2.7.6.9 【国際共同試験】非転移性去勢抵抗性前立腺癌患者を対象とした第Ⅲ相試験：試験 17712（報告書番号 PH-39723）

参照項目：5.3.5.1.1 PH-39723

2.7.6.9.1 試験計画の概要

試験の標題：

ハイリスク[1)]の非転移性去勢抵抗性前立腺癌患者を対象としたダロルタミドの有効性及び安全性を検討する、無作為化、二重盲検、プラセボ対照、第Ⅲ相試験

実施医療機関：409 施設（カナダ、米国、日本、韓国、台湾、アルゼンチン、オーストリア、オーストラリア、ベラルーシ、ベルギー、ブラジル、ブルガリア、コロンビア、チェコ、エストニア、フィンランド、フランス、ドイツ、ハンガリー、イスラエル、イタリア、ラトビア、リトアニア、ペルー、ポーランド、ポルトガル、ルーマニア、ロシア連邦、セルビア、スロバキア、南アフリカ、スペイン、スウェーデン、トルコ、ウクライナ、英国：36 ヵ国）

試験期間：

最初の被験者の組入れ日：2014 年 9 月 12 日

最後の被験者の完了日： 2018 年 9 月 3 日
（データカットオフ）

開発のフェーズ：第Ⅲ相

目的：

主要目的

ハイリスクの非転移性去勢抵抗性前立腺癌（nmCRPC）患者を対象として、無転移生存期間（MFS）についてダロルタミドのプラセボに対する優越性を検討する。

副次目的

全生存期間（OS）、疼痛増悪までの期間、細胞傷害性薬剤による化学療法の初回開始までの期間、及び症候性骨関連事象（SSE）の初回発現までの期間について、プラセボと比較しダロルタミドの有効性を示し、かつ安全性及び忍容性を検討する。

試験方法：

本試験は、スクリーニング期間、治験薬投与期間と追跡調査期間で構成された。

適格基準を満たした被験者を、二重盲検下にて 2：1 の割合で、ダロルタミド群（ダロルタミドを 600mg 1 日 2 回投与）又はプラセボ群に無作為に割付けた。前立腺特異抗原倍加時間（PSADT、6 ヵ月以下又は 6 ヵ月超）及び破骨細胞標的薬の使用の有無を、割付け時の層別因子とした。

被験者は、第 1 日、第 15 日、第 29 日及び第 16 週、並びにその後 16 週ごとに治験実施医療機関に来院することとした。コンピュータ断層撮影法（CT）／磁気共鳴画像診断法（MRI）及び骨シンチグラフィをベースライン時及び転移が認められるまで 16 週ごとに実施した。転移の有無は、ベースライン時及び試験期間中に、盲検下の中央判定による読影により確認した。中央判定による変化の特定には、画像検査（CT／MRI 又は X 線検査）による確認を必要とした。転移が確認された又は忍容できない有害事象が認められた場合、被験者は治験薬の投与を中止し、来院又は電話連絡により試験終了まで 16 週ごとに、副次評価項目及びその他の評価項目について追跡調査を受けることとした。

二重盲検期間中、転移の確認前に併用禁止療法が開始された被験者は、治験薬の投与を中止し、生存状況のみの追跡調査期間に移行することとした。

二重盲検期間は、MFS イベントの総件数が約 385 件に達するまで継続することとした。本試験の結果

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1) 前立腺特異抗原倍加時間（PSADT）が 10 ヵ月以下で血清中 PSA 値が 2ng/mL 以上の患者をハイリスクの nmCRPC 患者とした。

が得られ、ダロルタミド投与によるベネフィットがリスクを上回ると治験依頼者が判断した場合は（本試験の運営委員会及び／又は規制当局の意見を考慮した上で）、治験薬を投与中の被験者に、非盲検下でダロルタミドの投与を受ける機会を提供することとした。

