasonal allergy, Benign prostatic hyperplasia, Carpal tunnel decompression, Aortic valve replacement, Drug hypersensitivity, Atrial fibrillation, Osteoarthritis, Cerebrovascular accident, Cardiac pacemaker insertion, Cardiac amyloidosis, Vitamin B12 deficiency, Dysphonia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: ALFUZOSIN, FLUTICASONE FUROATE, RIVAROXABAN, CLOPIDOGREL, SACUBITRIL/VALSARTAN, SILDENAFIL, SPIRONOLACTONE, FUROSEMIDE, BUPRENORPHINE, PARACETAMOL, HYDROXOCOBALAMIN, SACUBITRIL/VALSARTAN, TRIMETHOPRIM, COVID-19 VACCINE, COVID-19 VACCINE, I.V. SOLUTIONS, LOPERAMIDE, COVID-19 VACCINE, HYDROCORTISONE, SACUBITRIL/VALSARTAN, COVID-19 VACCINE, BUMETANIDE				
Non-Serious Adverse Event [4]: Urinary tract infection, Diarrhoea, Cough, Cardiac failure, Dehydration, Trigeminal neuralgia, Neck pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
起立性低血圧	POSTURAL HYPOTENSION	Day 36 / Day 41	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「起立性低血圧」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Back pain, Carpal tunnel syndrome, Bronchiectasis, Percutaneous coronary intervention, Prostate cancer, Carpal tunnel decompression, Hip arthroplasty, Hip arthroplasty, Dermatitis, Atrial fibrillation, Atrial tachycardia, Cardiac ablation, Atrial fibrillation, Cardiac amyloidosis, Dyspepsia, Cardiac ablation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: DABIGATRAN, FUROSEMIDE, ROSUVASTATIN, PERINDOPRIL, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, AMIODARONE, OMEPRAZOLE, BOTULINUM TOXIN TYPE A, PARACETAMOL, COVID-19 VACCINE, SPIRONOLACTONE, FUROSEMIDE, AMOXICILLIN, CLARITHROMYCIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, OMEPRAZOLE, SENNA ALEXANDRINA, MACROGOL, COVID-19 VACCINE, COVID-19 VACCINE, SENNA ALEXANDRINA, COVID-19 VACCINE, TRIMETHOPRIM, COVID-19 VACCINE, AVENA SATIVA FLUID EXTRACT, INFLUENZA VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Carpal tunnel syndrome, Constipation, Atrial fibrillation, Negative cardiac inotropic effect, Acute kidney injury, Nephrolithiasis, Urinary retention				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腎結石症	RENAL CALCULI	Day 748 / Day 752	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「腎結石症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: F	Age: 7[redacted]
Medical History [1]: Seborrhoeic keratosis, Thyroidectomy, Rheumatoid arthritis, Postmenopause, Carpal tunnel decompression, Carpal tunnel decompression, Basal cell carcinoma, Hip arthroplasty, Fatigue, Diverticulitis, Cardiac amyloidosis, Presyncope, Actinic keratosis, Hypercholesterolaemia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911		
Concomitant Medication [3]: LEVOTHYROXINE, ETANERCEPT, STERCULIA URENS, FUROSEMIDE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, FLUOROURACIL, COVID-19 VACCINE, ATORVASTATIN, COVID-19 VACCINE, PARACETAMOL, APIXABAN, ALLOPURINOL, METHOTREXATE, FOLIC ACID, COVID-19 VACCINE, BUDESONIDE, SERTRALINE, ALLOPURINOL, COVID-19 VACCINE, COVID-19 VACCINE, INFLUENZA VACCINE, PREDNISOLONE, AMOXICILLIN, DOXYCYCLINE				
Non-Serious Adverse Event [4]: Presyncope, Anxiety, Gout, COVID-19, Viral upper respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
三束ブロック	TRIFASCICULAR BLOCK	Day 225 / Day 231	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
浮動性めまい	DIZZINESS	Day 238 / Day 242	Not Related	Drug Interrupted	Recovered /Resolved	Mild
治験責任医師の見解：「三束ブロック」及び「浮動性めまい」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Coronary artery disease, Carpal tunnel decompression, Transient ischaemic attack, Aortic valve replacement, Coronary artery bypass, Cox-Maze procedure, Spinal decompression, Cardiac amyloidosis, Cardiac pacemaker insertion, Endocarditis staphylococcal				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 909		
Concomitant Medication [3]: APIXABAN, RAMIPRIL, BISOPROLOL, FUROSEMIDE, ROSUVASTATIN, FLUCLOXACILLIN, AMLODIPINE, AMOXICILLIN, COVID-19 VACCINE, COVID-19 VACCINE, BISOPROLOL, FUROSEMIDE, PARACETAMOL, FLUCLOXACILLIN, COVID-19 VACCINE, AMOXICILLIN, AMOXICILLIN, MORPHINE SULFATE, PARACETAMOL, NITROUS OXIDE/OXYGEN, BISOPROLOL, COVID-19 VACCINE, INFLUENZA VACCINE, DAPAGLIFLOZIN, BISOPROLOL, BISOPROLOL				
Non-Serious Adverse Event [4]: Thermal burn, Tooth infection, Supraventricular tachycardia, Prostatic specific antigen increased, Viral upper respiratory tract infection, Cardiac failure, Cellulitis, Gastroenteritis viral, Joint dislocation, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	PNEUMONIA	NA / Start Day + 26 Days	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「肺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Depression, Insomnia, Inguinal hernia, Gastrooesophageal reflux disease, Hypercholesterolaemia, Cardiac amyloidosis, Carpal tunnel decompression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: LANSOPRAZOLE, SIMVASTATIN, FUROSEMIDE, CITALOPRAM, COVID-19 VACCINE, COVID-19 VACCINE, APIXABAN, DILTIAZEM, COVID-19 VACCINE, PROMETHAZINE, BICALUTAMIDE, GOSERELIN ACETATE, FUROSEMIDE, DILTIAZEM, FUROSEMIDE, DIGOXIN, DAPAGLIFLOZIN, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Nausea, Atrial fibrillation, Supraventricular tachycardia, Basal cell carcinoma, Goitre, Squamous cell carcinoma of skin, Cardiac failure, Squamous cell carcinoma, Skin lesion				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
遠隔転移を伴う前立腺癌	METASTATIC PROSTATE CANCER	Day 645 / Day 1022	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
治験責任医師の見解：「遠隔転移を伴う前立腺癌」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■						
Treatment Arm: Acoramidis		Race: White		Country: UK	Sex: M	Age: 6■
Medical History [1]: Hypertension, Gout, Carpal tunnel decompression, Carpal tunnel syndrome, Knee arthroplasty, Hypothyroidism, Atrial fibrillation, Hypercholesterolaemia, Implantable defibrillator insertion, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 896			
Concomitant Medication [3]: ALLOPURINOL, LEVOTHYROXINE, APIXABAN, LISINOPRIL, ROSUVASTATIN, BISOPROLOL, FUROSEMIDE, SPIRONOLACTONE, DOXAZOSIN, BISOPROLOL, COVID-19 VACCINE, SPIRONOLACTONE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, CHLORAMPHENICOL, PREDNISOLONE, CYCLOPENTOLATE, INFLUENZA VACCINE, COVID-19 VACCINE						
Non-Serious Adverse Event [4]: Hypotension, Diarrhoea, Urinary hesitation, Gastroenteritis, COVID-19, Upper respiratory tract infection						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
黄斑円孔	MACULAR HOLE	NA / Start Day + 125 Days	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「黄斑円孔」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 6[redacted]
Medical History [1]: Diabetes mellitus, Hypercholesterolaemia, Osteoarthritis, Chronic kidney disease, Knee arthroplasty, Knee arthroplasty, Carpal tunnel decompression, Carpal tunnel decompression, Hypertension, Fibromyalgia, Atrial flutter, Pneumonia, Cardiac ablation, Gastrooesophageal reflux disease, Diabetic retinopathy, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: METFORMIN, NEBIVOLOL, GLYCERYL TRINITRATE, SPIRONOLACTONE, FUROSEMIDE, ATORVASTATIN, DIHYDROCODEINE, PARACETAMOL, AMITRIPTYLINE, GABAPENTIN, APIXABAN, OMEPRAZOLE, EPLERENONE, COLCHICINE, DOXYCYCLINE, COVID-19 VACCINE, DOXYCYCLINE, NAPROXEN, CODEINE, CLONAZEPAM, VALPROATE SODIUM, ISOSORBIDE MONONITRATE, AMOXICILLIN/CLAVULANATE POTASSIUM, CLARITHROMYCIN, I.V. SOLUTIONS, GABAPENTIN, COVID-19 VACCINE, DIHYDROCODEINE, NEFOPAM HYDROCHLORIDE, IMMUNOGLOBULIN HUMAN ANTI-TETANUS, FUROSEMIDE, COVID-19 VACCINE, AMOXICILLIN, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Gout, Pneumonia, COVID-19, Chest injury, Acute kidney injury, Lower respiratory tract infection, Myalgia, Orthostatic hypotension, Skin laceration, Diarrhoea, Occult blood positive, Lower respiratory tract infection, Vaccination complication				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
神経系障害（1）	NERVOUS SYSTEM DISORDER	NA / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
神経系障害（2）	NERVOUS SYSTEM DISORDER	NA / Start Day + 74 Days	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
肺炎	PNEUMONIA	Day 247 / Day 252	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
非心臓性胸痛	CHEST PAIN (NON CARDIAC)	Day 279 / Day 646	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate

治験責任医師の見解：「神経系障害（1）」、「神経系障害（2）」、「肺炎」及び「非心臓性胸痛」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: White		Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Osteoarthritis, Carpal tunnel syndrome, Atrial fibrillation, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 896			
Concomitant Medication [3]: RAMIPRIL, FUROSEMIDE, APIXABAN, SPIRONOLACTONE, CALCIUM CARBONATE/COLECALCIFEROL, COLECALCIFEROL, COLECALCIFEROL, COVID-19 VACCINE, ZOLEDRONIC ACID, COVID-19 VACCINE, COVID-19 VACCINE, INFLUENZA VACCINE						
Non-Serious Adverse Event [4]: SARS-CoV-2 carrier, Osteoporosis						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大腿骨頚部骨折	FRACTURED NECK OF FEMUR-RIGHT	Day 166 / Day 198	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「大腿骨頚部骨折」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Seasonal allergy, Chronic kidney disease, Cataract operation, Hypercholesterolaemia, Type 2 diabetes mellitus, Long QT syndrome congenital, Glaucoma, Malignant melanoma, Inguinal hernia, Atrial fibrillation, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 921		
Concomitant Medication [3]: APIXABAN, APIXABAN, ATORVASTATIN, METFORMIN, BRINZOLAMIDE, LATANOPROST, APIXABAN, PARACETAMOL, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, CHLORAMPHENICOL, KETOROLAC TROMETHAMINE, DEXAMETHASONE SODIUM PHOSPHATE, METFORMIN, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FLUCLOXACILLIN, AMOXICILLIN, BISOPROLOL, BISOPROLOL				
Non-Serious Adverse Event [4]: Muscle spasms, Dyspepsia, Muscle spasms, Weight increased, COVID-19, Basal cell carcinoma, Cardiac failure, Atrial fibrillation, Drug intolerance				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
三束ブロック	TRISFASCICULAR BLOCK	NA / Start Day + 23 Days	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate

治験責任医師の見解：「三束ブロック」は治験薬と関連なしと判断した。

Patient ID: ■■-■■■					
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 7■	
Medical History [1]: Appendicectomy, Knee operation, Carpal tunnel syndrome, Cataract, Atrial flutter, Cardiac amyloidosis, Drug eruption, Atrioventricular block complete, Cardiac pacemaker insertion					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896			
Concomitant Medication [3]: BISOPROLOL, BENZYL ALCOHOL/BENZYL BENZOATE/BENZYL CINNAMATE/WOOL FAT/ZINC OXIDE, EDOXABAN, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, DOXYCYCLINE, ANTIBIOTICS, CARBOHYDRATES NOS/FATS NOS/MINERALS NOS/PROTEINS NOS/VITAMINS NOS, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN, CURCUMA LONGA, STEROIDS, OTHER OPHTHALMOLOGICALS, KETOROLAC TROMETHAMINE, DEXAMETHASONE					
Non-Serious Adverse Event [4]: Mouth ulceration, COVID-19, Adverse drug reaction, Inguinal hernia					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺膿瘍	LEFT LUNG ABSCESS	NA / Start Day + 140 Days	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「肺膿瘍」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: Black or African American	Country: UK	Sex: F	Age: 7[redacted]	
Medical History [1]: Type 2 diabetes mellitus, Cerebrovascular accident, Asthma, Postmenopause, Hypertension, Atrial fibrillation, Parkinson's disease, Tricuspid valve incompetence, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 512			
Concomitant Medication [3]: RIVAROXABAN, BISOPROLOL, BISOPROLOL, SPIRONOLACTONE, BUMETANIDE, CARBIDOPA/LEVODOPA, FLUTICASONE/SALMETEROL, SALBUTAMOL, COVID-19 VACCINE, COVID-19 VACCINE, RIVAROXABAN, DIGOXIN, SPIRONOLACTONE, BUMETANIDE					
Non-Serious Adverse Event [4]: Asthenia					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
転倒	FALL	Day 507 / Day 525	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「転倒」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Glaucoma, Transurethral prostatectomy, Nephrectomy, Carpal tunnel decompression, Carpal tunnel decompression, Chronic kidney disease, Spinal operation, Atrial fibrillation, Cardiac amyloidosis, Asthma				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 908		
Concomitant Medication [3]: BRINZOLAMIDE, BIMATOPROST, BRIMONIDINE, RIVAROXABAN, DIGOXIN, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, RAMIPRIL, BISOPROLOL, FUROSEMIDE, BISOPROLOL, FUROSEMIDE, LOPERAMIDE, COVID-19 VACCINE, AMOXICILLIN/CLAVULANATE POTASSIUM, COVID-19 VACCINE, FUROSEMIDE, GLYCEROL, HYPROMELLOSE, ACETIC ACID, DICLOFENAC, COLCHICINE, OMEPRAZOLE, TRANEXAMIC ACID, PREDNISOLONE, LACTULOSE, SENNA ALEXANDRINA, CALCIUM CARBONATE/COLECALCIFEROL, RIVAROXABAN, PREDNISOLONE, FUROSEMIDE, PREDNISOLONE, BISOPROLOL, FUROSEMIDE, BISOPROLOL, PREDNISOLONE, COVID-19 VACCINE, BISOPROLOL, PREDNISOLONE, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, STEROIDS, PREDNISOLONE, PREDNISOLONE, PARAFFIN SOFT/PARAFFIN, LIQUID (WOOL FAT), PREDNISOLONE, DAPAGLIFLOZIN, EPLERENONE, BUMETANIDE				
Non-Serious Adverse Event [4]: Acute kidney injury, Back pain, Pulmonary amyloidosis, Gastrointestinal disorder, Blepharitis, Anaemia, Increased tendency to bruise, Cardiac failure, Otitis externa, Regurgitation, Adverse drug reaction, Gout, Cardiorenal syndrome, Retinal tear, Adverse drug reaction, Fall				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	NA / Start Day + 34 Days	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Mild
免疫性血小板減少症	IMMUNE THROMBOCYTOPENIC PURPURA	Day 701 / Day 708	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
治験責任医師の見解：「心不全」及び「免疫性血小板減少症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Belgium	Sex: F	Age: 8[redacted]
Medical History [1]: Varicose vein operation, Squamous cell carcinoma, Gout, Hyperlipidaemia, Hypertension, Angioplasty, Endarterectomy, Hypertensive urgency, Hip arthroplasty, Oedema peripheral, Cardiac failure, Pulmonary embolism, Deep vein thrombosis, Cardiac failure, Type 2 diabetes mellitus, Cardiac amyloidosis, Hypothyroidism, Iron deficiency				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: EZETIMIBE, OMEPRAZOLE, ALLOPURINOL, BISOPROLOL/HYDROCHLOROTHIAZIDE, LERCANIDIPINE, PRAVASTATIN, LINAGLIPTIN, BUMETANIDE, GLIQUIDONE, APIXABAN, AMLODIPINE, SPIRONOLACTONE, LEVOTHYROXINE, IRON, INFLUENZA VACCINE, MAGNESIUM, COVID-19 VACCINE, PARACETAMOL, COVID-19 VACCINE, AZITHROMYCIN, BUDESONIDE/FORMOTEROL FUMARATE, DOMPERIDONE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, MOXIFLOXACIN, ISOSORBIDE DINITRATE, BUMETANIDE, PARACETAMOL, POTASSIUM, BISOPROLOL, LOPERAMIDE, MOXIFLOXACIN, FOSFOMYCIN, ACETYLSALICYLIC ACID, DEXTROMETHORPHAN HYDROBROMIDE, PARACETAMOL, ACETYLCYSTEINE, ACETYLSALICYLIC ACID, TRAZODONE, BISOPROLOL, APIXABAN, SPIRONOLACTONE, PARACETAMOL, INSULIN, SPIRONOLACTONE, LOPERAMIDE, COVID-19 VACCINE, VITAMIN D NOS, FOSFOMYCIN, COVID-19 VACCINE, INFLUENZA VACCINE, CLINDAMYCIN				
Non-Serious Adverse Event [4]: Oedema peripheral, Squamous cell carcinoma of head and neck, Arthralgia, Pyrexia, Cardiac failure, Chills, Gastroenteritis viral, Renal failure, Urinary tract infection, Diarrhoea, Normocytic anaemia, Pleurisy, Back pain, Acute kidney injury, Hyperglycaemia, Lymphadenopathy, Hepatic lesion, Pain in extremity, Pyrexia, Sleep disorder, Arthralgia, Diarrhoea, White blood cells urine positive, Bacterial test positive, Vitamin D deficiency, Intermittent claudication, Protein urine present, Wound infection, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	PNEUMONIA	Day 396 / Day 422	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全	ACUTE EPISODE OF HEART FAILUE	Day 399 / Day 422	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「肺炎」及び「急性心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]	
Medical History [1]: Goitre, Benign prostatic hyperplasia, Arthralgia, Carpal tunnel decompression, Bundle branch block left, Hypertrophic cardiomyopathy, Arrhythmia supraventricular, Coronary artery disease, Dyspnoea exertional, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896			
Concomitant Medication [3]: BISOPROLOL, ACETYLSALICYLIC ACID, IRBESARTAN, FUROSEMIDE, CANRENONE, FUROSEMIDE, IRBESARTAN, DIOSMIN/HESPERIDIN, APIXABAN, BISOPROLOL, COVID-19 VACCINE, EPLERENONE, OMEPRAZOLE, TAPENTADOL, PARACETAMOL, CEFTRIAXONE, REMDESIVIR					
Non-Serious Adverse Event [4]: Dizziness, Head injury, Haematuria					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	SYMPTOMATIC BRADYCARDIA	NA / Start Day + 115 Days	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９	PAUCISINTOMATIC INFECTION WITH SARS COV 2	Day 771 / Day 781	Not Related	Drug Interrupted	Recovered /Resolved	Mild
治験責任医師の見解：「徐脈」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Chronic kidney disease, Intervertebral disc operation, Corneal transplant, Carpal tunnel decompression, Intervertebral disc operation, Cardioversion, Atrial flutter, Ischaemic stroke, Cardioversion, Pericarditis, Atrial fibrillation, Cardiac failure, Cardiac pacemaker insertion, Dyspnoea, Cardioversion, Endocarditis, Hyperthyroidism, Cardioversion, Hyperthyroidism, Impaired fasting glucose, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: PREDNISONE, APIXABAN, BISOPROLOL, FUROSEMIDE, LEVOSIMENDAN, APIXABAN, BISOPROLOL, EPLERENONE, FUROSEMIDE, ACETAZOLAMIDE, FUROSEMIDE, BISOPROLOL, COVID-19 VACCINE, FUROSEMIDE, ACETAZOLAMIDE, COVID-19 VACCINE, FUROSEMIDE, ALLOPURINOL, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, METOLAZONE, METOLAZONE, SPIRONOLACTONE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Oedema, Pruritus, Gynaecomastia, Constipation, Dysgeusia, Non-24-hour sleep-wake disorder, N-terminal prohormone brain natriuretic peptide increased, Oedema peripheral, Blood albumin decreased, Blood creatinine increased, Blood urea increased, Protein total decreased, Protein urine present, Urine albumin/creatinine ratio increased, Oedema peripheral				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE DECOMPENSATED HEART FAILURE	Day 49 / Day 65	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: F	Age: 8[redacted]	
Medical History [1]: Knee arthroplasty, Hypertension, Menopause, Carpal tunnel decompression, Carpal tunnel decompression, Atrial fibrillation, Dyspnoea exertional, Cardiac failure, Cardiac amyloidosis, Ischaemic stroke, Orthostatic hypotension					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 640			
Concomitant Medication [3]: EDOXABAN TOSILATE, OMEPRAZOLE, VALSARTAN, BISOPROLOL, CANRENONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, SODIUM ALGINATE, PANTOPRAZOLE, LEVOSULPIRIDE, EDOXABAN TOSILATE, VALSARTAN, CANRENONE, FUROSEMIDE					
Non-Serious Adverse Event [4]: Dyspepsia, Muscle spasms, Paraesthesia, Gastroenteritis, Urinary tract infection, Renal impairment, Escherichia urinary tract infection, Hyperuricaemia, Dyspepsia					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	HEART FAILURE DECOMPENSATION	NA / Start Day + 47 Days	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
心不全（2）	HEART FAILURE	Day 575 / NA	Not Related	Drug Interrupted	Recovering /Resolving	Moderate
急性腎障害	ACUTE RENAL FAILURE ON CHRONIC	Day 575 / Day 584	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
呼吸困難	WORSENING DYSPNOEA	Day 622 / Day 625	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「急性腎障害」及び「呼吸困難」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: F	Age: 8[redacted]
Medical History [1]: Hepatic cyst, Glucose tolerance impaired, Hypercholesterolaemia, Obesity, Osteoporosis, Chronic kidney disease, Renal cyst, Pulmonary embolism, Palpitations, Dyspnoea, Syncope, Urinary tract infection, Atrial fibrillation, Atrial flutter, Intracardiac thrombus, Cardiac amyloidosis, Intervertebral disc protrusion, Ischaemic nephropathy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: RIVAROXABAN, RAMIPRIL, BISOPROLOL, DIGOXIN, CANRENONE, FUROSEMIDE, FUROSEMIDE, ALLOPURINOL, TAPENTADOL, METOPROLOL, COVID-19 VACCINE, TAPENTADOL, COVID-19 VACCINE, TAPENTADOL, ALL OTHER THERAPEUTIC PRODUCTS, ALL OTHER THERAPEUTIC PRODUCTS, CANRENONE, ALLOPURINOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, FUROSEMIDE, CIPROFLOXACIN				
Non-Serious Adverse Event [4]: Nasal discomfort, Dyspnoea, Arthralgia, Herpes zoster, Epistaxis, Urinary tract infection, Renal impairment, Presyncope, Urinary tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
失神寸前の状態	PRE-SYNCOPE	Day 713 / Day 719	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性腎障害	ACUTE RENAL FAILURE	Day 713 / Day 719	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	BRADIFREQUENT ATRIAL FIBRILLATION	Day 888 / Day 892	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「失神寸前の状態」、「急性腎障害」及び「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]	
Medical History [1]: Aortic valve incompetence, Hepatic steatosis, Carpal tunnel syndrome, Dyspnoea, Cancer surgery, Carpal tunnel decompression, Cataract operation, Aortic dilatation, Hypertension, Atrial fibrillation, Cardiac amyloidosis, Swelling, Essential tremor, Colon cancer					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 898			
Concomitant Medication [3]: CARVEDILOL, VALSARTAN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUSIDIC ACID, FUROSEMIDE, FUROSEMIDE, FUSIDIC ACID, CIPROFLOXACIN, CYCLOPHOSPHAMIDE, CAPECITABINE, VALSARTAN, TAPENTADOL HYDROCHLORIDE, TAMSULOSIN					
Non-Serious Adverse Event [4]: Visual impairment, Hyperkeratosis, Hyperkeratosis, Memory impairment, Cystitis, Back pain, Urethral adenoma, Urethral stenosis					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肝転移	LIVER METASTASIS DUE TO COLON CANCER	NA / NA	Not Related	Drug Interrupted	Recovering /Resolving	Moderate
治験責任医師の見解：「肝転移」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Italy	Sex: M	Age: 7[redacted]	
Medical History [1]: Carotid arteriosclerosis, Dyspnoea, Carpal tunnel decompression, Haemorrhoid operation, Incisional hernia repair, Inguinal hernia repair, Hypertension, Mitral valve incompetence, Cardiac amyloidosis, Spinal operation, Atrial fibrillation, Swelling					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900			
Concomitant Medication [3]: TERAZOSIN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, BISOPROLOL, NEBIVOLOL, LOW MOLECULAR WEIGHT HEPARIN, SPIRONOLACTONE, BISOPROLOL, RIVAROXABAN, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, PREGABALIN, TAPENTADOL, FUROSEMIDE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, CEFIXIME, PARACETAMOL, CARBOCISTEINE					
Non-Serious Adverse Event [4]: Arrhythmia, COVID-19					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大動脈狭窄	LOW - FLOW, LOW GRADIENT SEVERE AORTIC STENOSIS	Day 762 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「大動脈狭窄」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Deafness, Hyperuricaemia, Inguinal mass, Lumbar spinal stenosis, Osteoarthritis, Meniscus removal, Nasal septal operation, Spinal operation, Hypertension, Appendicectomy, Anal fistula repair, Anxiety, Hepatic steatosis, Pneumonia, Pulmonary embolism, Deep vein thrombosis, Hypertensive heart disease, Cardiac amyloidosis, Atrial fibrillation, Cardiac pacemaker insertion, Craniocerebral injury, Carpal tunnel decompression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: ALLOPURINOL, PLANTAGO OVATA, LORAZEPAM, ESCITALOPRAM, HYDROCHLOROTHIAZIDE/VALSARTAN, APIXABAN, CIPROFLOXACIN, VALSARTAN, LACTULOSE, MACROGOL, VALSARTAN, RIVASTIGMINE, ENOXAPARIN, RIVASTIGMINE, DONEPEZIL, DONEPEZIL, ONDANSETRON, PANTOPRAZOLE, CEFAZOLIN, TRANEXAMIC ACID, DICLOFENAC SODIUM, DEXKETOPROFEN, PARACETAMOL, FENTANYL CITRATE, PROPOFOL, BUPIVACAINE, LIDOCAINE, MIDAZOLAM, DEXAMETHASONE, PANTOPRAZOLE, BEMIPARIN SODIUM, ALLOPURINOL, ENOXAPARIN SODIUM, LOSARTAN, TORASEMIDE, VALSARTAN, APIXABAN				
Non-Serious Adverse Event [4]: COVID-19, Constipation, Asthenia, Osteoarthritis, Cognitive disorder				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性関節症	COXARTHROSIS	Day 842 / Day 860	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「変形性関節症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Hypertensive heart disease, Haemorrhoids, Cholangitis, Large intestinal polypectomy, Large intestinal polypectomy, Hypertension, Carpal tunnel syndrome, Peptic ulcer, Portal vein phlebitis, Sepsis, Portal hypertensive gastropathy, Portal vein cavernous transformation, Intervertebral disc protrusion, Iron deficiency anaemia, Hip arthroplasty, Shoulder arthroplasty, Biliary tract disorder, Carpal tunnel decompression, Hypertonic bladder, Rheumatoid arthritis, Hand fracture, Cardiac pacemaker insertion, Cardiac amyloidosis, Seborrhoeic keratosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: URSODEOXYCHOLIC ACID, ACENOCOUMAROL, OMEPRAZOLE, ACENOCOUMAROL, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, ACENOCOUMAROL, RIFAXIMIN, HYDROXYCHLOROQUINE SULFATE, PREDNISONE, FUROSEMIDE, AVIBACTAM, FUROSEMIDE, BIFIDOBACTERIUM LONGUM/LACTOBACILLUS ACIDOPHILUS/STREPTOCOCCUS LACTIS/STREPTOCOCCUS THERMOPHILUS, RIFAXIMIN, CALCIFEDIOL, ERTAPENEM, FUROSEMIDE, PARACETAMOL, PARACETAMOL, OMEPRAZOLE, HYDROXYCHLOROQUINE SULFATE, PHYTOMENADIONE, MANIDIPINE, PREDNISONE, BEMIPARIN SODIUM, BEMIPARIN SODIUM, PREDNISONE, BEMIPARIN SODIUM, BEMIPARIN SODIUM, FUROSEMIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, MEGLUMINE AMIDOTRIZOATE/SODIUM AMIDOTRIZOATE, OMEPRAZOLE, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, PREDNISONE, URSODEOXYCHOLIC ACID, PANTOPRAZOLE, ERTAPENEM, PARACETAMOL, PARACETAMOL, URSODEOXYCHOLIC ACID, DAPTOMYCIN, BEMIPARIN SODIUM, PREDNISONE, METAMIZOLE, BEMIPARIN SODIUM, CINITAPRIDE, AMOXICILLIN/CLAVULANIC ACID, FUROSEMIDE, PARACETAMOL, PREDNISONE, MAGNESIUM LACTATE, AMPICILLIN, CEFTRIAXONE, BEMIPARIN SODIUM, PARACETAMOL, FUROSEMIDE, URSODEOXYCHOLIC ACID, BEMIPARIN SODIUM, MIDAZOLAM, FLUMAZENIL, SUXAMETHONIUM CHLORIDE, ROCURONIUM BROMIDE, PARACETAMOL, METAMIZOLE, FENTANYL, PROPOFOL, SUGAMMADEX SODIUM, URSODEOXYCHOLIC ACID, URSODEOXYCHOLIC ACID, PANTOPRAZOLE, CINITAPRIDE, MAGNESIUM LACTATE, HYDROXYCHLOROQUINE, BEMIPARIN SODIUM, FUROSEMIDE, PREDNISONE, GENTAMICIN, MEROPENEM, BEMIPARIN SODIUM, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, PREDNISONE, ACENOCOUMAROL, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, PARACETAMOL, BEMIPARIN SODIUM, FUROSEMIDE, PANTOPRAZOLE, BEMIPARIN SODIUM, PREDNISONE, BEMIPARIN SODIUM, BEMIPARIN SODIUM, TORASEMIDE, BEMIPARIN SODIUM, DEXAMETHASONE, BIFIDOBACTERIUM LONGUM/LACTOBACILLUS ACIDOPHILUS/STREPTOCOCCUS LACTIS/STREPTOCOCCUS THERMOPHILUS, CALCIFEDIOL, ACENOCOUMAROL, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, FUROSEMIDE, PREDNISONE, PREDNISONE, PREDNISONE, PREDNISONE, PREDNISONE, FUROSEMIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, FENTANYL, VANCOMYCIN, VANCOMYCIN, MEROPENEM, BEMIPARIN SODIUM, MANIDIPINE, PARACETAMOL, BETAHISTINE HYDROCHLORIDE, LEVOFLOXACIN, BEMIPARIN SODIUM, ROCURONIUM BROMIDE, PETHIDINE HYDROCHLORIDE, ETOMIDATE, PROPOFOL, LEVOFLOXACIN, BIFIDOBACTERIUM LONGUM/LACTOBACILLUS ACIDOPHILUS/STREPTOCOCCUS LACTIS/STREPTOCOCCUS THERMOPHILUS, URSODEOXYCHOLIC ACID, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, FUROSEMIDE, DAPTOMYCIN, AVIBACTAM/CEFTAZIDIME, MANIDIPINE, PARACETAMOL, SIMETICONE, ONDANSETRON, ROCURONIUM, FENTANYL, ETOMIDATE, SUGAMMADEX SODIUM, VANCOMYCIN, AZITHROMYCIN, AVIBACTAM/CEFTAZIDIME, FENTANYL, PROPOFOL, DIAZEPAM, IPRATROPIUM BROMIDE/SALBUTAMOL SULFATE, METHYLPREDNISOLONE, FUROSEMIDE, FUROSEMIDE, ENALAPRIL, FUROSEMIDE, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, VANCOMYCIN, CEFTAZIDIME, PARACETAMOL, VANCOMYCIN, BEMIPARIN SODIUM, LEVOFLOXACIN, RIFAXIMIN, APIXABAN, ENALAPRIL MALEATE/LERCANIDIPINE HYDROCHLORIDE, RIFAXIMIN, CYANOCOBALAMIN/FOLIC ACID, OMEPRAZOLE				
Non-Serious Adverse Event [4]: Renal impairment, Constipation, Medical device site infection, Anaemia, Vestibular disorder, Constipation, Pyrexia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胆管炎（1）	WORSENING OF CHOLANGITIS	Day 170 / Day 176	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
胆管炎（2）	WORSENING OF CHOLANGITIS	Day 190 / Day 226	Not Related	Drug Interrupted	Recovered /Resolved	Severe
胆管炎（3）	WORSENING OF CHOLANGITIS	Day 653 / Day 660	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
胆管炎（4）	WORSENING OF CHOLANGITIS	Day 682 / Day 709	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肺炎	NOCOSOMIAL PNEUMONIA	Day 698 / Day 739	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胆管炎（5）	RECURRENT CHOLANGITIS	Day 730 / Day 737	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「胆管炎（1）」、「胆管炎（2）」、「胆管炎（3）」、「胆管炎（4）」、「肺炎」及び「胆管炎（5）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Hypercholesterolaemia, Osteoarthritis, Benign prostatic hyperplasia, Bronchitis chronic, Appendicectomy, Inguinal hernia repair, Inguinal hernia repair, Transurethral prostatectomy, Inguinal hernia repair, Osteotomy, Osteoarthritis, Osteotomy, Osteoarthritis, Joint prosthesis user, Carpal tunnel syndrome, Carpal tunnel decompression, Knee arthroplasty, Diverticulitis, Lumbar spinal stenosis, Asthma, Chronic gastritis, Cataract traumatic, Carpal tunnel decompression, Herpes zoster, Haemorrhoids, Neuralgia, Constipation, Atrial fibrillation, Hypertension, Hypertensive cardiomyopathy, Shoulder operation, Cardiac amyloidosis, Cardiac failure				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: APIXABAN, LOSARTAN, FUROSEMIDE, TAMSULOSIN, PANTOPRAZOLE, FLUTICASONE FUROATE/UMECLIDINIUM BROMIDE/VILANTEROL TRIFENATATE, MUPIROCIN, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, PREDNICARBATE, NEBIVOLOL, GINSENG NOS/VITAMIN B NOS				
Non-Serious Adverse Event [4]: Limb discomfort, Seborrhoeic keratosis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房粗動	ATRIAL FLUTTER	Day 41 / Day 43	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房粗動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Asthma, Anal fistula repair, Atrial fibrillation, Dupuytren's contracture, Fasciectomy, Dupuytren's contracture, Cardiac pacemaker insertion, Osteoarthritis, Spinal osteoarthritis, Hip arthroplasty, Intervertebral disc protrusion, Joint prosthesis user, Chronic obstructive pulmonary disease, Hypertension, Cardiac ablation, Cardiac pacemaker replacement, Hypertensive heart disease, Vascular pseudoaneurysm, Arterial angioplasty, Seborrhoeic keratosis, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: ACENOCOUMAROL, ATORVASTATIN, HYDROCHLOROTHIAZIDE/VALSARTAN, FLUTICASONE FUROATE/VILANTEROL TRIFENATATE, AMOXICILLIN/CLAVULANATE POTASSIUM, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN, ONDANSETRON, PANTOPRAZOLE, BEMIPARIN SODIUM, KETOROLAC, DIAZEPAM, PARACETAMOL, METAMIZOLE, COVID-19 VACCINE, PREDNICARBATE, INFLUENZA VACCINE, COVID-19 VACCINE, LANSOPRAZOLE, APIXABAN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Ecchymosis, Urinary tract infection, Diarrhoea, Diarrhoea, Tooth abscess, Epistaxis, Gastroenteritis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼠径ヘルニア	INGUINAL HERNIA	Day 396 / Day 405	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
肺炎	PNEUMONIA	Day 840 / Day 846	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「鼠径ヘルニア」及び「肺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Gastrooesophageal reflux disease, Hypercholesterolaemia, Intervertebral disc protrusion, Spinal stenosis, Prostatitis, Carpal tunnel decompression, Renal colic, Spinal osteoarthritis, Psoriasis, Benign prostatic hyperplasia, Deafness, Venous thrombosis, Sleep apnoea syndrome, Urinary tract infection, Seborrhoeic keratosis, Eyelid cyst removal, Skin neoplasm excision, Cardiac pacemaker insertion, Arthritis, Erectile dysfunction, Ectropion, Back pain, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: LANSOPRAZOLE, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, MIRABEGRON, TADALAFIL, TIOTROPIUM BROMIDE, ATORVASTATIN, ACETYLSALICYLIC ACID, ENOXAPARIN SODIUM, AMINOLEVULINIC ACID, METAMIZOLE MAGNESIUM, IMIQUIMOD, APIXABAN, IMIQUIMOD, COVID-19 VACCINE, COVID-19 VACCINE, TAMSULOSIN, FINASTERIDE, VILANTEROL, FLUTICASONE FUROATE, LANSOPRAZOLE, PANTOPRAZOLE, TORASEMIDE, TAMSULOSIN, DUTASTERIDE, APIXABAN, PANTOPRAZOLE, VALACICLOVIR, MUPIROCIN, HYALURONIC ACID, PREDNISONE, PREDNISONE, PREDNISONE, AMOXICILLIN/CLAVULANATE POTASSIUM, PREDNISONE, VARICELLA ZOSTER VACCINE LIVE (OKA/MERCK), LEVOFLOXACIN, AMOXICILLIN/CLAVULANATE POTASSIUM, CEFUROXIME, CEFUROXIME, FOSFOMYCIN, LEVOFLOXACIN, CEFUROXIME, ROCURONIUM, PARACETAMOL, METAMIZOLE, FENTANYL, PROPOFOL, SUGAMMADEX SODIUM, CEFUROXIME, BEMIPARIN SODIUM, PARACETAMOL, FLUTICASONE FUROATE, OLODATEROL HYDROCHLORIDE/TIOTROPIUM BROMIDE MONOHYDRATE, METHYL AMINOLEVULINATE HYDROCHLORIDE, MUPIROCIN, LEVOFLOXACIN, MOXIFLOXACIN, DEXAMETHASONE, DEXAMETHASONE, DEXAMETHASONE, DEXAMETHASONE, DEXAMETHASONE, PARACETAMOL, METAMIZOLE				
Non-Serious Adverse Event [4]: Constipation, Tendonitis, Asthenia, Conjunctival haemorrhage, Atrial flutter, Vomiting, Pyrexia, Ear infection viral, Facial paralysis, Escherichia urinary tract infection, Paraesthesia, Prostatitis, Cataract, COVID-19, Neck pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心粗動	FLUTTER ABLATION	Day 227 / Day 228	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
前立腺炎	PROSTATITIS	Day 637 / Day 640	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「心粗動」及び「前立腺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Spain	Sex: M	Age: 7[redacted]	
Medical History [1]: Carpal tunnel syndrome, Dyslipidaemia, Hypertension, Benign prostatic hyperplasia, Osteoarthritis, Joint prosthesis user, Hyperuricaemia, Chronic obstructive pulmonary disease, Cardiac failure, Atrial fibrillation, Coronary artery bypass, Herpes zoster, Cardiac amyloidosis, Patella fracture					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 924			
Concomitant Medication [3]: ALLOPURINOL, OMEPRAZOLE, SIMVASTATIN, POTASSIUM ASCORBATE, EPLERENONE, ACENOCOUMAROL, FUROSEMIDE, VALSARTAN, TERAZOSIN, BUDESONIDE, OLODATEROL, TIOTROPIUM BROMIDE, EDOXABAN, METOCLOPRAMIDE, TRAMADOL, PARACETAMOL, FUROSEMIDE, COVID-19 VACCINE, EDOXABAN, TRANEXAMIC ACID, PARACETAMOL, FUROSEMIDE, AMOXICILLIN, AMOXICILLIN/CLAVULANIC ACID, CHLORTALIDONE					
Non-Serious Adverse Event [4]: Osteoarthritis, Post procedural haemorrhage, Neck pain, Eye abscess					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
人工関節周囲骨折	LEFT PERIPROSTHETIC FRACTURE TYPE A VANCOUVER	Day 891 / NA	Not Related	Drug Interrupted	Recovering /Resolving	Severe