治験薬の盲検解除時に非盲検下でダロルタミドの投与を受けることを選択した被験者は、非盲検投与開始来院を実施し、治験実施医療機関による判定で転移がみられるまで16週ごとに来院することとした。転移が確認された場合、治験薬の投与を中止し、副次評価項目及びその他の評価項目について16週ごとに追跡調査を受けた。

追跡調査期間中は16週ごとに被験者に連絡を取り、生存確認を行った。生存データは更に、生存調査を通して収集した。すなわち、MFS解析のデータカットオフ日の直後、及び以降のOS解析実施前の時点で生存とみなされている被験者全例に連絡を取り、生存調査を行った。

被験薬：

ダロルタミドフィルムコーティング錠300mg

用法・用量

ダロルタミド600mg（300mg錠×2）を食後に1日2回経口投与

投与期間

転移が確認されるまで又は忍容できない有害事象が認められるまで

対照薬：

ダロルタミドフィルムコーティング錠300mgと外観が同じプラセボ

用法・用量

プラセボ（2錠）を食後に1日2回経口投与

投与期間

転移が確認されるまで又は忍容できない有害事象が認められるまで

選択・除外基準：

主な選択基準

(1) 文書による同意を得たもの

(2) 組織診又は細胞診により神経内分泌分化又は小細胞の特徴が認められない前立腺の腺癌と確定診断されたもの

(3) 去勢抵抗性前立腺癌（CRPC）患者〔CRPCは、アンドロゲン遮断療法（ADT）施行中に1週間以上間隔を空けた前立腺特異抗原（PSA）測定で、最低値が確認された後、3回の上昇が認められることと定義した〕。抗アンドロゲン薬の使用歴があった患者の場合は、抗アンドロゲン薬の中止から4週間以上が経過した最新のPSA値を測定しなければならない。

(4) 性腺刺激ホルモン放出ホルモン（GnRH）アゴニスト療法若しくはアンタゴニスト療法の施行期間中、又は両側精巣摘除術後の血清テストステロン値が去勢レベル〔1.7nmol/L（50ng/dL）未満〕であるもの。両側精巣摘除術を受けていない患者は、試験期間中、GnRHアゴニスト療法若しくはアンタゴニスト療法を継続しなければならない。

(5) PSADTが10ヵ月間以下かつスクリーニング時のPSAが2ng/mL以上であるもの

(6) 米国東部腫瘍臨床試験グループのパフォーマンスステータス（ECOG-PS）が0～1であるもの

主な除外基準

(1) 転移の既往（時期は不問とする）又は治験薬投与開始前42日以内に撮像した画像で盲検下の中央判定により検知可能な転移が存在するもの。大動脈分岐部下の短径2cm未満の骨盤リンパ節の存在は可とした。

(2) 前立腺癌に起因する中等度／重度の尿路閉塞又は水腎症など、医学的処置を要する症候性の局所的病態を有するもの

(3) 以下の前治療歴があるもの

- 第2世代アンドロゲン受容体（AR）阻害薬（エンザルタミド、アパルタミド、ダロルタミ

ド、その他の治験中の AR 阻害薬など）

- チトクローム P450（CYP）17 酵素阻害薬（アビラテロン酢酸エステル、オルテロネルなど）
- 28 日間を超えるケトコナゾールの経口投与

(4) 無作為割付け前 28 日以内にエストロゲン又は 5-α 還元酵素阻害薬（フィナステリド、デュタステリド）を使用したもの及びスクリーニング前 28 日以内に AR 阻害薬（ビカルタミド、フルタミド、nilutamide、酢酸シプロテロン）を使用したもの

(5) 前立腺癌に対する化学療法又は免疫療法の施行歴があるもの。なお、無作為割付けの 2 年より前に完了した術前補助療法／術後補助療法は除く。

(6) 無作為割付け前 28 日以内に prednisone 換算で 10mg/日以上のコルチコステロイドの全身投与を受けたもの

(7) 無作為割付け前 12 週以内に放射線療法〔外部照射療法（EBRT）、近距離照射療法又は放射性医薬品〕を受けたもの

(8) 無作為割付け前 12 週以内に、骨関連事象の予防を目的として破骨細胞標的薬（ビスホスホネート又はデノスマブ）の投与を受けたもの。骨粗鬆症に適応される用量及びスケジュールで骨量減少の予防を目的として破骨細胞標的薬の投与を受けている患者は、同じ用量及びスケジュールで投与を継続できる。

(9) 悪性腫瘍の既往歴があるもの。適切に治療された皮膚の基底細胞癌若しくは扁平上皮癌、又は結合組織層を越えて浸潤していない表在性膀胱癌（すなわち、pTis、pTa 及び pT1）は可とする。また、それ以外の癌で、5 年以上前に治療が完了し、それ以降、患者が無病状態を維持している場合も可とする。

(10) 胃腸障害を有するもの又は治験薬の吸収を著しく障害することが予想される処置を受けたもの

(11) 無作為割付け前 28 日以内に他の治験薬の投与を受けたもの

(12) 治験手順の遵守が困難であると治験責任（分担）医師が判断する状態を有するもの

有効性の評価項目：

主要評価項目

MFS（無作為割付け時点から、転移が確認された日又はあらゆる原因による死亡のいずれか早い方が認められるまでの期間と定義）とした。

副次評価項目：

有効性副次評価項目は、逐次的ゲートキーピング法を用いて、以下の順に解析した。

- OS
- 疼痛増悪までの期間〔簡易疼痛調査用紙（縮小版）と初回のオピオイド使用により判定した〕
- 前立腺癌に対する細胞傷害性薬剤による化学療法の初回開始までの期間
- SSE（骨関連症状の緩和のための EBRT、新たな症候性の病的骨折、脊髄圧迫の発現、又は腫瘍関連の整形外科的処置と定義した）の初回発現までの期間

その他の評価項目

無増悪生存期間（PFS）、前立腺癌関連の初回侵襲的処置までの期間、PSA の奏効割合、次の抗腫瘍療法の開始までの期間、及び生活の質（QOL）など（結果は 5.3.5.1.1 PH-39723/Section 9.2.1.4 参照）

薬物動態の評価項目：

ダロルタミド、SR 体、SS 体及び M-1 の血漿中濃度

薬物動態の解析結果については別途報告する。

安全性の評価項目：

- 有害事象
- バイタルサイン（血圧及び心拍数）

- 12 誘導心電図
- 理学的検査
- 臨床検査（血液学的検査、血液生化学的検査、尿検査）

被験者数：

目標被験者数：

1,500 例（ダロルタミド群：1,000 例、プラセボ群：500 例）

設定根拠：

被験者数は、有効性の主要評価項目である MFS に基づいて決定した。

ダロルタミド群とプラセボ群のハザード比を 0.71 と仮定した。また、全体の第一種の過誤率を 0.05、割付け比を 2：1、検出力を 91%、プラセボ群における MFS の中央値を 25 ヵ月と仮定し、被験者数を定めた。

ログランク検定を用い、有意水準を両側 0.05 として MFS における統計学的有意差を検出する場合、385 の MFS イベントを観察することにより、約 91%の検出力が得られる。被験者の集積期間を 40 ヵ月、脱落率を 40%と仮定すると、約 1,500 例（ダロルタミド群：1,000 例、プラセボ群：500 例）の集積が必要となる。

解析方法：

最大の解析対象集団（FAS）：無作為割付けされたすべての被験者。すべての有効性評価項目の主要解析対象集団として用いた。

安全性解析対象集団（SAF）：治験薬投与を受けたすべての被験者。SAF を安全性の解析に用いた。

すべての有効性の解析において、割付け時の層別因子（PSADT 及び破骨細胞標的薬の使用の有無）による調整を行った。

有効性の主要評価項目

MFS におけるダロルタミド群のプラセボ群に対する優越性を示すため、約 385 件のイベントを収集し、有意水準を両側 0.05 として層別ログランク検定を用いて比較した。