治験責任医師の見解：「人工関節周囲骨折」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Brazil	Sex: M	Age: 8[redacted]
Medical History [1]: Tonsillectomy, Diabetes mellitus, Dyslipidaemia, Coronary artery disease, Hernia repair, Cholecystectomy, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: METFORMIN, ACETYLSALICYLIC ACID, TRIMETAZIDINE, ROSUVASTATIN, NEBIVOLOL, FUROSEMIDE, FUROSEMIDE, GLIMEPIRIDE, FUROSEMIDE, GLICLAZIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, PREDNISONE, FUROSEMIDE, DOBUTAMINE, NITROPRUSSIDE SODIUM, LINAGLIPTIN, CIPROFLOXACIN, FUROSEMIDE, COVID-19 VACCINE, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE, FUROSEMIDE, VITAMIN B12 NOS				
Non-Serious Adverse Event [4]: Cardiac failure chronic, Pain in extremity, Hypoglycaemia, Bronchitis, Urinary tract infection, Benign prostatic hyperplasia, Cardiac failure chronic, Vitamin B12 deficiency				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	DECOMPENSATED HEART FAILURE	Day 212 / Day 218	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Brazil	Sex: M	Age: 8[redacted]
Medical History [1]: Skin neoplasm excision, Benign prostatic hyperplasia, Cardiac failure, Hypothyroidism, Osteoarthritis, Dyspnoea exertional, Carpal tunnel decompression, Chronic kidney disease, Atrial fibrillation, Cardiac amyloidosis, Sinus node dysfunction, Dyslipidaemia, Hyperuricaemia, Cardiac pacemaker insertion, Cardiac failure, Cardiac failure				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: LEVOTHYROXINE, OMEPRAZOLE, APIXABAN, BISOPROLOL, AMIODARONE, FUROSEMIDE, ATORVASTATIN, ALLOPURINOL, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, METAMIZOLE SODIUM, LEVOTHYROXINE, COVID-19 VACCINE, COVID-19 VACCINE, CEFTRIAXONE, CEFTRIAXONE, DAPAGLIFLOZIN, FUROSEMIDE, LEVOTHYROXINE, FUROSEMIDE, MEROPENEM, LEVOTHYROXINE, FOSFOMYCIN TROMETAMOL, DUTASTERIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, AMIODARONE				
Non-Serious Adverse Event [4]: Hypothyroidism, Nail discolouration, Dysentery, Viral upper respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ウイルス性上気道感染	UPPER AIRWAY INFECTION OF VIRAL ETIOLOGY	Day 234 / Day 243	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（1）	HEART DISEASE DECOMPENSATION	Day 239 / Day 243	Not Related	Dose Not Changed	Recovered /Resolved	Severe
腎機能障害	WORSENING RENAL FUNCTION	Day 239 / Day 248	Not Related	Dose Not Changed	Recovered /Resolved	Severe
尿路感染（1）	URINARY TRACT INFECTION	Day 555 / Day 556	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	HEART DISEASE DECOMPENSATION	Day 661 / Day 669	Not Related	Dose Not Changed	Recovered /Resolved	Severe
尿路感染（2）	URINARY TRACT INFECTION	Day 661 / Day 669	Not Related	Dose Not Changed	Recovered /Resolved	Severe
上気道感染	UPPER AIRWAY INFECTION	Day 756 / Day 759	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「ウイルス性上気道感染」、「心不全（1）」、「腎機能障害」、「尿路感染（1）」、「心不全（2）」、「尿路感染（2）」及び「上気道感染」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Anxiety, Atrial fibrillation, Carpal tunnel decompression, Carpal tunnel syndrome, Carpal tunnel decompression, Carpal tunnel decompression, Osteoarthritis, Bursitis, Morton's neuralgia, Neuropathy peripheral, Knee arthroplasty, Prostatism, Knee arthroplasty, Acute myocardial infarction, Coronary arterial stent insertion, Cardiac failure, Gastrooesophageal reflux disease, Hypercholesterolaemia, Hypertension, Biopsy abdominal wall, Ventricular tachycardia, Cardiac assistance device user, Cardiac pacemaker insertion, Hip arthroplasty, Echocardiogram, Hernia repair, Biopsy heart, Cardiac amyloidosis, Hypopituitarism, Malacoplakia, Colonoscopy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 511		
Concomitant Medication [3]: PANTOPRAZOLE, APIXABAN, DIGOXIN, FUROSEMIDE, ATORVASTATIN, LEVOTHYROXINE SODIUM, PERINDOPRIL, BISOPROLOL, HYDROCORTISONE, FUROSEMIDE, INFLUENZA VACCINE, FUROSEMIDE, DIGOXIN, SILODOSIN, APIXABAN, APIXABAN, ONDANSETRON, GENTAMICIN, METARAMINOL, PARACETAMOL, FENTANYL, PROPOFOL, TESTOSTERONE UNDECANOATE, HYDROCORTISONE, HYDROCORTISONE, RED BLOOD CELLS, DIGOXIN, BISOPROLOL, POTASSIUM, PERINDOPRIL, FERRIC CARBOXYMALTOSE, APIXABAN, PERINDOPRIL, TESTOSTERONE UNDECANOATE, NORFLOXACIN, AMIODARONE, AMIODARONE, AMIODARONE, AMIODARONE, AMIODARONE, TRANEXAMIC ACID, FACTOR II (PROTHROMBIN)/FACTOR IX COMPLEX HUMAN/FACTOR VII (PROCONVERTIN)/FACTOR X (STUART PROWER FACTOR), RED BLOOD CELLS, PERINDOPRIL, OXYCODONE, FENTANYL, PARACETAMOL, FENTANYL, KETAMINE, HYDROCORTISONE, ROPIVACAINE, FUROSEMIDE, HYDROCORTISONE, DOCUSATE/SENNOSIDE B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, SODIUM CHLORIDE, SODIUM CHLORIDE, HYDROCORTISONE, HYDROCORTISONE, HYDROCORTISONE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, HYDROCORTISONE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, TRAMADOL, APIXABAN, FUROSEMIDE, HYDROCORTISONE, APIXABAN, FUROSEMIDE, FUROSEMIDE, HYDROCORTISONE, FERRIC CARBOXYMALTOSE, COLECALCIFEROL, CEFTRIAXONE, HYDROCORTISONE, COLECALCIFEROL, HYDROCORTISONE, HYDROCORTISONE, CEFALEXIN, FUROSEMIDE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, FUROSEMIDE, PARACETAMOL, FUROSEMIDE				
Non-Serious Adverse Event [4]: Blood creatinine increased, Dyspnoea, Benign prostatic hyperplasia, Urethral stenosis, Exercise tolerance decreased, Malaise, Iron deficiency anaemia, Hypokalaemia, Herpes zoster, Blood testosterone decreased, Urinary tract infection, Haemothorax, Loss of consciousness, Hyponatraemia, Anaemia, Bacterial test, Blood creatinine increased, Skin laceration, Fall, Contusion, Coagulopathy, Pneumothorax, Pleural effusion, Adrenocortical insufficiency acute, Hypervolaemia, Constipation, Iron deficiency anaemia, Wound infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	DECOMPENSATED HEART FAILURE	Day 274 / Day 279	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心室性頻脈	VENTRICULAR TACHYCARDIA WORSENING	Day 410 / Day 414	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肋骨骨折	FRACTURED RIBS RIGHT 4-6	Day 461 / Day 472	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「心不全」、「心室性頻脈」及び「肋骨骨折」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Acrodynia, Cholecystectomy, Lactose intolerance, Hip arthroplasty, Sinus operation, Hip arthroplasty, Tenoplasty, Finger amputation, Tenoplasty, Restless legs syndrome, Coronary artery disease, Anxiety, Depression, Hypertension, Haemangioma of liver, Biopsy bone marrow, Biopsy abdominal wall, Dyslipidaemia, Biopsy heart, Cardiac amyloidosis, Oedema peripheral, Open reduction of fracture, Haemorrhoids, Echocardiogram				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ASCORBIC ACID, ASCORBIC ACID, FISH OIL, ACETYLSALICYLIC ACID, ROSUVASTATIN, MAGNESIUM, CITALOPRAM, FUROSEMIDE, RAMIPRIL, FUROSEMIDE, ONDANSETRON, ENOXAPARIN, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, FUROSEMIDE, OXYCODONE HYDROCHLORIDE, FENTANYL, PARACETAMOL, FENTANYL, AMIODARONE, APIXABAN, AMIODARONE, MEBEVERINE, AMITRIPTYLINE, INFLUENZA VACCINE INACT SPLIT 4V, COVID-19 VACCINE, COVID-19 VACCINE, INFLUENZA VACCINE INACT SPLIT 4V, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Angina pectoris, Nausea, Atrial fibrillation, Irritable bowel syndrome, Dyskinesia, Fatigue, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
発熱	FEBRILE ILLNESS	Day 137 / Day 143	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「発熱」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel decompression, Hepatic cirrhosis, Hypertension, Cataract, Macular hole, Cardiac failure, Blood cholesterol increased, Vitrectomy, Echocardiogram, Cardiac amyloidosis, Implantable defibrillator insertion, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 533		
Concomitant Medication [3]: RIVAROXABAN, CARVEDILOL, SPIRONOLACTONE, FUROSEMIDE, ATORVASTATIN CALCIUM, SACUBITRIL/VALSARTAN, METRONIDAZOLE, CEFTRIAXONE, CALCIUM CHLORIDE DIHYDRATE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, SODIUM CHLORIDE, GLUCOSE, CALCIUM CHLORIDE DIHYDRATE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, CARVEDILOL, SPIRONOLACTONE, FUROSEMIDE, ATORVASTATIN, RIVAROXABAN, DOXYCYCLINE, CEFAZOLIN, CALCIUM CHLORIDE DIHYDRATE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, METARAMINOL, ALFENTANIL, FENTANYL, LIDOCAINE, RIVAROXABAN, GLUCOSAMINE, GENTAMICIN, AMOXICILLIN, METRONIDAZOLE, SODIUM CHLORIDE, OXYCODONE HYDROCHLORIDE, CEFTRIAXONE, PARACETAMOL, PARACETAMOL, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, RIVAROXABAN, SACUBITRIL/VALSARTAN, SPIRONOLACTONE, FUROSEMIDE, THIAMINE, SACUBITRIL/VALSARTAN, CARVEDILOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, THIAMINE, THIAMINE, CARVEDILOL, SACUBITRIL/VALSARTAN, CEFALEXIN, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE				
Non-Serious Adverse Event [4]: Abdominal pain, Skin infection, Bile duct stone, Skin lesion, Frontotemporal dementia, Urinary tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胆管結石	CHOLEDOCHOLITHIASIS	Day 48 / Day 53	Not Related	Drug Interrupted	Recovered /Resolved	Severe
胆管炎	CHOLANGITIS	Day 293 / Day 297	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「胆管結石」及び「胆管炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Carpal tunnel syndrome, Atrial fibrillation, Hypercholesterolaemia, Cerebral infarction, Echocardiogram, Cardiac amyloidosis, Asthma				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: APIXABAN, METOPROLOL, DIGOXIN, ROSUVASTATIN, BUDESONIDE, COVID-19 VACCINE, INFLUENZA VACCINE INACT SPLIT 3V, DICLOFENAC DIETHYLAMINE, COVID-19 VACCINE, OXYCODONE, TRAMADOL, DOCUSATE SODIUM/SENNOSIDE B, OXYCODONE, PARACETAMOL, ELECTROLYTES NOS/MACROGOL, PARACETAMOL, PREGABALIN, OXYCODONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE, TRAMADOL, PROCHLORPERAZINE, PREGABALIN, PREGABALIN, TRAMADOL				
Non-Serious Adverse Event [4]: Carpal tunnel syndrome, Osteoarthritis, Arthralgia, Staphylococcal infection, C-reactive protein increased, Intervertebral disc protrusion, Rotator cuff syndrome, Bursitis, Vertebral foraminal stenosis, Bursitis, Vertigo, Microsleep, Sleep apnoea syndrome				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性関節症	OSTEOARTHRITIS OF LEFT SHOULDER (PREVIOUSLY WORSENING OF LEFT SHOULDER PAIN)	Day 480 / Day 495	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「変形性関節症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Seasonal allergy, Hip arthroplasty, Carpal tunnel decompression, Rotator cuff repair, Erectile dysfunction, Blood cholesterol increased, Gouty arthritis, Malignant melanoma, Knee arthroplasty, Actinic keratosis, Varicose vein, Transient ischaemic attack, Glaucoma, Muscle spasms, Hypertension, Atrial fibrillation, Cardiac failure, Vitamin D deficiency, Chronic kidney disease, Dyspnoea, Cardiac amyloidosis, Cholelithiasis, Gastrooesophageal reflux disease, Type 2 diabetes mellitus, Pleural effusion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: FEXOFENADINE HYDROCHLORIDE, SILDENAFIL CITRATE, ATORVASTATIN CALCIUM, MAGNESIUM, METOPROLOL, BIMATOPROST/TIMOLOL, VITAMIN D NOS, APIXABAN, FUROSEMIDE, FUROSEMIDE, METFORMIN, ALLOPURINOL, AMIODARONE, SPIRONOLACTONE, ESOMEPRAZOLE SODIUM, ATORVASTATIN CALCIUM, GLYCERYL TRINITRATE, ISOSORBIDE DINITRATE, METFORMIN, APIXABAN, DICLOFENAC, CODEINE PHOSPHATE/PARACETAMOL, ESOMEPRAZOLE, PANTOPRAZOLE, ASCORBIC ACID, OXYCODONE, TEMAZEPAM, SPIRONOLACTONE, ESOMEPRAZOLE, FUROSEMIDE, TIMOLOL MALEATE/TRAVOPROST, BRIMONIDINE TARTRATE/BRINZOLAMIDE, APIXABAN, MAGNESIUM, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE, COVID-19 VACCINE, FLUTICASONE FUROATE, TERBINAFINE HYDROCHLORIDE, FLUTICASONE FUROATE, COVID-19 VACCINE, CODEINE PHOSPHATE/PARACETAMOL, ESOMEPRAZOLE, DAPAGLIFLOZIN/METFORMIN, DOXYCYCLINE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE				
Non-Serious Adverse Event [4]: Parotid gland enlargement, Gamma-glutamyltransferase increased, Angina pectoris, Ascites, Dry skin, Back pain, Pulmonary mass, Melaena, Insomnia, Epistaxis, Abdominal distension, Tinea pedis, Headache, Cough, Lower respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
中毒性腎症	NSAIDS INDUCED ACUTE KIDNEY INJURY	Day 337 / Day 341	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「中毒性腎症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Intracardiac thrombus, Blindness unilateral, Cerebrovascular accident, Urinary tract infection, Gout, Hypercholesterolaemia, Asthma, Atrial fibrillation, Cardiac failure, Haemangioma of skin, Vitamin D deficiency, Pulmonary embolism, Haematuria, Benign prostatic hyperplasia, Transurethral prostatectomy, Cardiac ablation, Cardiac amyloidosis, Aortic stenosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: ATORVASTATIN, ALLOPURINOL, FOLIC ACID, BUDESONIDE/FORMOTEROL FUMARATE, TIOTROPIUM BROMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, ERGOCALCIFEROL, AMIODARONE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, APIXABAN, POTASSIUM CHLORIDE, SOTALOL, APIXABAN, POTASSIUM CHLORIDE, SPIRONOLACTONE, INFLUENZA VACCINE, INFLUENZA VACCINE INACT SPLIT 3V, ISOPRENALINE, MAGNESIUM, APIXABAN, CEFAZOLIN, CEFAZOLIN, FENTANYL, MIDAZOLAM, SOTALOL, APIXABAN, ALLOPURINOL, CEFALEXIN, BETAMETHASONE DIPROPIONATE, GRISEOFULVIN, COVID-19 VACCINE, INFLUENZA VACCINE, COVID-19 VACCINE, TRIMETHOPRIM, ATORVASTATIN, COVID-19 VACCINE, METHYLPREDNISOLONE ACETATE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, INFLUENZA VACCINE, COVID-19 VACCINE, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE/GLYCOPYRRONIUM BROMIDE				
Non-Serious Adverse Event [4]: Gamma-glutamyltransferase increased, Diarrhoea, Dizziness, Muscle spasms, Urinary tract infection, Dermatitis, Urinary tract infection, Occult blood positive, Bursitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心停止	VENTRICULAR STANDSTILL	Day 320 / Day 323	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心停止」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Carpal tunnel decompression, Carpal tunnel decompression, Osteotomy, Arthroscopy, Arthroscopy, Nasal septum deviation, Knee arthroplasty, Arthroscopy, Cataract, Knee arthroplasty, Polypectomy, Intraocular lens implant, Blood cholesterol increased, Shoulder operation, Arthroscopy, Stress, Dysphonia, Biopsy larynx, Laryngoscopy, Biopsy larynx, Laryngoscopy, Thrombocytopenia, Androgen deficiency, Coronary angioplasty, Dyspnoea, Cardiac amyloidosis, Obesity, Vitamin D deficiency, Cardiac failure, Aortic stenosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 899		
Concomitant Medication [3]: VITAMIN B-COMPLEX (PLAIN), FUROSEMIDE, CURCUMIN, COLECALCIFEROL, CETIRIZINE, UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE, EZETIMIBE/SIMVASTATIN, ACETYLSALICYLIC ACID, EZETIMIBE, SIMVASTATIN, CALAMINE, LORATADINE, TESTOSTERONE, DIETARY SUPPLEMENT, PANTOPRAZOLE SODIUM SESQUIHYDRATE, COVID-19 VACCINE, ESOMEPRAZOLE, COVID-19 VACCINE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, COVID-19 VACCINE, CEFUROXIME, PARACETAMOL				
Non-Serious Adverse Event [4]: Reflux laryngitis, Oropharyngeal pain, Pruritus, Urticaria, Thrombocytopenia, Basal cell carcinoma, Gastrointestinal disorder, Back pain, Upper respiratory tract infection, Arthralgia, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
低血圧	HYPOTENSION	Day 251 / Day 257	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「低血圧」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Urinary incontinence, Appendicectomy, Inguinal hernia repair, Lower limb fracture, Medical device implantation, Limb traumatic amputation, Inguinal hernia repair, Rotator cuff repair, Rotator cuff repair, Chest pain, Intervertebral disc operation, Back pain, Tenosynovitis, Depression, Carpal tunnel decompression, Intervertebral disc operation, Spinal fusion surgery, Carpal tunnel syndrome, Tinnitus, Carpal tunnel decompression, Allergy to arthropod bite, Restless legs syndrome, Ventricular tachycardia, Hypergammaglobulinaemia benign monoclonal, Gastrooesophageal reflux disease, Hyperlipidaemia, Dizziness postural, Glaucoma, Cardiac amyloidosis, Osteoarthritis, Aortic dilatation, Abdominal distension, Cardiac failure, Hydrocele, Coronary artery disease, Sinus bradycardia, Bundle branch block left				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 892		
Concomitant Medication [3]: CODEINE PHOSPHATE, PARACETAMOL, CITALOPRAM, FEXOFENADINE HYDROCHLORIDE, PRAMIPEXOLE, GLYCERYL TRINITRATE, ISOSORBIDE MONONITRATE, ROSUVASTATIN, LATANOPROST, FUROSEMIDE, ACETYLSALICYLIC ACID, PANTOPRAZOLE, INFLUENZA VACCINE, CORTISONE, PALMIDROL, SIMETICONE, PALMIDROL, FLUOROURACIL, FUROSEMIDE, PALMIDROL, PALMIDROL, METOPROLOL, DIPHTHERIA VACCINE TOXOID/PERTUSSIS VACCINE ACELLULAR/TETANUS VACCINE TOXOID, OTHER VIRAL VACCINES, CORTISONE, CLAVULANIC ACID, AMOXICILLIN, PREGABALIN, COVID-19 VACCINE, INFLUENZA VACCINE, GRAMICIDIN/NEOMYCIN SULFATE/NYSTATIN/TRIAMCINOLONE ACETONIDE, COVID-19 VACCINE, OXYCODONE, PARACETAMOL, DOCUSATE SODIUM/SENNOSIDE A+B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, ENOXAPARIN, FUROSEMIDE, IBUPROFEN, OXYCODONE, NALOXONE, FUROSEMIDE, MELATONIN, DENOSUMAB, ATROPINE, CEFAZOLIN, METARAMINOL, OXYCODONE, FENTANYL, PROPOFOL, PALMIDROL, PALMIDROL, CEFALEXIN, PALMIDROL, COVID-19 VACCINE, PALMIDROL, PALMIDROL, CEFAZOLIN, DOXYCYCLINE, DIPHTHERIA VACCINE TOXOID/TETANUS VACCINE TOXOID, IBUPROFEN, OXYCODONE, NUTRIENTS NOS, DOCUSATE SODIUM/SENNOSIDE A+B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, EPHEDRINE, ROSUVASTATIN CALCIUM, OXYCODONE, FENTANYL, FENTANYL, PROPOFOL, DICLOXACILLIN, PALMIDROL, PALMIDROL, DICLOFENAC, PREGABALIN, SALBUTAMOL, PREGABALIN, DEXAMETHASONE, PREGABALIN				
Non-Serious Adverse Event [4]: Tendonitis, Tenosynovitis, Fatigue, Cataract, Synovial cyst, Actinic keratosis, Renal impairment, Upper respiratory tract infection, Post vaccination syndrome, Procedural dizziness, Hyperplasia, Fall, Haematuria, Haematoma, Splenic neoplasm malignancy unspecified, Bladder hypertrophy, Constipation, Osteopenia, Insomnia, Basal cell carcinoma, Presyncope, Fall, Arthralgia, Fall, Wheezing, Back pain, Headache				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肋骨骨折	MULTIPLE FRACTURED RIBS	Day 512 / Day 570	Not Related	Dose Not Changed	Recovered /Resolved	Severe
足関節部骨折	FRACTURED RIGHT ANKLE	Day 749 / Day 766	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
皮膚裂傷	NUMEROUS LACERATIONS TO RIGHT FOOT	Day 749 / Day 766	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「肋骨骨折」、「足関節部骨折」及び「皮膚裂傷」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Skin injury, Dupuytren's contracture, Dupuytren's contracture operation, Dupuytren's contracture, Benign prostatic hyperplasia, Dupuytren's contracture operation, Transurethral prostatectomy, Pernicious anaemia, Varicose vein operation, Varicose vein, Varicose vein, Cardiac pacemaker insertion, Glaucoma, Cardiac failure, Humerus fracture, Cognitive disorder, Abnormal behaviour, Cerebral infarction, Atrial fibrillation, Pruritus, Carotid artery disease, Osteoporosis, Skin ulcer, Sleep apnoea syndrome, Positive airway pressure therapy, Rash, Arteriosclerosis coronary artery, Cardiac amyloidosis, Acetabulum fracture, Lower limb fracture, Cardiac pacemaker replacement, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: CANDESARTAN, SPIRONOLACTONE, FUROSEMIDE, ROSUVASTATIN, MOMETASONE, PREGABALIN, PREGABALIN, BIMATOPROST, RABEPRAZOLE, APIXABAN, BISOPROLOL, BETAMETHASONE VALERATE, PARACETAMOL, PROPYLPARABEN, FUROSEMIDE, DENOSUMAB, FUROSEMIDE, SPIRONOLACTONE, CANDESARTAN CILEXETIL, FUROSEMIDE, CALCIUM GLUCONATE, PANTOPRAZOLE, CLAVULANIC ACID, AMOXICILLIN, APIXABAN, RABEPRAZOLE, FUROSEMIDE, BISOPROLOL, SPIRONOLACTONE, BISOPROLOL, RABEPRAZOLE, ROSUVASTATIN, FUROSEMIDE, BISOPROLOL, FUROSEMIDE, BISOPROLOL, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, CLOTRIMAZOLE, COVID-19 VACCINE, FLUOROURACIL, SALICYLIC ACID/SULFUR/TRICLOSAN, MEDICATED DRESSINGS, APIXABAN, INFLUENZA VACCINE, MAGNESIUM, COVID-19 VACCINE, BENZYL ALCOHOL/BENZYL BENZOATE/BENZYL CINNAMATE/WOOL FAT/ZINC OXIDE, PROBIOTICS [UMBRELLA TERM], CEFALEXIN, POVIDONE-IODINE, FUROSEMIDE, CEFALEXIN, FUROSEMIDE, CALAMINE, FUROSEMIDE, BETAMETHASONE DIPROPIONATE, COVID-19 VACCINE, CEFALEXIN, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, APIXABAN, BETAMETHASONE DIPROPIONATE, FUROSEMIDE, MULTIVITAMINS (PLAIN), BISOPROLOL, SPIRONOLACTONE, BETAMETHASONE, LEVOTHYROXINE SODIUM, OTHER ANTIVIRALS				
Non-Serious Adverse Event [4]: Hypotension, Acute kidney injury, Presyncope, Basal cell carcinoma, Pulmonary oedema, Eye contusion, Squamous cell carcinoma of skin, Muscle spasms, Scab, Hypervolaemia, Rectal haemorrhage, Hypothyroidism, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路感染	URINARY TRACT INFECTION	Day 14 / Day 28	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性腎障害	ACUTE KIDNEY INJURY (SECONDARY TO HYPOTENSION)	Day 14 / Day 29	Not Related	Dose Not Changed	Recovered /Resolved	Severe
起立性低血圧	POSTURAL HYPOTENSION	Day 23 / Day 25	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「尿路感染」、「急性腎障害」及び「起立性低血圧」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Nasal septum deviation, Nasal turbinate hypertrophy, Spinal laminectomy, Carpal tunnel syndrome, Osteoarthritis, Hypertension, Cardiac failure congestive, Pulmonary mass, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: PERINDOPRIL, FUROSEMIDE, ANGELICA ARCHANGELICA ROOT/CARUM CARVI FRUIT/CHELIDONIUM MAJUS HERB/GLYCYRRHIZA GLABRA ROOT/IBERIS AMARA/MATRICARIA CHAMOMILLA FLOWER/MELISSA OFFICINALIS LEAF/MENTHA X PIPERITA LEAF/SILYBUM MARIANUM F, FUROSEMIDE, EPINEPHRINE, LORATADINE, PROMETHAZINE, PREDNISOLONE, HYDRALAZINE, FUROSEMIDE, PARACETAMOL, CODEINE PHOSPHATE/PARACETAMOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, TEMAZEPAM, MAGNESIUM, FUROSEMIDE, CODEINE PHOSPHATE/PARACETAMOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, SPIRONOLACTONE, SPIRONOLACTONE, BETAMETHASONE DIPROPIONATE, FUROSEMIDE, VALSARTAN, MIRTAZAPINE, SPIRONOLACTONE, HYDROCHLOROTHIAZIDE, HYDROCHLOROTHIAZIDE, MORPHINE, DOCUSATE/SENNA ALEXANDRINA, MACROGOL 3350, TAPENTADOL, GABAPENTIN, CEFAZOLIN, CEFALEXIN				
Non-Serious Adverse Event [4]: Abdominal distension, Abdominal discomfort, Oedema peripheral, Insomnia, Muscle spasms, Fall, Pleural effusion, Rash, Dyspnoea, Fall, Rib fracture, Dyspnoea exertional				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血管浮腫	ANGIOEDEMA -ACE INHIBITOR INDUCED	Day 66 / Day 68	Not Related	Dose Not Changed	Recovered /Resolved	Severe
転倒	MECHANICAL FALL FROM ROOF	Day 828 / Day 828	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
尾骨骨折	MULTI TRAUMA - FRACTURED COCCYX	Day 828 / Day 897	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肋骨骨折	MULTI TRAUMA - FRACTURED RIBS	Day 828 / Day 897	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
脳出血	MULTI TRAUMA - SMALL BRAIN BLEED	Day 828 / Day 897	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
徐脈	POSSIBLE WORSENING OF BRADYCARDIA	Day 831 / Day 833	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性腎障害	ACUTE ON CHRONIC KIDNEY DISEASE	Day 834 / Day 835	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「血管浮腫」、「転倒」、「尾骨骨折」、「肋骨骨折」、「脳出血」、「徐脈」及び「急性腎障害」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Food allergy, Spondylolisthesis, Carpal tunnel syndrome, Insomnia, Spinal stenosis, Carpal tunnel syndrome, Knee arthroplasty, Dupuytren's contracture operation, Spinal fusion surgery, Ischaemic stroke, Atrial fibrillation, Thrombocytopenia, Transient ischaemic attack, Coronary artery bypass, Myocardial ischaemia, Cataract operation, Skin neoplasm excision, Gastrooesophageal reflux disease, Transient ischaemic attack, Hyperlipidaemia, Knee arthroplasty, Osteoarthritis, Urosepsis, Sinus node dysfunction, Cardiac pacemaker insertion, Amyloidosis, Pleural effusion, Pleural effusion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: PARACETAMOL, WARFARIN, SIMVASTATIN, TRAMADOL, OXAZEPAM, ESOMEPRAZOLE SODIUM, POTASSIUM CHLORIDE, FUROSEMIDE, ESOMEPRAZOLE SODIUM, ESOMEPRAZOLE SODIUM, VANCOMYCIN, CEFAZOLIN, ISOPRENALINE, FENTANYL, MIDAZOLAM, CEFALEXIN, FUROSEMIDE, COLCHICINE, PREDNISONE				
Non-Serious Adverse Event [4]: Nausea, Headache, Nausea, Skin ulcer, Gout, SARS-CoV-2 test positive, Rheumatoid arthritis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼠径ヘルニア	WORSENING RIGHT INGUINAL HERNIA	Day 285 / Day 286	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「鼠径ヘルニア」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Haematuria, Hypertension, Hypercholesterolaemia, Prostate cancer, Carpal tunnel decompression, Gout, Transient ischaemic attack, Malignant melanoma, Shoulder operation, Spinal stenosis, Spinal laminectomy, Aortic arteriosclerosis, Acute myocardial infarction, Atrial fibrillation, Atrial fibrillation, Arterial stent insertion, Myocardial ischaemia, Cardiac amyloidosis, Presyncope				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: PERINDOPRIL ERBUMINE, ALLOPURINOL, HYDROXOCOBALAMIN, PARACETAMOL, EZETIMIBE/SIMVASTATIN, CLOPIDOGREL, APIXABAN, SOTALOL, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, PERINDOPRIL ERBUMINE, OXYCODONE HYDROCHLORIDE, CODEINE PHOSPHATE/PARACETAMOL, APIXABAN, GENTAMICIN, FLUCLOXACILLIN, POTASSIUM CHLORIDE, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE INACT SAG 4V, AMIODARONE, COVID-19 VACCINE, SOTALOL, BISOPROLOL, INFLUENZA VACCINE INACT SAG 4V, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Soft tissue injury, Spinal compression fracture, Presyncope, Adverse drug reaction, Cataract, Cataract, SARS-CoV-2 test positive				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
低血圧	HYPOTENSION	Day 17 / Day 18	Related	Dose Not Changed	Recovered /Resolved	Moderate
失神	SYNCOPE	Day 34 / Day 34	Related	Dose Not Changed	Recovered /Resolved	Severe
徐脈	BRADYCARDIA DUE TO SOTOLOL	Day 126 / Day 128	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
発熱	FEVER OF UNKNOWN ORIGIN	Day 347 / Day 350	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心房細動	EXACERBATION OF AF	Day 527 / Day 600	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「低血圧」及び「失神」は治験薬と関連ありと判断した。「徐脈」、「発熱」及び「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Carpal tunnel syndrome, Prostate cancer, Congenital inguinal hernia, Exposure to chemical pollution, Inguinal hernia repair, Rotator cuff repair, Depression, Atrial fibrillation, Cardiac failure, Nail operation, Gout, Compartment syndrome, Haematoma, Sleep apnoea syndrome, Knee arthroplasty, Type 2 diabetes mellitus, Carpal tunnel decompression, Carpal tunnel decompression, Joint stabilisation, Radical prostatectomy, Cardiac failure congestive, Urinary incontinence, Urinary bladder suspension, Helicobacter infection, Hip arthroplasty, Urinary tract infection, Hypertonic bladder, Hypertension, Bronchitis, Dermatitis, Cardiac amyloidosis, Vomiting, Gastrooesophageal reflux disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 908		
Concomitant Medication [3]: FISH OIL, POTASSIUM CHLORIDE, ALLOPURINOL, EMPAGLIFLOZIN/METFORMIN HYDROCHLORIDE, DABIGATRAN ETEXILATE MESILATE, VENLAFAXINE HYDROCHLORIDE, VENLAFAXINE HYDROCHLORIDE, METOPROLOL, FUROSEMIDE, FUROSEMIDE, VENLAFAXINE HYDROCHLORIDE, CODEINE PHOSPHATE/PARACETAMOL, TAPENTADOL HYDROCHLORIDE, PARACETAMOL, AMITRIPTYLINE, APIXABAN, ATORVASTATIN, FUROSEMIDE, NUCLEOSIDES AND NUCLEOTIDES EXCL. REVERSE TRANSCRIPTASE INHIBITORS				
Non-Serious Adverse Event [4]: SARS-CoV-2 test positive				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
四肢損傷	L SHOULDER INJURY	Day 167 / Day 296	Not Related	Dose Not Changed	Recovered /Resolved	Severe
深部静脈血栓症	SMALL VASUCLAR CLOT IN R LOWER LEG	Day 324 / Day 331	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「四肢損傷」及び「深部静脈血栓症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertension, Carpal tunnel syndrome, Carpal tunnel syndrome, Gout, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis, Neuropathy peripheral				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 904			
Concomitant Medication [3]: CANDESARTAN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, MELOXICAM, COLCHICINE, FUROSEMIDE, AMITRIPTYLINE, COVID-19 VACCINE, PARACETAMOL, AMITRIPTYLINE, VALSARTAN, FUROSEMIDE, FUROSEMIDE, PREGABALIN, FUROSEMIDE, FUROSEMIDE, PREDNISOLONE, ALLOPURINOL, MAGNESIUM, MULTIVITAMINS (PLAIN), VITAMIN B NOS, ALLOPURINOL, ESOMEPRAZOLE, POTASSIUM CHLORIDE, DAPAGLIFLOZIN, COVID-19 VACCINE, INFLUENZA VACCINE INACT SAG 4V				
Non-Serious Adverse Event [4]: Gout, Rash, Basal cell carcinoma, Musculoskeletal pain, Renal impairment, Synovitis, Hypokalaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
末梢腫脹	BILATERAL HAND SWELLING	Day 642 / Day 905	Not Related	Dose Not Changed	Recovered /Resolved	Severe
末梢性ニューロパチー	WORSENING PERIPHERAL NEUROPATHY	Day 676 / Day 806	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「末梢腫脹」及び「末梢性ニューロパチー」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]	
Medical History [1]: Shoulder operation, Aortic aneurysm, Carpal tunnel syndrome, Hypertension, Coronary artery disease, Dyslipidaemia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ROSUVASTATIN, EZETIMIBE, ISOSORBIDE, ATENOLOL, CANDESARTAN, ATENOLOL, ATENOLOL, ISOSORBIDE, GLYCERYL TRINITRATE, ROSUVASTATIN, COVID-19 VACCINE, INFLUENZA VACCINE INACT SPLIT 3V, COVID-19 VACCINE, COVID-19 VACCINE, COLCHICINE, OTHER ANTIVIRALS, CANDESARTAN, PARACETAMOL					
Non-Serious Adverse Event [4]: Dizziness, Chest discomfort, Dry eye, Dry mouth, Delirium					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９	COVID-19 INFECTION	Day 821 / Day 827	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Asthma, Varicose vein, Depression, Cerebrovascular accident, Atrial fibrillation, Hypercholesterolaemia, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: CETIRIZINE HYDROCHLORIDE, ACETYLSALICYLIC ACID, SIMVASTATIN, QUETIAPINE, APIXABAN, FUROSEMIDE, MAGNESIUM, MELATONIN, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN, PREDNISOLONE, COVID-19 VACCINE, FUROSEMIDE, COVID-19 VACCINE, MOMETASONE FUROATE, XYLOMETAZOLINE HYDROCHLORIDE, COVID-19 VACCINE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/SIMETICONE, INFLUENZA VACCINE INACT SPLIT 4V				
Non-Serious Adverse Event [4]: Sinusitis, Sinusitis, Rectal haemorrhage, Nasal polyps, Gastrooesophageal reflux disease, Influenza				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
副鼻腔炎	SINUSITIS	Day 515 / Day 606	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「副鼻腔炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Developmental hip dysplasia, Kyphosis, Gastrooesophageal reflux disease, Hypercholesterolaemia, Hypertension, Drug hypersensitivity, Diverticulitis, Lower gastrointestinal haemorrhage, Colon adenoma, Spinal osteoarthritis, Colon adenoma, Carpal tunnel syndrome, Cardiac failure, Cardiac amyloidosis, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: OMEPRAZOLE, PARACETAMOL, IRBESARTAN, HYDROCHLOROTHIAZIDE, ATORVASTATIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, TRAMADOL, ALLOPURINOL, COLCHICINE, FUROSEMIDE, COLCHICINE, IRBESARTAN, AMLODIPINE, COVID-19 VACCINE, INFLUENZA VACCINE INACT SPLIT 3V, ALLOPURINOL, COVID-19 VACCINE, RIVAROXABAN, METOPROLOL, AMIODARONE, RIVAROXABAN, PANTOPRAZOLE, MAGNESIUM SULFATE, TRANEXAMIC ACID, BLOOD PLASMA, RED BLOOD CELLS, POTASSIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM/SODIUM CHLORIDE/SODIUM LACTATE, METARAMINOL, HEPARIN, SALBUTAMOL, POTASSIUM CHLORIDE/SODIUM CARBONATE ANHYDROUS/SODIUM CHLORIDE/SODIUM SULFATE ANHYDROUS, ALLOPURINOL, FENTANYL, PROPOFOL, AMIODARONE, MAGNESIUM, ALBUMIN HUMAN, SALBUTAMOL, FUROSEMIDE, FUROSEMIDE, IPRATROPIUM BROMIDE, PANTOPRAZOLE, BISOPROLOL, FUROSEMIDE, ENOXAPARIN, FERRIC HYDROXIDE POLYMALTOSE COMPLEX, BUDESONIDE, COVID-19 VACCINE, BISOPROLOL, PREDNISOLONE, COLCHICINE, ALLOPURINOL, AMIODARONE, OXYCODONE, INFLUENZA VACCINE INACT SAG 4V, COVID-19 VACCINE, FUROSEMIDE, POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Eye haemorrhage, Muscle strain, Diarrhoea, Acute kidney injury, Hypoaesthesia, Paraesthesia, Sleep apnoea syndrome, Hypervolaemia, Liver function test abnormal, Developmental hip dysplasia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
二束ブロック	BIFASICULAR BLOCK	Day 542 / Day 605	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	ATRIAL FIBRILLATION	Day 585 / Day 730	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
上部消化管出血	UPPER GASTOINTESTINAL BLEEDING	Day 628 / Day 641	Not Related	Drug Interrupted	Recovered /Resolved	Severe
関節痛	ACUTE LEFT HIP PAIN	Day 752 / Day 756	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「二束ブロック」、「心房細動」、「上部消化管出血」及び「関節痛」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: F	Age: 8[redacted]
Medical History [1]: Hysterectomy, Arthroscopy, Spinal operation, Back pain, Spinal operation, Carpal tunnel decompression, Rotator cuff repair, Gastrooesophageal reflux disease, Hiatus hernia, Vitrectomy, Hypercholesterolaemia, Spinal operation, Carpal tunnel decompression, Cholecystectomy, Hypertension, Ventricular tachycardia, Bradyarrhythmia, Cardiac assistance device user, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: CODEINE PHOSPHATE/DOXYLAMINE SUCCINATE/PARACETAMOL, ESOMEPRAZOLE, AMIODARONE, ROSUVASTATIN, PERINDOPRIL, FUROSEMIDE, TAPENTADOL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, CELECOXIB, ALGINIC ACID/ALUMINIUM HYDROXIDE/MAGNESIUM TRISILICATE/SODIUM BICARBONATE, FENTANYL, PREGABALIN, COVID-19 VACCINE, COVID-19 VACCINE, FAMCICLOVIR, COVID-19 VACCINE, FENTANYL, VITAMIN D NOS				
Non-Serious Adverse Event [4]: Rib fracture, Herpes zoster, COVID-19, Bursitis, Skin cancer, Back pain, Anal incontinence, Vitamin D deficiency, Hypoaesthesia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
転倒	MECHANICAL FALL	Day 58 / Day 58	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
頭部損傷	HEADSTRIKE	Day 58 / Day 63	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
肋骨骨折	RIGHT FRACTURED RIB	Day 58 / Day 100	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
上腹部痛	EPIGASTRIC PAIN	Day 72 / Day 73	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「転倒」、「頭部損傷」、「肋骨骨折」及び「上腹部痛」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: F	Age: 8[redacted]
Medical History [1]: Hysterectomy, Seasonal allergy, Hypertension, Migraine, Knee arthroplasty, Osteoarthritis, Cataract, Atrial fibrillation, Gastrooesophageal reflux disease, Back pain, Chronic obstructive pulmonary disease, Osteoporosis, Macular degeneration, Hepatic steatosis, Shoulder arthroplasty, Thyroidectomy, Acute myocardial infarction, Troponin increased, Cholelithiasis, Cardiac amyloidosis, Cardiac failure, Bursitis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 383			
Concomitant Medication [3]: FEXOFENADINE HYDROCHLORIDE, DILTIAZEM HYDROCHLORIDE, APIXABAN, TAPENTADOL HYDROCHLORIDE, PREGABALIN, MAGNESIUM, UBIDECARENONE, ASCORBIC ACID/CUPRIC OXIDE/TOCOPHERYL ACID SUCCINATE/ZINC OXIDE, COLECALCIFEROL, DENOSUMAB, FUROSEMIDE, CALCITRIOL, MOMETASONE FUROATE, DILTIAZEM HYDROCHLORIDE, FUROSEMIDE, SPIRONOLACTONE, METOPROLOL, FUROSEMIDE, METOPROLOL, FUROSEMIDE, FUROSEMIDE, BISOPROLOL, MIDODRINE, MIDODRINE, SPIRONOLACTONE, FUROSEMIDE, PARACETAMOL, POTASSIUM CHLORIDE, FUROSEMIDE, PARACETAMOL, MIDAZOLAM, MIDODRINE, MIDODRINE, ONDANSETRON, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, ACETYLSALICYLIC ACID, DOCUSATE SODIUM/SENNOSIDE A+B, LACTULOSE, ENOXAPARIN SODIUM, BISOPROLOL, PANTOPRAZOLE, CEFALEXIN, ENOXAPARIN, METARAMINOL, SPIRONOLACTONE, ZINC OXIDE, TAPENTADOL, FENTANYL, PROPOFOL, LIDOCAINE, LIDOCAINE HYDROCHLORIDE, SODIUM PHOSPHATE MONOBASIC (ANHYDROUS), CYANOCOBALAMIN, CLOTRIMAZOLE, METHADONE, APIXABAN, APIXABAN, CALCIUM CARBONATE, CALCIUM CARBONATE, CALCIUM GLUCONATE, POTASSIUM CHLORIDE, AMIODARONE, LEVETIRACETAM, QUETIAPINE				
Non-Serious Adverse Event [4]: Exercise tolerance decreased, Cardiac failure acute, Orthostatic hypotension, Diarrhoea, Acute kidney injury, Blood creatine phosphokinase increased, Fall, Skin maceration, Delirium, Thrombophlebitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
転倒	FALL	Day 216 / Day 218	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
足関節部骨折	RIGHT TRIMALLEOLAR FRACTURE	Day 361 / Day 637	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心筋虚血	RATE RELATED, ATRIAL FIBRILLATION, ISCHAEMIA WITH TROPONIN RISE	Day 369 / Day 376	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
低カルシウム血症	HYPOCALCAEMIA-1.80L[2.10-2.60MMOL/L	Day 379 / Day 383	Not Related	Drug Withdrawn	Recovered /Resolved	Moderate

治験責任医師の見解：「転倒」、「足関節部骨折」、「心筋虚血」及び「低カルシウム血症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertension, Back pain, Osteoarthritis, Drug hypersensitivity, Asthma, Carpal tunnel syndrome, Carpal tunnel syndrome, Muscle spasms, Gastritis, Hypokalaemia, Atrial fibrillation, Gout, Hypercholesterolaemia, Cardiac failure, Renal infarct, Polycystic liver disease, Congenital cystic kidney disease, Acute myocardial infarction, Myocardial infarction, Cardiac amyloidosis, Cataract				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 904			
Concomitant Medication [3]: CANDESARTAN, TAPENTADOL, LERCANIDIPINE, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, SALBUTAMOL, APIXABAN, SIMVASTATIN, ALLOPURINOL, SPIRONOLACTONE, FUROSEMIDE, MORPHINE, OXYCODONE, FUROSEMIDE, FUROSEMIDE, APIXABAN, FUROSEMIDE, EMPAGLIFLOZIN, FENTANYL, PROPOFOL, MIDAZOLAM, LIDOCAINE, PANTOPRAZOLE, AMOXICILLIN, LEVOFLOXACIN, SALBUTAMOL, PREDNISOLONE, MOXIFLOXACIN, APIXABAN, SODIUM CHLORIDE, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, SALBUTAMOL, PREDNISOLONE, CALCIUM POLYSTYRENE SULFONATE, PREDNISOLONE, CANDESARTAN, SPIRONOLACTONE, FUROSEMIDE, KETOROLAC TROMETHAMINE, CELECOXIB, OXYCODONE, TAPENTADOL, PARACETAMOL, ACETYLSALICYLIC ACID, SPIRONOLACTONE, PANTOPRAZOLE, AMOXICILLIN, METRONIDAZOLE, LEVOFLOXACIN, COVID-19 VACCINE, PREGABALIN, PANTOPRAZOLE, LERCANIDIPINE, CLINDAMYCIN, DIPHTHERIA VACCINE TOXOID/TETANUS VACCINE TOXOID, BUPRENORPHINE, TRAMADOL, PARACETAMOL, ONDANSETRON, FENTANYL, PROPOFOL, LIDOCAINE, CLINDAMYCIN				
Non-Serious Adverse Event [4]: Helicobacter gastritis, Gastritis erosive, Acute kidney injury, Hyperkalaemia, COVID-19, Abdominal pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE KIDNEY INJURY	Day 7 / Day 28	Not Related	Drug Interrupted	Recovered /Resolved	Mild
喘息	INFECTIVE EXACERBATION OF ASTHMA	Day 284 / Day 324	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
頚髄神経根障害	ACUTE C5 RADICULOPATHY	Day 319 / Day 385	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
四肢膿瘍	ABSCESS OF DORSUM OF MID RIGHT HAND	Day 806 / Day 822	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性腎障害」、「喘息」、「頚髄神経根障害」及び「四肢膿瘍」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Spinal operation, Osteoarthritis, Hip arthroplasty, Diverticulum, Gout, Nephrolithiasis, Hypertension, Gastrooesophageal reflux disease, Carpal tunnel decompression, Spinal operation, Hyperlipidaemia, Muscle spasms, Left ventricular failure, Angina pectoris, Prostatism, Wheezing, Chronic obstructive pulmonary disease, Acute myocardial infarction, Coronary artery disease, Neuralgia, Cardiac amyloidosis, Chronic kidney disease, Pain in extremity, Constipation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 907		
Concomitant Medication [3]: ALLOPURINOL, ACETYLSALICYLIC ACID, OMEPRAZOLE, SIMVASTATIN, FINASTERIDE, SPIRONOLACTONE, BUMETANIDE, AMITRIPTYLINE, GLYCOPYRRONIUM/INDACATEROL, SALBUTAMOL, BISOPROLOL, TRAMADOL, ISOSORBIDE MONONITRATE, MORPHINE SULFATE, PREGABALIN, DOCUSATE SODIUM, SPIRONOLACTONE, BECLOMETASONE, ROXITHROMYCIN, LORATADINE, PSYLLIUM HYDROPHILIC MUCILLOID, ROXITHROMYCIN, ATORVASTATIN, ROXITHROMYCIN, ISOSORBIDE MONONITRATE, SODIUM CHLORIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, ENOXAPARIN SODIUM, BISOPROLOL, FUROSEMIDE, PREDNISONE, AMOXICILLIN/CLAVULANATE POTASSIUM, CLOPIDOGREL, AMOXICILLIN/CLAVULANATE POTASSIUM, ROXITHROMYCIN, ACETYLSALICYLIC ACID, AMOXICILLIN/CLAVULANATE POTASSIUM, PARACETAMOL, ZOPICLONE, ROXITHROMYCIN, CEFTRIAXONE, SODIUM CHLORIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, FAMOTIDINE, BUMETANIDE, PREGABALIN, ATORVASTATIN, PREGABALIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, SODIUM CHLORIDE, SODIUM CHLORIDE, SODIUM CHLORIDE, BISOPROLOL, ISOSORBIDE MONONITRATE, BUMETANIDE, CODEINE, ONDANSETRON, ACETYLSALICYLIC ACID, TRANEXAMIC ACID, LIDOCAINE HYDROCHLORIDE/PHENYLEPHRINE HYDROCHLORIDE, CEFALEXIN, FENTANYL, OXYCODONE, OXYCODONE HYDROCHLORIDE, ALGINIC ACID/ALUMINIUM HYDROXIDE/MAGNESIUM TRISILICATE/SODIUM BICARBONATE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/SIMETICONE, ACETYLSALICYLIC ACID, MAGNESIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, DOXYCYCLINE, FINASTERIDE, BUMETANIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, ROXITHROMYCIN, ISOSORBIDE MONONITRATE, BISOPROLOL, RIVAROXABAN, ISOSORBIDE MONONITRATE, COVID-19 VACCINE, COVID-19 VACCINE, FLUCLOXACILLIN, AMOXICILLIN, FUROSEMIDE, BISOPROLOL, BUMETANIDE, FLUCLOXACILLIN, CEFTRIAXONE, SODIUM CHLORIDE, PARACETAMOL, SODIUM CHLORIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, ISOSORBIDE MONONITRATE, ISOSORBIDE MONONITRATE, COVID-19 VACCINE, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, CLARITHROMYCIN, SODIUM CHLORIDE, PREDNISONE, BISOPROLOL, GENTAMICIN, AMOXICILLIN/CLAVULANATE POTASSIUM, SODIUM CHLORIDE, AMITRIPTYLINE, AMOXICILLIN/CLAVULANATE POTASSIUM, PARACETAMOL, AMOXICILLIN/CLAVULANATE POTASSIUM, ROXITHROMYCIN, DIGOXIN, CLARITHROMYCIN, AMOXICILLIN/CLAVULANATE POTASSIUM, ROXITHROMYCIN, BUMETANIDE, TRAMADOL				
Non-Serious Adverse Event [4]: Pruritus, Fatigue, Productive cough, Arthralgia, Constipation, Lower respiratory tract infection, Respiratory tract infection, Pain in extremity, Angina pectoris, Gastrooesophageal reflux disease, Lower respiratory tract infection, Abdominal pain upper, Neuropathy peripheral, Vomiting, Fall, Confusional state, Epistaxis, Joint injury, Limb injury, Epistaxis, Mobility decreased, Lower respiratory tract infection, Bronchitis, Localised infection, Localised infection, Tooth infection, Dehydration, Confusional state, Fall, Contusion, Lower respiratory tract infection, Lower respiratory tract infection, Atrial fibrillation, Cough				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
気管支炎	BRONCHIAL INFECTION	Day 230 / Day 274	Not Related	Dose Not Changed	Recovered /Resolved	Severe

心房細動	HOSPITALIZATION NEW ONSET ATRIAL FIBRILLATION	Day 232 / Day 235	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
下気道感染（1）	LOWER RESPIRATORY TRACT INFECTION	Day 244 / Day 248	Not Related	Dose Not Changed	Recovered /Resolved	Severe
下気道感染（2）	LOWER RESPIRATORY TRACT INFECTION	Day 269 / Day 272	Not Related	Dose Not Changed	Recovered /Resolved	Severe
失神	HYPOTENSIVE SYNCOPE	Day 329 / Day 334	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性腎障害	ACUTE KIDNEY INJURY POSSIBLE ETIOLOGY OVER DIURESIS	Day 330 / Day 334	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
靱帯捻挫	SPRAIN LEFT HIP	Day 381 / Day 382	Not Related	Dose Not Changed	Recovered /Resolved	Severe
転倒	FALL - MULTIFACTORIAL ETIOLOGY	Day 489 / Day 489	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房粗動	SLOW ATRIAL FLUTTER	Day 489 / Day 491	Not Related	Dose Not Changed	Recovered /Resolved	Severe
洞結節機能不全	TACHY-BRADY SYNDROME	Day 497 / Day 507	Not Related	Dose Not Changed	Recovered /Resolved	Severe
感染による気管支拡張症の増悪	INFECTIVE EXACERBATION OF BRONCHIECTISIS	Day 525 / Day 534	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心筋梗塞	NON ST-ELEVATION MYOCARDIAL INFARCTION	Day 527 / Day 527	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	EXACERBATION OF CONGESTIVE HEART FAILURE	Day 656 / Day 659	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺炎（1）	BILATERAL BRONCHOPNEUMONIA	Day 697 / Day 712	Not Related	Dose Not Changed	Recovered /Resolved	Severe

下気道感染（3）	LOWER RESPIRATORY TRACT INFECTION	Day 820 / Day 822	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺炎（2）	COMMUNITY ACQUIRED PNEUMONIA	Day 852 / Day 862	Not Related	Dose Not Changed	Recovered /Resolved	Severe
下気道感染（4）	LOWER RESPIRATORY INFECTION	Day 875 / Day 893	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	DECOMPENSATED HEART FAILURE	Day 876 / Day 883	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
便秘	CONSTIPATION CAUSING HOSPITALIZATION	Day 925 / Day 930	Not Related	NA	Recovered /Resolved	Moderate
治験責任医師の見解：「気管支炎」、「心房細動」、「下気道感染（1）」、「下気道感染（2）」、「失神」、「急性腎障害」、「靭帯捻挫」、「転倒」、「心房粗動」、「洞結節機能不全」、「感染による気管支拡張症の増悪」、「急性心筋梗塞」、「急性心不全」、「肺炎（1）」、「下気道感染（3）」、「肺炎（2）」、「下気道感染（4）」、「心不全」及び「便秘」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Cardiac failure, Hypercholesterolaemia, Hypertension, Knee arthroplasty, Haemorrhoids, Blood thyroid stimulating hormone increased, Cardiac amyloidosis, Cerebrovascular accident, Abdominal distension, Abdominal pain lower				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: FUROSEMIDE, PROPRANOLOL, DOMPERIDONE, ACETYLSALICYLIC ACID, AMLODIPINE, ATORVASTATIN, BISOPROLOL, ROXITHROMYCIN, AMOXICILLIN/CLAVULANATE POTASSIUM, FUROSEMIDE, AMLODIPINE, PARACETAMOL, DABIGATRAN, OMEPRAZOLE, DABIGATRAN, BISOPROLOL, FUROSEMIDE, OMEPRAZOLE, LOPERAMIDE HYDROCHLORIDE, ACETYLSALICYLIC ACID, FUROSEMIDE, DABIGATRAN, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, TERBINAFINE, HYDROCORTISONE BUTYRATE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Orthostatic hypotension, Respiratory tract infection, Nausea, Abdominal pain upper, Decreased appetite, Diarrhoea, Atrial fibrillation, Erosive duodenitis, Rectal haemorrhage, Orthostatic hypotension, Anal candidiasis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
十二指腸炎	ACUTE DUODENITIS	Day 153 / Day 156	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「十二指腸炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Cardiac failure, Gastrooesophageal reflux disease, Hypertension, Exostosis, Atrial fibrillation, Arthritis bacterial, Cardiac amyloidosis, Constipation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: DABIGATRAN, OMEPRAZOLE, DOCUSATE SODIUM, QUINAPRIL HYDROCHLORIDE, METOPROLOL, SPIRONOLACTONE, FUROSEMIDE, ONDANSETRON, OMEPRAZOLE, MAGNESIUM, POTASSIUM CHLORIDE, ENOXAPARIN SODIUM, POTASSIUM CHLORIDE, SODIUM CHLORIDE, AMIODARONE, AMIODARONE, PARACETAMOL, SPIRONOLACTONE, FUROSEMIDE, OMEPRAZOLE, HEPARIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, GLYCERYL TRINITRATE, FUROSEMIDE, METAMIZOLE, FENTANYL, MIDAZOLAM, CLINDAMYCIN, POTASSIUM CHLORIDE, DABIGATRAN, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, QUINAPRIL HYDROCHLORIDE, SPIRONOLACTONE, METOPROLOL, METOPROLOL, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE, SPIRONOLACTONE, FUROSEMIDE, METOPROLOL, METOPROLOL, SPIRONOLACTONE, COVID-19 VACCINE, FUROSEMIDE, OMEPRAZOLE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Renal impairment, Palpitations, Asthenia, Sinusitis, Bradycardia, Hypokalaemia, Conjunctival haemorrhage, Hypervolaemia, Hypervolaemia, Tachyarrhythmia, Nipple pain, COVID-19, Epistaxis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心停止	VENTRICULAR TACHYCARDIC ARREST	Day 166 / Day 166	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「心停止」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertension, Hip arthroplasty, Renal impairment, Lymphoma, Carpal tunnel syndrome, Gastrooesophageal reflux disease, Knee arthroplasty, Cardiac failure, Coronary artery disease, Cardiac amyloidosis, Squamous cell carcinoma of skin, Neuropathy peripheral, Atrial fibrillation, Gout, Mitral valve incompetence, Pulmonary hypertension				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: OMEPRAZOLE, FUROSEMIDE, DABIGATRAN, ALLOPURINOL, AMIODARONE, AMOXICILLIN/CLAVULANIC ACID, ROXITHROMYCIN, OMEPRAZOLE, ESCITALOPRAM, ESCITALOPRAM, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, PREGABALIN, FUROSEMIDE, CHONDRUS CRISPUS EXTRACT, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, AMOXICILLIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, BISOPROLOL, ISOSORBIDE MONONITRATE, ATORVASTATIN, COLCHICINE, PARACETAMOL, PREDNISONE, ATORVASTATIN, MELATONIN, HEPARIN, ACETYLSALICYLIC ACID, FENTANYL, MIDAZOLAM, CODEINE, PREDNISONE, PREDNISONE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Abdominal pain upper, Abdominal distension, Fatigue, Cough, Asthenia, Cough, Nasopharyngitis, Fall, Electrocardiogram QT prolonged, Contusion, Hypervolaemia, COVID-19, Nausea, SARS-CoV-2 test positive				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
非心臓性胸痛	NON CARDIAC CHEST PAIN	Day 764 / Day 780	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「非心臓性胸痛」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperlipidaemia, Hypertension, Spinal column injury, Spinal stenosis, Pain in extremity, Carpal tunnel syndrome, Heart rate decreased, Aortic stenosis, Cardiac failure, Trigeminal neuralgia, Proteinuria, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 908		
Concomitant Medication [3]: METOPROLOL, ATORVASTATIN, ACETYLSALICYLIC ACID, FUROSEMIDE, PERINDOPRIL, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, GRAMICIDIN/NEOMYCIN SULFATE/NYSTATIN/TRIAMCINOLONE ACETONIDE, COVID-19 VACCINE, DOXYCYCLINE, LORATADINE, FLUTICASONE PROPIONATE, PROTEASE INHIBITORS, RITONAVIR, CARBAMAZEPINE, METOPROLOL, CARBAMAZEPINE, FLUCLOXACILLIN				
Non-Serious Adverse Event [4]: Ear infection, Sinusitis, Seasonal allergy, COVID-19, Post procedural haematoma				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
完全房室ブロック	COMPLETE HEART BLOCK	Day 876 / Day 881	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「完全房室ブロック」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperlipidaemia, Hypertension, Haemoglobin decreased, Nasal septal operation, Rotator cuff repair, Gastrooesophageal reflux disease, Type 2 diabetes mellitus, Knee arthroplasty, Carpal tunnel decompression, Lipoma, Muscle spasms, Large intestinal polypectomy, Pleural effusion, Atrial fibrillation, Cardiac failure, Gout, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: INSULIN GLARGINE, OMEPRAZOLE, CANDESARTAN, METFORMIN, RIVAROXABAN, FUROSEMIDE, METOPROLOL, ATORVASTATIN, ALLOPURINOL, FUROSEMIDE, METOPROLOL, IBUPROFEN, FUROSEMIDE, CALCIUM CARBONATE, CALCITRIOL, METOPROLOL, INSULIN GLARGINE, FUROSEMIDE, ACETYLSALICYLIC ACID, TICAGRELOR, ACETYLSALICYLIC ACID, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN, PREDNISONE, EMPAGLIFLOZIN/METFORMIN HYDROCHLORIDE, INSULIN GLARGINE, COVID-19 VACCINE, IBUPROFEN, DICLOFENAC, CORTISONE, COVID-19 VACCINE, DOCUSATE SODIUM/SENNOSIDE A+B, CODEINE PHOSPHATE/PARACETAMOL, CORTISONE				
Non-Serious Adverse Event [4]: Pruritus, Blood creatinine increased, Muscle spasms, Visual impairment, Hypocalcaemia, Bronchitis, Hyponatraemia, Back pain, Blood creatinine increased, Neuralgia, Blood thyroid stimulating hormone decreased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血中クレアチニン増加	WORSENING SERUM CREATININE RISE SECONDARY TO ATORVASTATIN	Day 92 / Day 183	Not Related	Drug Interrupted	Recovered /Resolved	Severe
背部痛	SEVERE BACK PAIN	Day 197 / Day 199	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「血中クレアチニン増加」及び「背部痛」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 8[redacted]
Medical History [1]: Cholecystectomy, Arthritis, Tendon rupture, Muscle spasms, Scapula fracture, Light chain disease, Stem cell transplant, Arthritis, Dupuytren's contracture, Atrial flutter, Gastrointestinal carcinoma, Colectomy, Gynaecomastia, Appendicitis, Complicated appendicitis, Anaemia, Cardiac failure, Renal impairment, Cardiac ablation, Polyneuropathy, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: MAGNESIUM, FOLIC ACID, GLUCOSAMINE, FISH OIL, BUMETANIDE, BUMETANIDE, MELATONIN, RIVAROXABAN, GABAPENTIN, AMITRIPTYLINE HYDROCHLORIDE, IRON, TRIAMCINOLONE, ASCORBIC ACID/IRON, IRON/SACCHAROMYCES CEREVISIAE, RIVAROXABAN, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, ZOPICLONE, BUMETANIDE, IRON, BUMETANIDE, BUMETANIDE, SPIRONOLACTONE, METOLAZONE, METOLAZONE, POTASSIUM CHLORIDE, METOLAZONE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, COVID-19 VACCINE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, ZOPICLONE, SPIRONOLACTONE, RIVAROXABAN, RIVAROXABAN, BUMETANIDE, SPIRONOLACTONE, PREDNISONE, RIVAROXABAN, PREDNISONE, PREDNISONE, MELATONIN				
Non-Serious Adverse Event [4]: Sleep disorder, Muscle spasms, Dyspnoea, Abdominal pain, Atrial fibrillation, Muscle spasms, Limb injury, Bursitis, Feeling hot, Insomnia, Muscle spasms, Rectal haemorrhage, Rash, Muscle spasms, Cardiac failure acute, Hypokalaemia, Gout, Contusion, Skin papilloma, Joint swelling				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
失神	SYNCOPE CAUSE TO HAVE BEEN CARDIOGENIC	Day 585 / Day 590	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「失神」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 8[redacted]
Medical History [1]: Hip arthroplasty, Hip arthroplasty, Hip arthroplasty, Gastrooesophageal reflux disease, Drug hypersensitivity, Cough, Basal cell carcinoma, Cardiac failure, Hypertension, Leukoplakia oral, Inguinal hernia, Atrial fibrillation, Cardiac amyloidosis, Basal cell carcinoma, Basal cell carcinoma, Arthralgia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: OMEPRAZOLE, LOSARTAN, FUROSEMIDE, METOPROLOL, DABIGATRAN, PARACETAMOL, PARACETAMOL, BECLOMETASONE, LOPERAMIDE, GLUCOSE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM CITRATE, FENTANYL, ONDANSETRON, CEFAZOLIN SODIUM, METARAMINOL, ROCURONIUM, PROPOFOL, MIDAZOLAM, DABIGATRAN, ROXITHROMYCIN, PREDNISONE, PREDNISONE, ROXITHROMYCIN, PREDNISONE, PREDNISONE, ROXITHROMYCIN, PREDNISONE, PREDNISONE, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, CEFACLOR, CEFACLOR, CEFACLOR				
Non-Serious Adverse Event [4]: Hernia pain, Eosinophil count increased, Diarrhoea, Hernia pain, Dizziness, Cough, Upper respiratory tract infection, Papilloma, Squamous cell carcinoma, Basal cell carcinoma, Upper respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼡径ヘルニア	WORSENING INGUINAL HERNIA	Day 53 / Day 54	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「鼡径ヘルニア」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Cough, Carpal tunnel syndrome, Gout, Spinal stenosis, Spinal laminectomy, Tendon rupture, Transient ischaemic attack, Carotid artery stent insertion, Arteriosclerosis, Dyslipidaemia, Muscle spasms, Cardiac amyloidosis, Cardiac failure, Osteoarthritis, Sleep apnoea syndrome, Cerebrovascular accident, Foot deformity, Myositis, Tendon rupture				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 905		
Concomitant Medication [3]: CLOPIDOGREL, ATORVASTATIN, SPIRONOLACTONE, DICLOFENAC, FUROSEMIDE, CHROMIC CHLORIDE/MAGNESIUM AMINO ACID CHELATE/PYRIDOXINE HYDROCHLORIDE/SELENOMETHIONINE/ZINC SULFATE MONOHYDRATE, SELENIUM, PREDNISONE, PARACETAMOL, FLUCLOXACILLIN, FLUCLOXACILLIN, COVID-19 VACCINE, COVID-19 VACCINE, FEBUXOSTAT, PREDNISONE, VITAMIN B COMPLEX, COVID-19 VACCINE, AMOXICILLIN TRIHYDRATE, ROSUVASTATIN, ROSUVASTATIN, ACETYLSALICYLIC ACID, SPIRONOLACTONE, ROSUVASTATIN, CLOPIDOGREL, FLUCLOXACILLIN, AMOXICILLIN				
Non-Serious Adverse Event [4]: Muscle spasms, Dyspnoea exertional, Fall, Skin abrasion, Arthritis, Fall, Skin lesion, Skin lesion, Dizziness postural, Skin laceration, Nausea, Decreased appetite, Anaemia, Acute kidney injury, Hyponatraemia, Cardiac failure, Localised infection, Electrocardiogram QT prolonged				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
虚血性脳卒中	RIGHT OCCIPIAL ISCHAEMIC STROKE	Day 798 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe
治験責任医師の見解：「虚血性脳卒中」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Appendicectomy, Myalgia, Hip arthroplasty, Thyroidectomy, Gastrooesophageal reflux disease, Osteoarthritis, Hypothyroidism, Hypertension, Vertigo positional, Renal cancer, Nephrectomy, Large intestinal polypectomy, Seasonal allergy, Knee arthroplasty, Dyslipidaemia, Atrial fibrillation, Cerebrovascular accident, Cardiomyopathy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: PARACETAMOL, LEVOTHYROXINE SODIUM, FEXOFENADINE HYDROCHLORIDE, ROSUVASTATIN, VALSARTAN, RIVAROXABAN, RIVAROXABAN, DIGOXIN, DIGOXIN, MAGNESIUM, IBUPROFEN, LEVOTHYROXINE SODIUM, COVID-19 VACCINE, INFLUENZA VACCINE INACT SPLIT 3V, PNEUMOCOCCAL VACCINES, COVID-19 VACCINE, LEVOTHYROXINE SODIUM, CEFALEXIN, PREDNISOLONE, PREDNISOLONE, COVID-19 VACCINE, MELOXICAM, INFLUENZA VACCINE INACT SPLIT 3V, TAMSULOSIN, DUTASTERIDE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Venous pressure jugular increased, Muscle spasms, Muscle spasms, Vision blurred, Back pain, Pruritus, Gout, Back pain, Gout, Pain in extremity, Cognitive disorder, Arthralgia, Malaise, Pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血尿	HAEMATURIA	Day 713 / Day 727	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「血尿」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Left atrial enlargement, Arthralgia, Carpal tunnel syndrome, Constipation, Carpal tunnel decompression, Atrial fibrillation, Amyloidosis senile, Cardiac amyloidosis, Haematuria, Cardiac dysfunction				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911		
Concomitant Medication [3]: CYANOCOBALAMIN, VITAMIN D NOS, CYANOCOBALAMIN, AVENA SATIVA OIL/COCOS NUCIFERA OIL/GLYCINE MAX/HELIANTHUS ANNUUS OIL/LINUM USITATISSIMUM SEED OIL/OENOTHERA BIENNIS OIL/ORYZA SATIVA OIL/SESAMUM INDICUM SEED OIL/TOCOPHEROLS MIXED, MAGNESIUM, FISH OIL, TRIGLYCERIDES, IODINE, ASCORBIC ACID, FUROSEMIDE, FISH OIL, CETIRIZINE, TRANEXAMIC ACID, TRANEXAMIC ACID, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/SIMETICONE, PANTOPRAZOLE, TRANEXAMIC ACID, CODEINE PHOSPHATE/PARACETAMOL, ONDANSETRON, ESOMEPRAZOLE, PARACETAMOL, CEFAZOLIN, METARAMINOL, FENTANYL, PROPOFOL, PARACETAMOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, FUROSEMIDE, METHYLPREDNISOLONE ACEPONATE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, LACTULOSE, TEMAZEPAM, HYDROCHLOROTHIAZIDE, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, ACETYLSALICYLIC ACID, FUROSEMIDE, FUROSEMIDE, KRILL OIL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, METHYLPREDNISOLONE ACEPONATE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PREBIOTICS NOS/PROBIOTICS NOS, HERBAL PREPARATION, COVID-19 VACCINE, CHARCOAL, ACTIVATED, DIPEPTIDYL PEPTIDASE 4 (DPP-4) INHIBITORS, LACTITOL/PLANTAGO INDICA, FIBRE, DIETARY, LACTITOL/PLANTAGO INDICA, ACETYLSALICYLIC ACID, UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE, PROBIOTICS [UMBRELLA TERM], IRON, ESOMEPRAZOLE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, MACROGOL, DOCUSATE SODIUM, MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER, ESOMEPRAZOLE, FUROSEMIDE, COVID-19 VACCINE, HYDROCHLOROTHIAZIDE, IRON, MAGNESIUM, PANTOPRAZOLE, FISH OIL, SPIRONOLACTONE, SPIRONOLACTONE, PANTOPRAZOLE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, MINERALS NOS/VITAMINS NOS, MINERALS NOS/VITAMINS NOS, MAGNESIUM, FUROSEMIDE, COVID-19 VACCINE, OTHER ANTIVIRALS, MAGNESIUM, MAGNESIUM, HYDROCHLOROTHIAZIDE, HYDROCHLOROTHIAZIDE, SODIUM POLYSTYRENE SULFONATE, ESOMEPRAZOLE, DOCUSATE SODIUM/SENNOSIDE A+B, METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA, FUROSEMIDE, FUROSEMIDE, MOMETASONE FUROATE, ESOMEPRAZOLE, MAGNESIUM, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, OMEPRAZOLE, ATROPINE, ESOMEPRAZOLE, GENTAMICIN, FLUCLOXACILLIN, CEFAZOLIN, FUROSEMIDE, FENTANYL, PARACETAMOL, ESOMEPRAZOLE, SPIRONOLACTONE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, FUROSEMIDE, FUROSEMIDE, FLUCLOXACILLIN, DOCUSATE SODIUM/SENNOSIDE A+B, FUROSEMIDE, FLUCLOXACILLIN, FUROSEMIDE, BUMETANIDE, COLCHICINE, PREDNISOLONE, INDAPAMIDE, COLCHICINE, ENOXAPARIN, PREDNISOLONE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, POTASSIUM CHLORIDE, ELECTROLYTE SOLUTIONS [UMBRELLA TERM], METHOXY POLYETHYLENE GLYCOL-EPOETIN BETA, SPIRONOLACTONE, FUROSEMIDE, LORATADINE, PREDNISOLONE, ESOMEPRAZOLE, RED BLOOD CELLS (CONCENTRATED), RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, ESOMEPRAZOLE, RED BLOOD CELLS (CONCENTRATED), FUROSEMIDE, FUROSEMIDE, ESOMEPRAZOLE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FLUCLOXACILLIN, HEPARIN, AMOXICILLIN				

Non-Serious Adverse Event [4]: Chest pain, Dyspnoea, Rash, Prostatomegaly, Oral mucosal blistering, Rash, Renal impairment, Anaemia, Nausea, Hypervolaemia, Sleep disorder, Hypervolaemia, Haematuria, Constipation, Pruritus, Muscle spasms, Hypervolaemia, Abdominal distension, Contusion, Skin laceration, Eructation, Tremor, Skin laceration, Dyspnoea, Chronic kidney disease, Abdominal distension, Flatulence, Basal cell carcinoma, Skin lesion, Dyspnoea exertional, Faeces discoloured, Fatigue, Constipation, Superficial vein thrombosis, Gastritis erosive, Hypervolaemia, Nausea, Blood creatinine increased, Faeces discoloured, Asthenia, Pyrexia, Headache, Oropharyngeal pain, COVID-19, Cough, Rhinorrhoea, Muscle spasms, Melaena, Dyspnoea, Blood potassium increased, Anaemia, Heart rate irregular, Hyperkalaemia, Hypokalaemia, Urinary retention, Bradycardia, Hypotension, Hypervolaemia, Cardiac failure, Melaena, Hyponatraemia, Chronic kidney disease, Hypokalaemia, Hypovolaemia, Hypervolaemia, Incisional hernia, Iron deficiency, Hypokalaemia, Hypervolaemia, Cyanosis, Iron deficiency anaemia						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血尿（1）	EXACERBATION OF HAEMATURIA	Day 56 / Day 63	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
血尿（2）	WORSENING HAEMATURIA	Day 64 / Day 67	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
尿閉	URINARY RETENTION	Day 71 / Day 78	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
貧血（1）	SEVERE ANAEMIA	Day 436 / Day 461	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
胃腸出血	GASTROINTESTINAL HAEMORRHAGE	Day 645 / Day 652	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
腎前性腎不全	ACUTE PRERENAL INSUFFICIENCY FAILURE	Day 648 / Day 652	Not Related	Drug Interrupted	Recovered/ Resolved	Severe
血尿（3）	EXACERBATION OF HAEMATURIA	Day 713 / Day 719	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
完全房室ブロック	COMPLETE ATRIOVENTRICULAR BLOCK	Day 719 / NA	Not Related	Dose Not Changed	Not Recovered/ Not Resolved	Severe
うっ血性心不全	WORSENING OF CONGESTIVE HEART FAILURE	Day 738 / Day 756	Not Related	Drug Interrupted	Recovered/ Resolved	Severe
蜂巣炎	CELLULITIS OF LEFT LOWER LEG	Day 738 / Day 756	Not Related	Drug Interrupted	Recovered/ Resolved	Severe
痛風	ACUTE GOUT	Day 738 / Day 756	Not Related	Drug Interrupted	Recovered/ Resolved	Severe
腎機能障害	WORSENING RENAL IMPAIRMENT	Day 738 / Day 756	Not Related	Drug Interrupted	Recovered/ Resolved	Severe

薬疹	ALLERGIC DRUG RASH-BUMETANIDE AND INDAPAMIDE	Day 758 / Day 763	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
血液量増加症	FLUID OVERLOAD	Day 772 / Day 786	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
貧血（2）	WORSENING ANAEMIA	Day 780 / Day 786	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
下気道感染	LOWER RESPIRATORY TRACT INFECTION	Day 871 / Day 891	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
リンパ浮腫	RIGHT LEG LYMPHOEDEMA	Day 874 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
心不全	WORSENING HEART FAILURE	Day 927 / Day 940	Not Related	NA	Recovered/ Resolved	Severe
治験責任医師の見解：「血尿（1）」、「血尿（2）」、「尿閉」、「貧血（1）」、「胃腸出血」、「腎前性腎不全」、「血尿（3）」、「完全房室ブロック」、「うっ血性心不全」、「蜂巣炎」、「痛風」、「腎機能障害」、「薬疹」、「血液量増加症」、「貧血（2）」、「下気道感染」、「リンパ浮腫」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: Asian		Country: South Korea	Sex: M	Age: 7[redacted]
Medical History [1]: Diabetes mellitus, Prostate cancer, Prostatectomy, Atrial fibrillation, Cardiac failure congestive, Lumbar spinal stenosis, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 904			
Concomitant Medication [3]: EDOXABAN, BISOPROLOL, CANDESARTAN, SPIRONOLACTONE						
Non-Serious Adverse Event [4]: Lumbosacral radiculopathy						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性脊椎症	SPONDYLOSIS LUMBOSACRAL REGION	Day 127 / Day 133	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「変形性脊椎症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Occult blood positive, Benign prostatic hyperplasia, Transurethral prostatectomy, Atrial fibrillation, Atrial flutter, Cardiac ablation, Cardiac failure acute, Chronic obstructive pulmonary disease, Hypertension, Spinal osteoarthritis, Carpal tunnel syndrome, Cardiac pacemaker insertion, Chronic kidney disease, Cardiac failure acute, Liver disorder, Anaemia macrocytic, Gastric disorder, Glucose tolerance impaired, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: RIVAROXABAN, VALSARTAN, FUROSEMIDE, IPRATROPIUM BROMIDE, TAMSULOSIN HYDROCHLORIDE, PANTOPRAZOLE, BISOPROLOL FUMARATE, FUROSEMIDE, VALSARTAN, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Urinary tract infection, Chronic kidney disease, Haemorrhoids, Hypotension, Diabetes mellitus, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	CARDIAL DECOMPENSATION AT CHRONIC HEART FAILURE BASED ON ATTR-CM	Day 264 / Day 271	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: F	Age: 7[redacted]
Medical History [1]: Glaucoma, Lumbar spinal stenosis, Osteoarthritis, Osteoarthritis, Spinal pain, Cataract operation, Asthma, Rhinitis allergic, Deep vein thrombosis, Carpal tunnel decompression, Carpal tunnel syndrome, Spinal decompression, Mixed anxiety and depressive disorder, Hypertension, Atrial fibrillation, High frequency ablation, Amblyopia, Hypercholesterolaemia, Knee arthroplasty, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: LEVOCETIRIZINE DIHYDROCHLORIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, DIOSMIN/HESPERIDIN, PERINDOPRIL ARGININE, LAMOTRIGINE, VORTIOXETINE, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, FLUTICASONE PROPIONATE/SALMETEROL XINAFOATE, DABIGATRAN ETEXILATE MESILATE, METOPROLOL SUCCINATE, PENTOXIFYLLINE, CALCIUM CARBONATE/COLECALCIFEROL, CALCIUM CARBONATE/COLECALCIFEROL, ALFACALCIDOL, DENOSUMAB, LATANOPROST, DIGOXIN, SPIRONOLACTONE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, ROSUVASTATIN CALCIUM, COVID-19 VACCINE, METOPROLOL SUCCINATE, COVID-19 VACCINE, BISOPROLOL FUMARATE, BISOPROLOL FUMARATE, SPIRONOLACTONE, BENFOTIAMINE/PYRIDOXINE HYDROCHLORIDE, LAMOTRIGINE, CYANOCOBALAMIN/FISH OIL/FOLIC ACID/GINKGO BILOBA LEAF/PHOSPHATIDYL SERINE/TOCOPHEROL, FUROSEMIDE, DIOSMIN/HESPERIDIN, LATANOPROST, DABIGATRAN ETEXILATE MESILATE, FERRIC HYDROXIDE POLYMALTOSE COMPLEX, BISOPROLOL FUMARATE, SPIRONOLACTONE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, DIOSMIN/HESPERIDIN, BISOPROLOL FUMARATE, VORTIOXETINE, BISOPROLOL FUMARATE, BROMAZEPAM, VORTIOXETINE, CEFUROXIME AXETIL, PENTOXIFYLLINE, NADROPARIN CALCIUM, DABIGATRAN ETEXILATE MESILATE				
Non-Serious Adverse Event [4]: Heart rate increased, Depression, Blood creatine phosphokinase increased, Melanocytic naevus, Respiratory tract infection, Syncope				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大腿動脈塞栓症	EMBOLIZATION OF THE FEMORAL ARTERY COMMUNIS IN THE LEFT LOWER LIMB	Day 539 / Day 543	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「大腿動脈塞栓症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Phimosis, Osteoarthritis, Carpal tunnel syndrome, Essential hypertension, Orchidectomy, Carpal tunnel decompression, Abdominal hernia repair, Chronic obstructive pulmonary disease, Hernia hiatus repair, Gastrooesophageal reflux disease, Hiatus hernia, Abdominal hernia repair, Arthroscopy, Sciatica, Cataract, Osteoarthritis, Circumcision, Bladder diverticulum, Benign prostatic hyperplasia, Hypercholesterolaemia, Type 2 diabetes mellitus, Hyperparathyroidism primary, Abdominal hernia repair, Barrett's oesophagus, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis, Cardioversion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 889		
Concomitant Medication [3]: OMEPRAZOLE, FUROSEMIDE, ROSUVASTATIN CALCIUM, TELMISARTAN, FUROSEMIDE, IBANDRONATE SODIUM, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, SALBUTAMOL, THEOPHYLLINE, CINACALCET HYDROCHLORIDE, POTASSIUM CHLORIDE, APIXABAN, NEBIVOLOL HYDROCHLORIDE, SPIRONOLACTONE, WARFARIN, FUROSEMIDE, TELMISARTAN, FUROSEMIDE, TELMISARTAN, FUROSEMIDE, TRIMECAINE HYDROCHLORIDE, METHYLPREDNISOLONE ACETATE, NIMESULIDE, DABIGATRAN ETEXILATE MESILATE, EPLERENONE, METOCLOPRAMIDE HYDROCHLORIDE, ASCORBIC ACID, THIAMINE, METRONIDAZOLE, MEROPENEM, ENOXAPARIN SODIUM, FUROSEMIDE, METAMIZOLE, BISULEPIN HYDROCHLORIDE, ACETYLCYSTEINE, IPRATROPIUM BROMIDE, HYDROCORTISONE, AMIODARONE HYDROCHLORIDE, NEBIVOLOL HYDROCHLORIDE, HEPARIN SODIUM, DIOSMIN/HESPERIDIN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Hypotension, Osteoarthritis, Nipple pain, Abdominal pain upper, Viral infection, Thrombophlebitis, Cardiac failure, Limb injury, Hypotension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
感染性胆嚢炎	GANGRENOUS CHOLECYSTITIS	Day 327 / Day 340	Not Related	Drug Interrupted	Recovered /Resolved	Severe
敗血症	SEPSIS (OF ALREADY REPORTED CHOLECYSTITIS ORIGIN)	Day 329 / Day 340	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「感染性胆嚢炎」及び「敗血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Benign prostatic hyperplasia, Hepatitis, Peripheral venous disease, Varicose vein, Cholecystectomy, Hyperbilirubinaemia, Hyperlipidaemia, Chronic kidney disease, Peripheral sensorimotor neuropathy, Pseudoradicular syndrome, Prostatectomy, Cataract, Diabetes mellitus, Knee arthroplasty, Atrial fibrillation, Hypertension, Dyspepsia, Atrial fibrillation, Insomnia, Cardiac failure, Liver disorder, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: ATORVASTATIN CALCIUM, PARACETAMOL/TRAMADOL HYDROCHLORIDE, PARACETAMOL/TRAMADOL HYDROCHLORIDE, WARFARIN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, METOPROLOL SUCCINATE, DIGOXIN, ZOLPIDEM TARTRATE, MAGNESIUM CARBONATE/MAGNESIUM OXIDE, SPIRONOLACTONE, FUROSEMIDE, SACUBITRIL/VALSARTAN, SACUBITRIL/VALSARTAN, COVID-19 VACCINE, SPIRONOLACTONE, CLONAZEPAM, METOPROLOL SUCCINATE, COLECALCIFEROL, DABIGATRAN ETEXILATE MESILATE, COVID-19 VACCINE, FERRIC HYDROXIDE POLYMALTOSE COMPLEX, GABAPENTIN, EMPAGLIFLOZIN, FUROSEMIDE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, DRUGS FOR ACID RELATED DISORDERS, EMPAGLIFLOZIN, ANTIBIOTICS, SOLUTIONS AFFECTING THE ELECTROLYTE BALANCE, MUCOLYTICS, CORTICOSTEROIDS, IPRATROPIUM BROMIDE, VERICIGUAT, EPLERENONE				
Non-Serious Adverse Event [4]: Anxiety, Hyperkalaemia, COVID-19, Post viral fatigue syndrome, Anaemia, Neuropathy peripheral, Skin ulcer, Nasopharyngitis, Cardiac failure, Hyperkalaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
塞栓性脳卒中	ISCHAEMIC STROKE OF CARDIOEMBOLIC ORIGIN (PREVIOUSLY REPORTED AS DIZZINESS)	Day 308 / Day 309	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
気管支炎	ACUTE BRONCHITIS (PREVIOUSLY REPORTED AS BRONCHITIS)	Day 862 / Day 870	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「塞栓性脳卒中」及び「気管支炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperuricaemia, Hypertension, Rhinitis, Pneumonia, Spinal pain, Chronic obstructive pulmonary disease, Gastrooesophageal reflux disease, Aortic stenosis, Atrial fibrillation, Cardiac failure, Cardiac failure, Cardiac amyloidosis, Normochromic normocytic anaemia, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ALLOPURINOL, PERINDOPRIL ARGININE, OMEPRAZOLE, FENOTEROL HYDROBROMIDE/IPRATROPIUM BROMIDE, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, TIOTROPIUM BROMIDE, WARFARIN, WARFARIN, AMIODARONE HYDROCHLORIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, PERINDOPRIL ARGININE, FUROSEMIDE, WARFARIN, FUROSEMIDE, SPIRONOLACTONE, ENOXAPARIN SODIUM, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), SIMETICONE, ASCORBIC ACID/FERROUS SULFATE, APIXABAN, AMIODARONE HYDROCHLORIDE, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: COVID-19, Eosinophilia, Blood potassium increased, Urinary tract infection, Cardiac failure, Blood potassium increased, Iron deficiency anaemia, Hiatus hernia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE RENAL FAILURE OF PRERENAL DEHYDRATION (PREVIOUSLY REPORTED WORSENING OF RENAL FAILURE)	Day 410 / Day 416	Not Related	Drug Interrupted	Recovered /Resolved	Severe
腸炎	ACUTE ENTEROCOLITIS SYNDROME	Day 473 / Day 485	Not Related	Dose Not Changed	Recovered /Resolved	Severe
腎機能障害	ACUTE RENAL IMPAIRMENT OF PRERENAL ETIOLOGY	Day 473 / Day 485	Not Related	Dose Not Changed	Recovered /Resolved	Severe
正色素性正球性貧血	WORSENING OF NORMOCHROMIC NORMOCYTIC ANAEMIA	Day 806 / Day 836	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「急性腎障害」、「腸炎」、「腎機能障害」及び「正色素性正球性貧血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Spinal pain, Calculus urinary, Spinal operation, Hyperacusis, Benign prostatic hyperplasia, Tendon rupture, Carpal tunnel decompression, Adjustment disorder with depressed mood, Spinal laminectomy, Carpal tunnel decompression, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: SERTRALINE HYDROCHLORIDE, FUROSEMIDE, VALSARTAN, CARVEDILOL, SACUBITRIL, SPIRONOLACTONE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, ALLOPURINOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, RIVAROXABAN, FEBUXOSTAT, FUROSEMIDE, FUROSEMIDE, FEBUXOSTAT, ATORVASTATIN CALCIUM, CARVEDILOL, CALCIUM, COLECALCIFEROL, PARACETAMOL, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, VALSARTAN, SACUBITRIL, GLUCOSAMINE HYDROCHLORIDE				
Non-Serious Adverse Event [4]: Hyperuricaemia, Supraventricular tachycardia, Ventricular tachycardia, Rash, Renal impairment, COVID-19, Fatigue, Atrial fibrillation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心室性頻脈	WORSENING OF NON SUSTAINED VENTRICULAR TACHYCARDIA ICD IMPLANTATION	Day 317 / Day 320	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心室性頻脈」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Vasectomy, Large intestine polyp, Osteoarthritis, Carpal tunnel decompression, Depression, Tendon sheath incision, Spinal stenosis, Spinal claudication, Tendon rupture, Vertigo positional, Essential tremor, Spinal laminectomy, Spinal laminectomy, Hyperlipidaemia, Hypertension, Cataract, Cardiomyopathy, Coronary artery disease, Erectile dysfunction, Dry eye, Chronic kidney disease, Dry skin, Spinal laminectomy, Atrial fibrillation, Pulmonary embolism, Cardiac failure congestive, Blood bilirubin increased, Atrioventricular block first degree, Cardiac amyloidosis, Blood alkaline phosphatase increased, Syncope, Bradycardia, Cardiac resynchronisation therapy, Arthralgia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 322		
Concomitant Medication [3]: FISH OIL/OMEGA-3 FATTY ACIDS, SIMVASTATIN, ACETYLSALICYLIC ACID, DULOXETINE, CICLOSPORIN, TRIAMCINOLONE, PARACETAMOL, APIXABAN, CANNABIS SATIVA OIL, POTASSIUM CHLORIDE, FUROSEMIDE, TRAMADOL, PREGABALIN, TORASEMIDE, FUROSEMIDE, FUROSEMIDE, PREDNISONE, TORASEMIDE, INFLUENZA VACCINE, VARICELLA ZOSTER VACCINE RGE (CHO), ALLOPURINOL, ALLOPURINOL, MACROGOL/PROPYLENE GLYCOL/SIMETICONE/SORBIC ACID/SORBITOL/WHITE SOFT PARAFFIN, SIMVASTATIN, CURCUMA LONGA, CEFAZOLIN/GLUCOSE, SODIUM CHLORIDE, FENTANYL, PROPOFOL, PROPOFOL, BUPIVACAINE HYDROCHLORIDE, LIDOCAINE, IODIXANOL, VANCOMYCIN, PARACETAMOL, CEFALEXIN, PARACETAMOL, PIPERACILLIN/TAZOBACTAM, VANCOMYCIN, SODIUM CHLORIDE, COLCHICINE, DIPHENHYDRAMINE HYDROCHLORIDE/PARACETAMOL, ACETYLSALICYLIC ACID, APIXABAN, COLCHICINE, LOPERAMIDE, COLCHICINE, SPIRONOLACTONE, POTASSIUM CHLORIDE, TORASEMIDE, TORASEMIDE, PANTOPRAZOLE, RED BLOOD CELLS (CONCENTRATED), CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, LIDOCAINE, PANTOPRAZOLE, SODIUM CHLORIDE, TORASEMIDE, CORTICOSTEROIDS (OTHER COMBINATIONS), CALCITRIOL, FERROUS SULFATE, APIXABAN, SODIUM CHLORIDE, BUMETANIDE, FUROSEMIDE, METOLAZONE, MELATONIN, GLYCEROL/HYPROMELLOSE/MACROGOL, LIDOCAINE, MIDAZOLAM HYDROCHLORIDE, ALL OTHER NON-THERAPEUTIC PRODUCTS				
Non-Serious Adverse Event [4]: Abdominal discomfort, Gouty arthritis, Pain in extremity, Rash papular, Medical device site haematoma, Pericardial effusion, Pericarditis, Diarrhoea, Pleuritic pain, Jaundice, Cachexia, Decreased appetite, Weight decreased, Fall, Fall, Abdominal fat apron, Chronic left ventricular failure, Peripheral swelling, Gastric ulcer, Blister, Rash maculo-papular, Iron deficiency anaemia, Hyperparathyroidism secondary, Skin laceration, Epistaxis, Melaena				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性左室不全	CHRONIC DIASTOLIC HEART FAILURE, NYHA CLASS 3	Day 104 / Day 106	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心膜炎	PROBABLE PERICARDITIS (SYMPTOM: CHEST PAIN)	Day 112 / Day 114	Not Related	Dose Not Changed	Recovered /Resolved	Severe
胸痛	CHEST PAIN UNSPECIFIED TYPE	Day 115 / Day 117	Not Related	Dose Not Changed	Recovered /Resolved	Severe
上部消化管出血	UPPER GI BLEED	Day 268 / Day 271	Not Related	Drug Interrupted	Recovered /Resolved	Severe

急性左室不全	ACUTE DIASTOLIC CONGESTIVE HEART FAILURE NYHA CLASS 3	Day 290 / Day 297	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「慢性左室不全」、「心膜炎」、「胸痛」、「上部消化管出血」及び「急性左室不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Osteoarthritis, Hypertension, Colectomy, Ileostomy, Prostatectomy, Hypoacusis, Osteoarthritis, Diverticulitis, Carpal tunnel decompression, Appendicectomy, Insomnia, Hyperlipidaemia, Atrial fibrillation, Cardiomyopathy, Cardiac amyloidosis, Pericardial effusion, Hypotension, Coronary artery disease, Coronary artery bypass, Cardiac failure congestive, Hypothyroidism				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, WARFARIN, METOPROLOL TARTRATE, ATORVASTATIN, PARACETAMOL, MACROGOL 3350, DIPHENHYDRAMINE HYDROCHLORIDE/PARACETAMOL, FUROSEMIDE, CALCIUM CARBONATE/COLECALCIFEROL/INULIN, LEVOTHYROXINE, SENNOSIDE A+B, PREDNISONE, MACROGOL 400/PROPYLENE GLYCOL, LEVOTHYROXINE, LEVOTHYROXINE, MOXIFLOXACIN, FENTANYL CITRATE, MIDAZOLAM, TIMOLOL MALEATE, EPINEPHRINE, FLURBIPROFEN, LIDOCAINE HYDROCHLORIDE, TETRACAINE HYDROCHLORIDE, CYCLOPENTOLATE, TROPICAMIDE, PHENYLEPHRINE, OTHER OPHTHALMOLOGICALS, SODIUM CHLORIDE, CHONDROITIN SULFATE SODIUM/HYALURONATE SODIUM, ASCORBIC ACID/BETACAROTENE/CUPRIC OXIDE/TOCOPHERYL ACETATE/ZINC OXIDE, COVID-19 VACCINE, ALLANTOIN/ALOE VERA/CITRUS AURANTIUM/MAGNESIUM SULFATE HEPTAHYDRATE/SILVER COLLOIDAL/TOCOPHERYL ACETATE, METOPROLOL TARTRATE, AMIODARONE, METOPROLOL SUCCINATE, AMIODARONE				
Non-Serious Adverse Event [4]: Hyperkalaemia, Contusion, Oral mucosal exfoliation, Tongue exfoliation, Tongue haemorrhage, Tongue haematoma, Oropharyngeal pain, Dry eye, Astigmatism, Cataract, Dry age-related macular degeneration, Hypermetropia, Myopia, Presbyopia, Benign neoplasm of choroid, Lymphadenopathy, Joint range of motion decreased, Pain in extremity, Oedema peripheral, Cardiac failure, Muscle spasms, Bradycardia, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	ATRIAL FIBRILLATION WITH RAPID VENTICULAR RESPONSE	Day 884 / Day 885	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Coronary artery disease, Sinus node dysfunction, Hyperlipidaemia, Osteoarthritis, Rheumatoid arthritis, Insomnia, Major depression, Calculus urinary, Arthroscopy, Carpal tunnel decompression, Knee arthroplasty, Shoulder arthroplasty, Shoulder arthroplasty, Spinal fusion surgery, Syncope, Cardiac failure congestive, Atrioventricular block complete, Cataract operation, Hip surgery, Restrictive cardiomyopathy, Atrial fibrillation, Amyloidosis senile, Sleep apnoea syndrome				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 637		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), ACETYLSALICYLIC ACID, COLECALCIFEROL, POTASSIUM CHLORIDE, BUPROPION HYDROCHLORIDE, ATORVASTATIN CALCIUM, LOSARTAN POTASSIUM, METOPROLOL SUCCINATE, BUMETANIDE, METOLAZONE, MACROGOL, DIPHENHYDRAMINE HYDROCHLORIDE/PARACETAMOL, MELATONIN, DIPHENHYDRAMINE/PARACETAMOL, SPIRONOLACTONE, WOOL ALCOHOLS, MAGNESIUM SULFATE, BISACODYL, SODIUM FLUOROPHOSPHATE, SODIUM FLUOROPHOSPHATE, ENOXAPARIN, FUROSEMIDE, SODIUM CHLORIDE, BUMETANIDE, CLARITHROMYCIN, PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, CEFALEXIN, DIPHENHYDRAMINE/IBUPROFEN, CEFADROXIL, POTASSIUM CHLORIDE, BACLOFEN				
Non-Serious Adverse Event [4]: Hyperkeratosis, Myalgia, Fall, Weight decreased, Fall, Fall, Pain in extremity, Pain in extremity, Skin discolouration, Peripheral arterial occlusive disease, Hypokalaemia, Cardiac failure acute, Oedema, Skin abrasion, Ventricular tachycardia, Dry mouth, Dizziness postural, Haematuria, Urinary tract infection, Herpes zoster, Skin laceration, Fall, Skin laceration, Fall, Fall, Cellulitis, Neck pain, Fall, Gait disturbance, Muscle atrophy, Senile dementia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE ON CHRONIC CONGESTIVE HEART FAILURE, WORSENING	Day 358 / Day 373	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Back pain, Erectile dysfunction, Hypertension, Prostate cancer, Radiotherapy, Hyperlipidaemia, Cystitis glandularis, Atrioventricular block first degree, Myocardial infarction, Lymphadenectomy, Radical prostatectomy, Prostate cancer recurrent, Tinnitus, Vertigo, Inner ear disorder, Meniere's disease, Coronary artery disease, Obesity, Type 2 diabetes mellitus, Supraventricular extrasystoles, Supraventricular extrasystoles, Ventricular extrasystoles, Deafness bilateral, Chest discomfort, Pulmonary mass, Urinary incontinence, Syncope, Lip squamous cell carcinoma, Artificial urinary sphincter implant, Abscess drainage, Abscess drainage, Osteomyelitis, Nephrostomy, Aortic valve sclerosis, Paraesthesia, Oxygen saturation abnormal, Muscle operation, Pleural effusion, Cardiac failure congestive, Ureteric repair, Urinary cystectomy, Cardiac amyloidosis, Aortic valve incompetence, Pericardial effusion, Nasal congestion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894		
Concomitant Medication [3]: METOLAZONE, ALL OTHER NON-THERAPEUTIC PRODUCTS, ALL OTHER NON-THERAPEUTIC PRODUCTS, ALL OTHER NON-THERAPEUTIC PRODUCTS, TESTS FOR DIABETES, PARACETAMOL, ENALAPRIL MALEATE, ACETYLSALICYLIC ACID, METFORMIN HYDROCHLORIDE, SIMVASTATIN, METOPROLOL TARTRATE, AMLODIPINE BESILATE, ALL OTHER NON-THERAPEUTIC PRODUCTS, LACTOBACILLUS RHAMNOSUS, INSULIN GLARGINE, FUROSEMIDE, FLUTICASONE PROPIONATE, INSULIN ASPART, SODIUM CHLORIDE, SODIUM CHLORIDE, SENNOSIDE A+B, HEPARIN PORCINE, SODIUM CHLORIDE, OTHER DERMATOLOGICAL PREPARATIONS, SODIUM BICARBONATE, SODIUM BICARBONATE, ASCORBIC ACID/FERROUS FUMARATE, MACROGOL 3350, POTASSIUM CHLORIDE, TROLAMINE SALICYLATE, METOLAZONE, SODIUM CHLORIDE, LIDOCAINE, TRIAMCINOLONE ACETONIDE, TORASEMIDE, EMPAGLIFLOZIN, APIXABAN, DOCUSATE SODIUM, GLUCAGON, LIDOCAINE, GLUCAGON HYDROCHLORIDE, LIDOCAINE, COVID-19 VACCINE, HYALURONATE SODIUM, LIDOCAINE, MELATONIN, FERROUS SULFATE, ZALEPLON, ALL OTHER THERAPEUTIC PRODUCTS, ALBUMIN HUMAN, LIDOCAINE, ANTIVIRAL MONOCLONAL ANTIBODIES, ONDANSETRON, OMEPRAZOLE, ENOXAPARIN SODIUM, SODIUM CHLORIDE, HYDRALAZINE, HYDROMORPHONE HYDROCHLORIDE, COUGH AND COLD PREPARATIONS, METOPROLOL TARTRATE, FUROSEMIDE, SODIUM CHLORIDE, ATORVASTATIN, LIDOCAINE, LIDOCAINE, LIDOCAINE, LIDOCAINE, COLECALCIFEROL, APIXABAN, LIDOCAINE				
Non-Serious Adverse Event [4]: Malaise, Urine output decreased, Stoma complication, Iron deficiency anaemia, Constipation, Hypokalaemia, Arthralgia, Acute left ventricular failure, Stoma complication, Atrial fibrillation, Arthralgia, Arthritis, Fatigue, Constipation, Swelling, Swelling, Hypokalaemia, Chronic kidney disease, Ascites, Inguinal hernia, Anal incontinence, Insomnia, Sleep apnoea syndrome, COVID-19, Blood urine present, Muscle spasms, Incisional hernia, Syncope				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE ON CHRONIC RENAL FAILURE(CAUSALITY INTRAVASCULAR VOLUME DEPLETION)	Day 31 / Day 96	Not Related	Drug Interrupted	Recovered /Resolved	Severe
小腸閉塞	SMALL BOWEL OBSTRUCTION	Day 567 / Day 573	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「急性腎障害」及び「小腸閉塞」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Placebo	Race: White	Country: US	Sex: F	Age: 9■
Medical History [1]: Menopause, Hepatitis, Bunion operation, Varicose vein operation, Arthroscopy, Tinnitus, Vertigo, Hyperlipidaemia, Osteoarthritis, Transient ischaemic attack, Deafness, Seborrhoeic keratosis, Glaucoma, Neuropathy peripheral, Cataract operation, Eye laser surgery, Carpal tunnel decompression, Osteonecrosis, Arthritis, Cardiac failure congestive, Hypertension, Retinal vein occlusion, Biliary sphincterotomy, Cholelithiasis, Atrioventricular block first degree, Sinus bradycardia, Drug-induced liver injury, Jaundice cholestatic, Pruritus, Thrombocytopenia, Atrial fibrillation, Hip fracture, Open reduction of fracture, Bundle branch block left, Arteriosclerosis coronary artery, Cardiac amyloidosis, Atelectasis, Pulmonary fibrosis, Atrial flutter, Sleep apnoea syndrome, Goitre, Cerebral artery stenosis, Arteriosclerosis, Pericardial effusion, Tricuspid valve incompetence, Chest discomfort, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: AMOXICILLIN, MULTIVITAMINS (PLAIN), WARFARIN SODIUM, CARMELLOSE SODIUM, LISINOPRIL, TORASEMIDE, SPIRONOLACTONE, SPIRONOLACTONE, TROPICAMIDE, PHENYLEPHRINE, COVID-19 VACCINE, TROPICAMIDE, PHENYLEPHRINE, SODIUM CHLORIDE, MUPIROCIN, CEFAZOLIN SODIUM, CHLORHEXIDINE GLUCONATE, LIDOCAINE, IOHEXOL, COVID-19 VACCINE, PARACETAMOL, KETOROLAC TROMETHAMINE, TROPICAMIDE, PHENYLEPHRINE, LIDOCAINE/SODIUM BICARBONATE, PARAFFIN, HYDROCORTISONE, HYDROCORTISONE, CLINDAMYCIN HYDROCHLORIDE, DOXYCYCLINE HYCLATE, DIPHTHERIA VACCINE TOXOID/PERTUSSIS VACCINE ACELLULAR/TETANUS VACCINE TOXOID, AMPICILLIN SODIUM/SULBACTAM SODIUM, VANCOMYCIN, POLYVINYL ALCOHOL, ONDANSETRON, MACROGOL 3350, SODIUM CHLORIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, LIDOCAINE HYDROCHLORIDE, DEXAMETHASONE, DEXAMETHASONE, POTASSIUM CHLORIDE, IOHEXOL, PHYTOMENADIONE, COLESTYRAMINE, CLOBETASOL PROPIONATE, PREDNISONE, ENOXAPARIN SODIUM, KETOROLAC TROMETHAMINE, KETOROLAC TROMETHAMINE				
Non-Serious Adverse Event [4]: Lacrimation increased, Dizziness, Fall, Neck pain, Neck pain, Autoimmune thyroiditis, Retinal haemorrhage, Wound, Visual impairment, Rash papular, Erythema, Cellulitis, Dysphagia, Odynophagia, Tenosynovitis, Joint swelling, Hepatitis cholestatic, Rash, Basal cell carcinoma, Neck pain, Headache, Urinary tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
完全房室ブロック	BLOCK ATRIOVENTRICULAR COMPLETE	Day 521 / Day 524	Not Related	Drug Interrupted	Recovered /Resolved	Severe
腱鞘炎	TENOSYNOVITIS FINGER FLEXOR RIGHT	Day 824 / Day 826	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「完全房室ブロック」及び「腱鞘炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Hernia repair, Benign prostatic hyperplasia, Ankle fracture, Wrist fracture, Osteoarthritis, Atrial fibrillation, Cardiac failure congestive, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 904			
Concomitant Medication [3]: IBUPROFEN, ALFUZOSIN, FINASTERIDE, CHONDROITIN/GLUCOSAMINE, POTASSIUM CHLORIDE, COLECALCIFEROL, APIXABAN, METOPROLOL, FUROSEMIDE, METOPROLOL, DIMETICONE/GLYCEROL/PETROLATUM, POTASSIUM CHLORIDE, FUROSEMIDE, PARACETAMOL, MIRTAZAPINE, METOPROLOL, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, TAFAMIDIS, COVID-19 VACCINE, COVID-19 VACCINE, MULTIVITAMINS (PLAIN), COVID-19 VACCINE, MIDODRINE HYDROCHLORIDE, MIDODRINE				
Non-Serious Adverse Event [4]: Pruritus, Depression, Nasopharyngitis, Cough, Skin laceration, Cachexia, Hypoalbuminaemia, Hypothyroidism				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
膵腺癌	PANCREATIC HEAD ADENOCARCINOMA	Day 781 / Day 808	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Severe
起立性低血圧	ORTHOSTATIC HYPOTENSION	Day 788 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
治験責任医師の見解：「膵腺癌」及び「起立性低血圧」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Rhinitis allergic, Asthma, Atrial fibrillation, Hypertension, Coronary artery disease, Aortic stenosis, Hyperlipidaemia, Cardiac failure, Aortic valve replacement, Atrial appendage closure, Coronary artery bypass, Cerebrovascular accident, Iron deficiency anaemia, Cardiac amyloidosis, Cataract operation, Productive cough				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: AMOXICILLIN, BUDESONIDE/FORMOTEROL FUMARATE, SALBUTAMOL SULFATE, MONTELUKAST SODIUM, ACETYLSALICYLIC ACID, ROSUVASTATIN, LACTOBACILLUS ACIDOPHILUS, MAGNESIUM CITRATE, MULTIVITAMINS (PLAIN), FOLIC ACID, VITAMIN B12 NOS, SILODOSIN, CHONDROITIN/GLUCOSAMINE, LORATADINE, CURCUMA LONGA, POTASSIUM CHLORIDE, BUMETANIDE, BUMETANIDE, APIXABAN, DIGOXIN, IRON, CLARITHROMYCIN, METHOTREXATE, METOPROLOL, IBUPROFEN, VANCOMYCIN, CEFALEXIN, DOXYCYCLINE HYCLATE, TRAMADOL, HYDROCODONE, OXYCODONE, HYDROCODONE, OXYCODONE, BUMETANIDE, PREDNISONE, LOSARTAN, IVERMECTIN, EMPAGLIFLOZIN, IVERMECTIN, BUMETANIDE, SPIRONOLACTONE, CIPROFLOXACIN, AMOXICILLIN, IVERMECTIN, AZITHROMYCIN, PREDNISONE				
Non-Serious Adverse Event [4]: Sinusitis, Ejection fraction decreased, Arthritis, Respiratory tract infection, Bronchitis, Sinusitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
感染性腱鞘炎	INFECTIOUS TENOSYNOVITIS	Day 101 / Day 111	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「感染性腱鞘炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Not reported	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Hypertension, Carpal tunnel decompression, Herpes zoster, Cardiac amyloidosis, Atrial fibrillation, Cerebrovascular accident, Aortic valve incompetence, Cardiac failure, Atrial appendage closure, Coronary artery disease, Aortic valve replacement, Myalgia, Bladder cancer				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: ASCORBIC ACID, FUROSEMIDE, METOPROLOL, APIXABAN, ATORVASTATIN, DONEPEZIL, GEMCITABINE, Not coded: Tafamidis, TAFAMIDIS, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, MEMANTINE, BUMETANIDE, FUROSEMIDE, FUROSEMIDE, AMIODARONE, PANTOPRAZOLE, PANTOPRAZOLE, PANTOPRAZOLE, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Bladder cancer recurrent, Urinary tract infection, Atrial tachycardia, Fatigue, Cardiac failure acute, Facial bones fracture				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
徐脈	BRADYCARDIA	Day 471 / Day 477	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
呼吸困難	DYSPNEA	Day 471 / Day 483	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE CONGESTIVE HEART FAILURE EPISODE	Day 705 / Day 708	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胃腸出血	GASTROINTESTINAL HEMORRHAGE	Day 794 / Day 795	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「徐脈」、「呼吸困難」、「急性心不全」及び「胃腸出血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]	
Medical History [1]: Deep vein thrombosis, Hypertension, Coagulopathy, Coronary artery disease, Hyperlipidaemia, Pulmonary embolism, Gout, Pain, Carpal tunnel decompression, Atrial fibrillation, Cardiac failure, Congestive cardiomyopathy, Thyroid disorder, Seasonal allergy, Prostate cancer, Atrial fibrillation, Appendicectomy, Appendicitis, Colectomy, Amyloidosis, Atrial fibrillation, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 917			
Concomitant Medication [3]: WARFARIN, ATORVASTATIN, PARACETAMOL, FUROSEMIDE, LEVOTHYROXINE, SPIRONOLACTONE, MUPIROCIN, COVID-19 VACCINE, COVID-19 VACCINE, COLECALCIFEROL, ASCORBIC ACID, FLUTICASONE PROPIONATE, CETIRIZINE HYDROCHLORIDE, OXYCODONE, CYCLOBENZAPRINE, COVID-19 VACCINE					
Non-Serious Adverse Event [4]: Squamous cell carcinoma, Blood calcium decreased, Fall, Syncope, Bursitis					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
頚椎骨折	NONDISPLACED DENS FRACTURE	Day 860 / Day 951	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「頚椎骨折」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]	
Medical History [1]: Gout, Hyperlipidaemia, Coronary artery disease, Percutaneous coronary intervention, Embolism venous, Percutaneous coronary intervention, Oedema, Sleep disorder, Chronic kidney disease, Tenosynovitis stenosans, Pulmonary mass, Chronic obstructive pulmonary disease, Eyelid disorder, Cardiac failure congestive, Atrial fibrillation, Hypokalaemia, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 255			
Concomitant Medication [3]: ALLOPURINOL, SIMVASTATIN, POTASSIUM CHLORIDE, MIRTAZAPINE, TEMAZEPAM, BUMETANIDE, WARFARIN SODIUM, WARFARIN SODIUM, POTASSIUM CHLORIDE, WARFARIN SODIUM, WARFARIN SODIUM, NAPROXEN SODIUM					
Non-Serious Adverse Event [4]: Dysuria, Skin laceration, Fall, Contusion, Fall					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
中毒性腎症	ACUTE KIDNEY INJURY SECONDARY TO NAPROXEN	Day 255 / Day 309	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「中毒性腎症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: M	Age: 5[redacted]
Medical History [1]: Osteoarthritis, Osteomyelitis, Carpal tunnel syndrome, Drug abuse, Type V hyperlipidaemia, Catheterisation cardiac, Carpal tunnel decompression, Finger amputation, Chronic left ventricular failure, Coronary artery disease, Hypertension, Left ventricular hypertrophy, Ventricular tachycardia, Gastrooesophageal reflux disease, Troponin increased, Cardiac amyloidosis, Renal infarct, Mitral valve incompetence, Tricuspid valve incompetence, Chronic kidney disease, Atrial flutter, Dry eye, Bundle branch block right, Constipation, Pericardial effusion, Type 2 diabetes mellitus, Hypertension				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 93		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, WARFARIN, WARFARIN, EYE LUBRICANTS, MULTIVITAMINS (PLAIN), METOPROLOL, SPIRONOLACTONE, DOCUSATE, MACROGOL 3350, TORASEMIDE				
Non-Serious Adverse Event [4]: No event				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	ACUTE ON CHRONIC CONGESTIVE HEART FAILURE	Day 106 / Day 111	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Not reported	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperlipidaemia, Type 2 diabetes mellitus, Benign prostatic hyperplasia, Hypertension, Aortic valve sclerosis, Glaucoma, Aortic arteriosclerosis, Cardiac failure, Cardiac amyloidosis, Carpal tunnel syndrome				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 900		
Concomitant Medication [3]: TAMSULOSIN, PRAVASTATIN, METFORMIN, SACUBITRIL/VALSARTAN, TORASEMIDE, EMPAGLIFLOZIN, FUROSEMIDE, OSELTAMIVIR, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Acute kidney injury, Cardiac failure, Cardiac failure, Peripheral swelling, Traumatic ulcer				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
インフルエンザ	INFLUENZA	Day 107 / Day 112	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「インフルエンザ」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: F	Age: 7[redacted]
Medical History [1]: Hysterectomy, Migraine, Spinal operation, Supraventricular tachycardia, Carpal tunnel decompression, Arthritis, Hypertension, Pulmonary embolism, Gastrooesophageal reflux disease, Rotator cuff repair, Hyperlipidaemia, Cardiac failure, Anxiety, Diverticulum, Haemorrhoids, Osteoarthritis, Meniscus operation, Mass excision, Tendon sheath incision, Tendon sheath incision, Dyspnoea exertional, Sleep apnoea syndrome, Cardiac amyloidosis, Restrictive cardiomyopathy, Pulmonary arterial hypertension, Implantable defibrillator insertion, Conduction disorder, Ventricular tachycardia, Knee arthroplasty				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 715		
Concomitant Medication [3]: SPIRONOLACTONE, BUMETANIDE, POTASSIUM, APIXABAN, AMLODIPINE BESILATE, ONDANSETRON, HYDROMORPHONE, MORPHINE, PANTOPRAZOLE, MAGNESIUM CITRATE, HEPARIN, HYDROMORPHONE, OXYCODONE, ONDANSETRON, MACROGOL, PHENYLEPHRINE, PROPOFOL, LIDOCAINE, EPINEPHRINE, LISINOPRIL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, RANOLAZINE, DICLOFENAC, Not coded: Tafamidis, TAFAMIDIS, BUMETANIDE, SENNOSIDE A+B CALCIUM, ENEMAS, MACROGOL 3350, SUCRALFATE, AMOXICILLIN/CLAVULANATE POTASSIUM, TRAMADOL, DICYCLOVERINE, FAMOTIDINE, FUROSEMIDE, FUROSEMIDE, DOBUTAMINE, FUROSEMIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, DOBUTAMINE				
Non-Serious Adverse Event [4]: Arthritis, Venous pressure jugular increased, Atrioventricular block second degree, Urine analysis abnormal, Constipation, Hypervolaemia, Abnormal loss of weight, Dyspnoea exertional				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腹痛（1）	ABDOMINAL PAIN	Day 384 / Day 387	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全（1）	ACUTE DECOMPENSATED HEART FAILURE	Day 473 / Day 475	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
非心臓性胸痛	CHEST PAIN; NON-CARDIAC	Day 473 / Day 477	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性左室不全（1）	ACUTE ON CHRONIC SYSTOLIC AND DIASTOLIC HEART FAILURE	Day 526 / Day 528	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胸痛（1）	ATYPICAL CHEST PAIN	Day 526 / Day 528	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性左室不全（2）	ACUTE ON CHRONIC COMBINED DIASTOLIC/SYSTOLIC HEART FAILURE	Day 566 / Day 570	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胸痛（2）	ATYPICAL CHEST PAIN	Day 566 / Day 570	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