有効性の主要評価項目について、正式な中間解析は計画していなかった。

有効性の副次評価項目

副次評価項目について、MFS 解析時及びそれ以降にも統計的有意性を評価した。主要評価項目と同様に、層別ログランク検定を用いてダロルタミド群とプラセボ群を比較した。

MFS 解析時に実施する解析を中間解析、それ以降に行う解析を最終解析とみなした。また、有意性の検定を伴わない更なる解析を行う可能性があった。

安全性

治験薬投与開始から治験薬投与終了後 30 日までに発現した有害事象を治験薬投与下で発現した有害事象（TEAE）とした。有害事象は、ICH 国際医薬用語集（MedDRA）Ver.21.0 を用いてコーディングし、各有害事象の発現例数、発現割合及び曝露期間で調整した発現率（100 人年あたり）を示した。

有害事象の重症度（グレード）は、NCI-CTCAE Ver.4.03 を用いて評価し、最悪グレードで集計した。

独立した安全性データモニタリング委員会（DSMB）が、被験者の安全性に関するダロルタミドのベネフィット／リスクプロファイルを定期的に確認した。

治験薬との因果関係が否定できない毒性に対する用量調節及び投与の中断

重症度グレード (NCI-CTCAE v 4.03)	用量調節	治験薬の投与中止
グレード0～2	予定通りに投与する。 治験責任（分担）医師の判断に従い治験薬の投与を中断又は減量する [a, b]。	-
グレード3又は4	グレード 2 以下に回復するまで投与を中断する [a]。 重症度がグレード 2 以下に回復した後、300mg 1 日 2 回に減量し、投与を再開する [b, c]。	治験薬の用量を一時的に又は完全に 300mg 1 日 2 回に減量し、300mg 1 日 2 回投与時に治験薬と因果関係が否定できないグレード 3 以上の有害事象が発現した場合、治験薬の投与を中止する。

臨床的に重要でなく、症状を伴わない臨床検査値異常は除外する。

略語：NCI-CTCAE v 4.03 = 米国 National Cancer Institute 有害事象共通用語規準 第 4.03 版

a 28 日間を超えて回復が認められない場合、投与を完全に中止すること。

b 有害事象がベースラインまで回復、又は消失した場合は、治験責任（分担）医師の判断で 600mg 1 日 2 回投与への増量を検討してもよい。

c 用量を 600mg に増量した後で、2 回目の治験薬との因果関係を否定できないグレード 3 以上の有害事象が発現した場合は、永久的に減量する。3 回目のグレード 3 以上の治験薬との因果関係を否定できない有害事象が発現した場合は、治験薬の投与を完全に中止する。