急性左室不全（3）	ACUTE ON CHRONIC SYSTOLIC HEART FAILURE	Day 625 / Day 638	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
腹痛（2）	ABDOMINAL PAIN	Day 625 / Day 638	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
胃食道逆流性疾患	EXACERBATION OF GERD	Day 625 / Day 638	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心筋梗塞	NSTEMI TYPE II	Day 656 / Day 661	Not Related	Dose Not Changed	Recovered /Resolved	Mild
急性心不全（2）	ACUTE ON CHRONIC HEART FAILURE WITH REDUCED EJECTION FRACTION	Day 656 / Day 661	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心原性ショック	CARDIOGENIC SHOCK	Day 656 / Day 661	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性腎障害	AKI	Day 673 / Day 676	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「腹痛（1）」、「急性心不全（1）」、「非心臓性胸痛」、「急性左室不全（1）」、「胸痛（1）」、「急性左室不全（2）」、「胸痛（2）」、「急性左室不全（3）」、「腹痛（2）」、「胃食道逆流性疾患」、「急性心筋梗塞」、「急性心不全（2）」、「心原性ショック」及び「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Appendicectomy, Tonsillectomy, Osteoarthritis, Chondroplasty, Meniscus removal, Vasectomy, Chondroplasty, Atrial fibrillation, Gout, Dermatitis, Mitral valve incompetence, Cardiac amyloidosis, Pulmonary hypertension				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 916		
Concomitant Medication [3]: MAGNESIUM OXIDE, ASCORBIC ACID, COLECALCIFEROL, DIET FORMULATIONS FOR TREATMENT OF OBESITY, PROTEIN SUPPLEMENTS, HERBAL IMMUNOMODULATORS, HERBAL PREPARATION, ASCORBIC ACID/ECHINACEA PURPUREA/ZINC, BRASSICA OLERACEA, APIXABAN, DOFETILIDE, LOPERAMIDE HYDROCHLORIDE, ACETYLSALICYLIC ACID, METOPROLOL, Not coded: Tafamidis, TAFAMIDIS, CLOPIDOGREL, BISOPROLOL, TORASEMIDE, ATORVASTATIN, ATORVASTATIN, AMOXICILLIN/CLAVULANATE POTASSIUM, SILDENAFIL				
Non-Serious Adverse Event [4]: Diarrhoea, Hyperlipidaemia, Nasopharyngitis, Cardiac stress test abnormal, Angina pectoris, Cellulitis, Erectile dysfunction				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
呼吸困難	SHORTNESS OF BREATH REQUIRING HOSPITALIZATION	Day 48 / Day 49	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動（1）	WORSENING OF RAPID ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 447 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
心房細動（2）	WORSENING OF RAPID ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 487 / Day 489	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
虚血性肝炎	ISCHEMIC HEPATITIS	Day 490 / Day 513	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE DECOMPENSATED HEART FAILURE	Day 572 / Day 578	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
非心臓性胸痛	CHEST PAIN; NON CARDIAC	Day 572 / Day 578	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「呼吸困難」、「心房細動（1）」、「心房細動（2）」、「虚血性肝炎」、「急性心不全」及び「非心臓性胸痛」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Joint dislocation, Shoulder operation, Inguinal hernia repair, Knee operation, Pneumonia, Gout, Hypertension, Nephrolithiasis, Keratomileusis, Clavicle fracture, Carpal tunnel decompression, Carpal tunnel decompression, Anxiety, Knee arthroplasty, Arthritis, Depression, Benign prostatic hyperplasia, Sciatica, Thyroid adenoma, Neck pain, Thyroidectomy, Gastrooesophageal reflux disease, Erectile dysfunction, Chronic left ventricular failure, Mitral valve incompetence, Pulmonary hypertension, Cardiac amyloidosis, Sleep apnoea syndrome, Nasal congestion, Penile prosthesis insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 890		
Concomitant Medication [3]: LOSARTAN POTASSIUM, ALFUZOSIN HYDROCHLORIDE, LORAZEPAM, FUROSEMIDE, LEVOTHYROXINE, CETIRIZINE HYDROCHLORIDE, FLUTICASONE PROPIONATE, APIXABAN, HYDROCODONE/PARACETAMOL, PARACETAMOL, PARACETAMOL, ACETYLSALICYLIC ACID, LORAZEPAM, PARACETAMOL, LORAZEPAM, CEFAZOLIN, PROPOFOL, MIDAZOLAM, CEFAZOLIN, METOPROLOL SUCCINATE, COVID-19 VACCINE, COVID-19 VACCINE, CEFALEXIN, CEFALEXIN, HYDROCODONE/PARACETAMOL, ONDANSETRON HYDROCHLORIDE				
Non-Serious Adverse Event [4]: Back pain, Atrioventricular block second degree, Atrioventricular block second degree, Dyspepsia, Skin laceration, Pain in extremity, Metatarsalgia, Foot deformity, Nausea				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
筋骨格系胸痛	MUSCULOSKELETAL CHEST PAIN	Day 102 / Day 108	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
医療機器機能不良	CARDIAC PACEMAKER LEAD MALFUNCTION	Day 106 / Day 109	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「筋骨格系胸痛」及び「医療機器機能不良」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Herpes zoster, Intervertebral discitis, Benign prostatic hyperplasia, Essential hypertension, Transurethral prostatectomy, Atrial fibrillation, Cardiac failure congestive, Congestive cardiomyopathy, Acute kidney injury, Intervertebral discitis, Chronic kidney disease, Cardioversion, Inguinal hernia, Inguinal hernia repair, Inguinal hernia, Inguinal hernia repair, Syncope, Implantable cardiac monitor insertion, Chronic obstructive pulmonary disease, Hypothyroidism, Cerebrovascular accident, Visual field defect, Headache, Orthostatic hypotension, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, TRAMADOL, SPIRONOLACTONE, LEVOTHYROXINE, MIDODRINE HYDROCHLORIDE, LOSARTAN, VALACICLOVIR, MIDODRINE, VITAMIN D NOS, METOPROLOL, FUROSEMIDE, APIXABAN, DOFETILIDE, LEVOTHYROXINE, PHENYLEPHRINE, PROPOFOL, PROPOFOL, SODIUM CHLORIDE, DOFETILIDE, FUROSEMIDE, LEVOTHYROXINE, FUROSEMIDE, SPIRONOLACTONE, METOPROLOL, METOPROLOL, EPLERENONE, Not coded: Tafamidis, TAFAMIDIS, METOPROLOL, METOPROLOL, METOPROLOL, METOPROLOL, COVID-19 VACCINE, COVID-19 VACCINE, METOPROLOL, FUROSEMIDE				
Non-Serious Adverse Event [4]: Muscle spasms, Herpes zoster, Cardiac failure, Bradycardia, Atrial fibrillation, Cardiac failure, Contusion, Atrial fibrillation, Gynaecomastia, Abnormal loss of weight, Diarrhoea, Fatigue, Dizziness, Bradycardia, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	PAROXYSMAL ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 203 / Day 223	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性腎障害	ACUTE ON CHRONIC KIDNEY DISEASE SECONDARY TO OVERDIURESIS	Day 224 / Day 268	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心房細動」及び「急性腎障害」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Tonsillectomy, Lacrimal duct procedure, Carpal tunnel syndrome, Carpal tunnel decompression, Carpal tunnel decompression, Sleep apnoea syndrome, Rhinitis allergic, Syncope, Cataract, Cataract operation, Palpitations, Dupuytren's contracture, Glucose-galactose malabsorption, Diverticulum intestinal, Large intestine polyp, Dyslipidaemia, Vitamin D deficiency, Osteoarthritis, Erectile dysfunction, Left ventricular failure, Mitral valve incompetence, Pulmonary hypertension, Ventricular tachycardia, Cardiac amyloidosis, Cardiac resynchronisation therapy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 921		
Concomitant Medication [3]: FLUTICASONE, COLECALCIFEROL, ERGOCALCIFEROL, ATORVASTATIN, ACETYLSALICYLIC ACID, THIAMINE, FOLIC ACID, BUPIVACAINE, METHYLPREDNISOLONE ACETATE, VARICELLA ZOSTER VACCINE RGE (CHO), FUROSEMIDE, VARICELLA ZOSTER VACCINE RGE (CHO), EMPAGLIFLOZIN, APIXABAN, FAMOTIDINE, DOFETILIDE, CARVEDILOL, COVID-19 VACCINE, COVID-19 VACCINE, CEFALEXIN, METHYLPREDNISOLONE, DOFETILIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Alcohol poisoning, Brow ptosis, Osteoarthritis, Cough, Oedema peripheral, Fatigue, Apathy, Dyspnoea, Skin laceration, Nausea, Myalgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	NEW ONSET ATRIAL FIBRILLATION	Day 380 / Day 384	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Hypersensitivity, Insomnia, Rotator cuff syndrome, Atrial fibrillation, Oral herpes, Amyloidosis senile, Vitamin D deficiency, Pulmonary hypertension, Atrial fibrillation, Carpal tunnel syndrome, Sleep apnoea syndrome, Oedema peripheral, Iron deficiency anaemia, Peptic ulcer				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 945		
Concomitant Medication [3]: SALBUTAMOL, BACLOFEN, ACICLOVIR, COLECALCIFEROL, APIXABAN, ZINC SULFATE, CURCUMA LONGA, GABAPENTIN, PANTOPRAZOLE, METOPROLOL, SPIRONOLACTONE, TORASEMIDE, FERROUS SULFATE, CEFALEXIN, METOPROLOL, AMIODARONE, THIOCTIC ACID, TORASEMIDE, AMIODARONE, HYDROCORTISONE, PARACETAMOL, CEFALEXIN, TORASEMIDE, COVID-19 VACCINE, PROPOFOL, AMIODARONE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, PARACETAMOL, DAPAGLIFLOZIN, DAPAGLIFLOZIN, COVID-19 VACCINE, INFLUENZA VACCINE, AMOXICILLIN, DOXYCYCLINE, CEFTRIAXONE, VANCOMYCIN, DOXYCYCLINE, HEPARIN SODIUM, SODIUM CHLORIDE, OXYCODONE, PARACETAMOL, VANCOMYCIN				
Non-Serious Adverse Event [4]: Dizziness, Bradycardia, Conjunctivitis, Atrial fibrillation, Squamous cell carcinoma, Atrial fibrillation, Basal cell carcinoma, Medical device site joint infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	EXACERBATION OF ATRIAL FIBRILLATION WITH RAPID VENTRICULAR RESPONSE	Day 128 / Day 128	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心不全	ACUTE DECOMPENSATED HEART FAILURE	Day 128 / Day 131	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
パスツレラ菌性敗血症	INFECTION AND SEPSIS DUE TO PASTEURELLA MULTOCIDA	Day 493 / Day 496	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
医療機器関連感染	RIGHT SHOULDER PERIPROSTHETIC JOINT INFECTION	Day 785 / Day 914	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心房細動」、「急性心不全」、「パスツレラ菌性敗血症」及び「医療機器関連感染」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel syndrome, Deep vein thrombosis, Chronic lymphocytic leukaemia, Prostate cancer, Barrett's oesophagus, Diabetes mellitus, Hyperlipidaemia, Neuropathy peripheral, Gout, Hypothyroidism, Chronic kidney disease, Coronary artery disease, Left ventricular failure, Gastrooesophageal reflux disease, Aortic stenosis, Hypomagnesaemia, Atrial fibrillation, Atrial flutter, Aortic valve repair, Cardiac amyloidosis, Hypertension, Nephrolithiasis, Anaemia, Vision blurred, Arthralgia, Back pain, Dizziness, Cough				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: GABAPENTIN, FUROSEMIDE, FOLIC ACID, ATORVASTATIN, METFORMIN, METOPROLOL SUCCINATE, GLIMEPIRIDE, LEVOTHYROXINE, WARFARIN, MAGNESIUM OXIDE, FAMOTIDINE, SOTALOL, MAGNESIUM OXIDE, OMEPRAZOLE, IBUPROFEN, COLECALCIFEROL, CEFALEXIN, ALLOPURINOL, METOPROLOL SUCCINATE, FUROSEMIDE, METOPROLOL SUCCINATE, FUROSEMIDE, METOPROLOL, DOFETILIDE, COVID-19 VACCINE, DILTIAZEM, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, IRON/SUCROSE, FUROSEMIDE, FUROSEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, METOLAZONE, GLIMEPIRIDE, AMIODARONE, METFORMIN, AMIODARONE, TORASEMIDE, TORASEMIDE, AMIODARONE, TORASEMIDE, TORASEMIDE, INFLUENZA VACCINE, COVID-19 VACCINE, CEFALEXIN, ALLOPURINOL				
Non-Serious Adverse Event [4]: Rash, Joint swelling, Dyspnoea exertional, Skin ulcer, Dyspnoea, Iron deficiency anaemia, Hypervolaemia, Abdominal discomfort, Hypervolaemia, Cellulitis, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全	CONGESTIVE HEART FAILURE EXACERBATION	Day 642 / Day 648	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房粗動	RECURRENT ATRIAL FLUTTER	Day 724 / Day 727	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「急性心不全」及び「心房粗動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Vitamin D deficiency, Adenotonsillectomy, Squamous cell carcinoma, Large intestine polyp, Colonoscopy, Polypectomy, Drug hypersensitivity, Transient global amnesia, Carpal tunnel decompression, Carpal tunnel syndrome, Benign prostatic hyperplasia, Colonoscopy, Colonoscopy, Polypectomy, Inguinal hernia repair, Atrial fibrillation, Essential hypertension, Umbilical hernia repair, Retinopathy, Sleep apnoea syndrome, Spinal stenosis, Stasis dermatitis, Stress urinary incontinence, Hypokalaemia, Amyloidosis, Chronic kidney disease, Cardiac failure, Renal cyst, Therapeutic nerve ablation, Gout				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 927		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), PARACETAMOL, APIXABAN, TAMSULOSIN HYDROCHLORIDE, METOLAZONE, BUMETANIDE, ALLOPURINOL, POTASSIUM CHLORIDE, CEFTRIAXONE, PHENAZOPYRIDINE, CEFPODOXIME, CEFPODOXIME, COVID-19 VACCINE, STEROIDS, STEROIDS, POTASSIUM CHLORIDE, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: No event				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
尿路感染	URINARY TRACT INFECTION	Day 145 / Day 152	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「尿路感染」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Abscess drainage, Debridement, Ventricular septal defect repair, Seasonal allergy, Atrial fibrillation, Upper respiratory tract infection, Hypertension, Endocarditis bacterial, Aortic aneurysm, Mitral valve incompetence, Lithotripsy, Urinary tract infection, Hyperlipidaemia, Hypokalaemia, Hypomagnesaemia, Acute kidney injury, Urine analysis abnormal, Cardiac failure, Tricuspid valve incompetence, Drug hypersensitivity, Drug hypersensitivity, Umbilical hernia repair, Sleep apnoea syndrome, Cardiac amyloidosis, Hypothyroidism, Mitral valve repair, Tricuspid valve repair, Vascular pseudoaneurysm, Cardiac ablation, Acquired diaphragmatic eventration				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 552		
Concomitant Medication [3]: FLUTICASONE PROPIONATE, METOPROLOL TARTRATE, ATORVASTATIN CALCIUM, COLECALCIFEROL, LEVOTHYROXINE SODIUM, APIXABAN, TORASEMIDE, POTASSIUM CHLORIDE, LOSARTAN, AMIODARONE, SODIUM CHLORIDE, INFLUENZA VACCINE, TELMISARTAN, INSULIN, METRONIDAZOLE, CEFEPIME, CALCIUM GLUCONATE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, SODIUM BICARBONATE, GLUCOSE, BUMETANIDE, PANTOPRAZOLE, PHYTOMENADIONE, ALBUMIN HUMAN, DOBUTAMINE, PHENYLEPHRINE, FENTANYL, PROPOFOL, DEXMEDETOMIDINE, LEVOTHYROXINE, MAGNESIUM OXIDE, POTASSIUM CHLORIDE, CALCIUM GLUCONATE, MILRINONE, TORASEMIDE, TRAMADOL, ONDANSETRON, PANTOPRAZOLE, INSULIN, POTASSIUM CHLORIDE, POTASSIUM PHOSPHATE DIBASIC/SODIUM, OXYCODONE HYDROCHLORIDE/PARACETAMOL, PARACETAMOL, CLINDAMYCIN HYDROCHLORIDE, SODIUM CHLORIDE/VANCOMYCIN HYDROCHLORIDE, SODIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, DILTIAZEM, DILTIAZEM, BUMETANIDE, HYDROCODONE/PARACETAMOL, PARACETAMOL, ACETYLSALICYLIC ACID, ONDANSETRON, POTASSIUM CHLORIDE, LIDOCAINE, EPHEDRINE SULFATE, PHENYLEPHRINE, PROPOFOL, PROMETHAZINE, VITAMIN K NOS, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE/SODIUM CHLORIDE, DOCUSATE SODIUM/SENNOSIDE A+B, SPIRONOLACTONE, GABAPENTIN, VANCOMYCIN HYDROCHLORIDE, ACETYLSALICYLIC ACID/OXYCODONE HYDROCHLORIDE/OXYCODONE TEREPHTHALATE, LIDOCAINE, SODIUM CHLORIDE, CAPSAICIN, LACTULOSE, FUROSEMIDE, TRAZODONE, MELATONIN, COVID-19 VACCINE, FERUMOXYTOL, DIPHENHYDRAMINE, DEXAMETHASONE, FERUMOXYTOL, DIPHENHYDRAMINE, DEXAMETHASONE, COVID-19 VACCINE, ACETYLSALICYLIC ACID, ONDANSETRON, LACTULOSE, SODIUM CHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, FUROSEMIDE, PARACETAMOL, TRAZODONE HYDROCHLORIDE, MELATONIN, PROMETHAZINE, CHLORHEXIDINE GLUCONATE, TRIAMCINOLONE, OLANZAPINE, DOXYCYCLINE MONOHYDRATE, MAGNESIUM SULFATE, POTASSIUM CHLORIDE, SULFAMETHOXAZOLE/TRIMETHOPRIM				
Non-Serious Adverse Event [4]: Inguinal hernia, International normalised ratio increased, Liver function test increased, Anaemia, Confusional state, Post procedural haematoma, Non-cardiac chest pain, Abdominal pain, Non-cardiac chest pain, Abdominal hernia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心原性ショック	CARDIOGENIC SHOCK	Day 258 / Day 262	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心房細動	ATRIAL FIBRILLATION WITH RVR	Day 347 / Day 358	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全	ACUTE ON CHRONIC RIGHT HEART FAILURE	Day 404 / Day 409	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

肝性脳症	HEPATIC ENCEPHALOPATHY	Day 542 / Day 547	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心原性ショック」、「心房細動」、「急性心不全」及び「肝性脳症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 8[redacted]
Medical History [1]: Appendicectomy, Inguinal hernia repair, Dengue fever, Malignant melanoma, Lumbar spinal stenosis, Spinal laminectomy, Intervertebral disc degeneration, Basal cell carcinoma, Skin neoplasm excision, Squamous cell carcinoma, Hypogonadism, Hyperlipidaemia, Type 2 diabetes mellitus, Peroneal nerve palsy, Spinal laminectomy, Cervical radiculopathy, Depression, Actinic keratosis, Cancer surgery, Vitamin D deficiency, Micrographic skin surgery, Skin neoplasm excision, Skin neoplasm excision, Erectile dysfunction, Chronic obstructive pulmonary disease, Osteopenia, Carpal tunnel syndrome, Insomnia, Osteoarthritis, Carpal tunnel decompression, Coronary artery disease, Supraventricular tachycardia, Oedema peripheral, Dyspnoea exertional, Haematuria, Bladder neoplasm surgery, Atrial fibrillation, Vertigo positional, Bladder cancer, Bladder neoplasm, Drug hypersensitivity, Drug hypersensitivity, Thrombocytopenia, Bladder neoplasm surgery, Pulmonary hypertension, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 896			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, SODIUM FLUORIDE, COLECALCIFEROL, DOCOSAHEXAENOIC ACID/EICOSAPENTAENOIC ACID/FISH OIL, UROLOGICALS, CURCUMA LONGA, GABAPENTIN, ADEMETIONINE, PLANTAGO SPP., DIETARY SUPPLEMENT, DIETARY SUPPLEMENT, BOSWELLIA SERRATA, CYANOCOBALAMIN, FLUOXETINE HYDROCHLORIDE, CHONDROITIN SULFATE/GLUCOSAMINE, MELATONIN, CUPRIC OXIDE/FOLIC ACID/NICOTINIC ACID/ZINC OXIDE, TORASEMIDE, PRAVASTATIN, TESTOSTERONE, FLUTICASONE FUROATE/VILANTEROL TRIFENATATE, SALBUTAMOL SULFATE, METFORMIN, RIVAROXABAN, METOPROLOL SUCCINATE, GLYCERYL TRINITRATE, EPINEPHRINE/LIDOCAINE, CANAGLIFLOZIN, METOPROLOL, EMPAGLIFLOZIN, ONDANSETRON, GLYCOPYRRONIUM BROMIDE, CEFAZOLIN SODIUM, HEPARIN, SODIUM CHLORIDE, PHENYLEPHRINE, PROPOFOL, BUPIVACAINE/LIDOCAINE, LIDOCAINE, ATORVASTATIN, DOXYCYCLINE, BUPROPION HYDROCHLORIDE, FLUOXETINE HYDROCHLORIDE, LIDOCAINE, CLINDAMYCIN, IOPAMIDOL, DOXYCYCLINE, EPINEPHRINE/LIDOCAINE, IPRATROPIUM/SALBUTAMOL, INFLUENZA VACCINE INACT SPLIT 4V, BCG VACCINE, BCG VACCINE, BCG VACCINE, SEMAGLUTIDE, ATORVASTATIN CALCIUM, Not coded: Tafamidis, TAFAMIDIS, COVID-19 VACCINE, SPIRONOLACTONE, TESTOSTERONE, COVID-19 VACCINE, EPINEPHRINE/LIDOCAINE, EPINEPHRINE/LIDOCAINE, VENLAFAXINE HYDROCHLORIDE, EPINEPHRINE/LIDOCAINE, ALENDRONATE SODIUM, CEFAZOLIN SODIUM, HEXAMINOLEVULINATE HYDROCHLORIDE, SODIUM CHLORIDE, OXYCODONE, ATROPA BELLADONNA EXTRACT/PAPAVER SOMNIFERUM POWDER, PARACETAMOL, IPRATROPIUM BROMIDE/SALBUTAMOL SULFATE, IOPAMIDOL, OXYBUTYNIN HYDROCHLORIDE, INFLUENZA VACCINE, CIPROFLOXACIN, CIPROFLOXACIN, COVID-19 VACCINE, EPINEPHRINE/LIDOCAINE, LORAZEPAM, LIDOCAINE, CEFAZOLIN SODIUM, GEMCITABINE HYDROCHLORIDE, HEXAMINOLEVULINATE HYDROCHLORIDE, CALCIUM CHLORIDE/POTASSIUM CHLORIDE/SODIUM LACTATE, OXYCODONE HYDROCHLORIDE, ATROPA BELLADONNA EXTRACT/PAPAVER SOMNIFERUM POWDER, PARACETAMOL, IOPAMIDOL, METFORMIN, LIDOCAINE, HEPARIN, SODIUM CHLORIDE/VANCOMYCIN HYDROCHLORIDE, PSYLLIUM HYDROPHILIC MUCILLOID, AMPICILLIN, DOCUSATE SODIUM, CEFTRIAXONE SODIUM, FENTANYL, LIDOCAINE, LIDOCAINE, MIDAZOLAM, MIDAZOLAM, POTASSIUM CHLORIDE, PARAFFIN, TRAZODONE HYDROCHLORIDE, MACROGOL 3350, LORAZEPAM, GLUCOSE/HEPARIN, POTASSIUM CHLORIDE, BENZONATATE, GUAIFENESIN, QUETIAPINE FUMARATE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, CEFTRIAXONE, FUROSEMIDE, FUROSEMIDE, ONDANSETRON, GLYCOPYRRONIUM BROMIDE, VANCOMYCIN, HEPARIN, PHENYLEPHRINE, FENTANYL, PROPOFOL, TRAZODONE, TRAZODONE, FERROUS SULFATE, SPIRONOLACTONE, QUETIAPINE, POTASSIUM CHLORIDE, TRIAMCINOLONE				
Non-Serious Adverse Event [4]: Dysphonia, Supraventricular tachycardia, Fall, Dizziness, Cough, Skin mass, Pulmonary mass, Fatigue, Weight decreased, Fall, Fall, Pain in extremity, Haematoma, Bladder spasm, Haematuria, Peripheral swelling, Urinary tract infection, Urinary tract infection, Anxiety, Fall, Anaemia, Endocarditis, Acute kidney injury, Dysphagia, Erythema				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity

尿路性敗血症	UROSEPSIS	Day 793 / Day 825	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
治験責任医師の見解：「尿路性敗血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: M	Age: 6[redacted]
Medical History [1]: Prostate cancer, Radiotherapy, Tendon sheath incision, Dyspnoea exertional, Rhinitis, Atrial flutter, Cardiac failure, Erectile dysfunction, Amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 897			
Concomitant Medication [3]: ONDANSETRON, RIVAROXABAN, METOPROLOL SUCCINATE, ATORVASTATIN, FUROSEMIDE, AMOXICILLIN, FUROSEMIDE, SILDENAFIL CITRATE, TAZOBACTAM, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, PIPERACILLIN, MORPHINE, METRONIDAZOLE, CEFTRIAXONE, COVID-19 VACCINE, COVID-19 VACCINE, TORASEMIDE, Not coded: Tafamidis, TAFAMIDIS, METOLAZONE, PARACETAMOL, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Cardiac failure, Blood urine present, Oedema peripheral, Physical examination abnormal				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
胆道仙痛	GALLBLADDER COLIC	Day 121 / Day 129	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
投薬過誤	MEDICATION ERROR (METOLAZONE)	Day 547 / Day 552	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「胆道仙痛」及び「投薬過誤」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: US	Sex: M	Age: 7[redacted]
Medical History [1]: Tinnitus, Knee operation, Hyperlipidaemia, Benign prostatic hyperplasia, Myocardial infarction, Coronary arterial stent insertion, Coronary artery disease, Hypertension, Supraventricular tachycardia, Myocardial infarction, Atrial fibrillation, Cardiac failure congestive, Pulmonary hypertension, Iron deficiency anaemia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), LISINOPRIL, METOPROLOL, ATORVASTATIN, TAMSULOSIN, BETA-SITOSTEROL/BORON/CHROMIUM/COPPER/GERMANIUM/IODINE/MANGANESE/MOLYBDENUM/SELENIUM/SILICON/VANADIUM/VITAMIN D NOS/ZINC, FISH OIL, FINASTERIDE, DABIGATRAN, POTASSIUM, FUROSEMIDE, MAGNESIUM OXIDE, FUROSEMIDE, FUROSEMIDE, PREDNISONE, METOPROLOL, Not coded: Tafamidis, TAFAMIDIS, COVID-19 VACCINE, COVID-19 VACCINE, COLECALCIFEROL, FUROSEMIDE, TORASEMIDE, SODIUM CHLORIDE				
Non-Serious Adverse Event [4]: Fluid retention, Arthralgia, Tachycardia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING OF ATRIAL FIBRILLATION REQUIRING CARDIOVERSION	Day 845 / Day 848	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
うっ血性心不全	CONGESTIVE HEART FAILURE	Day 845 / Day 848	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「心房細動」及び「うっ血性心不全」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Placebo	Race: Black or African American	Country: US	Sex: M	Age: 6■
Medical History [1]: Anaemia, Hypertension, Obesity, Colonoscopy, Colon adenoma, Oedema peripheral, Constipation, Syncope, Myocardial infarction, Ventricular tachycardia, Coronary arterial stent insertion, Atrioventricular block first degree, Cardiac failure congestive, Coronary artery disease, Dyslipidaemia, Peripheral venous disease, Restrictive cardiomyopathy, Diabetes mellitus, Cardiac amyloidosis, Cardiac pacemaker insertion, Implantable defibrillator insertion, Gastrooesophageal reflux disease, Chronic kidney disease, Carpal tunnel syndrome, Erectile dysfunction				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 450		
Concomitant Medication [3]: TICAGRELOR, FUROSEMIDE, GABAPENTIN, FERROUS SULFATE, ACETYLSALICYLIC ACID, LISINOPRIL, CARVEDILOL, ATORVASTATIN, VALACICLOVIR, BISACODYL, OMEPRAZOLE, MULTIVITAMINS (PLAIN), POTASSIUM CHLORIDE, METOLAZONE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Herpes zoster, Syncope, Atrial flutter				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
トロポニン増加	ELEVATED TROPONINE. FLAT CURVE WITHOUT CHEST PAIN	Day 87 / Day 89	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
結膜出血	BILATERAL SUBCONJUNCTIVAL HEMORRHAGE	Day 87 / Day 97	Not Related	Drug Interrupted	Recovered /Resolved	Mild
失神	SYNCOPE	Day 414 / Day 418	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
低カリウム血症	WORSENING HYPOKALEMIA	Day 453 / Day 454	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「トロポニン増加」、「結膜出血」、「失神」及び「低カリウム血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 7[redacted]
Medical History [1]: Back pain, Sciatica, Carpal tunnel syndrome, Carpal tunnel decompression, Blastocystis infection, Cardiac failure, Tendon rupture, Percutaneous coronary intervention, Coronary artery disease, Dyslipidaemia, Hypertension, Percutaneous coronary intervention, Tendon rupture, Amyloidosis senile, Blood creatine phosphokinase increased				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 905			
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), ACETYLSALICYLIC ACID, ROSUVASTATIN, CURCUMA LONGA, SPIRONOLACTONE, FUROSEMIDE, BETA-SITOSTEROL/BORON/CHROMIUM/COPPER/GERMANIUM/IODINE/MANGANESE/MOLYBDENUM/SELENIUM/SILICON/VANADIUM/VITAMIN D NOS/ZINC, NEPAFENAC, PREDNISOLONE, COVID-19 VACCINE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, SPIRONOLACTONE, HYDROCHLOROTHIAZIDE, APIXABAN, FUROSEMIDE				
Non-Serious Adverse Event [4]: Fatigue, Sensory disturbance, Cataract, Influenza, Blood creatine phosphokinase increased, Lymphocyte count increased, Blood glucose decreased, Asthenia, Back pain, Cardiac failure congestive, Blastocystis infection, Atrial fibrillation, Hypokalaemia, Oropharyngeal pain, Fatigue, Dyspnoea, Orthopnoea, Breath sounds abnormal, N-terminal prohormone brain natriuretic peptide increased, White blood cell count increased, Urine albumin/creatinine ratio increased, Dizziness, Weight decreased, Cough				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性リンパ性白血病	CHRONIC LYMPHOCYTIC LEUKEMIA	Day 765 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
急性腎障害	ACUTE RENAL FAILURE	Day 765 / Day 812	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「慢性リンパ性白血病」及び「急性腎障害」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 6[redacted]
Medical History [1]: Diabetes mellitus, Erectile dysfunction, Anaemia, Coronary artery disease, Dyslipidaemia, Hypertension, Chronic obstructive pulmonary disease, Prostatic varices, Gastrointestinal haemorrhage, Large intestine polyp, Cholelithiasis, Nephrolithiasis, Thyroid mass, Cardiac failure congestive, Hyperkalaemia, Sleep apnoea syndrome, Acute myocardial infarction, Mitral valve incompetence, Amyloidosis senile, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 183		
Concomitant Medication [3]: INSULIN LISPRO, ACETYLSALICYLIC ACID, TESTOSTERONE CIPIONATE, VITAMIN D NOS, GLUCOSAMINE, ROSUVASTATIN, IRON POLYSACCHARIDE COMPLEX, FUROSEMIDE, SALBUTAMOL, GLYCOPYRRONIUM BROMIDE, OXYGEN, PANTOPRAZOLE, RAMIPRIL, EMPAGLIFLOZIN, SODIUM POLYSTYRENE SULFONATE, CLOPIDOGREL BISULFATE, TADALAFIL, EMPAGLIFLOZIN, SODIUM POLYSTYRENE SULFONATE, GLYCERYL TRINITRATE, VITAMIN B12 NOS, IRON				
Non-Serious Adverse Event [4]: Limb injury, Atrial fibrillation, Coronary artery disease, Haematoma				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
貧血	WORSENED ANEMIA	Day 119 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
治験責任医師の見解：「貧血」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: F	Age: 8[redacted]
Medical History [1]: Uterine cancer, Hip arthroplasty, Chronic kidney disease, Osteoarthritis, Hypertension, Asthma, Atrial fibrillation, Cardiac failure congestive, Pulmonary fibrosis, Cardiac ablation, Cardiac pacemaker insertion, Amyloidosis senile, Carpal tunnel decompression, Varicose vein				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 906		
Concomitant Medication [3]: VITAMIN D NOS, BUDESONIDE/FORMOTEROL FUMARATE, SALBUTAMOL, IPRATROPIUM BROMIDE, FUROSEMIDE, VITAMIN K NOS, APIXABAN, POTASSIUM CHLORIDE, SPIRONOLACTONE, COVID-19 VACCINE, CEFIXIME, COVID-19 VACCINE, NITROFURANTOIN, FUROSEMIDE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, SPIRONOLACTONE, FUROSEMIDE, COVID-19 VACCINE, INFLUENZA VACCINE				
Non-Serious Adverse Event [4]: Urinary tract infection, Blood creatine phosphokinase increased, Urinary tract infection, Venous pressure jugular increased, Arthralgia, Urinary albumin/creatinine ratio increased, Venous pressure jugular increased, Rash				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
敗血症	SEPSIS	Day 916 / Day 938	Not Related	NA	Recovered /Resolved	Severe

治験責任医師の見解：「敗血症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Constipation, Arthralgia, Intervertebral disc degeneration, Depression, Benign prostatic hyperplasia, Follicular lymphoma, Gastrooesophageal reflux disease, Carpal tunnel syndrome, Dysphagia, Hypertension, Pulmonary embolism, Bladder transitional cell carcinoma, Subarachnoid haemorrhage, Cardiac failure, Aortic valve stenosis, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 114		
Concomitant Medication [3]: RIVAROXABAN, OXYBUTYNIN HYDROCHLORIDE, DEXLANSOPRAZOLE, PERINDOPRIL, CARVEDILOL, DULOXETINE, PANTOPRAZOLE, SODIUM CHLORIDE, PANTOPRAZOLE, DICLOFENAC, DEXLANSOPRAZOLE, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, PREDNISONE, PREDNISONE, SODIUM CHLORIDE, GLYCERYL TRINITRATE, FUROSEMIDE, PARACETAMOL				
Non-Serious Adverse Event [4]: Cardiac failure, Oedema peripheral, Muscle spasms, Hypokalaemia, Peripheral vein thrombus extension, Atrial fibrillation, Hyperkalaemia, Hypokalaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
血便排泄	BLOOD IN STOOL	Day 57 / Day 60	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	WORSENING HEART FAILURE	Day 114 / Day 121	Not Related	Dose Not Changed	Recovered /Resolved	Severe
肺塞栓症	SEGMENTAL PULMONARY EMBOLISM WHILE ON DIRECT ORAL ANTICOAGULANT	Day 135 / Day 212	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「血便排泄」、「心不全」及び「肺塞栓症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 8[redacted]
Medical History [1]: Single functional kidney, Benign prostatic hyperplasia, Inguinal hernia, Inguinal hernia repair, Transurethral prostatectomy, Insomnia, Primary familial brain calcification, Meniere's disease, Precancerous skin lesion, Blood bilirubin increased, Mitral valve incompetence, Tricuspid valve incompetence, Hepatic cyst, Chronic kidney disease, Fatigue, Dizziness postural, Aortic valve incompetence, Atrioventricular block first degree, Bundle branch block right, Cardiac amyloidosis, Ventricular tachycardia, Hypokalaemia				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: DUTASTERIDE, BETAHISTINE, SPIRONOLACTONE, POTASSIUM, METOLAZONE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, FUROSEMIDE, FUROSEMIDE, HEPARIN, WARFARIN, ZOPICLONE, Not coded: Tafamidis, TAFAMIDIS MEGLUMINE, FUROSEMIDE, FUROSEMIDE, ZOPICLONE, FUROSEMIDE, APIXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, ALLOPURINOL, HYDROCORTISONE, FUROSEMIDE, FEBUXOSTAT, HYDRALAZINE, ISOSORBIDE MONONITRATE, APIXABAN, LEVETIRACETAM				
Non-Serious Adverse Event [4]: Cardiac failure chronic, Meniere's disease, Hypovolaemia, Atrial fibrillation, Hypervolaemia, Gout, Rash, Dyspnoea, Dizziness, Syncope				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
末梢動脈閉塞性疾患	RIGHT LOWER LIMB ACUTE ARTERIAL OCCLUSION	Day 407 / Day 412	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「末梢動脈閉塞性疾患」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 5[redacted]
Medical History [1]: Arthritis, Allergy to arthropod sting, Drug hypersensitivity, Cardiac failure, Carpal tunnel decompression, Transient ischaemic attack, Diverticulitis, Gout, Type 2 diabetes mellitus, Diabetic neuropathy, Atrial fibrillation, Knee operation, Knee operation, Anaemia, Urinary tract infection, Dyslipidaemia, Depression, Hypotension, Obesity, Drug hypersensitivity, Drug hypersensitivity, Drug hypersensitivity, Cardiac resynchronisation therapy, Cardiac amyloidosis, Vitrectomy, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: ALLOPURINOL, ATORVASTATIN, APIXABAN, METFORMIN, FUROSEMIDE, SERTRALINE, HYDROMORPHONE, ENALAPRIL, HYDROMORPHONE, MIDODRINE, PREGABALIN, PREGABALIN, DOMPERIDONE, ACETYLSALICYLIC ACID, COVID-19 VACCINE, HYDROMORPHONE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Tremor, Blood thyroid stimulating hormone decreased, Contusion, Erythema				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
不全片麻痺	TRANSIENT RIGHT SIDED HEMIPARESIS	Day 32 / Day 34	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate

治験責任医師の見解：「不全片麻痺」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Canada	Sex: M	Age: 8[redacted]	
Medical History [1]: Dyslipidaemia, Hypertension, Dry eye, Osteoarthritis, Glucose tolerance impaired, Atrial fibrillation, Cardiac pacemaker insertion, Cardiac amyloidosis, Cardiac failure					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897			
Concomitant Medication [3]: PARACETAMOL, OTHER OPHTHALMOLOGICALS, CILAZAPRIL, RETINOL, VITAMIN D NOS, BISOPROLOL, EDOXABAN, FUROSEMIDE, METFORMIN, DICLOFENAC, AMLODIPINE, AMLODIPINE, COVID-19 VACCINE, ROSUVASTATIN, COVID-19 VACCINE, COVID-19 VACCINE, HYDROMORPHONE, CODEINE PHOSPHATE/PARACETAMOL, METFORMIN					
Non-Serious Adverse Event [4]: Dizziness, Haematuria, Ligament sprain, Fall, Vertigo					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
半月板損傷	TORN MENISCUS LEFT KNEE	Day 487 / Day 554	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「半月板損傷」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: F	Age: 8[redacted]
Medical History [1]: Cataract, Dyslipidaemia, Hyperuricaemia, Type 2 diabetes mellitus, Chronic kidney disease, Sleep apnoea syndrome, Postmenopause, Hypertension, Cardiac pacemaker insertion, Cardiac failure, Arthralgia, Aphasia, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 884		
Concomitant Medication [3]: LINAGLIPTIN, BISOPROLOL, ALLOPURINOL, PARACETAMOL, ACETYLSALICYLIC ACID, ATORVASTATIN, APIXABAN, FERROUS SULFATE, FOSFOMYCIN, MACROGOL 3350, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, PANTOPRAZOLE, INSULIN PORCINE, CEFTRIAXONE, ENALAPRIL, URAPIDIL, HYDROCHLOROTHIAZIDE, ATORVASTATIN, LEVETIRACETAM, SERTRALINE, IPRATROPIUM BROMIDE, CEFUROXIME, ATORVASTATIN, ESLICARBAZEPINE ACETATE, APIXABAN, BROMAZEPAM, OLMESARTAN, OLMESARTAN, LEVETIRACETAM, LAMOTRIGINE, OLMESARTAN MEDOXOMIL, LAMOTRIGINE, CEFUROXIME, BISOPROLOL, SERTRALINE, VALACICLOVIR, PAROXETINE, PAROXETINE, MEMANTINE, FOSFOMYCIN TROMETAMOL, CEFIXIME, LAMOTRIGINE, QUETIAPINE, PAROXETINE, VORTIOXETINE, VORTIOXETINE				
Non-Serious Adverse Event [4]: Epilepsy, Syncope, Myalgia, Urinary tract infection, Constipation, Urinary tract infection, Hypertensive crisis, Syncope, Weight decreased, Parkinson's disease, Anxiety, Mouth haemorrhage, Dizziness, Bronchitis, Hypertensive crisis, Petit mal epilepsy, Limb injury, Epilepsy, Hypotension, Oral herpes, Urinary tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳血管発作	ICTUS	Day 105 / Day 106	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「脳血管発作」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: Black or African American	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Blood cholesterol increased, Hypertension, Benign prostatic hyperplasia, Constipation, Glaucoma, Aortic aneurysm, Cardiac failure, Dizziness postural, Cardiac amyloidosis, Ventricular arrhythmia, Implantable defibrillator insertion					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 167			
Concomitant Medication [3]: EPLERENONE, ATORVASTATIN, TAMSULOSIN, FINASTERIDE, LACTULOSE, LATANOPROST, BISOPROLOL, FUROSEMIDE, OMEPRAZOLE, APIXABAN, FUROSEMIDE, BUMETANIDE, EPLERENONE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, BUMETANIDE, VITAMIN D NOS					
Non-Serious Adverse Event [4]: No event					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	DECOMPENSATED HEART FAILURE	Day 33 / Day 40	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Spinal fusion surgery, Knee arthroplasty, Cardiac failure, Cardiac amyloidosis, Atrioventricular block complete, Cardiac pacemaker insertion, Carpal tunnel decompression, Atrial fibrillation, Cardioversion, Chronic kidney disease, Cardiac ablation, Cardioversion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: CURCUMIN, ALLIUM SATIVUM, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, AMOXICILLIN, DOXYCYCLINE, FUROSEMIDE, FUROSEMIDE, RAMIPRIL, BISOPROLOL, FUROSEMIDE, LANSOPRAZOLE, MEBEVERINE HYDROCHLORIDE, FUROSEMIDE, BISOPROLOL, METOCLOPRAMIDE, ZOPICLONE, AMIODARONE, MEBEVERINE, VITAMIN D NOS, FERROUS GLUCONATE/HERBAL NOS/VITAMINS NOS, FLUCLOXACILLIN, FUROSEMIDE, SENNA ALEXANDRINA, OMEPRAZOLE, FUROSEMIDE, FUROSEMIDE, LACTULOSE, METOCLOPRAMIDE, FUROSEMIDE, FUROSEMIDE, ERYTHROMYCIN, FUROSEMIDE, FUROSEMIDE, POTASSIUM BICARBONATE/POTASSIUM CHLORIDE, TORASEMIDE, BUMETANIDE, SPIRONOLACTONE, CETIRIZINE, TORASEMIDE, BETAMETHASONE VALERATE, ISOPROPYL MYRISTATE/PARAFFIN (LIQUID), MORPHINE, CROTAMITON, METOLAZONE, TRAMADOL, OXYCODONE, FENTANYL				
Non-Serious Adverse Event [4]: Fatigue, Lower respiratory tract infection, Lower respiratory tract infection, Change of bowel habit, Cough, Abdominal distension, Insomnia, Hypotension, Nail bed infection, Dyspnoea, Decreased appetite, Gastrooesophageal reflux disease, Nasal congestion, Hyperbilirubinaemia, Abdominal pain, Oedema peripheral, Cardiac failure, Pruritus				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 616 / Day 626	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全（2）	DECOMPENSATED HEART FAILURE	Day 744 / Day 749	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 6[redacted]
Medical History [1]: Carpal tunnel decompression, Cardiac pacemaker insertion, Atrial fibrillation, Cardiac resynchronisation therapy, Cardiac failure, Gastrooesophageal reflux disease, Peripheral vascular disorder, Implantable defibrillator insertion, Chronic kidney disease, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 812		
Concomitant Medication [3]: RIVAROXABAN, SACUBITRIL/VALSARTAN, EPLERENONE, FUROSEMIDE, OMEPRAZOLE, INFLUENZA VACCINE, FONDAPARINUX, ACETYLSALICYLIC ACID, TICAGRELOR, FUROSEMIDE, OMEPRAZOLE, AMOXICILLIN, METOCLOPRAMIDE, AMOXICILLIN/CLAVULANATE POTASSIUM, OMEPRAZOLE, VITAMIN D NOS, FUROSEMIDE, DIGOXIN, FUROSEMIDE, CODEINE PHOSPHATE/PARACETAMOL, COVID-19 VACCINE, COVID-19 VACCINE, RIVAROXABAN, FUROSEMIDE, AMOXICILLIN, CLARITHROMYCIN, FUROSEMIDE, LEVOFLOXACIN, FUROSEMIDE, BISOPROLOL, BUMETANIDE, NEBIVOLOL, EPLERENONE, EPLERENONE, FUROSEMIDE, APIXABAN, FUROSEMIDE, SACUBITRIL/VALSARTAN, FUROSEMIDE, EPLERENONE, BUMETANIDE, METOLAZONE, BUMETANIDE, HYOSCINE BUTYLBROMIDE, METOLAZONE, OXYCODONE, HALOPERIDOL, MIDAZOLAM, CYCLIZINE, SACUBITRIL/VALSARTAN				
Non-Serious Adverse Event [4]: Biliary colic, Dysphagia, Weight decreased, Mesenteric artery thrombosis, Biliary colic, Diarrhoea, Lower respiratory tract infection, Cholecystitis, Pleural effusion, Lower respiratory tract infection, Sinus congestion, Dyspnoea, Oedema peripheral				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
筋骨格系胸痛	MUSCULOSKELETAL CHEST PAIN	Day 96 / Day 97	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
胆石症	CHOLELITHIASIS	Day 205 / Day 216	Not Related	Drug Interrupted	Recovered/ Resolved	Moderate
心不全（1）	DECOMPENSATED HEART FAILURE	Day 732 / Day 735	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 747 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe

治験責任医師の見解：「筋骨格系胸痛」、「胆石症」、「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Hip arthroplasty, Hypertension, Benign prostatic hyperplasia, Atrioventricular block complete, Cardiac pacemaker insertion, Sleep apnoea syndrome, Atrial fibrillation, Cardiac failure, Cardiac pacemaker replacement, Carpal tunnel syndrome, Carpal tunnel decompression, Amyloidosis, Iron deficiency anaemia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 901			
Concomitant Medication [3]: BISOPROLOL, PANTOPRAZOLE, SPIRONOLACTONE, TAMSULOSIN, DUTASTERIDE, FUROSEMIDE, RIVAROXABAN, FERROUS SULFATE, RAMIPRIL, RIVAROXABAN, SODIUM CHLORIDE, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, HYDROCHLOROTHIAZIDE, COVID-19 VACCINE, PREDNISONE, PREDNISONE, PREDNISONE, PREDNISONE, ALLOPURINOL, COLCHICINE, METOCLOPRAMIDE, TAZOBACTAM, PIPERACILLIN, ENOXAPARIN, SODIUM CHLORIDE, GLUCOSE, FUROSEMIDE, TRAMADOL, PARACETAMOL, METAMIZOLE, OMEPRAZOLE, PHYTOMENADIONE, FUROSEMIDE, FINASTERIDE, OMEPRAZOLE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, FUROSEMIDE, PETHIDINE, PARACETAMOL, METAMIZOLE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, SODIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, ACETYLCYSTEINE, FUROSEMIDE, ENOXAPARIN, FUROSEMIDE, PARACETAMOL, FUROSEMIDE, SPIRONOLACTONE, ALBUMIN HUMAN, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE, FERROUS SULFATE, ENOXAPARIN, HYDROCHLOROTHIAZIDE, TAMSULOSIN, DUTASTERIDE, SODIUM CHLORIDE, FUROSEMIDE, CEFDITOREN, FUROSEMIDE, DEXKETOPROFEN, CEFIXIME, FUROSEMIDE, RICINUS COMMUNIS OIL, MYROXYLON BALSAMUM VAR. PEREIRAE BALSAM, MEDICATED DRESSINGS, CHLORHEXIDINE, FUROSEMIDE, CARMELLOSE, RIVAROXABAN, CEFDITOREN, COVID-19 VACCINE, PANTOPRAZOLE, ENOXAPARIN, BISOPROLOL, FUROSEMIDE, DEXKETOPROFEN, PARACETAMOL, PANTOPRAZOLE, FUROSEMIDE, RIVAROXABAN, MOMETASONE, PREDNISONE, PREDNISONE, PREDNISONE, FERROUS SULFATE, ALLOPURINOL				
Non-Serious Adverse Event [4]: Limb injury, Cardiac failure, Inflammation, Hyperuricaemia, Inguinal hernia, Urinary tract infection, Fall, Skin laceration, Skin laceration, Hypovolaemia, Renal impairment, Fall, Limb injury, Wound infection, Gout, Type 2 diabetes mellitus				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
四肢膿瘍	LEFT GLUTEAL ABSCESS	Day 518 / Day 548	Not Related	Drug Interrupted	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９	COVID19 INFECTION	Day 532 / Day 548	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心不全	DECOMPENSATED HEART FAILURE	Day 539 / Day 631	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「四肢膿瘍」、「ＣＯＶＩＤ－１９」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]		
Medical History [1]: Cholecystectomy, Thyroidectomy, Asthma, Iron deficiency anaemia, Cardiac failure, Myalgia, Capillary fragility, Hypertension, Haematoma, Cardiac amyloidosis, Oedema peripheral						
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 658					
Concomitant Medication [3]: BUDESONIDE/FORMOTEROL FUMARATE, TIOTROPIUM BROMIDE, OMEPRAZOLE, APIXABAN, BISOPROLOL, SPIRONOLACTONE, CHLORTALIDONE, FUROSEMIDE, FUROSEMIDE, ENOXAPARIN SODIUM, FUROSEMIDE, ACENOCOUMAROL, SPIRONOLACTONE, POTASSIUM, APIXABAN						
Non-Serious Adverse Event [4]: Anaemia, Head injury, Syncope						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ＣＯＶＩＤ－１９肺炎	BILATERIAL PNEUMONIA COVID 19	Day 308 / Day 323	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
完全房室ブロック	COMPLETE ATRIOVENTRICULAR BLOCK	Day 455 / Day 461	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	DECOMPENSATION HEART FAILURE	Day 571 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Mild
治験責任医師の見解：「ＣＯＶＩＤ－１９肺炎」、「完全房室ブロック」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Placebo		Race: White		Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Thrombocytosis, Pleural effusion, Hyperuricaemia, Chronic gastritis, Cardiac amyloidosis, Cardiac failure, Dyspnoea, Ischaemic cardiomyopathy						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 110			
Concomitant Medication [3]: CARVEDILOL, CANRENONE, FUROSEMIDE, ACETYLSALICYLIC ACID, ALLOPURINOL						
Non-Serious Adverse Event [4]: No event						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	Day 86 / Day 97	Not Related	Drug Interrupted	Recovered /Resolved	Severe
ＳＡＲＳ－ＣｏＶ－２検査陽性	POSITIVE COVID-19	Day 93 / Day 133	Not Related	Drug Interrupted	Recovered /Resolved	Mild
治験責任医師の見解：「心不全」及び「ＳＡＲＳ－ＣｏＶ－２検査陽性」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Benign prostatic hyperplasia, Transurethral prostatectomy, Hypertension, Cardiac failure, Atrial fibrillation, Hypercholesterolaemia, Cardiac amyloidosis, Anaemia, Cardiac resynchronisation therapy				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 617			
Concomitant Medication [3]: RAMIPRIL, PANTOPRAZOLE, EDOXABAN, CLOPIDOGREL, ATORVASTATIN, FUROSEMIDE, FERROUS SULFATE, FOLIC ACID, ROSUVASTATIN CALCIUM, ALLOPURINOL, FUROSEMIDE, OLMESARTAN, COVID-19 VACCINE, EDOXABAN, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, METOLAZONE, ROSUVASTATIN CALCIUM, DESOXIMETASONE, ALLOPURINOL, WARFARIN, PREDNISONE, PREDNISONE, PARACETAMOL, PREDNISONE, IRON, DARBEPOETIN ALFA, FUROSEMIDE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), PIPERACILLIN/TAZOBACTAM, OXACILLIN, SPIRONOLACTONE, ZOLPIDEM, FOLIC ACID, Not coded: Tafamidis, TAFAMIDIS				
Non-Serious Adverse Event [4]: Blood uric acid increased, Insomnia, Nausea, Cough, Blood creatinine increased, Myalgia, Dyspnoea, Constipation, Rash, Cutaneous vasculitis, Blood creatinine increased, Asthenia, Back pain, Muscle spasms, Dizziness postural, Oedema peripheral, Vasculitis, Anaemia, Haematuria, Decreased appetite, Spinal fracture, Back injury, Hyponatraemia, Gait disturbance				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING OF HEART FAILURE	Day 544 / Day 576	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ブドウ球菌性敗血症	S. AREUS SEPSIS	Day 549 / Day 573	Not Related	Dose Not Changed	Recovered /Resolved	Severe
錯乱状態	CONFUSIONAL STATE	Day 617 / Day 618	Not Related	Drug Withdrawn	Recovered /Resolved	Severe

治験責任医師の見解：「心不全」、「ブドウ球菌性敗血症」及び「錯乱状態」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]	
Medical History [1]: Renal failure, Cardiac failure, Hypertrophic cardiomyopathy, Cardiac amyloidosis, Implantable defibrillator insertion, Atrial fibrillation					
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 271				
Concomitant Medication [3]: PANTOPRAZOLE, APIXABAN, BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, ALLOPURINOL, SACUBITRIL/VALSARTAN, ALLOPURINOL, PAROXETINE, PANTOPRAZOLE, APIXABAN					
Non-Serious Adverse Event [4]: Depression, Insomnia, Dyspepsia, Nausea, Decreased appetite, Vomiting, Chronic gastritis, Duodenitis, Gastrooesophageal sphincter insufficiency, Pleural effusion, Pneumothorax, Cardiac failure congestive, Head injury					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	HEART FAILURE	Day 154 / Day 164	Not Related	NA	Recovered /Resolved	Moderate
治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。						

Patient ID: ■■-■■■				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: F	Age: 7■
Medical History [1]: Dolichocolon, Constipation, Hiatus hernia, Hypercalcaemia, Osteoarthritis, Nephrolithiasis, Menopause, Hyperparathyroidism primary, Hypothyroidism, Autoimmune thyroiditis, Cholecystectomy, Carpal tunnel decompression, Carpal tunnel decompression, Back pain, Spinal fracture, Cardiac failure, Anxiety, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: TORASEMIDE, HYDROCHLOROTHIAZIDE, GABAPENTIN, ALPRAZOLAM, LEVOTHYROXINE SODIUM, DULOXETINE HYDROCHLORIDE, BISOPROLOL, ESOMEPRAZOLE, BISPHOSPHONATES, ALLOPURINOL, VENLAFAXINE, BISOPROLOL, ARTIFICIAL TEARS [UMBRELLA TERM], COVID-19 VACCINE, COVID-19 VACCINE, APIXABAN, Not coded: Tafamidis, TAFAMIDIS, MAGNESIUM SULFATE, POTASSIUM CHLORIDE, BISOPROLOL, FERROUS SULFATE, AMIODARONE, FUROSEMIDE, OXYGEN, SPIRONOLACTONE				
Non-Serious Adverse Event [4]: Hyperuricaemia, Abdominal pain, Peripheral swelling, Decreased appetite, Depression, Fall, Alopecia, Fall, Incontinence, Vomiting, Eye pruritus, Fall, Diarrhoea, Atrial flutter, Ventricular tachycardia, Pneumonia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING OF HEART FAILURE	Day 549 / Day 576	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
失神	SYNCOPE	Day 618 / Day 618	Not Related	Dose Not Changed	Recovered /Resolved	Severe
完全房室ブロック	TOTAL ATRIOVENTRICULAR BLOCK	Day 619 / Day 623	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	WORSENING OF HEART FAILURE	Day 653 / Day 667	Not Related	Drug Interrupted	Recovered /Resolved	Mild

治験責任医師の見解：「心不全（1）」、「失神」、「完全房室ブロック」及び「心不全（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Hypothyroidism, Drug hypersensitivity, Asthma, Intervertebral disc protrusion, Carpal tunnel syndrome, Rotator cuff syndrome, Cholelithiasis, Supraventricular tachycardia, Cardiac ablation, Atrial fibrillation, Atrial flutter, Cardiac ablation, Polymyalgia rheumatica, Cardiac amyloidosis, Cardiac failure				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: PANTOPRAZOLE, COLECALCIFEROL, HYDROXYCHLOROQUINE, METHOTREXATE SODIUM, FOLIC ACID, METHYLPREDNISOLONE ACEPONATE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, RIVAROXABAN, EPLERENONE, FUROSEMIDE, FUROSEMIDE, PARACETAMOL, FUROSEMIDE, METOLAZONE, FUROSEMIDE, FUROSEMIDE, COLCHICINE, CODEINE/PARACETAMOL, COLECALCIFEROL, FUROSEMIDE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, NAPROXEN, INFLUENZA VACCINE INACT SAG 3V, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, METOLAZONE, METHYLPREDNISOLONE, DEXAMETHASONE, PREDNISONE, POTASSIUM CHLORIDE, FUROSEMIDE, INSULIN LISPRO, INSULIN GLARGINE, MIRTAZAPINE, CANAGLIFLOZIN, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, COVID-19 VACCINE, AMOXICILLIN/CLAVULANIC ACID, PIPERACILLIN/TAZOBACTAM, MEROPENEM TRIHYDRATE, CETIRIZINE, POTASSIUM CHLORIDE, METRONIDAZOLE, FUROSEMIDE, METHYLPREDNISOLONE, METHYLPREDNISOLONE, METOLAZONE, INFLUENZA VACCINE, ALLOPURINOL, COVID-19 VACCINE, EPLERENONE, FUROSEMIDE, POTASSIUM CHLORIDE, WARFARIN SODIUM, FEBUXOSTAT, DIAZEPAM, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Oropharyngeal pain, Dyspnoea, Cardiac failure, Toothache, Constipation, Cardiac failure, Blood potassium decreased, Renal failure, Type 2 diabetes mellitus, Depression, Drug hypersensitivity, Gouty tophus				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING HEART FAILURE	Day 369 / Day 380	Not Related	Dose Not Changed	Recovered /Resolved	Mild
敗血症	SEPTIC EPISODE	Day 540 / Day 550	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（2）	WORSENING HEART FAILURE	Day 695 / Day 700	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心不全（3）	WORSENING HEART FAILURE	Day 801 / Day 802	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「心不全（1）」、「敗血症」、「心不全（2）」及び「心不全（3）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Obesity, Osteoarthritis, Cataract, Diabetes mellitus, Acute myocardial infarction, Dyslipidaemia, Hyperuricaemia, Hypertension, Thyroidectomy, Acute myocardial infarction, Cardiac failure, Renal failure, Cardiac amyloidosis, Depression				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: METFORMIN, OMEPRAZOLE, ACETYLSALICYLIC ACID, BISOPROLOL, ATORVASTATIN, ZOFENOPRIL, ALLOPURINOL, LEVOTHYROXINE, LEVOTHYROXINE, INSULIN GLARGINE, GLYCERYL TRINITRATE, CANRENONE, FUROSEMIDE, EMPAGLIFLOZIN, ESCITALOPRAM, ALPRAZOLAM, NIMESULIDE, BETAMETHASONE/CHLORAMPHENICOL, INFLUENZA VACCINE, LEVOFLOXACIN HEMIHYDRATE, EYE LUBRICANTS, BROMFENAC SODIUM, PHOSPHOLIPIDS/RETINOL PALMITATE/TOCOPHEROL, FUROSEMIDE, ESCITALOPRAM, FUROSEMIDE, CLOPIDOGREL, AMOXICILLIN/CLAVULANIC ACID, FUROSEMIDE, BISOPROLOL, LEVETIRACETAM, METFORMIN, EMPAGLIFLOZIN, INSULIN GLARGINE, FUROSEMIDE, ALPRAZOLAM, INFLUENZA VACCINE, EDOXABAN, COVID-19 VACCINE, FUROSEMIDE, METOLAZONE, CHLORPHENAMINE MALEATE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Haematoma, Cardiac failure, Cognitive disorder, Seizure, Paraesthesia, Hypoxic-ischaemic encephalopathy, Cardiac failure, Ventricular tachycardia, Atrial fibrillation, Skin ulcer, Cardiac failure, Fall, Head injury, Fall, Drug eruption, Squamous cell carcinoma				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脱水	MUCOCUTANEOS DEHYDRATION	Day 732 / Day 733	Not Related	Dose Not Changed	Recovered /Resolved	Mild

治験責任医師の見解：「脱水」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: F	Age: 7[redacted]
Medical History [1]: Chronic kidney disease, Menopause, Appendicectomy, Thyroidectomy, Hypercholesterolaemia, Hypertension, Breast cancer, Breast conserving surgery, Carpal tunnel decompression, Hyperuricaemia, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: LEVOTHYROXINE SODIUM, FENOFIBRATE, OMEGA-3 TRIGLYCERIDES, ALLOPURINOL, CYANOCOBALAMIN, FUROSEMIDE, APIXABAN, AMIODARONE, VITAMINS NOS, APIXABAN, LANSOPRAZOLE, AMIODARONE, LEVOTHYROXINE SODIUM, BISOPROLOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CANRENOATE, FUROSEMIDE, AZITHROMYCIN, CEFTRIAXONE, ENOXAPARIN SODIUM, FUROSEMIDE, LEVOFLOXACIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, WARFARIN SODIUM, METOLAZONE, FUROSEMIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, COVID-19 VACCINE, COVID-19 VACCINE, FERROUS SULFATE, FOLIC ACID, LEVOTHYROXINE SODIUM, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, COVID-19 VACCINE, INFLUENZA VACCINE, NUCLEOSIDES AND NUCLEOTIDES EXCL. REVERSE TRANSCRIPTASE INHIBITORS, PARACETAMOL				
Non-Serious Adverse Event [4]: Alopecia, Depression, Cardiac failure, Pneumococcal infection, Asthenia, Occult blood, Anaemia, Hypotension, Large intestinal haemorrhage, Hyperthyroidism, Cardiac failure, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING OF HEART FAILURE IN AMYLOID-INDUCE CARDIOMIOPATHY	Day 184 / Day 185	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	WORSENING HEART FAILURE	Day 201 / Day 217	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Phlebectomy, Carpal tunnel syndrome, Inguinal hernia, Carpal tunnel syndrome, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: RIVAROXABAN, METOPROLOL, FUROSEMIDE, METOPROLOL, BISOPROLOL, BISOPROLOL, FUROSEMIDE, BISOPROLOL, CETIRIZINE HYDROCHLORIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, FUROSEMIDE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, BISOPROLOL, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS, PANTOPRAZOLE SODIUM SESQUIHYDRATE, COVID-19 VACCINE, CLOPIDOGREL BISULFATE, AMIODARONE, CANRENONE, FUROSEMIDE, EZETIMIBE/ROSUVASTATIN ZINC, INFLUENZA VACCINE				
Non-Serious Adverse Event [4]: Bradycardia, Palpitations, Palpitations, Ventricular tachycardia, Rash, Ventricular tachycardia, COVID-19, Coronary artery disease				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	WORSENING HEART FAILURE	Day 546 / Day 630	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心室性頻脈	SUSTAINED VENTRICULAR TACHYCARDIA	Day 827 / Day 839	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「心不全」及び「心室性頻脈」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Osteoarthritis, Carpal tunnel syndrome, Carpal tunnel syndrome, Asthma, Knee arthroplasty, Atrial fibrillation, Ocular hypertension, Angiocardiogram, Cardiac failure, Coronary artery disease, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: MONTELUKAST SODIUM, ACETYLSALICYLIC ACID, BUDESONIDE/FORMOTEROL FUMARATE, THEOPHYLLINE, TAFLUPROST, FUROSEMIDE, PARACETAMOL, INFLUENZA VACCINE, BISOPROLOL, PARACETAMOL, ENOXAPARIN, DICLOFENAC, TIZANIDINE, METHYLPREDNISOLONE, COVID-19 VACCINE, COVID-19 VACCINE, PARACETAMOL, ETORICOXIB, TIZANIDINE, ETORICOXIB, INFLUENZA VACCINE, COVID-19 VACCINE, DICLOFENAC, THIOCOLCHICOSIDE, ALLOPURINOL, PARACETAMOL, CODEINE PHOSPHATE/PARACETAMOL, INFLUENZA VACCINE, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Arthralgia, Ventricular tachycardia, Torticollis, Contusion, Arthralgia, Hyperuricaemia, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性関節症	PRIMARY GONARTHROSIS LEFT KNEE	Day 166 / Day 171	Not Related	Dose Not Changed	Recovered /Resolved	Mild
治験責任医師の見解：「変形性関節症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]		
Medical History [1]: Inguinal hernia, Hypertension, Inguinal hernia, Osteoarthritis, Atrial fibrillation, Chronic obstructive pulmonary disease, Cardiac pacemaker insertion, Cardiac failure chronic, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 894				
Concomitant Medication [3]: BISOPROLOL, FUROSEMIDE, APIXABAN, ENALAPRIL, TIOTROPIUM, FUROSEMIDE, BISOPROLOL, FUROSEMIDE, COVID-19 VACCINE, METOPROLOL, AZITHROMYCIN, REMDESIVIR, DEXAMETHASONE, REMDESIVIR, METHYLPREDNISOLONE, FEBUXOSTAT, PARACETAMOL						
Non-Serious Adverse Event [4]: Aortic stenosis, Gouty arthritis						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心室性頻脈	NON SUSTAINED VENTRICULAR TACHYCARDIA	Day 609 / Day 611	Not Related	Dose Not Changed	Recovered /Resolved	Severe
ＣＯＶＩＤ－１９肺炎	COVID-19 INFECTION/SARS-COV2 INFECTION/COVID-19 PNEUMONIA	Day 720 / Day 725	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心室性頻脈」及び「ＣＯＶＩＤ－１９肺炎」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 6[redacted]
Medical History [1]: Dyslipidaemia, Hyperuricaemia, Benign prostatic hyperplasia, Hypertension, Cardiac failure chronic, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 917		
Concomitant Medication [3]: FUROSEMIDE, RAMIPRIL, METOPROLOL, SPIRONOLACTONE, TAMSULOSIN, ALLOPURINOL, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, DAPAGLIFLOZIN, RAMIPRIL, METOPROLOL, FEBUXOSTAT, FUROSEMIDE, VALSARTAN, FEBUXOSTAT, SACUBITRIL, FUROSEMIDE, FUROSEMIDE, ALLOPURINOL, FUROSEMIDE, VANCOMYCIN, VALSARTAN, SACUBITRIL				
Non-Serious Adverse Event [4]: Hyperkalaemia, Cardiac failure, Asymptomatic COVID-19, Dyspnoea, Atrial fibrillation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心不全（1）	ACUTE HEART FAILURE	Day 775 / Day 784	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（2）	ACUTE HEART FAILURE	Day 816 / Day 825	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性心不全（3）	ACUTE HEART FAILURE	Day 887 / Day 908	Not Related	Drug Interrupted	Recovered /Resolved	Severe
ブドウ球菌感染	S.AUREUS INFECTION	Day 890 / Day 904	Not Related	Drug Interrupted	Recovered /Resolved	Severe
治験責任医師の見解：「急性心不全（1）」、「急性心不全（2）」、「急性心不全（3）」及び「ブドウ球菌感染」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Israel	Sex: M	Age: 7[redacted]
Medical History [1]: Hypertension, Haemorrhoids, Large intestine polyp, Ex-tobacco user, Spinal laminectomy, Hypercholesterolaemia, Carpal tunnel syndrome, Gastritis, Hiatus hernia, Oesophagitis, Impaired fasting glucose, Glaucoma, Asthma, Chronic obstructive pulmonary disease, Knee arthroplasty, Cardiomyopathy, Cardiac failure chronic, Deep vein thrombosis, Neuropathy peripheral, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 891			
Concomitant Medication [3]: ATORVASTATIN CALCIUM, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, DEXAMETHASONE SODIUM PHOSPHATE, CEFUROXIME AXETIL, PREDNISONE, SPIRONOLACTONE, FUROSEMIDE, UMECLIDINIUM BROMIDE, APIXABAN, AMIODARONE HYDROCHLORIDE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, SPIRONOLACTONE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, FLUTICASONE FUROATE/UMECLIDINIUM BROMIDE/VILANTEROL TRIFENATATE, BECLOMETASONE DIPROPIONATE/FORMOTEROL FUMARATE, FUROSEMIDE, AMOXICILLIN, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, METOLAZONE, COVID-19 VACCINE, DUPILUMAB, METOLAZONE, DUPILUMAB, FEXOFENADINE HYDROCHLORIDE, PREDNISONE, ACETYLSALICYLIC ACID, CEFALEXIN, FUROSEMIDE, CAFFEINE/CODEINE PHOSPHATE/PARACETAMOL, AMIODARONE HYDROCHLORIDE, MIDODRINE HYDROCHLORIDE, FUROSEMIDE, DIMETINDENE MALEATE, FEXOFENADINE HYDROCHLORIDE, DIFLUCORTOLONE VALERATE, DIGOXIN, APIXABAN, CEFALEXIN, COVID-19 VACCINE, DIGOXIN, ATORVASTATIN CALCIUM, CLOBETASOL PROPIONATE, FEXOFENADINE HYDROCHLORIDE, BISACODYL, COVID-19 VACCINE, CEFALEXIN				
Non-Serious Adverse Event [4]: Chronic obstructive pulmonary disease, Cardiac failure acute, Presyncope, Toothache, Pruritus, Microembolism, Pruritus, Acarodermatitis, Eczema, Constipation, Inflammation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
低ナトリウム血症	HYPONATREMIA	Day 16 / Day 21	Not Related	Dose Not Changed	Recovered /Resolved	Mild
胸水	PLEURAL EFFUSION	Day 16 / Day 21	Not Related	Dose Not Changed	Recovered /Resolved	Mild
喀血	HEMOPTYSIS	Day 496 / Day 504	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「低ナトリウム血症」、「胸水」及び「喀血」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Israel	Sex: M	Age: 8[redacted]
Medical History [1]: Colectomy, Adenomatous polyposis coli, Colon cancer, Constipation, Acromegaly, Gigantism, Thyroid disorder, Inguinal hernia, Prostate cancer, Radical prostatectomy, Peripheral motor neuropathy, Peripheral sensory neuropathy, Radiculopathy, Sleep apnoea syndrome, Neoplasm skin, Peripheral venous disease, Retinal vein occlusion, Mitral valve incompetence, Tricuspid valve incompetence, Abdominal hernia, Cardiac amyloidosis, Atrial fibrillation, Tumour excision, Cardiac failure congestive, Diarrhoea				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 906		
Concomitant Medication [3]: OMEPRAZOLE, RIVAROXABAN, AMIODARONE HYDROCHLORIDE, FUROSEMIDE, AMIODARONE HYDROCHLORIDE, CHLORAMPHENICOL/POLYMYXIN B, FERRIC CARBOXYMALTOSE, APIXABAN, ACETYLSALICYLIC ACID, CLOPIDOGREL BISULFATE, FUROSEMIDE, ATORVASTATIN CALCIUM, FUROSEMIDE, ESOMEPRAZOLE, APIXABAN, EPLERENONE, FUROSEMIDE, FERRIC SODIUM GLUCONATE COMPLEX, DOBUTAMINE HYDROCHLORIDE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, RAMIPRIL, FUROSEMIDE, DOBUTAMINE HYDROCHLORIDE, APIXABAN, AMIODARONE HYDROCHLORIDE, AMIODARONE HYDROCHLORIDE, COLCHICINE, PROPOFOL, COVID-19 VACCINE, APIXABAN, ACICLOVIR, AMIODARONE HYDROCHLORIDE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS				
Non-Serious Adverse Event [4]: Anaemia, Serum ferritin decreased, Eye inflammation, Myocardial ischaemia, Dyspepsia, Cardiac failure acute, Tricuspid valve incompetence, Dizziness, Vision blurred, Bone cancer metastatic, Localised infection, Oral herpes				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性心筋梗塞	ACUTE ST ELEVATION INFERIOR MI	Day 146 / Day 160	Not Related	Dose Not Changed	Recovered /Resolved	Severe
僧帽弁閉鎖不全症	MITRAL REGURGITATION EXACERBATION	Day 435 / Day 503	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性心筋梗塞」及び「僧帽弁閉鎖不全症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Ireland	Sex: M	Age: 8[redacted]
Medical History [1]: Ischaemic cardiomyopathy, Chronic lymphocytic leukaemia, Carotid artery stenosis, Pulmonary fibrosis, Rash maculo-papular, Rotator cuff repair, Carpal tunnel syndrome, Myocardial ischaemia, Urine flow decreased, Pulmonary hypertension, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: METFORMIN, ACETYLSALICYLIC ACID, BISOPROLOL, FUROSEMIDE, ROSUVASTATIN, TAMSULOSIN, ALLOPURINOL, TIOTROPIUM BROMIDE, OMEPRAZOLE, COVID-19 VACCINE, SPIRONOLACTONE, METFORMIN, COVID-19 VACCINE, FUSIDIC ACID, BISOPROLOL, AMOXICILLIN/CLAVULANATE POTASSIUM, Not coded: Tafamidis, TAFAMIDIS, ESOMEPRAZOLE, MAGNESIUM OXIDE, POTASSIUM CHLORIDE, SODIUM CHLORIDE, LACTULOSE, BISOPROLOL, CARBOHYDRATES NOS/CHOLINE/FATS NOS/MINERALS NOS/PROTEINS NOS/VITAMINS NOS, EZETIMIBE, FUROSEMIDE, FUROSEMIDE, AMOXICILLIN, PREDNISOLONE				
Non-Serious Adverse Event [4]: Dizziness, Fall, Muscle spasms, Conjunctivitis, Dyspnoea exertional, Urinary tract infection, Myalgia, Constipation, Renal injury, Arthralgia, Hypotension, Soft tissue injury, Viral infection, Fatigue, N-terminal prohormone brain natriuretic peptide increased				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
横紋筋融解症	RHABDOMYOLYSIS	Day 500 / Day 513	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「横紋筋融解症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Ireland	Sex: M	Age: 7[redacted]
Medical History [1]: Cardiomyopathy, Coronary artery disease, Glaucoma, Gastrooesophageal reflux disease, Cholelithiasis, Gout, Osteoarthritis, Erectile dysfunction, Hip arthroplasty, Spinal osteoarthritis, Sciatica, Carpal tunnel decompression, Atrial fibrillation, Type 2 diabetes mellitus, Asthma, Aortic stenosis, Amyloidosis senile, Renal impairment				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 729		
Concomitant Medication [3]: LANSOPRAZOLE, WARFARIN, RAMIPRIL, BUMETANIDE, ATORVASTATIN, SILDENAFIL, ALLOPURINOL, BISOPROLOL, BUMETANIDE, PARACETAMOL, SALBUTAMOL, BECLOMETASONE, KETOPROFEN, BUMETANIDE, BUMETANIDE, OXYCODONE HYDROCHLORIDE, CALAMINE, BISOPROLOL, BUMETANIDE, SPIRONOLACTONE, BUMETANIDE, COVID-19 VACCINE, FUROSEMIDE, ALLOPURINOL, POTASSIUM CHLORIDE, METOLAZONE, FUROSEMIDE, COVID-19 VACCINE, QUININE, FUROSEMIDE, BUMETANIDE, FUROSEMIDE, SPIRONOLACTONE, METOLAZONE, BUMETANIDE, METOLAZONE, BUMETANIDE, BUMETANIDE, BUMETANIDE, CEFUROXIME, CEFUROXIME AXETIL, FENTANYL, MIDAZOLAM, CEFALEXIN, METOLAZONE, Not coded: Tafamidis, TAFAMIDIS, FUROSEMIDE, LATANOPROST, SENNA ALEXANDRINA, POTASSIUM CHLORIDE, METOLAZONE, POTASSIUM CHLORIDE, BUMETANIDE, BUMETANIDE, METOLAZONE, SPIRONOLACTONE, ALLOPURINOL, POTASSIUM CHLORIDE, MIDODRINE, SENNA ALEXANDRINA, MAGNESIUM OXIDE, MIDODRINE, GABAPENTIN, BUMETANIDE, BUMETANIDE, BUMETANIDE, FUROSEMIDE, FUROSEMIDE, ZOPICLONE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, IRON ISOMALTOSIDE 1000, FUROSEMIDE, FUROSEMIDE, METFORMIN, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, METOLAZONE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, BUMETANIDE, BUMETANIDE, LINAGLIPTIN, SODIUM PHOSPHATE MONOBASIC (ANHYDROUS), POTASSIUM CHLORIDE, PANTOPRAZOLE, SENNA ALEXANDRINA, LINAGLIPTIN, POTASSIUM CHLORIDE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, CEFTRIAXONE, POTASSIUM CHLORIDE, SODIUM CHLORIDE, PARACETAMOL, DEXAMETHASONE, BUMETANIDE, INSULIN ASPART, AMOXICILLIN/CLAVULANATE POTASSIUM, INSULIN HUMAN/INSULIN HUMAN INJECTION (ISOPHANE), BUMETANIDE, BUMETANIDE, SODIUM PHOSPHATE MONOBASIC (ANHYDROUS), AMOXICILLIN, LACTULOSE, LINAGLIPTIN, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, POTASSIUM CHLORIDE, BUMETANIDE, BUMETANIDE, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, SODIUM CHLORIDE, FUROSEMIDE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, FUROSEMIDE, MAGNESIUM OXIDE, GENTAMICIN, PIPERACILLIN, FUROSEMIDE, GLICLAZIDE, SPIRONOLACTONE, POTASSIUM CHLORIDE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, HYDROCORTISONE/MICONAZOLE NITRATE, KETOCONAZOLE, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, BUMETANIDE, BUMETANIDE, MEROPENEM, BUMETANIDE, MORPHINE SULFATE, BUMETANIDE, BUMETANIDE				
Non-Serious Adverse Event [4]: Non-cardiac chest pain, Non-cardiac chest pain, Tendon rupture, Gamma-glutamyltransferase increased, Blood alkaline phosphatase increased, Pulmonary oedema, Non-cardiac chest pain, Pruritus, Renal impairment, Blood potassium decreased, Muscle spasms, Hypervolaemia, Spinal pain, Syncope, Contusion, Hypoacusis, Cardiac failure, Constipation, Blood iron decreased, Blood potassium decreased, Depressed mood, Acute kidney injury, Blood potassium decreased, Urinary tract infection, Bacteraemia, Hyperglycaemia, Hypoglycaemia, Cardiac failure, Depressed mood, Body tinea, Urinary retention, Haematuria, Cognitive disorder, Cervical vertebral fracture, Clavicle fracture, Acute kidney injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
うっ血性心不全	HOSPITAL ADMISSION FOR CONGESTIVE CARDIAC FAILURE	Day 211 / Day 220	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Mild

徐脈	SYMPTOMATIC BRADYCARDIA	Day 347 / Day 356	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（1）	DECOMPENSATED HEART FAILURE	Day 479 / Day 486	Not Related	Dose Not Changed	Recovered /Resolved	Severe
失神寸前の状態	PRESYNCOPE	Day 503 / Day 517	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 630 / Day 638	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９	COVID 19 INFECTION	Day 644 / Day 653	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
大腸菌性菌血症	BLOOD BORNE E-COLI INFECTION	Day 653 / Day 668	Not Related	Dose Not Changed	Recovered /Resolved	Severe
尿路感染	URINARY TRACT INFECTION	Day 653 / Day 668	Not Related	Dose Not Changed	Recovered /Resolved	Severe
急性腎障害	ACUTE KIDNEY INJURY	Day 653 / Day 668	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（3）	DECOMPENSATED HEART FAILURE	Day 657 / Day 668	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
転倒	FELL DOWN STAIRS	Day 712 / Day 734	Not Related	Drug Withdrawn	Recovered /Resolved	Severe
治験責任医師の見解：「うっ血性心不全」、「徐脈」、「心不全（1）」、「失神寸前の状態」、「心不全（2）」、「ＣＯＶＩＤ－１９」、「大腸菌性菌血症」、「尿路感染」、「急性腎障害」、「心不全（3）」及び「転倒」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Arthritis, Type 2 diabetes mellitus, Cerebrovascular accident, Atrial fibrillation, Constipation, Cardiac failure, Asthma, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: ALLOPURINOL, WARFARIN SODIUM, METOPROLOL SUCCINATE, PLANTAGO OVATA, FUROSEMIDE, FUROSEMIDE, TERBUTALINE, PARACETAMOL, RAMIPRIL, SITAGLIPTIN PHOSPHATE, SPIRONOLACTONE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, VANCOMYCIN, POTASSIUM, INSULIN ASPART, INSULIN ASPART, CEFUROXIME, INSULIN GLARGINE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, DENOSUMAB, CALCIUM/COLECALCIFEROL, VITAMIN D NOS, FUROSEMIDE, FUROSEMIDE, SALBUTAMOL, ZOPICLONE, BUMETANIDE, POTASSIUM, BUMETANIDE				
Non-Serious Adverse Event [4]: Rhinorrhoea, Clostridium difficile infection, Hypotension, Osteoarthritis, Spinal compression fracture, Fall, Hypocalcaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	INFECTION PNEUMONIA	Day 253 / Day 260	Not Related	Dose Not Changed	Recovered /Resolved	Severe
処置後感染	INFECTION RIGHT TOE POST SURGERY	Day 529 / Day 546	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全	WORSENING OF HEARTFAILURE	Day 751 / Day 756	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「肺炎」、「処置後感染」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Eczema, Constipation, Amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 897			
Concomitant Medication [3]: RIVAROXABAN, POTASSIUM CHLORIDE, FUROSEMIDE, AZELAIC ACID, FUSIDATE SODIUM, BETAMETHASONE, PARACETAMOL, MAGNESIUM HYDROXIDE, IMIDAZOLE, CORTICOSTEROIDS, METOPROLOL SUCCINATE, POTASSIUM CHLORIDE, FUROSEMIDE, FUROSEMIDE, METFORMIN, TAMSULOSIN, ATORVASTATIN, BICALUTAMIDE, LEUPRORELIN				
Non-Serious Adverse Event [4]: Fatigue, Dyspnoea, Oedema peripheral, Prostatic specific antigen increased, Type 2 diabetes mellitus, Hypoaesthesia, Dyslipidaemia, Prostate cancer				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
関節炎	HIP ARTHRITIS RIGHT SIDE	Day 819 / Day 820	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「関節炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]
Medical History [1]: Arteriosclerosis coronary artery, Hypertension, Gout, Gastrooesophageal reflux disease, Asthma, Cardiac failure, Chronic kidney disease, Atrial fibrillation, Glaucoma, Arthritis, Amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 897			
Concomitant Medication [3]: LANSOPRAZOLE, TERBUTALINE, FORMOTEROL, BUDESONIDE, FUROSEMIDE, LATANOPROST, SIMVASTATIN, POTASSIUM CHLORIDE, APIXABAN, AMIODARONE, LOSARTAN, PILOCARPINE, ALLOPURINOL, DORZOLAMIDE, PARACETAMOL, ALLOPURINOL, COLCHICINE, ACETAZOLAMIDE, FUROSEMIDE, MICONAZOLE, SODIUM CHLORIDE, ALLOPURINOL, LEVOTHYROXINE SODIUM, LACTULOSE, COLECALCIFEROL, CARVEDILOL, ALLOPURINOL, FUROSEMIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, FUROSEMIDE, METOLAZONE, DESLORATADINE, ALLOPURINOL, ALLOPURINOL				
Non-Serious Adverse Event [4]: Oral candidiasis, Infected bunion, Oedema peripheral, Lentigo maligna, Skin ulcer, Gout, Dehydration, Hypothyroidism, Constipation, Iron deficiency, Blood thyroid stimulating hormone increased, Seasonal allergy, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
全身健康状態悪化	GENERAL PHYSICAL HEALTH DETERIORATION	NA / Start Day + 86 Days	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「全身健康状態悪化」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]	
Medical History [1]: Gastrooesophageal reflux disease, Amyloidosis, Calcium deficiency, Retroperitoneal abscess, Magnesium deficiency, Atrial fibrillation					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 924			
Concomitant Medication [3]: MULTIVITAMINS (PLAIN), LANSOPRAZOLE, CALCIUM/COLECALCIFEROL, FUROSEMIDE, VITAMIN B NOS, MAGNESIUM HYDROXIDE, METOPROLOL, WARFARIN, POTASSIUM, POTASSIUM, PIPERACILLIN/TAZOBACTAM, TRAMADOL HYDROCHLORIDE, PARACETAMOL, DALTEPARIN SODIUM, FENTANYL, MIDAZOLAM, FUROSEMIDE, FUROSEMIDE, AMIODARONE, DEXAMETHASONE, DEXAMETHASONE/TOBRAMYCIN					
Non-Serious Adverse Event [4]: Macular hole, Arthralgia, Eye inflammation					

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
後腹膜膿瘍	RECURRENT RETROPERITONEAL ABSCESS	Day 230 / Day 237	Not Related	Dose Not Changed	Recovered /Resolved	Severe
血液量増加症	CARDIAC FLUID OVERLOAD	Day 693 / Day 697	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「後腹膜膿瘍」及び「血液量増加症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 7[redacted]
Medical History [1]: Deep vein thrombosis, Hypertension, Dyslipidaemia, Type 2 diabetes mellitus, Amyloidosis, Insomnia, Spinal stenosis, Urticaria, Cardiac failure				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 891			
Concomitant Medication [3]: SIMVASTATIN, METFORMIN, RIVAROXABAN, ZOPICLONE, PARACETAMOL, CETIRIZINE HYDROCHLORIDE, PREDNISOLONE, LOSARTAN, CODEINE PHOSPHATE, POTASSIUM CHLORIDE, AMLODIPINE, FUROSEMIDE, SEMAGLUTIDE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, METRONIDAZOLE, METOLAZONE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, POTASSIUM CHLORIDE, BISACODYL, CALCIUM, VITAMIN D NOS, METOCLOPRAMIDE, OXYCODONE HYDROCHLORIDE, OXYCODONE HYDROCHLORIDE, AZELAIC ACID, FUROSEMIDE, FLUCONAZOLE, ISOSORBIDE MONONITRATE, NYSTATIN, SEMAGLUTIDE, TAMSULOSIN HYDROCHLORIDE, FINASTERIDE, BENDROFLUMETHIAZIDE/POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Cardiac failure, Atrial fibrillation, Rosacea, Dyspnoea, Dyspnoea, Oral fungal infection, Acute kidney injury, Benign prostatic hyperplasia, Bursitis, Dehydration, Diarrhoea, Lower urinary tract symptoms, Renal impairment, Cardiac failure, Fall				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
腹水	ASCITIS	Day 259 / Day 262	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
中毒性腎症	KIDNEY FUNCTION IMPAIRED, DRUG INDUCED	Day 298 / Day 444	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（1）	WORSENING HEART FAILURE	Day 315 / Day 323	Not Related	Dose Not Changed	Recovered /Resolved	Severe
大腿骨骨折	PERTROCHANTERIC FRACTURE	Day 381 / Day 653	Not Related	Dose Not Changed	Recovered /Resolved	Severe
処置による疼痛	INCREASED PAIN DUE TO HIP SURGERY IN FEB.2021	Day 478 / Day 486	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	WORSENING HEART FAILURE	Day 529 / Day 532	Not Related	Dose Not Changed	Recovered /Resolved	Severe
変形性関節症	SEVERE HIP ARTHROSIS RIGHT HIP	Day 620 / Day 653	Not Related	Dose Not Changed	Recovered /Resolved	Severe
丹毒	ERYSIPELAS	Day 816 / Day 835	Not Related	Dose Not Changed	Recovered /Resolved	Severe
起立性低血圧	ORTOSTATIC HYPOTENSION	Day 885 / Day 889	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「腹水」、「中毒性腎症」、「心不全（1）」、「大腿骨骨折」、「処置による疼痛」、「心不全（2）」、「変形性関節症」、「丹毒」及び「起立性低血圧」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Denmark	Sex: M	Age: 8[redacted]	
Medical History [1]: Hypertension, Calcium deficiency, Aortic stenosis, Osteoporosis, Prostate cancer, Lung adenocarcinoma, Granuloma annulare, Amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903			
Concomitant Medication [3]: CALCIUM, VITAMIN D NOS, GOSERELIN, DENOSUMAB, CLOBETASOL, AMLODIPINE, MOMETASONE, POTASSIUM, BENDROFLUMETHIAZIDE, APIXABAN, LOSARTAN, POTASSIUM, BENDROFLUMETHIAZIDE, HYDROCORTISONE BUTYRATE, MIRTAZAPINE, PARACETAMOL, DICLOXACILLIN					
Non-Serious Adverse Event [4]: Dyspnoea, Atrial fibrillation, Prostate cancer, Insomnia, Rash, Oedema peripheral					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
再発肺腺癌	RECURRENCE ADENOCARCINOMA LUNG DXT	Day 243 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「再発肺腺癌」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Left ventricular failure, Hypertension, Cardiac ablation, Cardiac ablation, Chronic obstructive pulmonary disease, Intervertebral disc protrusion, Intervertebral disc operation, Atrial fibrillation, Sinus bradycardia, Atrial fibrillation, Atrial fibrillation, Mitral valve incompetence, Tricuspid valve incompetence, Cardiac failure, Sleep apnoea syndrome, Hypercholesterolaemia, Left ventricular hypertrophy, Haematuria, Renal cell carcinoma, Nephrectomy, Cardiac amyloidosis, Cardiac resynchronisation therapy, Cardiac ablation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 904		
Concomitant Medication [3]: ATORVASTATIN, FLUTICASONE FUROATE/VILANTEROL TRIFENATATE, BISOPROLOL FUMARATE, RIVAROXABAN, BUMETANIDE, PERINDOPRIL ARGININE, EPLERENONE, AMYLMETACRESOL/ASCORBIC ACID/DICHLOROBENZYL ALCOHOL/SODIUM ASCORBATE, DEXAMETHASONE/TOBRAMYCIN, PARACETAMOL, RIVAROXABAN, BUMETANIDE, BUMETANIDE, DICLOFENAC, PARACETAMOL, COVID-19 VACCINE, DICLOFENAC, DICLOFENAC, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, PARACETAMOL, IBUPROFEN, DICLOFENAC, FLUTICASONE FUROATE/UMECLIDINIUM BROMIDE/VILANTEROL TRIFENATATE, COVID-19 VACCINE, INFLUENZA VACCINE, CIPROFLOXACIN, CODEINE PHOSPHATE HEMIHYDRATE/PARACETAMOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, DOMPERIDONE, IBUPROFEN, IBUPROFEN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, ERYTHROMYCIN STEARATE, PHYTOMENADIONE, ENOXAPARIN SODIUM, BLOOD PLASMA, PANTOPRAZOLE SODIUM SESQUIHYDRATE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, RIVAROXABAN, PERINDOPRIL, BISOPROLOL, ETILEFRINE HYDROCHLORIDE, BUMETANIDE				
Non-Serious Adverse Event [4]: Blood uric acid increased, Urinary casts, Oropharyngeal pain, Dyspnoea, Fatigue, Ankle impingement, Eye contusion, Carpal tunnel syndrome, Cardiac failure, Pain in extremity, Pain in extremity, Renal impairment, Chest pain, Tendon injury, COVID-19, Ventricular tachycardia, Hypertension, Inflammation, Cystitis, Pain in extremity, International normalised ratio increased, Hypotension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
マロリー・ワイス症候群	MALLORY WEISS LESION	Day 892 / Day 896	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「マロリー・ワイス症候群」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Pleurisy, Hypertension, Hypercholesterolaemia, Benign prostatic hyperplasia, Rectal adenocarcinoma, Cancer surgery, Colostomy, Influenza like illness, Central venous catheterisation, Cystitis radiation, Haematuria, Anaemia, Gastroenteritis radiation, Pneumonia, Hepatic steatosis, Bundle branch block right, Diastolic dysfunction, Left ventricular hypertrophy, Ileus, Renal cyst, Intestinal resection, Anaemia, Diaphragmatic hernia, Gastrooesophageal reflux disease, Contusion, Bone fissure, Cholelithiasis, Hepatic cyst, Pancreatitis, Cholecystitis acute, Cholecystectomy, Bronchiolitis, Cataract, Cataract, Cataract operation, Cataract operation, Syncope, Pneumonia, Stomal hernia, Hernia repair, Ventricular extrasystoles, Arteriosclerosis coronary artery, Lenticular opacities, Bundle branch block left, Coronary artery bypass, Cough, Cardiac failure, Stomal hernia, Pulmonary hypertension, Mitral valve incompetence, Cardiac amyloidosis, Osteoarthritis, Cardiac failure, Chronic kidney disease				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: PANTOPRAZOLE SODIUM SESQUIHYDRATE, TAMSULOSIN, ACETYLSALICYLIC ACID, PERINDOPRIL ARGININE, BISOPROLOL, SPIRONOLACTONE, SIMVASTATIN, ACETYLCYSTEINE, PARACETAMOL, INFLUENZA VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, AMOXICILLIN, SALBUTAMOL, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, SALBUTAMOL, CITRIC ACID/MAGNESIUM OXIDE/SODIUM PICOSULFATE, IOXITALAMATE MEGLUMINE, BARIUM, COVID-19 VACCINE, MOMETASONE, PARACETAMOL, AMOXICILLIN, MAGNESIUM SULFATE, BUMETANIDE, FUROSEMIDE, QUININE SULFATE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, SACUBITRIL/VALSARTAN, BUMETANIDE, Not coded: Tafamidis, TAFAMIDIS, BUMETANIDE				
Non-Serious Adverse Event [4]: Microalbuminuria, Diarrhoea, Upper respiratory tract infection, Dyspnoea, Albuminuria, N-terminal prohormone brain natriuretic peptide increased, Blood creatinine increased, Nasopharyngitis, N-terminal prohormone brain natriuretic peptide increased, Back pain, Dyspnoea, Metabolic acidosis, Bilirubin conjugated increased, Loss of consciousness, Nasopharyngitis, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全	CARDIAC DECOMPENSATION	Day 754 / Day 760	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心不全」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: F	Age: 8[redacted]
Medical History [1]: Hypercholesterolaemia, Spinal osteoarthritis, Cataract operation, Arthralgia, Dacryocystorhinostomy, Tenosynovitis, Tendon rupture, Synovial rupture, Carpal tunnel syndrome, Carpal tunnel syndrome, Meniscus injury, Osteoarthritis, Neurolysis, Neurolysis, Diverticulum, Large intestine polyp, Gastrointestinal angiodysplasia, Polypectomy, Cardiac failure, Hypokalaemia, Left ventricular hypertrophy, Iron deficiency anaemia, Pulmonary hypertension, Diastolic dysfunction, Polypectomy, Gastrointestinal angiodysplasia, Cardiac amyloidosis, Atrioventricular block first degree				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 893		
Concomitant Medication [3]: ROSUVASTATIN CALCIUM, EZETIMIBE, BUMETANIDE, VITAMIN D NOS, BUMETANIDE, BUMETANIDE, FERROUS SULFATE, INFLUENZA VACCINE, VITAMINS NOS, PETHIDINE, MIDAZOLAM, COVID-19 VACCINE, FERROUS SULFATE, COVID-19 VACCINE, FERROUS SULFATE, COVID-19 VACCINE, FERROUS SULFATE, BUMETANIDE, DICLOFENAC, BUMETANIDE, BUMETANIDE, BUMETANIDE, FERRIC CARBOXYMALTOSE, RED BLOOD CELLS (CONCENTRATED), BUMETANIDE, ASCORBIC ACID/MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM ASCORBATE/SODIUM CHLORIDE/SODIUM SULFATE, BUMETANIDE, BUMETANIDE, LIDOCAINE, PANTOPRAZOLE, FERROUS SULFATE, PETHIDINE, MIDAZOLAM, BUMETANIDE, COVID-19 VACCINE, BUMETANIDE, POTASSIUM GLUCONATE, SPIRONOLACTONE, BUMETANIDE, ACETAZOLAMIDE, FERRIC CARBOXYMALTOSE, RED BLOOD CELLS (CONCENTRATED), BUMETANIDE, PARACETAMOL, POTASSIUM GLUCONATE, MAGNESIUM SULFATE, POTASSIUM CHLORIDE, POTASSIUM GLUCONATE, QUININE SULFATE, PARACETAMOL, COLECALCIFEROL, BUMETANIDE, ALIZAPRIDE HYDROCHLORIDE, PARACETAMOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, RED BLOOD CELLS (CONCENTRATED), BUMETANIDE, BUMETANIDE, BUMETANIDE, ACETAZOLAMIDE, COVID-19 VACCINE, RED BLOOD CELLS (CONCENTRATED), BUMETANIDE, ACETAZOLAMIDE, PARACETAMOL, LIDOCAINE/TETRACAINE, POTASSIUM GLUCONATE, POTASSIUM CHLORIDE, ACETAZOLAMIDE, QUININE SULFATE, BUMETANIDE, ACETAZOLAMIDE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, PARACETAMOL, POTASSIUM CHLORIDE, BUMETANIDE, ALGINIC ACID/GLUCOSE/GLUCOSE OXIDASE/GUAIACOL/LACTOPEROXIDASE/MACROGOL, SPIRONOLACTONE, FERRIC CARBOXYMALTOSE, RED BLOOD CELLS (CONCENTRATED), BUMETANIDE, BUMETANIDE, ACETAZOLAMIDE, ENOXAPARIN SODIUM, RED BLOOD CELLS (CONCENTRATED), POTASSIUM CHLORIDE, GLUCOSE, POTASSIUM GLUCONATE, BUMETANIDE, ALBUMIN HUMAN, EZETIMIBE/ROSUVASTATIN CALCIUM				
Non-Serious Adverse Event [4]: Headache, Iron deficiency, Fatigue, Peripheral swelling, Iron deficiency, Iron deficiency, Liver function test increased, Oedema peripheral, Fluid retention, Atrial fibrillation, Congestive hepatopathy, Gastrooesophageal reflux disease, Rectal haemorrhage, Rectal polyp, Cardiac failure, Hyponatraemia, Acute kidney injury, Hypokalaemia, Cardiac failure, Thrombocytopenia, Hyponatraemia, Liver function test increased, Reticulocytosis, Acute kidney injury, Hypokalaemia, Iron deficiency anaemia, Hepatic cyst, Hypokalaemia, Blood albumin decreased, Melaena, Urinary tract infection, COVID-19				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	CORDECOMPENSATION	NA / Start Day + 101 Days	Not Related	Dose Not Changed	Recovered/ Resolved	Mild
鉄欠乏性貧血（1）	WORSENING OF FERRIPRIVE ANEMIA	Day 625 / Day 716	Not Related	Dose Not Changed	Recovered/ Resolved	Mild
鉄欠乏性貧血（2）	WORSENING OF FERRIPRIVE ANEMIA	Day 750 / Day 753	Not Related	Dose Not Changed	Recovered/ Resolved	Mild