2.7.6.9.2 成績

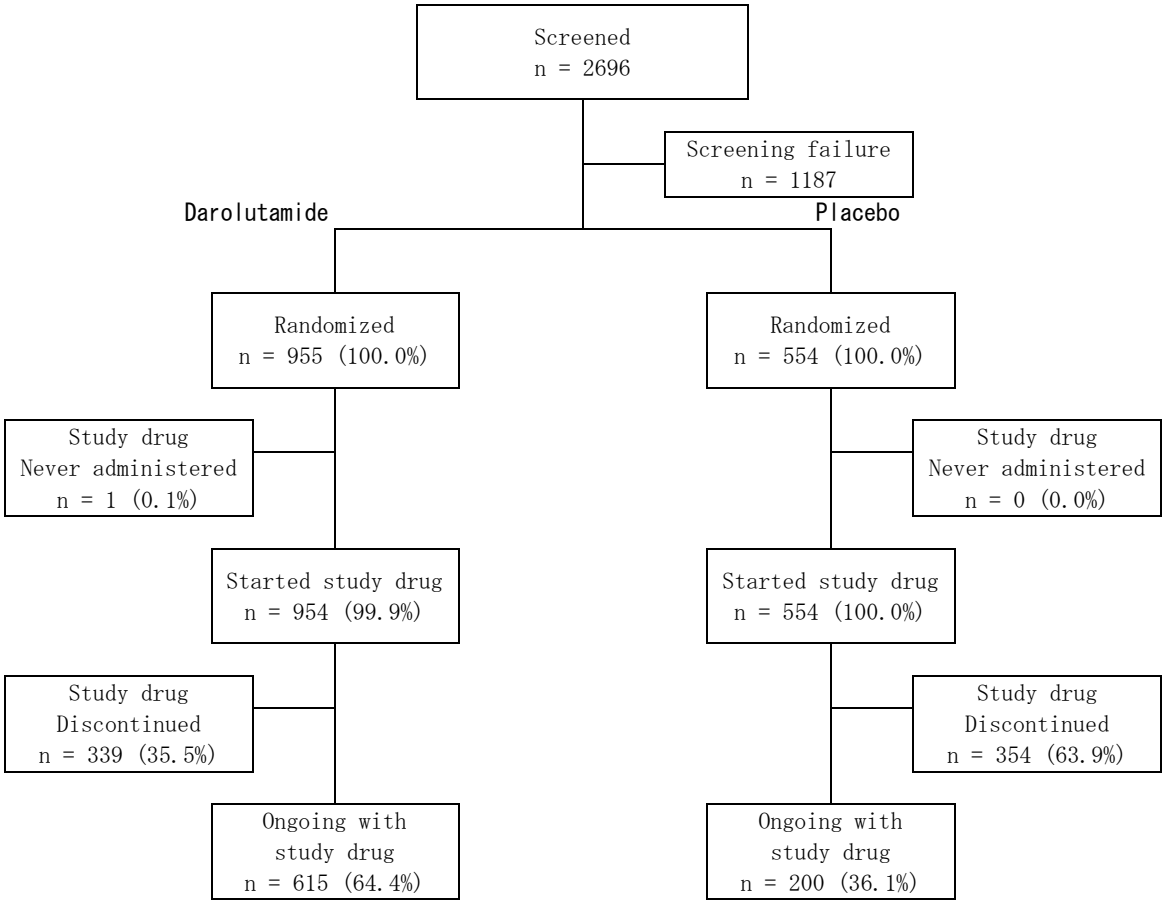
2.7.6.9.2.1 試験対象集団

2.7.6.9.2.1.1 被験者の内訳

被験者の内訳を図 2.7.6.9-1 及び表 2.7.6.9-1 に示す。

2,696 例の被験者が組入れられ、1,187 例（44.0%）がスクリーニングで不適格となった。ダロルタミド群に 955 例、プラセボ群に 554 例が割付けられ、ダロルタミド群 954 例、プラセボ群 554 例の合計 1,508 例が治験薬の投与を受けた。

データカットオフ日（2018 年 9 月 3 日）時点で治験薬投与中の被験者数は、ダロルタミド群 615 例（64.4%）、プラセボ群 200 例（36.1%）で、投与を中止した被験者数は、それぞれ 339 例（35.5%）及び 354 例（63.9%）であった。



Source：5.3.5.1.1 PH-39723/Table 14.1.1/5

図 2.7.6.9-1 被験者の内訳（組入れられた全被験者）

表 2.7.6.9-1 被験者の内訳（組入れられた全被験者）

Patient disposition		
Enrolled [a]	2696	
Screening failures [b]	1187	
	Darolutamide	Placebo
Randomized (N=1509; included in FAS)	955 (100.0%)	554 (100.0%)
Study drug never administered	1/955 (0.1%)	0/554
Started treatment (N = 1508; included in SAF)	954/955 (99.9%)	554/554 (100.0%)
Ongoing with treatment (as of the cut-off date)	615/955 (64.4%)	200/554 (36.1%)
Discontinued study treatment	339/955 (35.5%)	354/554 (63.9%)
Entered follow-up [c]	291/955 (30.5%)	332/554 (59.9%)
Ongoing with follow-up [d]	117/291 (40.2%)	169/332 (50.9%)
Discontinued follow-up [d]	174/291 (59.8%)	163/332 (49.1%)