心不全（2）	CORDECOMPENSATION	Day 750 / Day 753	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
胸水	WORSENING PLEURAL EFFUSION LEFT	Day 816 / Day 824	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
急性心不全（1）	ACUTE HEART FAILURE	Day 852 / Day 864	Not Related	Dose Not Changed	Recovered/ Resolved	Moderate
鉄欠乏性貧血（3）	WORSENING OF FERRIPRIVE ANEMIA	Day 856 / Day 864	Not Related	Dose Not Changed	Recovered/ Resolved	Mild
骨髄異形成症候群	MYELODYSPLASTIC SYNDROME	Day 858 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Moderate
急性心不全（2）	ACUTE HEART FAILURE	Day 883 / NA	Not Related	Dose Not Changed	Not Recovered/ Not Resolved	Moderate
治験責任医師の見解：「心不全（1）」、「鉄欠乏性貧血（1）」、「鉄欠乏性貧血（2）」、「心不全（2）」、「胸水」、「急性心不全（1）」、「鉄欠乏性貧血（3）」、「骨髄異形成症候群」及び「急性心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Pulmonary embolism, Pneumonia cytomegaloviral, Hypercholesterolaemia, Hypertension, Gastritis, Left ventricular hypertrophy, Biopsy heart, Cardiac amyloidosis, Syncope, Orthostatic hypotension, Hyperthyroidism, Cardioversion, Atrial fibrillation, Atrioventricular block first degree, Cardiac ablation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: PANTOPRAZOLE SODIUM SESQUIHYDRATE, AMIODARONE HYDROCHLORIDE, APIXABAN, NEBIVOLOL, LEVOTHYROXINE, FUROSEMIDE, SPIRONOLACTONE, INFLUENZA VACCINE, COVID-19 VACCINE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, EMPAGLIFLOZIN, BUMETANIDE, BUMETANIDE, ONDANSETRON, HEPARIN, HEPARIN, NOREPINEPHRINE, ROCURONIUM, FENTANYL CITRATE, REMIFENTANIL, PROPOFOL, DEXAMETHASONE, GLYCOPYRRONIUM BROMIDE, APIXABAN, CHLORHEXIDINE, ALGINIC ACID/GLUCOSE/GLUCOSE OXIDASE/GUAIACOL/LACTOPEROXIDASE/MACROGOL, TAMSULOSIN, CHLORHEXIDINE GLUCONATE/LIDOCAINE HYDROCHLORIDE, TAMSULOSIN, CIPROFLOXACIN, DUTASTERIDE, BUMETANIDE, COVID-19 VACCINE, BUMETANIDE, CEFAZOLIN, APIXABAN, PARACETAMOL, COLECALCIFEROL, TAMSULOSIN, LEVOTHYROXINE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, ANTIBIOTICS, INFLUENZA VACCINE, BUMETANIDE				
Non-Serious Adverse Event [4]: Abdominal distension, Cardiac failure, Cardiac failure, Sleep apnoea syndrome, Aspartate aminotransferase increased, Prostatic cyst, Haematuria, Vitamin D deficiency, Urinary tract infection, Bronchitis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房粗動	ATRIAL FLUTTER	Day 717 / Day 766	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
房室ブロック	AV CONDUCTION BLOCK	Day 765 / Day 802	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房粗動」及び「房室ブロック」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 8[redacted]
Medical History [1]: Inguinal hernia perforation, Benign prostatic hyperplasia, Cough, Tracheitis, Atrial fibrillation, Hypertrophic cardiomyopathy, Aortic aneurysm, Cardiac amyloidosis, Polycythaemia, Sleep apnoea syndrome, Epistaxis, Cautery to nose				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: EDOXABAN TOSILATE, PERINDOPRIL, NEBIVOLOL, COLECALCIFEROL, EDOXABAN TOSILATE, COVID-19 VACCINE, COVID-19 VACCINE, EDOXABAN TOSILATE, NITROFURANTOIN, COVID-19 VACCINE, OFLOXACIN, MAGNESIUM, CEFUROXIME AXETIL, BUMETANIDE, COLECALCIFEROL, PAMIDRONATE DISODIUM, PAMIDRONATE DISODIUM, PARACETAMOL, PARACETAMOL, BUMETANIDE, ALIZAPRIDE HYDROCHLORIDE, PAMIDRONATE DISODIUM, PARACETAMOL, PAMIDRONATE DISODIUM, PARACETAMOL, ZOLEDRONIC ACID MONOHYDRATE, ZOLEDRONIC ACID MONOHYDRATE, PARACETAMOL, AMOXICILLIN/CLAVULANATE POTASSIUM, ACETYLCYSTEINE, ZOLEDRONIC ACID MONOHYDRATE, PARACETAMOL, DEXPANTHENOL				
Non-Serious Adverse Event [4]: Bundle branch block right, Haematocrit increased, Hypercalcaemia, Eye irritation, Rash, Cystitis, Rash, Haematoma, Vertigo, Myalgia, Diverticulitis, Respiratory tract infection, Vitamin D deficiency, Cardiac failure, Influenza, Complication associated with device, Eczema				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
慢性リンパ性白血病	CHRONIC LYMPHATIC LEUKEMIA	Day 373 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe

治験責任医師の見解：「慢性リンパ性白血病」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Joint prosthesis user, Hypercholesterolaemia, Hypertension, Atrial fibrillation, Vasectomy, Lung disorder, Cardiomyopathy, Amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 78		
Concomitant Medication [3]: RIVAROXABAN, ATORVASTATIN CALCIUM, BUMETANIDE, CHLORTALIDONE, MAGNESIUM OXIDE, SPIRONOLACTONE, PANTOPRAZOLE, RIVAROXABAN, SPIRONOLACTONE, CHLORTALIDONE, FLUCLOXACILLIN, SPIRONOLACTONE, COLECALCIFEROL, PARACETAMOL, ITRACONAZOLE, ROSUVASTATIN CALCIUM, LEVOCETIRIZINE DIHYDROCHLORIDE, TERBINAFINE, BUMETANIDE, CEFEPIME, MEROPENEM				
Non-Serious Adverse Event [4]: Restless legs syndrome, Renal impairment, Back pain, Fungal infection, Head injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
ブドウ球菌性敗血症	STAPHYLOCOCCUS AUREUS SEPSIS	Day 52 / Day 72	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
医療機器関連敗血症	CATHETER SEPSIS WITH ACINETOBACTER	Day 71 / Day 78	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「ブドウ球菌性敗血症」及び「医療機器関連敗血症」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Aortic valve sclerosis, Gouty arthritis, Joint prosthesis user, Carpal tunnel syndrome, Cardiac pacemaker insertion, Hypercholesterolaemia, Cardiac failure, Cardiac amyloidosis, Medical device site infection, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: SIMVASTATIN, FEBUXOSTAT, ACETYLSALICYLIC ACID, SPIRONOLACTONE, BUMETANIDE, PANTOPRAZOLE, BUMETANIDE, BUMETANIDE, SPIRONOLACTONE, BUMETANIDE, BUMETANIDE, SPIRONOLACTONE, PARACETAMOL, BUMETANIDE, SACUBITRIL/VALSARTAN, APIXABAN, Not coded: Tafamidis, TAFAMIDIS, BUMETANIDE, BUMETANIDE				
Non-Serious Adverse Event [4]: Abdominal pain upper, Abdominal pain upper, Cardiac failure, Chest pain, Face injury, Urine albumin/creatinine ratio increased, Rales, Fatigue, Urine albumin/creatinine ratio increased, Back pain, Paraesthesia, Atrial fibrillation, Renal impairment, Hypotension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
鼡径ヘルニア	INGUINAL HERNIA	Day 581 / Day 616	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「鼡径ヘルニア」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Placebo	Race: Not reported	Country: Netherlands	Sex: F	Age: 8[redacted]		
Medical History [1]: Squamous cell carcinoma, Sigmoidectomy, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis						
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 365					
Concomitant Medication [3]: APIXABAN, SPIRONOLACTONE, ISOSORBIDE MONONITRATE, BUMETANIDE, PANTOPRAZOLE, COLECALCIFEROL, FUROSEMIDE, FLUCLOXACILLIN, AMOXICILLIN, FUROSEMIDE, COVID-19 VACCINE, COVID-19 VACCINE, BUMETANIDE, SPIRONOLACTONE, BUMETANIDE						
Non-Serious Adverse Event [4]: Urinary tract infection, Oedema peripheral, Fatigue, Wound						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	WORSENING HEART FAILURE	Day 283 / Day 288	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（2）	WORSENING HEART FAILURE	Day 314 / Day 317	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Not reported	Country: Netherlands	Sex: M	Age: 6[redacted]
Medical History [1]: Carpal tunnel syndrome, Cardiac failure, Atrial fibrillation, Cardiac amyloidosis, Anaemia, Gastrointestinal angiodysplasia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 893			
Concomitant Medication [3]: RIVAROXABAN, LOSARTAN, FUROSEMIDE, PANTOPRAZOLE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), FERROUS FUMARATE, FUROSEMIDE, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), APIXABAN, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, PNEUMOCOCCAL VACCINES, INFLUENZA VACCINE, CODEINE SULFATE, Not coded: Tafamidis, TAFAMIDIS, BLOOD TRANSFUSION (AUXILIARY PRODUCTS), INFLUENZA VACCINE, NOSCAPINE				
Non-Serious Adverse Event [4]: Cough, Gynaecomastia, Basal cell carcinoma, Abnormal faeces, Cough				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
貧血（1）	WORSENING ANEMIA	Day 83 / Day 87	Not Related	Dose Not Changed	Recovered /Resolved	Severe
貧血（2）	WORSENING ANEMIA	Day 160 / Day 166	Not Related	Dose Not Changed	Recovered /Resolved	Severe
貧血（3）	WORSENING ANEMIA	Day 687 / Day 693	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「貧血（1）」、「貧血（2）」及び「貧血（3）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Not reported	Country: Netherlands	Sex: M	Age: 7[redacted]
Medical History [1]: Varicose vein, Carpal tunnel syndrome, Prostate cancer, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: PERINDOPRIL, COVID-19 VACCINE, COVID-19 VACCINE, OMEPRAZOLE, DICLOFENAC, COVID-19 VACCINE, INFLUENZA VACCINE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, Not coded: Tafamidis, TAFAMIDIS, BICALUTAMIDE, GOSERELIN				
Non-Serious Adverse Event [4]: Contusion, Arthritis, Urinary tract infection, Hyperglycaemia, Gout, Oedema peripheral, Arthralgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
遠隔転移を伴う前立腺癌	METASTASIZED PROSTATE CARCINOMA	Day 637 / NA	Not Related	Dose Not Changed	Not Recovered/Not Resolved	Severe

治験責任医師の見解：「遠隔転移を伴う前立腺癌」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: Not reported	Country: Netherlands	Sex: F	Age: 8[redacted]
Medical History [1]: Anaemia, Chronic gastritis, Transient ischaemic attack, Non-cardiac chest pain, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 915		
Concomitant Medication [3]: FERROUS FUMARATE, EDOXABAN, METOPROLOL, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, AMIODARONE, PREDNISOLONE, PANTOPRAZOLE, COLECALCIFEROL, HYDROXOCOBALAMIN, DEXTRAN, METOPROLOL, METOPROLOL, GLYCERYL TRINITRATE, GLYCERYL TRINITRATE, METOPROLOL, TRAMADOL, PARACETAMOL, FERROUS FUMARATE, CARVEDILOL, ALGELDRATE/MAGNESIUM HYDROXIDE, METOPROLOL, EDOXABAN				
Non-Serious Adverse Event [4]: Angina pectoris, Dry eye, Fatigue, Angina pectoris, Alopecia, Contusion, Muscle spasms, Fall, Angina pectoris, Abdominal discomfort, Atrial fibrillation, Fatigue, Fall				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
全身健康状態悪化	OVERALL DECLINE	Day 517 / Day 520	Not Related	Dose Not Changed	Recovered /Resolved	Mild
肺炎	PNEUMONIA	Day 783 / Day 789	Not Related	Dose Not Changed	Recovered /Resolved	Severe
大腿骨骨折	PETROCHANTARY FEMURFRACTURE RIGHT	Day 863 / Day 905	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「全身健康状態悪化」、「肺炎」及び「大腿骨骨折」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Belgium	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel syndrome, Rotator cuff syndrome, Hypertension, Hypercholesterolaemia, Cardiac amyloidosis, Cardiac failure, Electrocardiogram abnormal, Cardiac resynchronisation therapy, Cardioversion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: ESOMEPRAZOLE, ATORVASTATIN, EDOXABAN TOSILATE, AMIODARONE HYDROCHLORIDE, BUMETANIDE, PARACETAMOL, MOXIFLOXACIN, FENOTEROL HYDROBROMIDE/IPRATROPIUM BROMIDE, DEXAMETHASONE, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, TRAMADOL HYDROCHLORIDE, TRAMADOL HYDROCHLORIDE, COVID-19 VACCINE, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, SPIRONOLACTONE, INFLUENZA VACCINE, AMOXICILLIN, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, COVID-19 VACCINE, PARACETAMOL				
Non-Serious Adverse Event [4]: COVID-19, Bone contusion, Nasopharyngitis, Cardiac failure, Atrial fibrillation, Atrial fibrillation, Hypervolaemia, Vaccination site discomfort				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
急性腎障害	ACUTE PRERENAL FAILURE	Day 94 / Day 105	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９	WORSENING OF COVID INFECTION	Day 94 / Day 135	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房細動	PERMANENT ATRIAL FIBRILLATION	Day 582 / Day 583	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「急性腎障害」、「ＣＯＶＩＤ－１９」及び「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]						
Treatment Arm: Placebo		Race: White		Country: Greece	Sex: M	Age: 8[redacted]
Medical History [1]: Hypertension, Dyslipidaemia, Atrial fibrillation, Coronary artery disease, Dyspnoea, Amyloidosis						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 901			
Concomitant Medication [3]: AMLODIPINE BESILATE/VALSARTAN, VALSARTAN, AMLODIPINE, SIMVASTATIN, SIMVASTATIN, PANTOPRAZOLE, DABIGATRAN ETEXILATE MESILATE, APIXABAN, AMIODARONE, AMIODARONE						
Non-Serious Adverse Event [4]: No event						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING OF ATRIAL FIBRILLATION GR3.(TTR AMYLOIDOSIS RELATED)	Day 90 / Day 92	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Placebo	Race: White	Country: Greece	Sex: M	Age: 8[redacted]		
Medical History [1]: Dyslipidaemia, Atrial fibrillation, Hyperuricaemia, Neuropathy peripheral, Dyspnoea, Amyloidosis						
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 364					
Concomitant Medication [3]: ALLOPURINOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, APIXABAN, AMLODIPINE BESILATE/BISOPROLOL FUMARATE, SIMVASTATIN, SACUBITRIL/VALSARTAN, EPLERENONE, FUROSEMIDE, POTASSIUM GLUCONATE, FUROSEMIDE						
Non-Serious Adverse Event [4]: Oedema peripheral						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
脳血管発作	STROKE	Day 365 / Day 381	Not Related	Drug Withdrawn	Recovered /Resolved With Sequelae	Severe
治験責任医師の見解：「脳血管発作」は治験薬と関連なしと判断した。						

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: Other	Country: UK	Sex: M	Age: 7[redacted]	
Medical History [1]: Osteoarthritis, Hip arthroplasty, Hypercholesterolaemia, Type 2 diabetes mellitus, Hypertension, Trigger finger, Carpal tunnel decompression, Gastrooesophageal reflux disease, Cardiac amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 221			
Concomitant Medication [3]: ACETYLSALICYLIC ACID, RAMIPRIL, BISOPROLOL, ATORVASTATIN, DAPAGLIFLOZIN, METFORMIN, SPIRONOLACTONE, BUMETANIDE, BUMETANIDE, OLOPATADINE, GLICLAZIDE, LANSOPRAZOLE, LACTULOSE, BISOPROLOL, ATORVASTATIN, CITALOPRAM					
Non-Serious Adverse Event [4]: Dry eye, Pruritus, Constipation, Depression, Delirium, Pneumonia					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 233 / NA	Not Related	NA	Recovering /Resolving	Severe
心不全（2）	DECOMPENSATED HEART FAILURE	Day 233 / NA	Not Related	NA	Recovering /Resolving	Severe
治験責任医師の見解：「心不全（1）」及び「心不全（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Osteoarthritis, Chronic kidney disease, Atrial fibrillation, Cardiac amyloidosis, Cardiac resynchronisation therapy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 915		
Concomitant Medication [3]: WARFARIN, WARFARIN, FUROSEMIDE, SPIRONOLACTONE, OMEPRAZOLE, CODEINE PHOSPHATE/PARACETAMOL, FLUCLOXACILLIN, FLUCLOXACILLIN, SENNA ALEXANDRINA, DOCUSATE, INFLUENZA VACCINE, NEBIVOLOL, AMIODARONE, AMIODARONE, AMIODARONE, AMIODARONE, SPIRONOLACTONE, FUROSEMIDE, AMIODARONE, BUMETANIDE, AMIODARONE, IBUPROFEN, RAMIPRIL, SPIRONOLACTONE, BUMETANIDE, COVID-19 VACCINE, BUMETANIDE, BUMETANIDE, INFLUENZA VACCINE, TAMSULOSIN, MACROGOL, DAPAGLIFLOZIN, BISOPROLOL, AMIODARONE, EPLERENONE, BUMETANIDE, BUMETANIDE, CODEINE PHOSPHATE/PARACETAMOL				
Non-Serious Adverse Event [4]: Headache, Nausea, Oral blood blister, Muscle spasms, Osteoarthritis, Benign prostatic hyperplasia, Fall, Rib fracture, Dizziness, Mobility decreased, Fibula fracture				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
蜂巣炎	CELLULITIS	Day 69 / Day 79	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心室性頻脈（1）	VENTRICULAR TACHYCARDIA	Day 109 / NA	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心室性頻脈（2）	VENTRICULAR TACHYCARDIA	Day 889 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe
治験責任医師の見解：「蜂巣炎」、「心室性頻脈（1）」及び「心室性頻脈（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 8[redacted]
Medical History [1]: Hip arthroplasty, Type 2 diabetes mellitus, Hypertension, Blood cholesterol increased, Carpal tunnel decompression, Carpal tunnel decompression, Bronchiectasis, Cardiac amyloidosis, Arthralgia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 965			
Concomitant Medication [3]: RAMIPRIL, SIMVASTATIN, RAMIPRIL, BISOPROLOL, EPLERENONE, FUROSEMIDE, EMPAGLIFLOZIN, COVID-19 VACCINE, COVID-19 VACCINE, GLICLAZIDE, COVID-19 VACCINE, FUROSEMIDE, LINAGLIPTIN, LOPERAMIDE, GLICLAZIDE, COVID-19 VACCINE, GLYCEROL, FUROSEMIDE, LATANOPROST, INFLUENZA VACCINE, COVID-19 VACCINE, SENNOSIDE A+B, MACROGOL, DIHYDROCODEINE, PARACETAMOL, COLECALCIFEROL, COLECALCIFEROL, ANTIBIOTICS, APIXABAN, RAMIPRIL, DIGOXIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Cough, Weight decreased, Diarrhoea, Viral upper respiratory tract infection, Glaucoma, Anal incontinence, Mobility decreased, Atrial fibrillation, Fall, Gastroenteritis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
人工関節周囲骨折	LEFT SIDED PERI-PROSTHETIC HIP FRACTURE	Day 816 / NA	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
心不全	WORSENING HEART FAILURE	NA / Start Day +73 Days	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
治験責任医師の見解：「人工関節周囲骨折」及び「心不全」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 5[redacted]
Medical History [1]: Migraine, Hip arthroplasty, Chronic obstructive pulmonary disease, Carpal tunnel decompression, Carpal tunnel decompression, Cardiac amyloidosis, Cholecystectomy, Manipulation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 893		
Concomitant Medication [3]: BUDESONIDE/FORMOTEROL FUMARATE, SALBUTAMOL, PARACETAMOL, BISOPROLOL, DAPAGLIFLOZIN, BISOPROLOL, OMEPRAZOLE, COLECALCIFEROL, EPLERENONE, ATORVASTATIN, FUROSEMIDE, OMEPRAZOLE, BISOPROLOL, NADOLOL, CODEINE PHOSPHATE/PARACETAMOL, PARACETAMOL, CLOTRIMAZOLE/FLUCONAZOLE				
Non-Serious Adverse Event [4]: Cardiac failure, Ventricular tachycardia, COVID-19, Gastrooesophageal reflux disease, Balanitis candida, Orthostatic hypotension, Upper respiratory tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心室性頻脈（1）	VENTRICULAR TACHYCARDIA	Day 325 / Day 330	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心室性頻脈（2）	VENTRICULAR TACHYCARDIA	Day 387 / Day 392	Not Related	Dose Not Changed	Recovered /Resolved	Mild
心室性頻脈（3）	VENTRICULAR TACHYCARDIA	Day 408 / Day 421	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心室性頻脈（4）	VENTRICULAR TACHYCARDIA	Day 808 / Day 808	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心室性頻脈（1）」、「心室性頻脈（2）」、「心室性頻脈（3）」及び「心室性頻脈（4）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: UK	Sex: M	Age: 7[redacted]
Medical History [1]: Chronic kidney disease, Carpal tunnel syndrome, Eye operation, Knee arthroplasty, Knee arthroplasty, Hypercholesterolaemia, Cardiac amyloidosis, Spinal stenosis, Implantable defibrillator insertion				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 469			
Concomitant Medication [3]: PREGABALIN, ACETYLSALICYLIC ACID, RAMIPRIL, FUROSEMIDE, SIMVASTATIN, EPLERENONE, GABAPENTIN, AMOXICILLIN/CLAVULANATE POTASSIUM, BUMETANIDE, BUMETANIDE, BUMETANIDE, APIXABAN, AMIODARONE, AMIODARONE, AMIODARONE, ATORVASTATIN, MIRTAZAPINE, ROSUVASTATIN, FLUCLOXACILLIN, FUROSEMIDE, METOLAZONE, DIGOXIN, FUROSEMIDE, BENDROFLUMETHIAZIDE, LINAGLIPTIN, ANTIBIOTICS, DIURETICS				
Non-Serious Adverse Event [4]: Dyskinesia, Cardiac failure, Anxiety, Eye infection, Atrial fibrillation, Urinary incontinence, Acute kidney injury, Depression, Urinary tract infection, Cellulitis, Diabetes mellitus, Adverse drug reaction, Fall, Hypophagia, Spinal stenosis, Hyponatraemia, Acute kidney injury, Cardiac failure, Constipation, Pneumonia, Acute kidney injury, Haematuria, Seborrhoeic dermatitis, Pneumonia, Hypokalaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
失神（1）	SYNCOPE	Day 147 / Day 149	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
失神（2）	SYNCOPE	Day 166 / Day 169	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（1）	DECOMPENSATED HEART FAILURE	Day 207 / Day 212	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 354 / Day 364	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
蜂巣炎	RIGHT ARM CELLULITIS	Day 469 / Day 510	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
滑液包炎	OLECRANON BURSITIS	Day 469 / Day 510	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「失神（1）」、「失神（2）」、「心不全（1）」、「心不全（2）」、「蜂巣炎」及び「滑液包炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 8[redacted]
Medical History [1]: Diabetes mellitus, Chronic obstructive pulmonary disease, Hypertension, Atrial fibrillation, Cardiac failure, Cardiac amyloidosis, Cardiac failure, Cardiac failure, Cardiac resynchronisation therapy, Cardiac failure				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 379		
Concomitant Medication [3]: TIOTROPIUM BROMIDE, PANTOPRAZOLE, RIVAROXABAN, RAMIPRIL, BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, ALLOPURINOL, OXYGEN, FUROSEMIDE, ASCORBIC ACID/FERRIC PYROPHOSPHATE/VITAMIN B12 NOS, PARNAPARIN SODIUM, PROTON PUMP INHIBITORS, FERRIC CARBOXYMALTOSE, RED BLOOD CELLS, FONDAPARINUX, OMEPRAZOLE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Fall, Gastrointestinal haemorrhage, Facial bones fracture, Fall, Abdominal pain upper, Dyspnoea, Dyspnoea, Dyspnoea, Dyspnoea				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
背部損傷	LUMBAR TRAUMA	Day 93 / Day 103	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Moderate
上部消化管出血	UPPER GASTROINTESTINAL BLEEDING	Day 224 / Day 248	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全（1）	WORSENING OF HEART FAILURE	Day 268 / Day 272	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
急性心不全	ACUTE HEART FAILURE	Day 292 / Day 296	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心不全（2）	WORSENING OF HEART FAILURE	Day 379 / Day 383	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「背部損傷」、「上部消化管出血」、「心不全（1）」、「急性心不全」及び「心不全（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: F	Age: 7[redacted]	
Medical History [1]: Thyroid disorder, Dyspepsia, Heart rate increased, Hypercholesterolaemia, Chronic kidney disease, Hypertension, Chest pain, Dyspnoea exertional, Hiatus hernia, Splenic artery aneurysm, Cholelithiasis, Cancer surgery, Cardiac amyloidosis, Sinus bradycardia, Mitral valve disease, Bronchitis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897			
Concomitant Medication [3]: RAMIPRIL, BRINZOLAMIDE, FUROSEMIDE, ANASTROZOLE, ALLOPURINOL, CANRENONE, MAGALDRATE, COVID-19 VACCINE, COVID-19 VACCINE, LEVOTHYROXINE SODIUM, LEVOTHYROXINE SODIUM, AMOXICILLIN/CLAVULANATE POTASSIUM, FOLIC ACID, RAMIPRIL					
Non-Serious Adverse Event [4]: Bronchitis, Oedema peripheral, Post procedural infection, Influenza					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
悪性黒色腫	MALIGNANT MELANOMA	Day 639 / Day 720	Not Related	Unknown	Recovered /Resolved	Mild
治験責任医師の見解：「悪性黒色腫」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Italy	Sex: M	Age: 7[redacted]
Medical History [1]: Retinal detachment, Diverticulum intestinal, Gastrooesophageal reflux disease, Large intestine polyp, Drug hypersensitivity, Drug hypersensitivity, Urethral meatus stenosis, Appendicectomy, Phlebectomy, Hypertension, Mitral valve incompetence, Polypectomy, Endocarditis, Aortic valve replacement, Mitral valve replacement, Pulmonary valve replacement, Atrial fibrillation, Pulmonary hypertension, Urethral operation, Syncope, Cardiac pacemaker insertion, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: PANTOPRAZOLE, BISOPROLOL, SILODOSIN, DELORAZEPAM, VALSARTAN, RIVAROXABAN, COVID-19 VACCINE, ACETYLSALICYLIC ACID, CLOPIDOGREL, BISOPROLOL, SPIRONOLACTONE, FUROSEMIDE, DELORAZEPAM, COVID-19 VACCINE, ENOXAPARIN, WARFARIN SODIUM, BISOPROLOL, DIGOXIN, SPIRONOLACTONE, RIVAROXABAN, VALSARTAN, EPLERENONE, Not coded: Tafamidis, TAFAMIDIS, BACILLUS COAGULANS/FRUCTOOLIGOSACCHARIDES/LACTOBACILLUS ACIDOPHILUS/LACTOBACILLUS RHAMNOSUS, CEFIXIME, CODEINE, PARACETAMOL				
Non-Serious Adverse Event [4]: Thrombocytopenia, Proteinuria, Proteinuria, Urethral stricture post infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
冠動脈疾患	CORONARY ARTERY DISEASE	Day 107 / Day 180	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「冠動脈疾患」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 7[redacted]
Medical History [1]: Oedema peripheral, Tendon rupture, False positive investigation result, Hyperuricaemia, Osteoarthritis, Osteoarthritis, Pain in extremity, Stasis dermatitis, Large intestinal polypectomy, Varicose vein operation, Hypertension, Carpal tunnel decompression, Joint prosthesis user, Chronic obstructive pulmonary disease, Glottis carcinoma, Atrial fibrillation, Cardiac pacemaker insertion, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 898		
Concomitant Medication [3]: LOSARTAN, APIXABAN, ALLOPURINOL, TIOTROPIUM BROMIDE MONOHYDRATE, PANTOPRAZOLE, BISOPROLOL, EPLERENONE, FUROSEMIDE, ATORVASTATIN, LEVOFLOXACIN, LEVOFLOXACIN, INFLUENZA VACCINE, COVID-19 VACCINE, CEFDITOREN, ACETYLCYSTEINE, ATORVASTATIN/EZETIMIBE				
Non-Serious Adverse Event [4]: Asthenia, Rhinorrhoea, Diarrhoea, Upper respiratory tract infection, Carotid artery stenosis				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
細菌性肺炎	BACTERIAL PENUMONIA	Day 187 / Day 191	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「細菌性肺炎」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Spain	Sex: M	Age: 8[redacted]
Medical History [1]: Cardiac failure, Proctitis, Pneumonia, Depression, Benign prostatic hyperplasia, Transurethral prostatectomy, Carpal tunnel decompression, Atrial fibrillation, Respiratory failure, Liver disorder, Asthma, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 904			
Concomitant Medication [3]: ACENOCOUMAROL, ACENOCOUMAROL, FUROSEMIDE, FLUVOXAMINE, LORAZEPAM, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, FLUTICASONE PROPIONATE, FUROSEMIDE, FUROSEMIDE, FLUVOXAMINE, PANTOPRAZOLE, FUROSEMIDE, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, MUPIROCIN, DICLOFENAC, ACECLOFENAC, SPIRONOLACTONE, COVID-19 VACCINE, PANTOPRAZOLE, AZITHROMYCIN, CEFTRIAXONE, REMDESIVIR, FUROSEMIDE, PARACETAMOL, BUDESONIDE, BEMIPARIN SODIUM, ONDANSETRON, DOMPERIDONE, MACROGOL 4000, ASPARTIC ACID/POTASSIUM ASCORBATE, FUROSEMIDE, FUROSEMIDE, FLUTICASONE PROPIONATE, PANTOPRAZOLE, CEFAZOLIN, PARACETAMOL, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, FUROSEMIDE, TAMSULOSIN, ASPARTIC ACID/POTASSIUM ASCORBATE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FLUVOXAMINE, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, LEVOFLOXACIN, LEVOFLOXACIN, BEMIPARIN SODIUM, FUROSEMIDE, FUROSEMIDE, FLUTICASONE PROPIONATE, ASCORBIC ACID/ASPARTIC ACID/POTASSIUM, LEVOFLOXACIN, FUROSEMIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMIKACIN, PANTOPRAZOLE, PARACETAMOL, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, PARACETAMOL, PREDNISONE, FUROSEMIDE, GLYCOPYRRONIUM BROMIDE/INDACATEROL MALEATE, PREDNISONE, PREDNISONE, PREDNISONE, ACENOCOUMAROL, SPIRONOLACTONE, SPIRONOLACTONE, FUROSEMIDE, SPIRONOLACTONE, EMPAGLIFLOZIN, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Bursitis, Respiratory tract infection viral, Epicondylitis, Diarrhoea				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	HEART FAILURE DECOMPENSATION	Day 43 / Day 47	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
ＣＯＶＩＤ－１９肺炎	COVID-19 PNEUMONIA	Day 351 / Day 359	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心房細動	WORSENING ATRIAL FIBRILATION	Day 548 / Day 557	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 563 / Day 577	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（3）	CARDIAC INSUFICIENCY	Day 612 / Day 614	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（4）	HEART FAILURE	Day 758 / Day 761	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（5）	HEART FAILURE DESCOMPENSATION	Day 828 / Day 834	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心不全（1）」、「ＣＯＶＩＤ－１９肺炎」、「心房細動」、「心不全（2）」、「心不全（3）」、「心不全（4）」及び「心不全（5）」は治験薬と関連なしと判断した。

Patient ID: [redacted]					
Treatment Arm: Placebo	Race: White	Country: Brazil	Sex: M	Age: 8[redacted]	
Medical History [1]: Bundle branch block left, Ventricular extrasystoles, Dyspepsia, Varicocele repair, Vasectomy, Gout, Osteoarthritis, Benign prostatic hyperplasia, Amyloidosis					
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902			
Concomitant Medication [3]: ESOMEPRAZOLE, FAMOTIDINE, COLECALCIFEROL, DOXAZOSIN MESILATE, LYCOPENE, ALLOPURINOL, OXACEPROL, PRIMIDONE, DOXAZOSIN/FINASTERIDE, METOPROLOL SUCCINATE, FUROSEMIDE, MAGNESIUM PIDOLATE, COVID-19 VACCINE, COVID-19 VACCINE, COVID-19 VACCINE, AZITHROMYCIN, ESOMEPRAZOLE SODIUM, MIKANIA GLOMERATA, APIXABAN					
Non-Serious Adverse Event [4]: Paraesthesia, Gastrooesophageal reflux disease, COVID-19, Nasopharyngitis					
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	BRONCHOPNEUMONIA	Day 664 / Day 675	Not Related	Dose Not Changed	Recovered /Resolved	Severe
網膜動脈閉塞	CENTRAL RETINAL ARTERY OCCLUSION	Day 810 / Day 813	Not Related	Dose Not Changed	Recovered /Resolved With Sequelae	Moderate
治験責任医師の見解：「肺炎」及び「網膜動脈閉塞」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Brazil	Sex: F	Age: 8[redacted]
Medical History [1]: Hip arthroplasty, Hip arthroplasty, Dyslipidaemia, Carpal tunnel decompression, Retinal detachment, Visual acuity reduced, Vitamin D deficiency, Intervertebral disc protrusion, Cardiac failure, Hypothyroidism, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 934		
Concomitant Medication [3]: VITAMIN D NOS, CHLORTALIDONE, ROSUVASTATIN, LEVOTHYROXINE, AZITHROMYCIN, PREDNISONE, EDOXABAN TOSILATE, AMIODARONE, COVID-19 VACCINE, LIDOCAINE, EDOXABAN TOSILATE, COVID-19 VACCINE, FUROSEMIDE, Not coded: Tafamidis, TAFAMIDIS, LEVETIRACETAM, LACOSAMIDE, CEFTRIAXONE, MEROPENEM, LINEZOLID, LEVETIRACETAM				
Non-Serious Adverse Event [4]: Upper respiratory tract infection, Atrial fibrillation, Intervertebral disc protrusion, Hypoaesthesia, Cardiac failure chronic, Age-related macular degeneration, Visual acuity reduced, Urinary tract infection, Seizure, Pneumonia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
頭蓋脳損傷	TRAUMATIC CRANIOENCEPHALIC	Day 877 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe
徐脈性不整脈	SYNCOPE DUE TO BRADYARRHYTHMIA	Day 877 / Day 921	Not Related	Dose Not Changed	Recovered/ Resolved	Severe
硬膜下血腫	SUBDURAL HEMATOMA	Day 886 / NA	Not Related	Dose Not Changed	Recovering /Resolving	Severe

治験責任医師の見解：「頭蓋脳損傷」、「徐脈性不整脈」及び「硬膜下血腫」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Benign prostatic hyperplasia, Psoriasis, Hypertension, Hypercholesterolaemia, Carpal tunnel decompression, Osteoarthritis, Spinal stenosis, Actinic keratosis, Carpal tunnel decompression, Squamous cell carcinoma, Coronary arterial stent insertion, Coronary artery disease, Muscle atrophy, Atrial fibrillation, Cardiac amyloidosis, Cardiac failure congestive, Haematuria, Blood alkaline phosphatase increased				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ATORVASTATIN CALCIUM, APIXABAN, AMIODARONE, SPIRONOLACTONE, FUROSEMIDE, FUROSEMIDE, INFLUENZA VACCINE INACT SPLIT 3V, FUROSEMIDE, FICUS CARICA SEED DRY EXTRACT/PHOENIX DACTYLIFERA/SENNA ALEXANDRINA LEAF POWDER, GLYCEROL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, DOCUSATE SODIUM/SENNOSIDE B, CLOBETASOL, DOCUSATE SODIUM/SENNOSIDE B, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, PANTOPRAZOLE, NIZATIDINE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, APIXABAN, COVID-19 VACCINE				
Non-Serious Adverse Event [4]: Upper respiratory tract infection, Presyncope, Gynaecomastia, Raynaud's phenomenon, Bowen's disease, Larynx irritation, Constipation, Dysphagia, Fatigue, Constipation, Hypervolaemia, Contusion				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
良性前立腺肥大症	WORSENING OF BENIGN PROSTATIC HYPERPLASIA	Day 213 / Day 221	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「良性前立腺肥大症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 6[redacted]
Medical History [1]: Spinal laminectomy, Spinal laminectomy, Carpal tunnel decompression, Carpal tunnel decompression, Gout, Arthroscopy, Arthroscopy, Inguinal hernia, Pleural fibrosis, Polyp, Bursitis, Osteoarthritis, Colonoscopy, Cardiac failure, Dyspnoea exertional, Cardiac amyloidosis, Gamma-glutamyltransferase increased				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: DICLOFENAC, PARACETAMOL, FUROSEMIDE, PREDNISOLONE, PREDNISOLONE, IBUPROFEN, CEFAZOLIN, ENOXAPARIN, PARECOXIB, DEXAMETHASONE, FUROSEMIDE, PANTOPRAZOLE, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, ENOXAPARIN, ACETYLSALICYLIC ACID, TICAGRELOR, METOPROLOL, DIGOXIN, AMIODARONE, CEFAZOLIN, HEPARIN, MAGNESIUM SULFATE, POTASSIUM PHOSPHATE MONOBASIC, SODIUM PHOSPHATE MONOBASIC (ANHYDROUS), AMIODARONE, AMIODARONE, NOREPINEPHRINE, MILRINONE, FUROSEMIDE, LEVOSIMENDAN, TEMAZEPAM, DOCUSATE/SENNOSIDE A+B, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, APIXABAN, DIGOXIN, VANCOMYCIN, ESMOLOL, MELATONIN, METOPROLOL, METOPROLOL, METOPROLOL, FUROSEMIDE, METOPROLOL, AMIODARONE, FUROSEMIDE, AMIODARONE, FUROSEMIDE, DIGOXIN, FUROSEMIDE, DIGOXIN, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, AMIODARONE, DIGOXIN, FUROSEMIDE, DIGOXIN, DIGOXIN, WARFARIN, METOPROLOL, PANTOPRAZOLE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, FUROSEMIDE, METOPROLOL, FUROSEMIDE, FUROSEMIDE, METARAMINOL TARTRATE, AMIODARONE, FUROSEMIDE, FUROSEMIDE, MOMETASONE FUROATE, COVID-19 VACCINE, FUROSEMIDE, AMIODARONE, INFLUENZA VACCINE INACT SAG 4V, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, AMIODARONE				
Non-Serious Adverse Event [4]: Peripheral swelling, Osteoarthritis, Rheumatoid arthritis, Gamma-glutamyltransferase increased, Haemorrhoids, Groin pain, Pleural effusion, Dyspnoea exertional, Inflammatory marker increased, Atrial thrombosis, Insomnia, Acute kidney injury, Haematuria, Hyponatraemia, Constipation, Anaemia, Exercise tolerance decreased, Nausea, Hyperlactacidaemia, Liver function test abnormal, Coagulopathy, Medical device site necrosis, Blood alkaline phosphatase increased, Blood bilirubin increased, Chronic kidney disease, Hypervolaemia, Atrial flutter, Paranasal sinus inflammation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
絞扼性鼠径ヘルニア	R) STRANGULATED INGUINAL HERNIA	Day 343 / Day 345	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心房細動	RAPID AF WITH RAPID VENTRICULAR RESPONSE(PREVIOUSLY CALLED CHEST PAIN)	Day 434 / Day 451	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心原性ショック（1）	CARDIOGENIC SHOCK	Day 440 / Day 451	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心不全（1）	DECOMPENSATED HEART FAILURE	Day 457 / Day 461	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

心不全（2）	DECOMPENSATED HEART FAILURE	Day 476 / Day 479	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心原性ショック（2）	CARDIOGENIC SHOCK	Day 531 / Day 540	Not Related	Drug Interrupted	Recovered /Resolved	Severe
急性腎障害	ACUTE KIDNEY INJURY	Day 531 / Day 593	Not Related	Drug Interrupted	Recovered /Resolved	Severe
心タンポナーデ	PERICARDIAL EFFUSION WITH TAMPONADE	Day 532 / Day 533	Not Related	Drug Interrupted	Recovered /Resolved	Severe
外傷性血胸	LEFT HAEMOHYDROPNEUMOTHORAX	Day 532 / Day 538	Not Related	Drug Interrupted	Recovered /Resolved	Severe
血液量増加症	FLUID OVERLOAD	Day 589 / Day 593	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房粗動	ATRIAL FLUTTER - SYMPTOMATIC	Day 749 / Day 755	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心原性ショック（3）	CARDIOGENIC SHOCK	Day 751 / Day 751	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「絞扼性臍径ヘルニア」、「心房細動」、「心原性ショック（1）」、「心不全（1）」、「心不全（2）」、「心原性ショック（2）」、「急性腎障害」、「心タンポナーデ」、「外傷性血胸」、「血液量増加症」、「心房粗動」及び「心原性ショック（3）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Sleep apnoea syndrome, Gout, Carpal tunnel syndrome, Cholecystitis, Carpal tunnel decompression, Cholecystectomy, Atrial fibrillation, Benign prostatic hyperplasia, Depression, Skin papilloma, Papilloma excision, Squamous cell carcinoma of skin, Skin neoplasm excision, Actinic keratosis, Skin lesion removal, Basal cell carcinoma, Skin neoplasm excision, Seborrhoeic keratosis, Actinic keratosis, Skin lesion removal, Skin lesion removal, Actinic keratosis, Skin lesion removal, Actinic keratosis, Neuropathy peripheral, Oedema peripheral, Cardiac amyloidosis, Obesity, Cardiac failure				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 896		
Concomitant Medication [3]: OXYGEN, ALLOPURINOL, RIVAROXABAN, DUTASTERIDE/TAMSULOSIN HYDROCHLORIDE, MIRTAZAPINE, FUROSEMIDE, METOPROLOL, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, NICOTINAMIDE, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, FUROSEMIDE, TAMSULOSIN, SALBUTAMOL, IPRATROPIUM BROMIDE, AMOXICILLIN, DOXYCYCLINE, AMOXICILLIN, DOXYCYCLINE, INFLUENZA VACCINE, VITAMIN B12 NOS, THIOCTIC ACID, ACETYLCARNITINE, MIRTAZAPINE, CEFUROXIME, COVID-19 VACCINE, MIRTAZAPINE, COVID-19 VACCINE, VITAMIN D NOS, COVID-19 VACCINE, PANTOPRAZOLE, CLOPIDOGREL, RAMIPRIL, NEBIVOLOL, PARACETAMOL, ACETYLSALICYLIC ACID, GLYCERYL TRINITRATE, MORPHINE, MORPHINE, ACETYLSALICYLIC ACID, FUROSEMIDE, FUROSEMIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, ADRENERGIC AND DOPAMINERGIC AGENTS, FUROSEMIDE, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, DOCUSATE SODIUM/SENNOSIDE A+B, METRONIDAZOLE, CEFTRIAXONE, TRAMADOL, FUROSEMIDE, TRAMADOL, FENTANYL, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, TAPENTADOL, FUROSEMIDE, PARACETAMOL, NALOXONE HYDROCHLORIDE/OXYCODONE HYDROCHLORIDE, PLANTAGO OVATA, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, POTASSIUM CHLORIDE, MIRTAZAPINE, INFLUENZA VACCINE, SPIRONOLACTONE, COVID-19 VACCINE, SPIRONOLACTONE, DOCUSATE SODIUM/SENNOSIDE A+B, POTASSIUM CHLORIDE, ROSUVASTATIN, POTASSIUM CHLORIDE				
Non-Serious Adverse Event [4]: Dysgeusia, Hypokalaemia, Dyspnoea at rest, Pneumonia, Lower respiratory tract infection, Oedema peripheral, Atrial fibrillation, Renal impairment, Myocardial ischaemia, Arteriosclerosis, Cardiac failure acute, Hypokalaemia, Procedural pain, Constipation, Pneumonia, Skin lesion, Pleural effusion, Constipation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
筋骨格系胸痛	MUSCULOSKELETAL CHEST PAIN	Day 288 / Day 292	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
急性心筋梗塞	ANTERIOR STEMI	Day 701 / Day 726	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
心停止	VENTRICULAR FIBRILLATION ARREST	Day 703 / Day 726	Not Related	Drug Interrupted	Recovered /Resolved	Severe

治験責任医師の見解：「筋骨格系胸痛」、「急性心筋梗塞」及び「心停止」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Scoliosis, Hypercholesterolaemia, Prostate cancer, Radical prostatectomy, Gout, Hearing aid user, Hip arthroplasty, Pancreatic carcinoma, Pancreatectomy, Splenectomy, Muscle spasms, Bursitis, Skin neoplasm excision, Gastrooesophageal reflux disease, Hypertension, Actinic keratosis, Cardiac amyloidosis, Bundle branch block right				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 897		
Concomitant Medication [3]: PARACETAMOL, FISH OIL, CALCIUM CARBONATE/COLECALCIFEROL, CALCIUM/COLECALCIFEROL/MAGNESIUM, OMEPRAZOLE, TELMISARTAN, AMLODIPINE, FERROUS FUMARATE, ATORVASTATIN, OMEPRAZOLE, ESOMEPRAZOLE MAGNESIUM, INDOMETACIN, COVID-19 VACCINE, ESOMEPRAZOLE MAGNESIUM, INFLUENZA VACCINE, COVID-19 VACCINE, METHYLPREDNISOLONE ACEPONATE, IBUPROFEN, OXYCODONE, PARACETAMOL, COVID-19 VACCINE, FUROSEMIDE, ATORVASTATIN, INFLUENZA VACCINE, COVID-19 VACCINE, INDOMETACIN, BISACODYL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, NADROPARIN CALCIUM, RED BLOOD CELLS (CONCENTRATED), ETORICOXIB, BACLOFEN, TEMAZEPAM, MUPIROCIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, OXYCODONE, SULFAMETHOXAZOLE, TRIMETHOPRIM, RIVAROXABAN, TAPENTADOL HYDROCHLORIDE, FUROSEMIDE, DOCUSATE SODIUM/SENNOSIDE A+B, FENTANYL, PROPOFOL, MIDAZOLAM, ENOXAPARIN SODIUM, OXYCODONE, NALOXONE, ENOXAPARIN SODIUM, GENTAMICIN, CEFTRIAXONE, BUPRENORPHINE, ONDANSETRON, FENTANYL, MIDAZOLAM, LACTULOSE, GENTAMICIN, VANCOMYCIN, CEFAZOLIN, ALBUMIN HUMAN, FUROSEMIDE, PARACETAMOL, FENTANYL, GENTAMICIN, TAPENTADOL HYDROCHLORIDE, MENTHA X PIPERITA OIL, GENTAMICIN, APIXABAN				
Non-Serious Adverse Event [4]: Trifascicular block, Basal cell carcinoma, Neurodermatitis, Barrett's oesophagus, Post vaccination syndrome, Hand fracture, Haematoma, Carpal tunnel syndrome, Tendon rupture, Back pain, Constipation, Anaemia, Cardiac failure, Cardiac failure, Non-cardiac chest pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
塞栓性脳卒中	EMBOLIC STROKE	Day 737 / Day 745	Not Related	Drug Interrupted	Recovered /Resolved	Severe
人工関節周囲骨折	PERIPROSTHETIC HIP FRACTURE	Day 737 / Day 750	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
医療機器位置異常	RECURRENT LEFT HIP DISLOCATION	Day 766 / Day 845	Not Related	NA	Recovered /Resolved With Sequelae	Moderate
肺塞栓症	PULMONARY EMBOLUS	Day 787 / NA	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「塞栓性脳卒中」、「人工関節周囲骨折」、「医療機器位置異常」及び「肺塞栓症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 7[redacted]
Medical History [1]: Meningitis, Gout, Pulmonary embolism, Carpal tunnel decompression, Carpal tunnel syndrome, Deep vein thrombosis, Lipoma, Spinal laminectomy, Spinal decompression, Carpal tunnel decompression, Polyp, Haemorrhoids, Intervertebral disc degeneration, Radiculopathy, Deafness bilateral, Ear haemorrhage, Carpal tunnel decompression, Atrial fibrillation, Skin papilloma, Cardiac failure, Hypothyroidism, Chronic kidney disease, Hypertension, Cataract, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 890			
Concomitant Medication [3]: WARFARIN, FUROSEMIDE, VITAMIN D NOS, ALLOPURINOL, FUROSEMIDE, CHLOROBUTANOL/MACROGOL/MACROGOL STEARATE, INFLUENZA VACCINE, COVID-19 VACCINE, CHLORAMPHENICOL, NEPAFENAC, DEXAMETHASONE, FUROSEMIDE, CHLORAMPHENICOL, NEPAFENAC, DEXAMETHASONE, FUROSEMIDE, FLUOROMETHOLONE, FLUOROMETHOLONE, CHLOROBUTANOL/MACROGOL/MACROGOL STEARATE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, FUROSEMIDE, LEVOTHYROXINE SODIUM, FUROSEMIDE, COVID-19 VACCINE, CLINDAMYCIN, SODIUM POLYSTYRENE SULFONATE, FUROSEMIDE, CLINDAMYCIN, WARFARIN, METARAMINOL, FENTANYL, PROPOFOL, FUROSEMIDE, LINCOMYCIN, HYDROCORTISONE ACETATE, CLINDAMYCIN, FUROSEMIDE, COLECALCIFEROL, VITAMIN D NOS, LEVOTHYROXINE, FUROSEMIDE, ALLOPURINOL, LEVOTHYROXINE, FUROSEMIDE, SALBUTAMOL, FUROSEMIDE, COLCHICINE, COLCHICINE, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Peripheral swelling, Ocular hyperaemia, Blood creatine phosphokinase increased, Post procedural erythema, Cardiac failure, Hypothyroidism, Fall, Skin lesion, Hyperkalaemia, Hypervolaemia, Confusional state, Stasis dermatitis, Fractured sacrum, Renal impairment, Fall, Haematoma, Dehydration, Hypernatraemia, Iron deficiency anaemia, Gout, Skin laceration, Cognitive disorder, Pleural effusion, Decubitus ulcer, Hypernatraemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
皮膚感染	MULTIPLE INFECTED SKIN LESIONS BILATERAL LOWER LEGS	Day 638 / Day 658	Not Related	Dose Not Changed	Recovered /Resolved	Severe
基底細胞癌	ULCERATED NODULAR BASAL CELL CARCINOMA	Day 644 / Day 658	Not Related	Dose Not Changed	Recovered /Resolved	Severe
植皮感染	INFECTED SKIN GRAFT	Day 678 / Day 686	Not Related	Dose Not Changed	Recovered /Resolved	Severe
無力症	PHYSICAL FRAILTY	Day 724 / Day 742	Not Related	Drug Interrupted	Recovered /Resolved With Sequelae	Severe
血液量増加症	FLUID OVERLOADED	Day 735 / Day 742	Not Related	Drug Interrupted	Recovered /Resolved	Moderate
交通事故	LOW SPEED MOTOR VEHICLE ACCIDENT	Day 822 / Day 822	Not Related	Dose Not Changed	Recovered /Resolved	Mild
急性腎障害	ACUTE KIDNEY INJURY	Day 890 / Day 896	Not Related	Dose Not Changed	Recovered /Resolved	Severe

治験責任医師の見解：「皮膚感染」、「基底細胞癌」、「植皮感染」、「無力症」、「血液量増加症」、「交通事故」及び「急性腎障害」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: F	Age: 6[redacted]
Medical History [1]: Dextrocardia, Carpal tunnel syndrome, Carpal tunnel decompression, Cardiac failure, Cardiac amyloidosis, Atrial flutter, Back pain				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 645		
Concomitant Medication [3]: TEMAZEPAM, RAMIPRIL, SPIRONOLACTONE, MAGNESIUM, RIVAROXABAN, NEBIVOLOL, FUROSEMIDE, OMEPRAZOLE, ACETYLSALICYLIC ACID, FUROSEMIDE, PRUNUS SPP./SENNA SPP. LEAF, COVID-19 VACCINE, ESTRADIOL, PARACETAMOL, METOCLOPRAMIDE, FLUCONAZOLE, FUROSEMIDE, CALCIUM CARBONATE, ALUMINIUM HYDROXIDE/MAGNESIUM HYDROXIDE/MAGNESIUM TRISILICATE, CALCIUM CARBONATE/SODIUM ALGINATE/SODIUM BICARBONATE, LACTULOSE, Not coded: Tafamidis, TAFAMIDIS, OMEPRAZOLE, MAGNESIUM, WARFARIN, GLYCERYL TRINITRATE, FERRIC CARBOXYMALTOSE, FUROSEMIDE, FUROSEMIDE, DAPAGLIFLOZIN, FUROSEMIDE, ESCITALOPRAM				
Non-Serious Adverse Event [4]: Dizziness, Neck pain, Exercise tolerance decreased, Cough, Gastrooesophageal reflux disease, Fatigue, Epistaxis, Wrist fracture, Gastrooesophageal reflux disease, Iron deficiency anaemia, Liver function test abnormal, Delirium, Pleural effusion, Subclavian vein thrombosis, Atrial fibrillation, Steroid diabetes, Urinary tract infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心不全（1）	DECOMPENSATED HEART FAILURE	Day 501 / Day 518	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（2）	DECOMPENSATED HEART FAILURE	Day 519 / Day 522	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（3）	DECOMPENSATED HEART FAILURE	Day 552 / Day 646	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全（4）	DECOMPENSATED HEART FAILURE	Day 646 / Day 646	Not Related	Drug Withdrawn	Recovered /Resolved	Severe
治験責任医師の見解：「心不全（1）」、「心不全（2）」、「心不全（3）」及び「心不全（4）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Arthroscopy, Hip arthroplasty, Myocardial ischaemia, Dyslipidaemia, Gout, Benign prostatic hyperplasia, Aortic stenosis, Hypertension, Large intestine polyp, Iron deficiency anaemia, Gastrooesophageal reflux disease, Diabetes mellitus, Back pain, Neuropathy peripheral, Cardiac amyloidosis, Cardiac failure, Atrial fibrillation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 895		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, ALLOPURINOL, PREGABALIN, ESOMEPRAZOLE, METFORMIN, DULAGLUTIDE, GLICLAZIDE, NORTRIPTYLINE, FUROSEMIDE, APIXABAN, AMIODARONE, APIXABAN, DOCUSATE SODIUM/SENNOSIDE A+B, SODIUM PHOSPHATE DIBASIC/SODIUM PHOSPHATE MONOBASIC, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, TEMAZEPAM, SPIRONOLACTONE, RAMIPRIL, RAMIPRIL, BISOPROLOL, ONDANSETRON, OFLOXACIN, LEVOTHYROXINE SODIUM, PREGABALIN, FUROSEMIDE, DOCUSATE SODIUM/SENNOSIDE A+B, ACETYLSALICYLIC ACID, CLOPIDOGREL, GLYCERYL TRINITRATE, TEMAZEPAM, TEMAZEPAM, HEPARIN, HEPARIN, ACETYLSALICYLIC ACID, CLOPIDOGREL, PARACETAMOL, LIDOCAINE, TEMAZEPAM, TAPENTADOL, EMPAGLIFLOZIN, SPIRONOLACTONE, IRBESARTAN, GLICLAZIDE				
Non-Serious Adverse Event [4]: Open globe injury, Hypothyroidism, Acute kidney injury, Lethargy, Nausea, Orthostatic hypotension, Dyspnoea, Dizziness, Dyspnoea, Anaemia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
便秘	CONSTIPATION	Day 62 / Day 71	Not Related	Dose Not Changed	Recovered /Resolved	Mild
急性心筋梗塞	NON ST ELEVATION MI	Day 290 / Day 294	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「便秘」及び「急性心筋梗塞」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Australia	Sex: M	Age: 8[redacted]
Medical History [1]: Hip arthroplasty, Skin cancer, Diverticulum, Colonoscopy, Gastrooesophageal reflux disease, Cardiac failure, Macular degeneration, Hypercholesterolaemia, Sleep apnoea syndrome, Hypertension, Atrial fibrillation, Coronary artery disease, Colonoscopy, Aortic valve replacement, Colonoscopy, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: ASCORBIC ACID/CUPRIC OXIDE/TOCOPHERYL ACID SUCCINATE/ZINC OXIDE, APIXABAN, VALSARTAN, SOTALOL, AMLODIPINE, FUROSEMIDE, FUROSEMIDE, SIMVASTATIN, VITAMIN B NOS, COLECALCIFEROL/RETINOL, BUPRENORPHINE, INFLUENZA VACCINE, FUROSEMIDE, FUROSEMIDE, COVID-19 VACCINE, ONDANSETRON, SODIUM BICARBONATE, CEFALEXIN, FUROSEMIDE, FUROSEMIDE, TAPENTADOL, PARACETAMOL, DOCUSATE SODIUM/SENNOSIDE A+B, LACTULOSE, NICOTINAMIDE, FLUCLOXACILLIN, CLINDAMYCIN, BUPRENORPHINE, SODIUM CITRATE/SODIUM LAURYL SULFOACETATE/SORBITOL, SODIUM PHOSPHATE DIBASIC/SODIUM PHOSPHATE MONOBASIC, PIPERACILLIN SODIUM/TAZOBACTAM SODIUM, VANCOMYCIN, TRANEXAMIC ACID, FACTOR II (PROTHROMBIN)/FACTOR IX COMPLEX HUMAN/FACTOR VII (PROCONVERTIN)/FACTOR X (STUART PROWER FACTOR), APIXABAN, FENTANYL, MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE, HEPARIN, AMOXICILLIN/CLAVULANIC ACID, VALSARTAN, NEBIVOLOL				
Non-Serious Adverse Event [4]: Osteoarthritis, Dizziness, Acute kidney injury, Limb injury				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
四肢損傷	INJURED RIGHT SHOULDER	Day 499 / Day 577	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
心不全	DECOMPENSATED HEART FAILURE	Day 806 / Day 810	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
蜂巣炎	CELLULITIS LEFT LOWER LEG	Day 806 / Day 933	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
直腸出血	BLEEDING PER RECTUM	Day 815 / Day 817	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「四肢損傷」、「心不全」、「蜂巣炎」及び「直腸出血」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Poliomyelitis, Coronary artery disease, Hyperlipidaemia, Hypertension, Hip arthroplasty, Gout, Aortic stenosis, Cardiac failure, Glucose tolerance impaired, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 908		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, METOPROLOL, ATORVASTATIN, EZETIMIBE, FUROSEMIDE, SPIRONOLACTONE, CORTISONE, SPIRONOLACTONE, MAGNESIUM, PREDNISONE, PREDNISONE, IBUPROFEN, SPIRONOLACTONE, PREDNISONE, PREDNISONE, COVID-19 VACCINE, COVID-19 VACCINE, ALLOPURINOL, COLCHICINE, NAPROXEN, FUROSEMIDE, FUROSEMIDE, ALLOPURINOL, SPIRONOLACTONE, FUROSEMIDE, SPIRONOLACTONE, ALLOPURINOL, FUROSEMIDE, PARACETAMOL, BISOPROLOL, MELATONIN, FUROSEMIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Arthralgia, Asthenia, Abdominal discomfort, Hypervolaemia, Muscle spasms, Gout, Gout, Cough, Nipple pain, Hypervolaemia, Decreased appetite, Ageusia, SARS-CoV-2 test positive, Abdominal discomfort, Aortic stenosis, Joint stiffness, Myalgia, Atrial flutter, Left ventricular dysfunction, Weight decreased, Glossitis, Myalgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
大動脈狭窄	WORSENING AORTIC STENOSIS	Day 719 / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Severe

治験責任医師の見解：「大動脈狭窄」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: New Zealand	Sex: M	Age: 7[redacted]
Medical History [1]: Carpal tunnel decompression, Carpal tunnel decompression, Haemorrhoids, Lipid metabolism disorder, Prostate cancer, Glucose tolerance impaired, Appendicectomy, Large intestinal polypectomy, Pneumonia, Transient global amnesia, Cardiac amyloidosis, Neuropathy peripheral, Restless legs syndrome, IVth nerve paralysis, Dizziness, Cardiac failure, Arthritis, Cataract operation				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 906		
Concomitant Medication [3]: FUROSEMIDE, FUROSEMIDE, FAMCICLOVIR, CELECOXIB, ORPHENADRINE CITRATE, GABAPENTIN, CELECOXIB, COVID-19 VACCINE, COVID-19 VACCINE, FUROSEMIDE, FUROSEMIDE, CODEINE PHOSPHATE/PARACETAMOL, PROTEASE INHIBITORS, RITONAVIR, PARACETAMOL, OMEPRAZOLE, GABAPENTIN, ACETYLSALICYLIC ACID, ACETYLSALICYLIC ACID, LOPERAMIDE, ONDANSETRON, HYOSCINE BUTYLBROMIDE, GLUCONATE SODIUM/MAGNESIUM CHLORIDE HEXAHYDRATE/POTASSIUM CHLORIDE/SODIUM ACETATE TRIHYDRATE/SODIUM CHLORIDE, PARACETAMOL, FUROSEMIDE, GABAPENTIN				
Non-Serious Adverse Event [4]: Soft tissue injury, Oral herpes, Back pain, Dizziness, Neuropathy peripheral, Urticaria, Pain, Gastrointestinal viral infection, Orthostatic hypotension				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
認知症	EARLY DEMENTIA	NA / NA	Not Related	Dose Not Changed	Not Recovered /Not Resolved	Moderate
ＣＯＶＩＤ－１９	COVID-19 INFECTION REQUIRING HOSPITALISATION	Day 727 / Day 734	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「認知症」及び「ＣＯＶＩＤ－１９」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: New Zealand	Sex: M	Age: 6[redacted]
Medical History [1]: Talipes, Asthma, Massage, Carpal tunnel decompression, Meniscus removal, Osteoarthritis, Tinnitus, Tendon rupture, Rotator cuff repair, Spinal decompression, Inguinal hernia repair, Carotid endarterectomy, Peripheral vascular disorder, Gait disturbance, Fall, Cardiac amyloidosis, Dyslipidaemia, Cardiac failure, Ventricular tachycardia, Back pain, Implantable defibrillator insertion, Cardiac resynchronisation therapy				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 898		
Concomitant Medication [3]: ACETYLSALICYLIC ACID, ATORVASTATIN, BUMETANIDE, IBUPROFEN, CELECOXIB, IBUPROFEN, PARACETAMOL, SPIRONOLACTONE, BISOPROLOL, RIVAROXABAN, BISOPROLOL, Not coded: Tafamidis, COVID-19 VACCINE, TAFAMIDIS, COVID-19 VACCINE, TAFAMIDIS, EPLERENONE, EPLERENONE, FUROSEMIDE, COVID-19 VACCINE, BISOPROLOL, AMOXICILLIN/CLAVULANATE POTASSIUM, CLAVULANIC ACID, AMOXICILLIN				
Non-Serious Adverse Event [4]: Dyspnoea, Arthralgia, Spinal stenosis, Muscle strain, Haematoma infection				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動（1）	RAPID ATRIAL FIBRILLATION	Day 407 / Day 409	Not Related	Unknown	Recovered /Resolved	Moderate
心房細動（2）	RAPID ATRIAL FIBRILLATION	Day 826 / Day 829	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「心房細動（1）」及び「心房細動（2）」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Czech Republic	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Gastritis, Liver disorder, Hypergammaglobulinaemia benign monoclonal, Clavicle fracture, Fracture treatment, Migraine, Inguinal hernia repair, Testicular operation, Inguinal hernia, Hip arthroplasty, Cholecystectomy, Hypercholesterolaemia, Carpal tunnel decompression, Knee arthroplasty, Right ventricular failure, Knee arthroplasty, Osteoarthritis, Prostate cancer, Right ventricular failure, Amyloidosis, Angiocardiogram, Coronary artery disease, Cardioversion, Bundle branch block right, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 898		
Concomitant Medication [3]: PARACETAMOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, ATORVASTATIN CALCIUM, TAMSULOSIN, FINASTERIDE, PARACETAMOL/TRAMADOL HYDROCHLORIDE, POTASSIUM CHLORIDE, FUROSEMIDE, RAMIPRIL, AMIODARONE HYDROCHLORIDE, DABIGATRAN ETEXILATE MESILATE, BISOPROLOL FUMARATE, BROMAZEPAM, LACTOBACILLUS ACIDOPHILUS/LACTOBACILLUS RHAMNOSUS/SACCHAROMYCES BOULARDII, PIRITRAMIDE, CEFAZOLIN SODIUM, NADROPARIN CALCIUM, TRAMADOL HYDROCHLORIDE, TRAMADOL HYDROCHLORIDE, PARACETAMOL, PARACETAMOL, METAMIZOLE SODIUM, METAMIZOLE SODIUM, NADROPARIN CALCIUM				
Non-Serious Adverse Event [4]: Insomnia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
変形性関節症	WORSENING OF ARTHROSIS OF THE RIGHT SHOULDER	NA / Start Day + 168 Days	Not Related	Drug Interrupted	Recovered /Resolved	Moderate

治験責任医師の見解：「変形性関節症」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Czech Republic	Sex: M	Age: 8[redacted]
Medical History [1]: Cholelithiasis, Rheumatoid arthritis, Osteoarthritis, Carpal tunnel decompression, Hypertension, Carpal tunnel decompression, Atrial fibrillation, Benign prostatic hyperplasia, Transient ischaemic attack, Hypothyroidism, Peripheral venous disease, Adjustment disorder with depressed mood, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: PREDNISONE, SPIRONOLACTONE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, WARFARIN, TAMSULOSIN, LEVOTHYROXINE SODIUM, SERTRALINE HYDROCHLORIDE, FUROSEMIDE, FUROSEMIDE, TAMSULOSIN HYDROCHLORIDE, SOLIFENACIN SUCCINATE, FUROSEMIDE, PYRIDOXINE HYDROCHLORIDE, BENFOTIAMINE, CYANOCOBALAMIN, FUROSEMIDE, IBUPROFEN, TRAMADOL HYDROCHLORIDE, PARACETAMOL, GABAPENTIN, PYRIDOXINE HYDROCHLORIDE, BENFOTIAMINE, CYANOCOBALAMIN, COVID-19 VACCINE, COVID-19 VACCINE, PREDNISONE, AMINO ACIDS NOS/ENTEROCOCCUS FAECIUM/ESCHERICHIA COLI/LACTOBACILLUS ACIDOPHILUS/LACTOBACILLUS HELVETICUS/MINERALS NOS, MAGNESIUM, DIOSMIN/HESPERIDIN, METAMIZOLE SODIUM, CURCUMIN/LECITHIN/MANGIFERA INDICA/PIPER NIGRUM/PYRIDOXINE HYDROCHLORIDE/RESVERATROL/RIBOFLAVIN, CALCIUM CARBONATE, TRAMADOL HYDROCHLORIDE, LEVOTHYROXINE SODIUM, PREDNISONE, RIVAROXABAN, PANTOPRAZOLE SODIUM SESQUIHYDRATE, CALCIUM CARBONATE/COLECALCIFEROL, COLECALCIFEROL, WARFARIN, WARFARIN, NIMESULIDE, COVID-19 VACCINE, COVID-19 VACCINE, APIXABAN, DICLOFENAC SODIUM, FUROSEMIDE				
Non-Serious Adverse Event [4]: Fall, Joint swelling, Osteoarthritis, Herpes zoster, Urinary incontinence, Anaemia, Polymyalgia rheumatica, Osteoarthritis, Rotator cuff syndrome, COVID-19, Dermatitis allergic, Peripheral swelling, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
肺炎	BRONCHOPNEUMONIA	Day 358 / Day 372	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
関節痛	JOINT PAINT - REHABILITATION	Day 480 / Day 498	Not Related	Dose Not Changed	Recovered /Resolved	Mild
嚢胞	CYST LOCATED ON THE LEFT SHOULDER	Day 559 / Day 720	Not Related	Dose Not Changed	Recovered /Resolved	Moderate
治験責任医師の見解：「肺炎」、「関節痛」及び「嚢胞」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Czech Republic	Sex: M	Age: 8[redacted]
Medical History [1]: Spinal fracture, Nephrectomy, Chronic kidney disease, Hypertension, Diabetes mellitus, Hyperlipidaemia, Goitre, Diverticulum intestinal, Haemorrhoids, Large intestinal polypectomy, Spinal pain, Cholelithiasis, Benign prostatic hyperplasia, Carpal tunnel decompression, Carpal tunnel decompression, Cardiac failure, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 902		
Concomitant Medication [3]: METFORMIN, DOXAZOSIN MESILATE, ALLOPURINOL, ACETYLSALICYLIC ACID, RAMIPRIL, METOPROLOL SUCCINATE, SIMVASTATIN, NIMESULIDE, SITAGLIPTIN PHOSPHATE, GLIMEPIRIDE, FUROSEMIDE, PANTOPRAZOLE SODIUM SESQUIHYDRATE, METAMIZOLE SODIUM, CALCIUM CARBONATE, CALCIUM PHOSPHATE, CODEINE PHOSPHATE, COVID-19 VACCINE, COVID-19 VACCINE, GLIQUIDONE, LINAGLIPTIN, GLIQUIDONE, PIOGLITAZONE HYDROCHLORIDE, IBUPROFEN, TRAMADOL HYDROCHLORIDE, PARACETAMOL, PARACETAMOL, POTASSIUM CHLORIDE, RIVAROXABAN, FUROSEMIDE, FUROSEMIDE, METOCLOPRAMIDE HYDROCHLORIDE, METOPROLOL SUCCINATE, ETOMIDATE, AMIODARONE HYDROCHLORIDE, FUROSEMIDE, METOCLOPRAMIDE HYDROCHLORIDE, ETOMIDATE, APIXABAN, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Diarrhoea, Phimosis, Peripheral swelling, Dyspnoea, Arthralgia, Back pain, Atrial fibrillation, Atrial fibrillation, Renal failure, Cardiac failure				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
出血性腸憩室	DIVERTICULUM INTESTINAL HAEMORRHAGIC	Day 663 / Day 674	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「出血性腸憩室」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Czech Republic	Sex: F	Age: 7[redacted]
Medical History [1]: Hip arthroplasty, Limb injury, Dyslipidaemia, Hypertension, Peripheral artery occlusion, Cervix operation, Hip arthroplasty, Cardiac failure chronic, Sinus bradycardia, Cardiac amyloidosis, Cardiac amyloidosis, Magnetic resonance imaging heart, Biopsy bone marrow				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 901		
Concomitant Medication [3]: TELMISARTAN, ACETYLSALICYLIC ACID/GLYCINE, BISOPROLOL FUMARATE, FUROSEMIDE, SPIRONOLACTONE, COVID-19 VACCINE, COVID-19 VACCINE, SPIRONOLACTONE, FUROSEMIDE, DABIGATRAN ETEXILATE MESILATE, FUROSEMIDE, COVID-19 VACCINE, NADROPARIN CALCIUM, BISOPROLOL FUMARATE, DABIGATRAN ETEXILATE MESILATE, BISOPROLOL FUMARATE				
Non-Serious Adverse Event [4]: Dyspnoea, Atrial fibrillation, Eye haemorrhage, Retinal haemorrhage, Atrial fibrillation				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動	WORSENING OF ATRIAL FIBRILATION	Day 791 / Day 813	Not Related	Dose Not Changed	Recovered /Resolved	Moderate

治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Placebo	Race: White	Country: Czech Republic	Sex: M	Age: 7[redacted]
Medical History [1]: Appendicectomy, Tobacco abuse, Tenoplasty, Hypercholesterolaemia, Hyperuricaemia, Polypectomy, Large intestine polyp, Carpal tunnel decompression, Hypertension, Atrial fibrillation, Gastric disorder, Melaena, Prostate cancer, Cardiac failure chronic, Cardiac amyloidosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 903		
Concomitant Medication [3]: BISOPROLOL, SIMVASTATIN, ALLOPURINOL, PANTOPRAZOLE SODIUM SESQUIHYDRATE, APIXABAN, TAMSULOSIN HYDROCHLORIDE, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, AMIODARONE, COVID-19 VACCINE, COVID-19 VACCINE, BISOPROLOL, AMIODARONE HYDROCHLORIDE, COVID-19 VACCINE, BISOPROLOL, AMILORIDE HYDROCHLORIDE/HYDROCHLOROTHIAZIDE, ATORVASTATIN CALCIUM/EZETIMIBE, ALLOPURINOL, PARACETAMOL/TRAMADOL HYDROCHLORIDE, AMIODARONE, METAMIZOLE SODIUM, DEXAMETHASONE, SPIRONOLACTONE, FUROSEMIDE, EPLERENONE				
Non-Serious Adverse Event [4]: COVID-19, Spinal pain, Cardiac failure chronic				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Severity
心房細動（1）	WORSENING OF ATRIAL FIBRILLATION	Day 406 / Day 409	Not Related	Dose Not Changed	Recovered /Resolved	Severe
心房細動（2）	WORSENING OF ATRIAL FIBRILLATION	Day 491 / Day 492	Not Related	Dose Not Changed	Recovered /Resolved	Severe
治験責任医師の見解：「心房細動（1）」及び「心房細動（2）」は治験薬と関連なしと判断した。						

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10 第 3 相試験【ALXN2060-TAC-302】（国内）［評価資料］

10.1 試験の概要

国内で実施した第 3 相試験【治験実施計画書番号：ALXN2060-TAC-302】の概要を Table 1 に示す。

Table 1: 第 3 相試験【治験実施計画書番号：ALXN2060-TAC-302】

治験の標題：日本人のトランスサイレチン型心アミロイドーシス患者を対象に、ALXN2060 を投与したときの有効性、安全性、薬物動態及び薬力学を評価する多施設共同、非盲検第 3 相試験	
治験実施計画書番号：ALXN2060-TAC-302	
治験実施施設：国内 14 施設（このうち 12 施設で患者を登録）	
治験期間： 最初の患者の登録日：2020 年 11 月 13 日 最後の患者の Month 30 来院日：2023 年 11 月 8 日	**開発段階：**第 3 相
目的： **主要目的：** Part A： • トランスサイレチン型心アミロイドーシス（ATTR-CM）を有する成人の日本人患者を対象に、アコラミジス塩酸塩 800 mg 1 日 2 回（BID）を経口投与したときの有効性を 6 分間歩行試験（6MWT）によって評価する。 Part B： • ATTR-CM を有する成人の日本人患者を対象に、アコラミジス塩酸塩 800 mg BID を経口投与したときの有効性を全死因死亡及び心血管症状に関連する入院によって評価する。 **副次目的：** Part A： • 6MWT に対するアコラミジス塩酸塩 800 mg BID の有効性を評価する。 • ATTR-CM を有する成人の日本人患者を対象に、Kansas City Cardiomyopathy Questionnaire Overall Summary Score（KCCQ-OS）測定によって健康関連生活の質（QoL）に対するアコラミジス塩酸塩 800 mg BID の有効性を評価する。 • ATTR-CM を有する成人の日本人患者を対象に、アコラミジス塩酸塩 800 mg BID の安全性及び忍容性を評価する。 • トランスサイレチン（TTR）安定化の in vivo バイオマーカーである血清中 TTR 濃度及び ex vivo アッセイである蛍光プローブ排除（FPE）法によって、アコラミジスの薬力学的作用（PD）を評価し、TTR 濃度／FPE 法とアコラミジスの薬物動態（PK）パラメータとの相関性を評価する。 Part B： • 6MWT に対するアコラミジス塩酸塩 800 mg BID の効果を評価する。 • ATTR-CM を有する成人の日本人患者を対象に、KCCQ-OS 測定によって健康関連 QoL に対するアコラミジス塩酸塩 800 mg BID の効果を評価する。 • ATTR-CM を有する成人の日本人患者にアコラミジス塩酸塩 800 mg BID を 30 ヵ月間投与し	

たときの安全性及び忍容性を評価する。
- TTR 安定化の in vivo バイオマーカーである血清中 TTR 濃度及び ex vivo アッセイである FPE 法によって、アコラミジスの PD を評価し、TTR 濃度／FPE 法とアコラミジスの PK パラメータとの相関性を評価する。

探索的目的：
- ATTR-CM を有する日本人患者を対象に、アコラミジス塩酸塩 800 mg BID を経口投与したときの有効性を全死因死亡及び心血管症状に関連する入院によって評価する（Part A のみ）。
- アコラミジス塩酸塩 800 mg BID を経口投与したときのアコラミジス及びその代謝物のポピュレーション PK を検討する。
- ATTR-CM を有する日本人患者を対象に、心筋壁張力及び微小血管虚血の血中バイオマーカーに対するアコラミジス塩酸塩 800 mg BID の有効性を評価する。
- ATTR-CM を有する日本人患者を対象に、EuroQol 5-dimentions 5-levels Health Outcomes Assessment（EQ-5D-5L）に対するアコラミジス塩酸塩 800 mg BID の有効性を評価する。
- ATTR-CM を有する日本人患者を対象に、心臓の構造、機能、組織の特性に及ぼすアコラミジス塩酸塩 800 mg BID の影響を、心臓 MRI によって評価する（特定の施設で同意が得られた患者のみ）。

方法：

本試験は、日本人の ATTR-CM 患者を対象に、アコラミジス塩酸塩 800 mg BID を経口投与したときの有効性、安全性、忍容性、PK 及び PD を評価する、第 3 相多施設共同オープンラベル試験であった。本試験は、スクリーニング期、治療期（Part A 及び Part B）、継続投与期及び追跡調査来院で構成された。

スクリーニング期に適格性が確認された患者は、治療期にアコラミジス塩酸塩 800 mg BID を 12 ヵ月投与された（Part A）。Part A の最終来院（Month 12）後、患者は Part B（Part A 後 18 ヵ月間、Day 1 から 30 ヵ月間）に移行し、アコラミジス塩酸塩 800 mg BID の経口投与を継続した。さらに、治療期での 30 ヵ月間の投与及び最終評価を完了した後、患者は継続投与期に移行し、アコラミジスの日本での承認又は最長 30 ヵ月間のいずれか早い時期まで、アコラミジス塩酸塩 800 mg BID の経口投与を継続できることとした。

患者数（計画時及び解析時）：

計画時：22 名

解析時：25 名（Full Analysis Set［FAS］：25 名、安全性解析対象集団：25 名、PK 解析対象集団：25 名、PD 解析対象集団：25 名）

診断及び組入れ基準：

［選択基準］

以下のすべての基準を満たす患者を本試験への組入れ対象とした。

1. 同意取得時に 20 歳以上 90 歳以下の男性又は女性。
2. 以下のいずれかの診断方法によって ATTR-CM（野生型 ATTR-CM［ATTRwt-CM］又は遺伝性 ATTR-CM［ATTRm-CM/ATTRv-CM］［遺伝子型判定により確認］）と確定診断されている者。
   a). 心筋生検で、免疫組織染色法、質量分析法又は免疫電子顕微鏡法のいずれかによる TTR

アミロイドタイピングの確認。

b). ピロリン酸テクネチウム（^{99m}Tc）又は ^{99m}Tc-ビスホスホネート（DPD 又は HMDP）シンチグラフィでの陽性像の確認かつ臨床検査による免疫グロブリン軽鎖（AL）アミロイドーシスの除外（血清及び尿の免疫固定法［IFE］、並びに血清免疫グロブリン遊離軽鎖分析の両方に基づく）及び心臓以外の生検（例えば、腹壁脂肪）による TTR アミロイド沈着の確認。

意義不明の単クローン性免疫グロブリン血症を有する患者は、免疫組織染色法、質量分析法又は免疫電子顕微鏡法のいずれかによる TTR アミロイドのタイピングで確認を行った組織生検による ATTR-CM の確定診断が必要である。

3. 以下のいずれかの心不全の病歴を有する者。
   a). 心不全による入院歴に基づく心不全の既往。
   b). 心不全による入院歴はないが、容量負荷や心内圧上昇の徴候・症状による心不全の臨床的エビデンス（例：頚静脈圧上昇、息切れ、X 線検査又は聴診での肺うっ血の徴候、末梢浮腫）。
   c). 利尿薬による治療を必要とした、又は継続的に必要とする心不全の症状。
4. ATTR-CM による New York Heart Association（NYHA）心機能分類 I～III の症状を有する者。
5. 利尿薬を除く心血管薬物治療を行っている場合、スクリーニング開始前の少なくとも 2 週間、用量が安定（50%以下の用量調節及び薬剤カテゴリーの変更なし）している者。
6. Day 1 前に 24 時間超かつ 3 週間以下の間隔を空けて、少なくとも 2 回実施した 6MWT で、150 m 以上の歩行を達成した者。2 回の試験で歩行した距離の差は 15%以内でなければならない。2 回の試験のいずれかが 150 m 以上でない場合、又は 2 回の試験の歩行距離の差が 15%以内でない場合、最初の試験から 3 週間以内に 3 回目の試験を実施する。3 回目の試験も 150 m 以上でない又は最初の 2 回の試験のいずれかの歩行距離との差が 15%以内でない場合、当該患者は参加不適格となる。
7. 経胸壁心エコー図検査又は心臓磁気共鳴（CMR）による測定で左室壁（心室中隔又は左室後壁）の厚さが 12 mm 以上であることが、スクリーニング開始前 10 年以内の病歴として記録されている、又はスクリーニング時の心エコー図検査若しくは CMR で認められる者。
8. スクリーニング時に心筋壁張力のバイオマーカーである脳性ナトリウム利尿ペプチド前駆体 N 端フラグメント（NT-proBNP）値が 300 pg/mL 以上の者。
9. 異性間性交渉を行う妊娠可能な女性の場合、スクリーニング時から治験薬の最終投与 30 日後まで有効な避妊法を使用することに同意できる者。妊娠可能な女性と性交渉を行う精管切除未実施の男性の場合、Day 1 から治験薬の最終投与 90 日後まで有効な避妊法を使用することに同意できる者。
10. 同意説明文書（ICF）を理解し、署名することができる者。ICF への署名は試験関連手順を開始する前に取得しなければならない。患者は、ICF 及び治験実施計画書に記載されている要件及び制限の遵守を含め、治験実施計画書に記載されているように ICF に署名できなければならない。

［除外基準］

以下のいずれかの基準に抵触する患者は、本試験から除外した。

1. スクリーニング開始前の 90 日以内に、急性心筋梗塞、急性冠症候群のエピソードの発症又

は冠動脈血行再建術を受けた者。
2. スクリーニング開始前の 90 日以内に脳卒中又は一過性脳虚血発作を発症した者。
3. スクリーニング時に、治験責任医師等が試験参加へのリスクが高すぎると判断する不安定な心血管血行動態を呈した者。
4. スクリーニング開始時から 1 年以内に心臓移植を受ける見込みがある者。
5. アコラミジス、その代謝物又は製剤の添加剤に対する過敏症が確認されている者。
6. 妊娠中又は授乳中の女性。授乳中の女性は、治験薬投与前に授乳を中止することに同意しなければならない。妊娠可能な女性は、スクリーニング時及び Day 1 の尿妊娠検査で陰性でなければならない。
7. 治験責任医師等又はメディカルモニターの判断で、臨床的に重要な医学的状態、臨床検査値異常又は患者の安全を脅かす、試験参加により患者のリスクが上昇する、若しくは試験に影響を及ぼす可能性のある状態を有する者。
8. ATTR-CM の治療としてタファミジス、ATTR-CM に対する適応のない既存薬（例：ジフルニサル、ドキシサイクリン）、天然物医薬品又は天然物誘導体（例：緑茶抽出物、タウロウルソデオキシコール酸／ursodiol）を治験薬の投与開始前 14 日以内に使用した者。パチシラン、inotersen 又は他の遺伝子サイレンシング薬を、パチシランは治験薬の投与開始前 90 日以内、inotersen は 180 日以内、他の遺伝子サイレンシング薬は半減期の 5 倍の期間に使用した者。
9. 刺激伝導系に作用するカルシウムチャネル遮断薬（ベラパミル、ジルチアゼム等）による治療が必要な者。ジヒドロピリジン系カルシウム拮抗薬は併用可能とする。ジギタリスの使用は、頻拍性の心房細動の管理に必要な場合にのみ許容される。
10. アコラミジス塩酸塩投与開始前の 30 日以内に、本試験の結果を交絡させる残存効果を有する可能性がある別の治験薬又は治験機器の試験に参加している者。
11. AL アミロイドーシスの確定診断を受けた者。
12. スクリーニング時に、アラニンアミノトランスフェラーゼ若しくはアスパラギン酸アミノトランスフェラーゼが基準値上限（ULN）の 3 倍を超える、又は総ビリルビンが ULN の 3 倍を超える肝機能検査異常がみられる者。
13. スクリーニング時の NT-proBNP が 8500 pg/mL 以上の者。
14. スクリーニング時に Modification of Diet in Renal Disease（MDRD）式によって算出された推算糸球体濾過率（eGFR）が 30 mL/min/1.73 m^2 未満の者。
15. 治験責任医師等又はメディカルモニターの判断で、薬物乱用歴、アルコール依存症又は精神疾患といった本治験実施計画書の遵守を妨げる状態を有する者。

治験薬、用法・用量：

すべての患者にアコラミジス塩酸塩 800 mg (2 × 400 mg 錠; ロット番号: [redacted]、[redacted]、[redacted]、[redacted]、[redacted]、[redacted]、[redacted]）を 1 日 2 回経口投与した。

治療期間：

スクリーニング～Month 30 来院まで : 最長約 32 ヵ月（スクリーニング期 : 最大 35 日間、治療期 : 30 ヵ月間）

（ただし、継続投与期へ移行した患者では最長約 60 ヵ月）

評価項目：

主要評価項目：

Part A：

- 6MWT の歩行距離のベースラインから Month 12 までの変化量

Part B：

- Month 30 までの全死因死亡割合及び心血管症状に関連する入院頻度

副次評価項目：

Part A：

- 6MWT の歩行距離のベースラインから Month 6 及び 9 までの変化量
- KCCQ-OS のベースラインから Month 6、9 及び 12 までの変化量
- 安全性パラメータ：重篤な有害事象及び有害事象、投与中止に至った有害事象、臨床的意義のある身体所見の異常、臨床的意義のあるバイタルサインの異常、臨床的意義のある心電図パラメータの異常及び臨床的に問題となる臨床検査パラメータの変化量
- Day 14 及び 28 並びにその後の来院日での、血清中 TTR 濃度（TTR 安定化の in vivo での指標）のベースラインからの変化量及び ex vivo アッセイである FPE 法による TTR 安定化率（%）

Part B：

- 6MWT の歩行距離のベースラインから Month 18、24 及び 30 までの変化量
- KCCQ-OS のベースラインから Month 18、24 及び 30 までの変化量
- 安全性パラメータ：重篤な有害事象及び有害事象、投与中止に至った有害事象、臨床的意義のある身体所見の異常、臨床的意義のあるバイタルサインの異常、臨床的意義のある心電図パラメータの異常及び臨床的に問題となる臨床検査パラメータの変化量
- 血清中 TTR 濃度（TTR 安定化の in vivo の指標）のベースラインからの変化量及び ex vivo アッセイである FPE 法による TTR 安定化率（%）

探索的評価項目：

- Month 12 までの全死因死亡及び心血管症状に関連する入院（Part A のみ）
- Month 30 までのアコラミジス及びその代謝物の PK の検討
- NT-proBNP 及びトロポニン I（TnI）のベースラインから Month 30 までの変化量
- EQ-5D-5L のベースラインから Month 30 までの変化量
- CMR パラメータのベースラインから Month 12、24 及び 30 までの変化量（特定の施設で同意が得られた患者のみ）

統計手法：

有効性：

有効性の主解析対象集団は FAS とし、その定義は「アコラミジス塩酸塩が 1 回以上投与されたすべての患者」とした。

Part A の主要評価項目「6MWT の歩行距離のベースラインから Month 12 までの変化量」及び Part B の主要評価項目「Month 30 までの全死因死亡及び心血管症状に関連する入院」に対して記述統計量を用いて結果を要約した。6MWT の歩行距離のベースラインから Month 12 までの変化量では平均値と 95%信頼区間を示した。また、全死因死亡では Month 12 及び Month 30 時点での

Kaplan-Meier 法による点推定値とその 95%信頼区間を示し、Kaplan-Meier 曲線も作成した。心血管症状に関連する入院の累積頻度は、共変量を含まないが各患者の試験期間の対数に等しいオフセット項をモデルに含めた負の二項回帰分析を用いて推定した。また、Month 30 時点の 1 年あたりの心血管症状に関連する入院頻度を 95%信頼区間とともに示した。
Part A での成功基準は、6MWT の歩行距離のベースラインから Month 12 までの変化量の 95%信頼区間の下限が-60 m を上回ることとした。
Part B での成功基準は、全死因死亡のみに基づき、Month 30 時点での推定生存割合が海外 AG10-301 試験のプラセボ群を上回ることとした。
6MWT の歩行距離及び KCCQ-OS のベースラインからの変化量は、ベースライン値及び来院で調整した反復測定混合効果モデルを用いて解析した。
なお、全死因死亡イベントには死因を問わない死亡、心臓移植及び心臓補助装置の使用が含まれた。また、心血管症状に関連する入院イベントには心血管症状に関連する入院（「心血管症状に関連した病的状態による急性期治療のための非選択的入院で、24 時間以上の滞在を要する入院」と定義）及び臨床的に注目すべき事象（「非代償性心不全のために利尿薬静注療法が実施された 24 時間未満の規定外来院」と定義）が含まれた。これらの入院の理由又は死因は独立した臨床イベント判定委員会（CEC）によってレビュー・判定され、治験実施計画書に規定された有効性評価項目の定義に合致しているか否かが決定された。

薬物動態／薬力学的作用：
PK 解析対象集団は「アコラミジス塩酸塩が 1 回以上投与され、評価可能なアコラミジス濃度を有するすべての患者」と定義した。PD 解析対象集団は「アコラミジス塩酸塩が 1 回以上投与され、評価可能な PD データを有するすべての患者」と定義した。
アコラミジスとその代謝物に対し、PK パラメータ及び PD パラメータの記述統計を示した。薬物曝露と治療効果の関係を評価するため、PK/PD 相関関係とポピュレーション PK 解析を実施した。

安全性：
安全性は安全性解析対象集団を対象に解析し、その定義は「アコラミジス塩酸塩が 1 回以上投与されたすべての患者」とした。
安全性データの要約には記述統計量を用い、安全性パラメータに関する正式な仮説検定は実施しなかった。有害事象は ICH 国際医薬用語集（MedDRA）Version 26.1 を用いてコード化した。有害事象の発現頻度は器官別大分類（SOC）及び基本語（PT）別に、すべての有害事象、治験薬との関連性が否定できない有害事象、重篤な有害事象、重症度別の有害事象、治験薬の投与中止に至った有害事象を集計した。有害事象の重症度は米国国立がん研究所（NCI）有害事象共通用語規準（CTCAE）Version 5.0 を用いてグレード分類した。
臨床検査値、バイタルサイン及び心電図の結果はベースラインからの平均変化量を示すとともに、ベースラインからの変化のシフトテーブル（例：正常から異常）を作成した。

中間解析：
本試験では、試験継続を判断するための正式な中間解析は計画されなかった。なお、当初 Part A の評価項目は Part A 完了時に解析する計画であったが、AG10-301 試験の Part A の結果を受け、Part B 完了時に Part A を含む治療期全体（30 ヵ月間）のすべての評価項目を解析することとした。

結果の要約：

本試験には 25 名が登録され、全員に治験薬が投与された。当該 25 名が FAS 及び安全性解析対象集団に含まれた。25 名中 22 名（88.0%）が治療期（Month 30）の投与を完了し、3 名（12.0%）が早期中止した。投与の中止理由は有害事象が 2 名（8.0%）、患者の意思が 1 名（4.0%）であった。また、治療期を完了した 22 名中 21 名が継続投与期に移行した。

FAS での年齢の平均値（標準偏差［SD］）は 76.5（6.31）歳、性別は男性が 88.0%であった。ATTR-CM 診断からの期間の平均値（SD）は 0.38（0.814）年、NYHA 心機能分類は I が 0%、II が 96.0%、III が 4.0%であった。ATTR-CM の遺伝子型は ATTRv-CM が 8.0%、ATTRwt-CM が 92.0%であった。また NT-proBNP は 3000 pg/mL 以下が 72.0%、3000 pg/mL 超が 28.0%、eGFR は 45 mL/min/1.73 m^2 以上が 100.0%、45 mL/min/1.73 m^2 未満が 0%であった。

有効性の結果：

Part A

- Part A の主要評価項目である「6MWT の歩行距離のベースラインから Month 12 までの変化量」では、Month 12 時点での 6MWT の歩行距離の平均値（SD）は 403.66（68.741）m、ベースラインからの変化量の平均値（SD）は-4.05（45.474）m であった。また、Month 12 時点で 6MWT の歩行距離のベースラインからの変化量の最小二乗平均［95%信頼区間］は-3.86［-22.85～15.13］m であった。ベースラインからの変化量の最小二乗平均の 95%信頼区間の下限が-60 m を上回っており、治験実施計画書で規定した Part A での成功基準を満たした。

治療期全体（Part A + Part B）

主要評価項目

- Month 30 時点で死亡は認められず、Month 30 時点での推定生存割合は 100.0%（同意撤回した患者が Month 30 まで生存していると仮定した場合の 95%信頼区間［0.863～1.000］、同意撤回した患者が Month 30 までに死亡していると仮定した場合の 95%信頼区間［0.796～0.999］）と推定された。当該推定生存割合は、海外 AG10-301 試験での Month 30 時点のプラセボ群での生存割合（約 74%）を上回っており、治験実施計画書で規定した Part B での成功基準を満たした。
- 心血管症状に関連する入院は 25 名中 5 名に 8 件認められ、その頻度は 0.1329 回/年であった。このうち、CEC によって臨床的に注目すべき事象と判定されたイベントはなかった。

副次評価項目

- 6MWT の歩行距離のベースラインから Month 30 までの変化量の最小二乗平均［95%信頼区間］は、-36.20［-58.54～-13.86］m であった。また、6MWT の歩行距離の実測値の平均値及びベースラインからの平均変化量は、Month 18 時点でそれぞれ 384.57 m、-25.69 m、Month 24 時点でそれぞれ 384.29 m、-25.08 m、Month 30 時点でそれぞれ 372.95 m、-36.42 m であった。
- KCCQ-OS のベースラインから Month 30 までの変化量の最小二乗平均［95%信頼区間］は、-6.97［-14.74～0.80］ポイントであった。また、KCCQ-OS の実測値の平均値及びベースラインからの平均変化量は、Month 18 時点でそれぞれ 72.36 ポイント、-5.18 ポイント、Month 24 時点でそれぞれ 76.51 ポイント、-0.13 ポイント、Month 30 時点でそれぞれ 70.15 ポイント、-6.49 ポイントであった。
- 血清 TTR 値のベースラインから Month 30 までの変化量の最小二乗平均［95%信頼区間］は

9.36［6.71～12.01］mg/dL であった。また、Day 14（初回評価）時点の血清 TTR 値の実測値の平均値は 32.39 mg/dL、ベースラインからの平均変化量は 9.62 mg/dL、Month 30 時点の血清 TTR 値の実測値の平均値は 31.33 mg/dL、ベースラインからの平均変化量は 9.40 mg/dL であった。

FPE 法を用いて TTR 安定化率を測定した結果、Month 30 時点での安定化率の平均値は 11.01%であったが、これは 1 名で投与開始後の各来院時に高い負の値がみられたためであり、中央値は 95.60%であった。そのため、事後解析として、当該 1 名を外れ値として除外し、FPE 法による TTR 安定化率の感度分析を実施した。感度分析の結果、Month 30 時点での安定化率の平均値は 96.62%であり、Month 30 までほぼ完全な（90%以上）の TTR 安定化が認められた。当該 1 名を除外した Month 30 時点での FPE 法を用いた TTR 安定化率の最小二乗平均は 97.71%［95%信頼区間：93.90%～101.51%］であった。

探索的評価項目

- NT-proBNP のベースラインから Month 30 までの幾何平均倍率変化［95%信頼区間］は 1.06 pg/mL［0.88～1.26 pg/mL］であった。また、Month 30 時点の NT-proBNP の実測値の平均値は 2434.5 pg/mL、ベースラインからの平均変化量は 53.2 pg/mL であった。
- TnI のベースラインから Month 30 までの変化量では、各患者の TnI 測定法がベースライン（標準的測定法）と Month 30（高感度測定法）で異なったため、変化量に対して正式な解釈をすることができなかった。
- EQ-5D-5L のベースラインから Month 30 までの変化量、並びに CMR 画像法パラメータ（1 名）のベースラインから Month 12、24 及び 30 までの変化量でも良好な結果が得られた。

薬物動態の結果：

- Month 30 時点のアコラミジスの定常状態でのトラフ濃度の平均値（SD）は 2535.2 (1007.82) ng/mL であり、アコラミジスの目標トラフ濃度 2340 ng/mL（約 8 μM）を上回って維持していた。

安全性の結果：

- 有害事象は 100.0%（25/25 名）に発現した。SOC 別の主な有害事象（発現割合 30%以上）は、「胃腸障害」（14 名、56.0%）、「感染症および寄生虫症」（13 名、52.0%）、「代謝および栄養障害」（11 名、44.0%）、「心臓障害」（10 名、40.0%）、「筋骨格系および結合組織障害」（9 名、36.0%）、「一般・全身障害および投与部位の状態」、「神経系障害」（各 8 名、32.0%）であった。PT 別の主な有害事象（発現割合 15%以上）は「便秘」（7 名、28.0%）、「上咽頭炎」（6 名、24.0%）、「発熱」、「背部痛」（各 5 名、20.0%）、「COVID-19」、「血尿」、「腎機能障害」（各 4 名、16.0%）であった。
- 治験薬との関連性が否定できない有害事象は 12.0%（3 名）に 4 件認められ、その内訳は「腎機能障害」（2 名、8.0%）、「便秘」、「薬疹」（各 1 名、4.0%）であった。
- 有害事象の重症度はほとんどが Grade 1 又は Grade 2 であり、Grade 3 の有害事象は 40.0%（10 名）、Grade 4 の有害事象は 4.0%（1 名、「洞停止」）に発現した。
- 本試験で死亡した患者はいなかった。
- 重篤な有害事象は 48.0%（12 名）に発現した。最も多く認められた SOC 別の重篤な有害事象は「心臓障害」（5 名、20.0%）であった。PT 別の重篤な有害事象は「大腸ポリープ」が 2