N = total number of patients

a: Number of patients enrolled is the number of patients who signed informed consent. Re-screened patients are only considered once (last enrollment captured).

b: One patient received two doses of study drug but was not randomized and was included as a screening failure (more than 28 days between screening and central imaging review), and therefore was not included in any analysis set.

c: Patients with end of treatment visit and/or follow-up visit and/or documented reason of discontinuation of follow-up were considered to have entered follow-up. Not all of the patients performed the first follow-up visit.

d: Percentages for patients ongoing with follow-up and patients who discontinued follow-up were manually calculated by treatment arm from patients who entered follow-up.

Source: 5.3.5.1.1 PH-39723/Table 14.1.1/5, 14.1.1/15

治験薬投与中止の主な理由を表 2.7.6.9-2 に示す。

投与中止理由で最も多かったものは、中央判定で確認された転移で、ダロルタミド群で 112 例（33.0%）、プラセボ群で 129 例（36.4%）であった（表 2.7.6.9-2）。中央判定により転移が同定されたことによる治験薬投与の中止は、ダロルタミド群で 955 例中 112 例（11.7%）、プラセボ群で 554 例中 129 例（23.3%）であった。有害事象による中止は、ダロルタミド群で 86 例（9.0%）、プラセボ群で 47 例（8.5%）であった。

治験実施計画書で規定したとおり、転移が確認された被験者は試験を中止することとしていた。中央判定で転移が同定された被験者は、ダロルタミド群で 180 例（18.8%）、プラセボ群で 197 例（35.6%）であった（表 2.7.6.9-5）。このうち、ベースライン時に既に転移があったことが有効性評価の中央判定で同定された被験者は、ダロルタミド群で 50 例、プラセボ群で 39 例であった。ダロルタミド群の 168 例（17.6%）、プラセボ群の 188 例（33.9%）は、中央判定の評価に基づき転移が確認されたものの試験を継続した（5.3.5.1.1 PH-39723/Table 14.2.1/156）。中央判定による転移の確認から治験薬投与中止までの期間は、ダロルタミド群で 2～1,146 日、プラセボ群で 2～1,012 日であった（5.3.5.1.1 PH-39723/Table 14.2.1/158）。

治験責任（分担）医師の判断による中止は、ダロルタミド群の 54 例（15.9%）、プラセボ群の 91 例（25.7%）で報告され、そのうち、臨床的病勢進行〔ダロルタミド群：54 例中 37 例（68.5%）、プラセボ群 91 例中 60 例（65.9%）〕、PSA 増加〔54 例中 6 例（11.1%）、91 例中 16 例（17.6%）〕及び治験責任（分担）医師の判断〔54 例中 6 例（11.1%）、91 例中 6 例（6.6%）〕が多かった（5.3.5.1.1 PH-39723/Table 14.1/3s3）。

個人的な理由による中止は、ダロルタミド群の 68 例（20.1%）、プラセボ群の 78 例（22.0%）で報告され、そのうち、PSA 増加〔ダロルタミド群：68 例中 2 例（2.9%）、プラセボ群：78 例