名（8.0%）に認められたほかは、いずれも各 1 名（4.0%）での発現であった。治験薬との関連性が否定できない重篤な有害事象はなかった。

- 治験薬の投与中止に至った有害事象は 8.0%（2 名）に発現し、その内訳は「腎機能障害」、「薬疹」（各 1 名、4.0%）であった。

結論：

- 本試験で死亡は認められず、その推定生存割合（100.0%）は海外 AG10-301 試験での Month 30 時点のプラセボ群での生存割合（約 74%）を上回っており、治験実施計画書で規定した Part B での成功基準を満たした。また、心血管症状に関連する入院の累積頻度は 0.1329 回/年であった。
- 本試験でアコラミジス塩酸塩を日本人 ATTR-CM 患者に投与したとき、全死因死亡、心血管症状に関連する入院に加え、6MWT、KCCQ-OS、TTR 値、TTR 安定化率及び NT-proBNP でも臨床的に意義のある治療効果が認められた。
- 本試験でアコラミジス塩酸塩を日本人の ATTR-CM 患者に投与したときの忍容性は良好であり、臨床的に問題となる安全性のシグナルは認められなかった。

報告書作成日：20[redacted]年[redacted]月[redacted]日

10.2 有害事象

すべての有害事象、治験薬との関連性が否定できない有害事象、重篤な有害事象及び治験薬の投与中止に至った有害事象を以下に示す。

すべての有害事象	Table 14.3.1.3.2.1
治験薬との関連性が否定できない有害事象	Table 14.3.1.3.3.2
重篤な有害事象	Table 14.3.1.3.5.1
治験薬の投与中止に至った有害事象	Table 14.3.1.3.8

10.3 個別被験者の詳細

本試験で死亡は認められなかった。重篤な有害事象を発現した患者の詳細を以下に示す。

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
Any Adverse Event	25 (100)	201
血液およびリンパ系障害	2 (8.0)	3
貧血	2 (8.0)	3
心臓障害	10 (40.0)	19
心房細動	2 (8.0)	2
心房粗動	2 (8.0)	2
完全房室ブロック	1 (4.0)	1
心不快感	1 (4.0)	1
心不全	3 (12.0)	3
慢性心不全	2 (8.0)	5
動悸	2 (8.0)	2
洞停止	1 (4.0)	1
洞結節機能不全	1 (4.0)	2
耳および迷路障害	2 (8.0)	3
回転性めまい	2 (8.0)	3

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
内分泌障害	1 (4.0)	1
甲状腺機能低下症	1 (4.0)	1
眼障害	4 (16.0)	7
眼瞼炎	1 (4.0)	2
白内障	1 (4.0)	1
アレルギー性結膜炎	1 (4.0)	1
ドライアイ	2 (8.0)	2
視力障害	1 (4.0)	1
胃腸障害	14 (56.0)	30
腹部膨満	1 (4.0)	1
上腹部痛	2 (8.0)	2
裂肛	1 (4.0)	1
便秘	7 (28.0)	7
憩室	1 (4.0)	1
出血性腸憩室	1 (4.0)	5
胃出血	1 (4.0)	1
痔核	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
胃腸障害（続き）		
鼠径ヘルニア	1 (4.0)	2
大腸ポリープ	2 (8.0)	2
悪心	2 (8.0)	3
嘔吐	3 (12.0)	4
一般・全身障害および投与部位の状態	8 (32.0)	11
疲労	1 (4.0)	1
注射部位発疹	1 (4.0)	1
倦怠感	2 (8.0)	3
非心臓性胸痛	1 (4.0)	1
発熱	5 (20.0)	5
肝胆道系障害	1 (4.0)	1
肝機能異常	1 (4.0)	1
免疫系障害	1 (4.0)	1
季節性アレルギー	1 (4.0)	1
感染症および寄生虫症	13 (52.0)	27

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
感染症および寄生虫症（続き）		
穿孔性虫垂炎	1 (4.0)	4
細菌性前立腺炎	1 (4.0)	2
ＣＯＶＩＤ－１９	4 (16.0)	4
膀胱炎	2 (8.0)	2
ヘリコバクター性胃炎	1 (4.0)	1
ヘリコバクター感染	1 (4.0)	1
爪感染	1 (4.0)	1
上咽頭炎	6 (24.0)	8
肺炎	1 (4.0)	1
肺炎球菌性肺炎	1 (4.0)	2
副鼻腔炎	1 (4.0)	1
傷害、中毒および処置合併症	6 (24.0)	8
顔面損傷	1 (4.0)	1
頭部損傷	1 (4.0)	1
熱射病	1 (4.0)	1
関節損傷	1 (4.0)	1
四肢損傷	2 (8.0)	2
肉離れ	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
傷害、中毒および処置合併症（続き）		
処置後出血	1 (4.0)	1
臨床検査	5 (20.0)	10
血中クレアチンホスホキナーゼＭＢ増加	1 (4.0)	3
血中クレアチニン増加	2 (8.0)	4
国際標準比増加	1 (4.0)	1
ＳＡＲＳ－ＣｏＶ－２検査陽性	1 (4.0)	1
体重減少	1 (4.0)	1
代謝および栄養障害	11 (44.0)	13
食欲減退	2 (8.0)	2
脱水	2 (8.0)	2
脂質異常症	1 (4.0)	1
痛風	2 (8.0)	2
高カリウム血症	2 (8.0)	2
高尿酸血症	2 (8.0)	2
低カリウム血症	1 (4.0)	1
２型糖尿病	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
筋骨格系および結合組織障害	9 (36.0)	16
関節痛	3 (12.0)	3
関節炎	1 (4.0)	1
背部痛	5 (20.0)	5
軟骨石灰化症	1 (4.0)	1
筋痙縮	2 (8.0)	2
筋肉痛	2 (8.0)	2
四肢痛	1 (4.0)	1
軟部組織腫瘤	1 (4.0)	1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (8.0)	2
膀胱癌	1 (4.0)	1
前立腺癌	1 (4.0)	1
神経系障害	8 (32.0)	9
手根管症候群	2 (8.0)	2
脳出血	1 (4.0)	1
浮動性めまい	1 (4.0)	1
感覚鈍麻	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
神経系障害（続き）		
神経痛	1 (4.0)	1
末梢性ニューロパチー	1 (4.0)	1
坐骨神経痛	1 (4.0)	1
傾眠	1 (4.0)	1
製品の問題	1 (4.0)	4
医療機器位置異常	1 (4.0)	4
精神障害	1 (4.0)	1
不眠症	1 (4.0)	1
腎および尿路障害	6 (24.0)	11
慢性腎臓病	1 (4.0)	1
血尿	4 (16.0)	5
腎機能障害	4 (16.0)	5
生殖系および乳房障害	4 (16.0)	4
良性前立腺肥大症	2 (8.0)	2
乳頭痛	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
生殖系および乳房障害（続き）		
精巣痛	1 (4.0)	1
呼吸器、胸郭および縦隔障害	5 (20.0)	8
咳嗽	1 (4.0)	1
間質性肺疾患	1 (4.0)	3
胸水	1 (4.0)	1
肺腫瘤	1 (4.0)	1
睡眠時無呼吸症候群	1 (4.0)	1
上気道の炎症	1 (4.0)	1
皮膚および皮下組織障害	7 (28.0)	9
皮膚炎	1 (4.0)	1
薬疹	1 (4.0)	1
皮膚乾燥	2 (8.0)	2
そう痒症	1 (4.0)	1
発疹	3 (12.0)	3
蕁麻疹	1 (4.0)	1
血管障害	2 (8.0)	3

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.2.1
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
血管障害（続き）		
起立性低血圧	1 (4.0)	1
静脈瘤	1 (4.0)	1
四肢静脈血栓症	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
Any Adverse Event	3 (12.0)	4	24 (96.0)	196
血液およびリンパ系障害	0	0	2 (8.0)	3
貧血	0	0	2 (8.0)	3
心臓障害	0	0	10 (40.0)	19
心房細動	0	0	2 (8.0)	2
心房粗動	0	0	2 (8.0)	2
完全房室ブロック	0	0	1 (4.0)	1
心不快感	0	0	1 (4.0)	1
心不全	0	0	3 (12.0)	3
慢性心不全	0	0	2 (8.0)	5
動悸	0	0	2 (8.0)	2
洞停止	0	0	1 (4.0)	1
洞結節機能不全	0	0	1 (4.0)	2
耳および迷路障害	0	0	2 (8.0)	3
回転性めまい	0	0	2 (8.0)	3

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
内分泌障害	0	0	1 (4.0)	1
甲状腺機能低下症	0	0	1 (4.0)	1
眼障害	0	0	4 (16.0)	7
眼瞼炎	0	0	1 (4.0)	2
白内障	0	0	1 (4.0)	1
アレルギー性結膜炎	0	0	1 (4.0)	1
ドライアイ	0	0	2 (8.0)	2
視力障害	0	0	1 (4.0)	1
胃腸障害	1 (4.0)	1	13 (52.0)	29
腹部膨満	0	0	1 (4.0)	1
上腹部痛	0	0	2 (8.0)	2
裂肛	0	0	1 (4.0)	1
便秘	1 (4.0)	1	6 (24.0)	6
憩室	0	0	1 (4.0)	1
出血性腸憩室	0	0	1 (4.0)	5
胃出血	0	0	1 (4.0)	1
痔核	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
胃腸障害（続き）				
鼠径ヘルニア	0	0	1 (4.0)	2
大腸ポリープ	0	0	2 (8.0)	2
悪心	0	0	2 (8.0)	3
嘔吐	0	0	3 (12.0)	4
一般・全身障害および投与部位の状態	0	0	8 (32.0)	11
疲労	0	0	1 (4.0)	1
注射部位発疹	0	0	1 (4.0)	1
倦怠感	0	0	2 (8.0)	3
非心臓性胸痛	0	0	1 (4.0)	1
発熱	0	0	5 (20.0)	5
肝胆道系障害	0	0	1 (4.0)	1
肝機能異常	0	0	1 (4.0)	1
免疫系障害	0	0	1 (4.0)	1
季節性アレルギー	0	0	1 (4.0)	1
感染症および寄生虫症	0	0	13 (52.0)	27

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
感染症および寄生虫症（続き）				
穿孔性虫垂炎	0	0	1 (4.0)	4
細菌性前立腺炎	0	0	1 (4.0)	2
ＣＯＶＩＤ－１９	0	0	4 (16.0)	4
膀胱炎	0	0	2 (8.0)	2
ヘリコバクター性胃炎	0	0	1 (4.0)	1
ヘリコバクター感染	0	0	1 (4.0)	1
爪感染	0	0	1 (4.0)	1
上咽頭炎	0	0	6 (24.0)	8
肺炎	0	0	1 (4.0)	1
肺炎球菌性肺炎	0	0	1 (4.0)	2
副鼻腔炎	0	0	1 (4.0)	1
傷害、中毒および処置合併症	0	0	6 (24.0)	8
顔面損傷	0	0	1 (4.0)	1
頭部損傷	0	0	1 (4.0)	1
熱射病	0	0	1 (4.0)	1
関節損傷	0	0	1 (4.0)	1
四肢損傷	0	0	2 (8.0)	2
肉離れ	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
傷害、中毒および処置合併症（続き）				
処置後出血	0	0	1 (4.0)	1
臨床検査	0	0	5 (20.0)	10
血中クレアチンホスホキナーゼＭＢ増加	0	0	1 (4.0)	3
血中クレアチニン増加	0	0	2 (8.0)	4
国際標準比増加	0	0	1 (4.0)	1
ＳＡＲＳ－ＣｏＶ－２検査陽性	0	0	1 (4.0)	1
体重減少	0	0	1 (4.0)	1
代謝および栄養障害	0	0	11 (44.0)	13
食欲減退	0	0	2 (8.0)	2
脱水	0	0	2 (8.0)	2
脂質異常症	0	0	1 (4.0)	1
痛風	0	0	2 (8.0)	2
高カリウム血症	0	0	2 (8.0)	2
高尿酸血症	0	0	2 (8.0)	2
低カリウム血症	0	0	1 (4.0)	1
２型糖尿病	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
筋骨格系および結合組織障害	0	0	9 (36.0)	16
関節痛	0	0	3 (12.0)	3
関節炎	0	0	1 (4.0)	1
背部痛	0	0	5 (20.0)	5
軟骨石灰化症	0	0	1 (4.0)	1
筋痙縮	0	0	2 (8.0)	2
筋肉痛	0	0	2 (8.0)	2
四肢痛	0	0	1 (4.0)	1
軟部組織腫瘤	0	0	1 (4.0)	1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0	2 (8.0)	2
膀胱癌	0	0	1 (4.0)	1
前立腺癌	0	0	1 (4.0)	1
神経系障害	0	0	8 (32.0)	9
手根管症候群	0	0	2 (8.0)	2
脳出血	0	0	1 (4.0)	1
浮動性めまい	0	0	1 (4.0)	1
感覚鈍麻	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
神経系障害（続き）				
神経痛	0	0	1 (4.0)	1
末梢性ニューロパチー	0	0	1 (4.0)	1
坐骨神経痛	0	0	1 (4.0)	1
傾眠	0	0	1 (4.0)	1
製品の問題	0	0	1 (4.0)	4
医療機器位置異常	0	0	1 (4.0)	4
精神障害	0	0	1 (4.0)	1
不眠症	0	0	1 (4.0)	1
腎および尿路障害	2 (8.0)	2	6 (24.0)	9
慢性腎臓病	0	0	1 (4.0)	1
血尿	0	0	4 (16.0)	5
腎機能障害	2 (8.0)	2	2 (8.0)	3
生殖系および乳房障害	0	0	4 (16.0)	4
良性前立腺肥大症	0	0	2 (8.0)	2
乳頭痛	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
生殖系および乳房障害（続き）				
精巣痛	0	0	1 (4.0)	1
呼吸器、胸郭および縦隔障害	0	0	5 (20.0)	8
咳嗽	0	0	1 (4.0)	1
間質性肺疾患	0	0	1 (4.0)	3
胸水	0	0	1 (4.0)	1
肺腫瘤	0	0	1 (4.0)	1
睡眠時無呼吸症候群	0	0	1 (4.0)	1
上気道の炎症	0	0	1 (4.0)	1
皮膚および皮下組織障害	1 (4.0)	1	6 (24.0)	8
皮膚炎	0	0	1 (4.0)	1
薬疹	1 (4.0)	1	0	0
皮膚乾燥	0	0	2 (8.0)	2
そう痒症	0	0	1 (4.0)	1
発疹	0	0	3 (12.0)	3
蕁麻疹	0	0	1 (4.0)	1
血管障害	0	0	2 (8.0)	3

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.3.2
Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term by Highest Relationship to Treatment
Parts A and B
Safety Set

	ALXN2060 N=25			
	Related		Not Related	
System Organ Class (SOC) Preferred Term (PT)	n (%)	E	n (%)	E
血管障害（続き）				
起立性低血圧	0	0	1 (4.0)	1
静脈瘤	0	0	1 (4.0)	1
四肢静脈血栓症	0	0	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
Highest relationship for each participant per SOC/PT is summarized.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1

Table 14.3.1.3.5.1
Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
Any Serious Adverse Event	12 (48.0)	25
心臓障害	5 (20.0)	7
心房細動	1 (4.0)	1
完全房室ブロック	1 (4.0)	1
心不快感	1 (4.0)	1
心不全	1 (4.0)	1
慢性心不全	1 (4.0)	1
洞停止	1 (4.0)	1
洞結節機能不全	1 (4.0)	1
胃腸障害	3 (12.0)	7
出血性腸憩室	1 (4.0)	4
単径ヘルニア	1 (4.0)	1
大腸ポリープ	2 (8.0)	2
感染症および寄生虫症	3 (12.0)	4
穿孔性虫垂炎	1 (4.0)	2
細菌性前立腺炎	1 (4.0)	1
肺炎球菌性肺炎	1 (4.0)	1
臨床検査	1 (4.0)	1
血中クレアチンホスホキナーゼＭＢ増加	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1.3

Table 14.3.1.3.5.1
Treatment-Emergent Serious Adverse Events by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
代謝および栄養障害	1 (4.0)	1
脱水	1 (4.0)	1
筋骨格系および結合組織障害	1 (4.0)	1
軟部組織腫瘤	1 (4.0)	1
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (8.0)	2
膀胱癌	1 (4.0)	1
前立腺癌	1 (4.0)	1
製品の問題	1 (4.0)	1
医療機器位置異常	1 (4.0)	1
呼吸器、胸郭および縦隔障害	1 (4.0)	1
間質性肺疾患	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1.3

Table 14.3.1.3.8
Treatment-Emergent Adverse Events Leading to Withdrawal of Study Drug by MedDRA System Organ Class and Preferred Term
Parts A and B
Safety Set

System Organ Class (SOC) Preferred Term (PT)	ALXN2060 N = 25 n (%)	E
Any Adverse Event	2 (8.0)	2
腎および尿路障害	1 (4.0)	1
腎機能障害	1 (4.0)	1
皮膚および皮下組織障害	1 (4.0)	1
薬疹	1 (4.0)	1

% = n/N*100. E = total number of events.
In summarizing n(%), a participant is counted only once for a particular SOC in case of multiple events under the SOC. Similarly, a participant is counted only once for a particular PT in case of multiple events under the PT.
SOCs and PTs were coded using MedDRA version 26.1.
Source listing(s): 16.2.7.1.5

10.3.1. 死亡に至った有害事象の詳細

該当なし

10.3.2. その他の重篤な有害事象の詳細

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: Asian		Country: Japan	Sex: M	Age: 8[redacted]
Medical History [1]: Atrial fibrillation, Chronic kidney disease, Constipation, Dyslipidaemia, Cardiac failure, Hypertension, Hypertonic bladder, Type 2 diabetes mellitus, Aortic valve stenosis, Atrioventricular block						
Treatment First Dose Day [2]: Day 1			Last Dose Day [2]: Day 918			
Concomitant Medication [3]: LEVOFLOXACIN, AMBROXOL HYDROCHLORIDE, CARBOCISTEINE, LEVOFLOXACIN, CEFTRIAXONE SODIUM SESQUATERHYDRATE, CARVEDILOL, GLIMEPIRIDE, RABEPRAZOLE SODIUM, MOMETASONE FUROATE MONOHYDRATE, REBAMIPIDE, PARACETAMOL, LOXOPROFEN SODIUM DIHYDRATE, CARVEDILOL, GLIMEPIRIDE, ENALAPRIL MALEATE, APIXABAN, TENELIGLIPTIN HYDROBROMIDE, MAGNESIUM OXIDE, ATORVASTATIN CALCIUM, TRICHLORMETHIAZIDE, NIFEDIPINE, IMIDAFENACIN						
Non-Serious Adverse Event [4]: Pneumonia pneumococcal, Sinusitis, Back pain						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
肺炎球菌性肺炎	Pneumococcal pneumonia	Day 285 / Day 303	Not Related	Drug Interrupted	Recovered/ Resolved	Grade 3
治験責任医師の見解：「肺炎球菌性肺炎」は治験薬と関連なしと判断した。						

F = female; M = male; MedDRA = Medical Dictionary for Regulatory Activities; NA = Not Available

[1] Medical history preferred terms are coded using MedDRA version 26.1.

[2] Relative to the first study drug administration.

[3] Concomitant medications are defined as any medication taken by a participant overlapping with the intake of study drug or with insufficient date to determine it is a prior medication.

[4] Adverse Event preferred terms are coded using MedDRA version 26.1.

[5] Toxicity is an assessment of Adverse Event intensity based on the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) v5.0, published 27 Nov 2017.

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Osteoarthritis, Chronic kidney disease, Diverticulum intestinal haemorrhagic, Cardiac failure, Hyperuricaemia, Hypertension, Graves' disease, Type 2 diabetes mellitus				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 918			
Concomitant Medication [3]: THIAMAZOLE, BILASTINE, MUCOPOLYSACCHARIDE POLYSULFURIC ACID ESTER, EZETIMIBE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, AZOSEMIDE, CEFTAZIDIME, PARACETAMOL, CEFMETAZOLE SODIUM, TAMSULOSIN HYDROCHLORIDE, CEFMETAZOLE SODIUM, FOSFOMYCIN CALCIUM, THIAMAZOLE, EDOXABAN TOSILATE, DEGARELIX ACETATE, DEGARELIX ACETATE, TOZINAMERAN, PARACETAMOL, CEFACLOR, GENTAMICIN SULFATE, THIAMAZOLE, FUSIDATE SODIUM, POVIDONE-IODINE/SUCROSE, BISOPROLOL FUMARATE, THIAMAZOLE, PARACETAMOL, CARVEDILOL, SODIUM PICOSULFATE MONOHYDRATE, NALOXONE HYDROCHLORIDE, LIDOCAINE, ASCORBIC ACID/MACROGOL 3350/POTASSIUM CHLORIDE/SODIUM ASCORBATE/SODIUM CHLORIDE/SODIUM SULFATE, GLUCAGON,PETHIDINE HYDROCHLORIDE, EDOXABAN TOSILATE, ENZALUTAMIDE, LEUPRORELIN ACETATE, THIAMAZOLE, THIAMAZOLE, PETHIDINE HYDROCHLORIDE, PETHIDINE HYDROCHLORIDE, GLUCAGON, PETHIDINE HYDROCHLORIDE, PETHIDINE HYDROCHLORIDE, GLUCAGON, PETHIDINE HYDROCHLORIDE, EDOXABAN TOSILATE, FERROUS SODIUM CITRATE, THIAMAZOLE, FERROUS SODIUM CITRATE, LOXOPROFEN SODIUM DIHYDRATE, RED BLOOD CELLS (CONCENTRATED), GLUCAGON, PETHIDINE HYDROCHLORIDE, GLUCAGON, PETHIDINE HYDROCHLORIDE, GLUCAGON, PETHIDINE HYDROCHLORIDE, EDOXABAN TOSILATE, EPLERENONE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, AZOSEMIDE, EDOXABAN TOSILATE, BISOPROLOL FUMARATE, FEBUXOSTAT, ESOMEPRAZOLE MAGNESIUM				
Non-Serious Adverse Event [4]: Anaemia, Anaemia, Abdominal distension, Constipation, Diverticulum intestinal haemorrhagic, Diverticulum, Injection site rash, Pyrexia, Hepatic function abnormal, Bacterial prostatitis, Dyslipidaemia, Back pain, Pain in extremity, Benign prostatic hyperplasia, Dermatitis, Dry skin				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
出血性腸憩室（1）	Colonic diverticular bleeding	Day 542 / Day 556	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
出血性腸憩室（2）	Colonic diverticular bleeding	Day 562 / Day 574	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
出血性腸憩室（3）	Colonic diverticular bleeding	Day 855 / Day 861	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
出血性腸憩室（4）	Colonic diverticular bleeding	Day 867 / Day 871	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
大腸ポリープ	Large intestine polyp	Day 856 / Day 899	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
細菌性前立腺炎	Acute bacterial prostatitis	Day 33 / Day 44	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
前立腺癌	Prostate cancer	Day 90 / Ongoing	Not Related	Dose Not Changed	Not Recovered/ Not Resolved	Grade 3

治験責任医師の見解：「出血性腸憩室（1）」、「出血性腸憩室（2）」、「出血性腸憩室（3）」、「出血性腸憩室（4）」、「大腸ポリープ」、「細菌性前立腺炎」及び「前立腺癌」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: F	Age: 7[redacted]
Medical History [1]: Anaemia, Viral hepatitis carrier, Chronic kidney disease, Hyperuricaemia, Cardiac failure chronic, Sinus node dysfunction, Hypothyroidism, Cardiac pacemaker insertion				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 911			
Concomitant Medication [3]: FEBUXOSTAT, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, AZOSEMIDE, AZOSEMIDE, GLYCERYL TRINITRATE, TORASEMIDE, TORASEMIDE, TORASEMIDE, TORASEMIDE, VERICIGUAT, PARACETAMOL, FERROUS SODIUM CITRATE, DIFENIDOL HYDROCHLORIDE, BETAHISTINE MESILATE, METOCLOPRAMIDE, ESOMEPRAZOLE MAGNESIUM, SALBUTAMOL SULFATE, BROMHEXINE HYDROCHLORIDE, GLYCERYL TRINITRATE, LIDOCAINE, DIMETICONE, DIFENIDOL HYDROCHLORIDE, SODIUM CHLORIDE, CARBOHYDRATES NOS/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, ATRACTYLODES LANCEA RHIZOME/CITRUS X AURANTIUM PEEL/GLYCYRRHIZA SPP. ROOT/PANAX GINSENG ROOT/PINELLIA TERNATA TUBER/PORIA COCOS SCLEROTIUM/ZINGIBER OFFICINALE RHIZOME/ZIZIPHUS JUJUB, MOSAPRIDE CITRATE, GLUCOSE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, GLYCERYL TRINITRATE, LIDOCAINE, DIMETICONE, PRONASE, SODIUM BICARBONATE, VONOPRAZAN FUMARATE, SENNOSIDE A+B CALCIUM, SODIUM PICOSULFATE MONOHYDRATE, LIDOCAINE, MACROGOL/POTASSIUM CHLORIDE/SODIUM BICARBONATE/SODIUM CHLORIDE/SODIUM SULFATE ANHYDROUS, DIMETICONE, GLUCAGON, AMINO ACIDS NOS/ELECTROLYTES NOS/GLUCOSE/THIAMINE HYDROCHLORIDE, VONOPRAZAN FUMARATE, TORASEMIDE, MOLNUPIRAVIR, FUROSEMIDE, GLYCERYL TRINITRATE, PARACETAMOL, MOLNUPIRAVIR, POTASSIUM CHLORIDE, TORASEMIDE, TOLVAPTAN, GLYCERYL TRINITRATE, MOLNUPIRAVIR, SENNOSIDE A+B, AMINO ACIDS NOS/ELECTROLYTES NOS/GLUCOSE/THIAMINE HYDROCHLORIDE, TOLVAPTAN, TORASEMIDE, TOLVAPTAN, FUROSEMIDE, FUROSEMIDE				
Non-Serious Adverse Event [4]: Cardiac failure chronic, Cardiac failure chronic, Vertigo, Vertigo, Nausea, Nausea, Vomiting, SARS-CoV-2 test positive, Orthostatic hypotension, Venous thrombosis limb				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
慢性心不全	Worsening of chronic heart failure	Day 709 / Day 719	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
脱水	Dehydration	Day 678 / Day 687	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
治験責任医師の見解：「慢性心不全」及び「脱水」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 8[redacted]
Medical History [1]: Essential tremor, Hypertension, Pruritus, Osteoporosis, Asthma, Gastrooesophageal reflux disease, Musculoskeletal stiffness, Constipation, Cardiac failure chronic, Tinea pedis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 910			
Concomitant Medication [3]: TOCOPHERYL NICOTINATE, ELDECALCITOL, ALENDRONATE SODIUM, EPLERENONE, CANDESARTAN CILEXETIL, LULICONAZOLE, BISOPROLOL FUMARATE, TOZINAMERAN, TOZINAMERAN, AZITHROMYCIN MONOHYDRATE, LOXOPROFEN SODIUM DIHYDRATE, TEPRENONE, CEFTRIAXONE SODIUM SESQUATERHYDRATE, CEFCAPENE PIVOXIL HYDROCHLORIDE HYDRATE, PREDNISOLONE, METHYLPREDNISOLONE SODIUM SUCCINATE, SULFAMETHOXAZOLE/TRIMETHOPRIM, MINOCYCLINE HYDROCHLORIDE, METHYLPREDNISOLONE SODIUM SUCCINATE, PIPERACILLIN/TAZOBACTAM, SULFAMETHOXAZOLE/TRIMETHOPRIM, MINOCYCLINE HYDROCHLORIDE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, ZOLPIDEM TARTRATE, BISOPROLOL FUMARATE, FUROSEMIDE, ELOBIXIBAT, CROTAMITON, SODIUM BICARBONATE/SODIUM PHOSPHATE MONOBASIC (ANHYDROUS), METHYLPREDNISOLONE, LEVOFLOXACIN, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, MINOCYCLINE HYDROCHLORIDE, PREDNISOLONE, PREDNISOLONE, MINOCYCLINE HYDROCHLORIDE, HEPARINOID, PREDNISOLONE, PREDNISOLONE, HYALURONATE SODIUM, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, L-CARBOCISTEINE, DIFLUCORTOLONE VALERATE, SULFAMETHOXAZOLE/TRIMETHOPRIM, PREDNISOLONE, PREDNISOLONE, PREDNISOLONE, CANNABIS SATIVA FRUIT/CITRUS SPP. UNRIPE FRUIT/MAGNOLIA SPP. BARK/PAEONIA LACTIFLORA ROOT/PRUNUS SPP. SEED/RHEUM SPP. RHIZOME, PREDNISOLONE, ENSITRELVIR FUMARIC ACID, PARACETAMOL, ENSITRELVIR FUMARIC ACID, AMBROXOL HYDROCHLORIDE, DEXTROMETHORPHAN HYDROBROMIDE MONOHYDRATE, AMBROXOL HYDROCHLORIDE, DIHYDROCODEINE PHOSPHATE, PREDNISOLONE, PETROLATUM/SALICYLIC ACID, FERROUS SODIUM CITRATE, FERROUS SODIUM CITRATE, ECABET SODIUM PENTAHYDRATE, PREDNISOLONE, FERROUS SODIUM CITRATE, BETAMETHASONE/DEXCHLORPHENIRAMINE MALEATE, CLONAZEPAM, OLOPATADINE HYDROCHLORIDE, LUBIPROSTONE, MAGNESIUM OXIDE, SODIUM PICOSULFATE MONOHYDRATE, ESOMEPRAZOLE MAGNESIUM, BUDESONIDE, THEOPHYLLINE, LOXOPROFEN SODIUM DIHYDRATE				
Non-Serious Adverse Event [4]: Palpitations, Gastric haemorrhage, COVID-19, Insomnia, Interstitial lung disease, Interstitial lung disease				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
間質性肺疾患	Interstitial pneumonia	Day 242 / Day 260	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3

治験責任医師の見解：「間質性肺疾患」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 7[redacted]
Medical History [1]: Atrioventricular block first degree, Cardiac failure, Cough, Dry skin, Dyslipidaemia, Hypertension, Carpal tunnel syndrome, Rotator cuff syndrome, Post herpetic neuralgia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 911			
Concomitant Medication [3]: FUROSEMIDE, ROSUVASTATIN CALCIUM, HYDROCORTISONE BUTYRATE, TOZINAMERAN, TOZINAMERAN, SACUBITRIL/VALSARTAN, SACUBITRIL/VALSARTAN, AMLODIPINE BESILATE, FUROSEMIDE, BILASTINE, CINNAMOMUM CASSIA BARK/COIX LACRYMA-JOBI VAR. MA-YUEN SEED/PAEONIA LACTIFLORA ROOT/PAEONIA X SUFFRUTICOSA ROOT BARK/PORIA COCOS SCLEROTIUM/PRUNUS SPP. SEED, HEPARINOID, TRANEXAMIC ACID, L-CARBOCISTEINE, PARACETAMOL, CEFTRIAXONE SODIUM SESQUATERHYDRATE, PANAX GINSENG ROOT/ZANTHOXYLUM PIPERITUM PERICARP/ZINGIBER OFFICINALE PROCESSED RHIZOME, AMOXICILLIN/CLAVULANATE POTASSIUM, CEFTRIAXONE SODIUM SESQUATERHYDRATE, AMOXICILLIN/CLAVULANATE POTASSIUM, SACUBITRIL/VALSARTAN, TOZINAMERAN, FUROSEMIDE, RIVAROXABAN, CELECOXIB, REBAMIPIDE, FUROSEMIDE, SPIRONOLACTONE, FUROSEMIDE, ROSUVASTATIN CALCIUM, HEPARINOID, AMLODIPINE BESILATE/VALSARTAN, LORATADINE, CLOBETASOL PROPIONATE, KETOPROFEN, LOXOPROFEN SODIUM DIHYDRATE, L-CARBOCISTEINE				
Non-Serious Adverse Event [4]: Atrial fibrillation, Cardiac failure, Constipation, Appendicitis perforated, Appendicitis perforated, Face injury, Joint injury, Limb injury, Haematuria, Renal impairment, Renal impairment				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
穿孔性虫垂炎（1）	Appendicitis purulent perforated	Day 432 / Day 454	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
穿孔性虫垂炎（2）	Appendicitis purulent perforated	Day 469 / Day 484	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3

治験責任医師の見解：「穿孔性虫垂炎（1）」及び「穿孔性虫垂炎（2）」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 5[redacted]
Medical History [1]: Cardiac failure, Dyslipidaemia, Osteoarthritis, Osteoarthritis, Seasonal allergy, Gastrooesophageal reflux disease, Meniscus injury, Rotator cuff syndrome, Carpal tunnel syndrome, Lumbar spinal stenosis				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911		
Concomitant Medication [3]: FEXOFENADINE HYDROCHLORIDE, RIVAROXABAN, APIXABAN, RABEPRAZOLE SODIUM, CEFAZOLIN SODIUM, LIDOCAINE, IOPAMIDOL, PROTAMINE SULFATE, HEPARIN SODIUM, DEXMEDETOMIDINE HYDROCHLORIDE, FENTANYL CITRATE, ADENOSINE TRIPHOSPHATE (DISODIUM SALT), TOZINAMERAN, TOZINAMERAN, PARACETAMOL, DEXTROMETHORPHAN HYDROBROMIDE MONOHYDRATE, L-CARBOCISTEINE, PARACETAMOL, CODEINE PHOSPHATE, DIMETICONE, MIDAZOLAM, PRONASE, SODIUM BICARBONATE, INFLUENZA VACCINE, CINNAMOMUM CASSIA BARK/EPHEDRA SPP. HERB/GLYCYRRHIZA SPP. ROOT/PAEONIA LACTIFLORA ROOT/PUERARIA MONTANA VAR. LOBATA ROOT/ZINGIBER OFFICINALE RHIZOME/ZIZIPHUS JUJU, PARACETAMOL, ELASOMERAN, LOXOPROFEN SODIUM DIHYDRATE, CHLORPHENAMINE MALEATE/DIHYDROCODEINE BITARTRATE/METHYLEPHEDRINE HYDROCHLORIDE-DL, CINNAMOMUM CASSIA BARK/EPHEDRA SPP. HERB/GLYCYRRHIZA SPP. ROOT/PAEONIA LACTIFLORA ROOT/PUERARIA MONTANA VAR. LOBATA ROOT/ZINGIBER OFFICINALE RHIZOME/ZIZIPHUS JUJU, LEVOFLOXACIN, CODEINE PHOSPHATE				
Non-Serious Adverse Event [4]: Atrial fibrillation, Malaise, Malaise, Pyrexia, COVID-19, Nasopharyngitis, Nasopharyngitis, Decreased appetite, Arthralgia, Myalgia				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
心房細動	Atrial fibrillation	Day 124 / Day 127	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
治験責任医師の見解：「心房細動」は治験薬と関連なしと判断した。						

Patient ID: [redacted]						
Treatment Arm: Acoramidis		Race: Asian	Country: Japan		Sex: M	Age: 6[redacted]
Medical History [1]: Cardiac failure, Hip arthroplasty, Spinal compression fracture, Carpal tunnel syndrome, Hypertension, Chronic obstructive pulmonary disease						
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911				
Concomitant Medication [3]: LIDOCAINE, FLURBIPROFEN AXETIL, DEXMEDETOMIDINE HYDROCHLORIDE, ESZOPICLONE, CEFAZOLIN SODIUM, PARACETAMOL, TOZINAMERAN, TOZINAMERAN, TOZINAMERAN, METOCLOPRAMIDE HYDROCHLORIDE, SODIUM BICARBONATE, AMOXICILLIN TRIHYDRATE, LOXOPROFEN SODIUM DIHYDRATE, REBAMIPIDE						
Non-Serious Adverse Event [4]: Hyperkalaemia, Arthritis, Gouty arthritis, Dizziness						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
軟部組織腫瘤	Soft tissue formation around the thoracic lumbar spine	Day 100 / Day 105	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
治験責任医師の見解：「軟部組織腫瘤」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 7[redacted]
Medical History [1]: Hyperlipidaemia, Hypertension, Hyperuricaemia, Gastrooesophageal reflux disease, Cardiac failure chronic, Cystoid macular oedema, Glaucoma, Diarrhoea, Large intestine polyp				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 910			
Concomitant Medication [3]: CLOSTRIDIUM BUTYRICUM, TOZINAMERAN, TOZINAMERAN, INFLUENZA VACCINE, TOZINAMERAN, COLCHICINE, LOXOPROFEN SODIUM DIHYDRATE, FEBUXOSTAT, LIDOCAINE HYDROCHLORIDE MONOHYDRATE, HEPARIN SODIUM, HYDROXYZINE HYDROCHLORIDE, PENTAZOCINE, CEFAZOLIN SODIUM, DIPHENHYDRAMINE, WHITE SOFT PARAFFIN, BRIMONIDINE TARTRATE, BROMFENAC SODIUM, DORZOLAMIDE HYDROCHLORIDE/TIMOLOL MALEATE, MOXIFLOXACIN HYDROCHLORIDE, ACETAZOLAMIDE, POTASSIUM ASPARTATE, LIDOCAINE HYDROCHLORIDE MONOHYDRATE, EPINEPHRINE, OFLOXACIN, BETAMETHASONE SODIUM PHOSPHATE, DICLOFENAC SODIUM, TRIAMCINOLONE ACETONIDE, PHENYLEPHRINE HYDROCHLORIDE, BUPIVACAINE HYDROCHLORIDE, OXYBUPROCAINE HYDROCHLORIDE, OXYBUPROCAINE HYDROCHLORIDE, ATROPINE SULFATE MONOHYDRATE, ATROPINE SULFATE MONOHYDRATE, PHENYLEPHRINE HYDROCHLORIDE/TROPICAMIDE, PARACETAMOL, HYALURONATE SODIUM, HYALURONATE SODIUM, BROMFENAC SODIUM, PHENYLEPHRINE HYDROCHLORIDE/TROPICAMIDE, LEVOFLOXACIN, BRIMONIDINE TARTRATE, DORZOLAMIDE HYDROCHLORIDE/TIMOLOL MALEATE, BETAMETHASONE SODIUM PHOSPHATE, SENNOSIDE A+B CALCIUM, BROMFENAC SODIUM, PHENYLEPHRINE HYDROCHLORIDE/TROPICAMIDE, PHENYLEPHRINE HYDROCHLORIDE/TROPICAMIDE, LEVOFLOXACIN, LEVOFLOXACIN, METHYLPREDNISOLONE, BETAMETHASONE SODIUM PHOSPHATE, BRIMONIDINE TARTRATE, METHYLPREDNISOLONE, VUTRISIRAN SODIUM, VITAMINS NOS, FEBUXOSTAT, BRIMONIDINE TARTRATE, DORZOLAMIDE HYDROCHLORIDE, BETAMETHASONE SODIUM PHOSPHATE, BROMFENAC SODIUM, PERINDOPRIL ERBUMINE, RIPASUDIL, ESOMEPRAZOLE MAGNESIUM, AZOSEMIDE, ATORVASTATIN CALCIUM, AMLODIPINE BESILATE						
Non-Serious Adverse Event [4]: Sinus node dysfunction, Blepharitis, Blepharitis, Constipation, Gout, Neuropathy peripheral, Device dislocation, Device dislocation, Device dislocation, Pruritus						
Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
洞結節機能不全	Sick sinus syndrome	Day 532 / Day 539	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
医療機器位置異常	Both intracular lens subluxation	Day 578 / Day 589	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
治験責任医師の見解：「洞結節機能不全」及び「医療機器位置異常」は治験薬と関連なしと判断た。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 8[redacted]
Medical History [1]: Seasonal allergy, Benign prostatic hyperplasia, Gout, Hyperuricaemia, Osteoporosis, Cerebral infarction, Inguinal hernia, Cardiac failure chronic, Ventricular extrasystoles, Angina pectoris, Chronic kidney disease, Percutaneous coronary intervention, Percutaneous coronary intervention				
Treatment First Dose Day [2]: Day 1		Last Dose Day [2]: Day 911		
Concomitant Medication [3]: ALLOPURINOL, NAFTOPIDIL, RISEDRONATE SODIUM, SOLIFENACIN SUCCINATE, ELDECALCITOL, FUROSEMIDE, BISOPROLOL FUMARATE, ACETYLSALICYLIC ACID, CLOPIDOGREL BISULFATE, VONOPRAZAN FUMARATE, ATORVASTATIN CALCIUM, EBASTINE, RUPATADINE FUMARATE, FUROSEMIDE, COVID-19 VACCINE MRNA, PARACETAMOL, RUPATADINE FUMARATE, ELASOMERAN, MAGNESIUM OXIDE, MAGNESIUM OXIDE, TOZINAMERAN, FUROSEMIDE, MAGNESIUM OXIDE, TOZINAMERAN, DESFLURANE, REMIFENTANIL HYDROCHLORIDE, CEFAZOLIN SODIUM, PARACETAMOL, RUPATADINE FUMARATE, ELASOMERAN, FERROUS SODIUM CITRATE				
Non-Serious Adverse Event [4]: Anaemia, Cardiac failure, Constipation, Inguinal hernia, Pyrexia, Chronic kidney disease				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
鼠径ヘルニア	Worsened right inguinal hernia	Day 676 / Day 679	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
治験責任医師の見解：「鼠径ヘルニア」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 8[redacted]
Medical History [1]: Age-related macular degeneration, Hyperuricaemia, Hypothyroidism, Inguinal hernia, Insomnia, Ventricular tachycardia, Prostate cancer, Atrial fibrillation, Cardiac failure chronic				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 916			
Concomitant Medication [3]: PIMOBENDAN, BISOPROLOL FUMARATE, TORASEMIDE, TOZINAMERAN, TOZINAMERAN, ELASOMERAN, EMPAGLIFLOZIN, ELASOMERAN, FEBUXOSTAT,PREGABALIN, CELECOXIB, REBAMIPIDE, PREGABALIN, BETAMETHASONE BUTYRATE PROPIONATE, BISOPROLOL FUMARATE, BISOPROLOL FUMARATE, BISOPROLOL FUMARATE, BISOPROLOL FUMARATE, FUROSEMIDE, AZOSEMIDE, LEMBOREXANT, AZOSEMIDE, HYDROCORTISONE, BACILLUS NOS, LACTOMIN, MOSAPRIDE CITRATE, FAMOTIDINE, TEPRENONE, MAGNESIUM OXIDE, AZOSEMIDE, MAGNESIUM OXIDE, SENNOSIDE A+B CALCIUM, FLUMAZENIL, THIOPENTAL SODIUM, LIDOCAINE, DEXMEDETOMIDINE HYDROCHLORIDE, MIDAZOLAM, CEFAZOLIN SODIUM, BISOPROLOL FUMARATE, POTASSIUM ASPARTATE, ANGELICA ACUTILOBA ROOT/ATRACTYLODES LANCEA RHIZOME/BUPLEURUM FALCATUM ROOT/GLYCYRRHIZA SPP. ROOT/LIGUSTICUM OFFICINALE RHIZOME/PORIA COCOS SCLEROTIUM/UNCARIA SPP. HOOK, SENNOSIDE A+B CALCIUM, ANGELICA ACUTILOBA ROOT/ATRACTYLODES LANCEA RHIZOME/BUPLEURUM FALCATUM ROOT/GLYCYRRHIZA SPP. ROOT/LIGUSTICUM OFFICINALE RHIZOME/PORIA COCOS SCLEROTIUM/UNCARIA SPP. HOOK, POTASSIUM CHLORIDE, BISOPROLOL FUMARATE, AZOSEMIDE, BISOPROLOL FUMARATE, DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE, FEBUXOSTAT, AZOSEMIDE, RIVAROXABAN, LEVOTHYROXINE SODIUM				
Non-Serious Adverse Event [4]: Palpitations, Abdominal pain upper, Anal fissure, Constipation, Hypokalaemia, Sciatica, Haematuria, Haematuria, Renal impairment, Rash, Urticaria				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
完全房室ブロック	AF bradycardia with complete AV block	Day 873 / Day 889	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
心不快感	Cardiac chest discomfort	Day 772 / Day 778	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
心不全	Exacerbation of heart failure	Day 843 / Day 856	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2
膀胱癌	Bladder cancer	Day 818 / Day 836	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 2

治験責任医師の見解：「完全房室ブロック」、「心不快感」、「心不全」及び「膀胱癌」は治験薬と関連なしと判断した。

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 7[redacted]
Medical History [1]: Atrial fibrillation, Cardiac failure chronic, Chronic obstructive pulmonary disease, Large intestine polyp, Constipation, Dyspepsia, Hypertension, Insomnia, Iron deficiency anaemia, Spinal stenosis				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 909			
Concomitant Medication [3]: SPIRONOLACTONE, LOSARTAN POTASSIUM, TOZINAMERAN, TOZINAMERAN, DICLOFENAC SODIUM, AMOXICILLIN TRIHYDRATE, VONOPRAZAN FUMARATE, METRONIDAZOLE, VONOPRAZAN FUMARATE, ACOTIAMIDE HYDROCHLORIDE TRIHYDRATE, TOZINAMERAN, VALSARTAN, ELASOMERAN, INFLUENZA VACCINE, ELASOMERAN, FEBUXOSTAT, DAPAGLIFLOZIN, RIVAROXABAN, TRANEXAMIC ACID, ASARUM SPP. ROOT/CINNAMOMUM CASSIA BARK/EPHEDRA SPP. HERB/GLYCYRRHIZA SPP. ROOT/PAEONIA LACTIFLORA ROOT/PINELLIA TERNATA TUBER/SCHISANDRA CHINENSIS FRUIT/ZINGIBER, LOXOPROFEN SODIUM DIHYDRATE, REBAMIPIDE, ANTIBIOTICS-RESISTANT LACTIC ACID BACTERIAE, AMOXICILLIN TRIHYDRATE/CLAVULANATE POTASSIUM, SODIUM GUALENATE HYDRATE, CEFDITOREN PIVOXIL, ASCORBIC ACID/CALCIUM PANTOTHENATE, FERROUS SODIUM CITRATE, RIVAROXABAN, MAGNESIUM OXIDE, ZOLPIDEM TARTRATE, TIOTROPIUM BROMIDE MONOHYDRATE				
Non-Serious Adverse Event [4]: Helicobacter gastritis, Nasopharyngitis, Heat stroke, Hyperuricaemia, Back pain				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
大腸ポリープ	Colorectal polyps	Day 325 / Day 326	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 1
治験責任医師の見解：「大腸ポリープ」は治験薬と関連なしと判断した。						

Patient ID: [redacted]				
Treatment Arm: Acoramidis	Race: Asian	Country: Japan	Sex: M	Age: 7[redacted]
Medical History [1]: Appendicitis, Carpal tunnel syndrome, Cardiac failure chronic, Atrioventricular block first degree, Gynaecomastia, Hyperuricaemia, Meniscus injury, Nephrolithiasis, Hypertension, Cerebral infarction, Cataract, Rotator cuff syndrome, Spinal osteoarthritis, Spinal osteoarthritis, Hyperlipidaemia				
Treatment First Dose Day [2]: Day 1	Last Dose Day [2]: Day 906			
Concomitant Medication [3]: ATORVASTATIN CALCIUM, AMLODIPINE BESILATE, AZOSEMIDE, KETOPROFEN, NIFEDIPINE, ENALAPRIL MALEATE, ALISMA PLANTAGO-AQUATICA SUBSP. ORIENTALE TUBER/ATRACTYLODES SPP. RHIZOME/BUPLEURUM FALCATUM ROOT/CINNAMOMUM CASSIA BARK/GLYCYRRHIZA SPP. ROOT/PANAX GINSENG ROOT/PINELLIA TERNATA TUBER/POLYP, FLUOROMETHOLONE, AZOSEMIDE, TOZINAMERAN, TOZINAMERAN, AZOSEMIDE, KETOPROFEN, LIDOCAINE, PRONASE, BARIUM SULFATE, AMOXICILLIN TRIHYDRATE, VONOPRAZAN FUMARATE, CLARITHROMYCIN, FUROSEMIDE, FEXOFENADINE HYDROCHLORIDE, DEXTROMETHORPHAN HYDROBROMIDE MONOHYDRATE, CARBOCISTEINE, CALCIUM CHLORIDE DIHYDRATE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, EPERISONE HYDROCHLORIDE, CALCIUM POLYSTYRENE SULFONATE, DESLORATADINE, PENTAZOCINE, CEFMETAZOLE SODIUM, EDOXABAN TOSILATE MONOHYDRATE, CEFMETAZOLE SODIUM, CARBAZOCHROME SODIUM SULFONATE, TOBRAMYCIN, THIAMYLAL SODIUM, HYDROXYZINE HYDROCHLORIDE, PENTAZOCINE, CALCIUM CHLORIDE DIHYDRATE/POTASSIUM CHLORIDE/SODIUM CHLORIDE/SODIUM LACTATE, DEXMEDETOMIDINE HYDROCHLORIDE, PARACETAMOL, AZOSEMIDE,NAPROXEN, ACETYLSALICYLIC ACID, FUROSEMIDE, EMPAGLIFLOZIN, FUROSEMIDE, NIFEDIPINE, TOZINAMERAN, AMOXICILLIN TRIHYDRATE, VONOPRAZAN FUMARATE, CLARITHROMYCIN, PARACETAMOL, CALCIUM POLYSTYRENE SULFONATE, LIDOCAINE, HYDROXYZINE HYDROCHLORIDE, HEPARIN SODIUM, PENTAZOCINE, ISOSORBIDE DINITRATE, ISOSORBIDE DINITRATE, IOHEXOL, HYALURONATE SODIUM, PREGABALIN, ENALAPRIL MALEATE, CARVEDILOL, ACETYLSALICYLIC ACID, FEBUXOSTAT				
Non-Serious Adverse Event [4]: Atrial flutter, Dry eye, Visual impairment, Nausea, Malaise, Helicobacter infection, Nasopharyngitis, Blood creatine phosphokinase MB increased, Blood creatine phosphokinase MB increased, Blood creatinine increased, Blood creatinine increased, Blood creatinine increased, Dehydration, Gout, Hyperkalaemia, Neuralgia, Haematuria, Pulmonary mass, Rash				

Serious Adverse Event (PT) [4]	Verbatim Term	Start Day/ End Day [2]	Relationship	Action Taken	Outcome	Toxicity [5]
洞停止	Sinus arrest	Day 470 / Day 484	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 4
血中クレアチンホスホキナーゼＭＢ増加	CK-MB elevation	Day 658 / Day 659	Not Related	Dose Not Changed	Recovered/ Resolved	Grade 3
治験責任医師の見解：「洞停止」及び「血中クレアチンホスホキナーゼＭＢ増加」は治験薬と関連なしと判断した。						