中 6 例（7.7%）〕及び新規の前立腺癌治療の開始〔68 例中 1 例（1.5%）、78 例中 8 例（10.3%）〕を含む同意撤回〔68 例中 52 例（76.5%）、78 例中 49 例（62.8%）〕が最も多かった（5.3.5.1.1 PH-39723/Table 14.1/3s3）。次いで、PSA 増加〔ダロルタミド群：68 例中 0 例（0.0%）、プラセボ群：78 例中 4 例（5.1%）〕及び新規の前立腺癌治療の開始〔68 例中 5 例（7.4%）、78 例中 4 例（5.1%）〕を含む被験者判断〔68 例中 11 例（16.2%）、78 例中 24 例（30.8%）〕が多かった。

その他〔ダロルタミド群：6 例（1.8%）、プラセボ群：2 例（0.6%）〕に分類された理由として、最も多かったのは 28 日以上の治験薬投与の中止であった（5.3.5.1.1 PH-39723/Table 14.1.1/9）。

表 2.7.6.9-2 治験薬投与中止の主な理由（FAS）

	Darolutamide		Placebo	
	Total N = 955 n (%)	Discontinued treatment N=339 [a] n (%)	Total N = 554 n (%)	Discontinued treatment N=554 [a] n (%)
Discontinued study treatment, Primary reason:	339/955 (35.5%)	339/339 (100.0%)	354/554 (63.9%)	354/354 (100.0%)
Adverse event	86/955 (9.0%)	86/339 (25.4%)	47/554 (8.5%)	47/354 (13.3%)
Confirmed metastasis	112/955 (11.7%)	112/339 (33.0%)	129/554 (23.3%)	129/354 (36.4%)
Judgment of the investigator	54/955 (5.7%)	54/339 (15.9%)	91/554 (16.4%)	91/354 (25.7%)
Other	6/955 (0.6%)	6/339 (1.8%)	2/554 (0.4%)	2/354 (0.6%)
Personal reason	68/955 (7.1%)	68/339 (20.1%)	78/554 (14.1%)	78/354 (22.0%)
Protocol deviation	13/955 (1.4%)	13/339 (3.8%)	7/554 (1.3%)	7/354 (2.0%)

N = total number of patients (100%); n = number of patients with event

a: Percentages for the primary reasons for discontinuation were manually calculated by treatment arm from the number of patients who discontinued study treatment.

Source: 5.3.5.1.1 PH-39723/Table 14.1.1/8

2.7.6.9.2.1.2 解析対象集団

無作為割付けされた 1,509 例（ダロルタミド群：955 例、プラセボ群：554 例）を FAS とした。無作為割付けされたが治験薬投与を受けなかった 1 例（1 例、0 例）を除いた 1,508 例（954 例、554 例）を SAF とした（5.3.5.1.1 PH-39723/Table 14.1.1/18）。

2.7.6.9.2.1.3 人口統計学的及びベースラインの特性

2.7.6.9.2.1.3.1 人口統計学的特性

人口統計学的特性を表 2.7.6.9-3 に示す。

FAS の 1,509 例は、すべて男性であった。人口統計学的特性は群間で同様であった。

人種は、白人がダロルタミド群 760 例（79.6%）及びプラセボ群 434 例（78.3%）、アジア人がそれぞれ 122 例（12.8%）及び 71 例（12.8%）であった。年齢の中央値は、いずれの投与群においても 74.0 歳であった。

表 2.7.6.9-3 人口統計学的特性 (FAS)

	Darolutamide N = 955 n (%)	Placebo N = 554 n (%)
Age (years)		
n	955	554
Mean	73.9	73.2
StD	7.8	8.2
Min	48	50
Median	74.0	74.0
Max	95	92
Age group (years), n (%)		
<65	113 (11.8%)	84 (15.2%)
65-74	373 (39.1%)	216 (39.0%)
75-84	384 (40.2%)	209 (37.7%)
≥85	85 (8.9%)	45 (8.1%)
Race, n (%)		
Missing [a]	36 (3.8%)	19 (3.4%)
Asian	122 (12.8%)	71 (12.8%)
Black or African American	28 (2.9%)	24 (4.3%)
Other	9 (0.9%)	6 (1.1%)
White	760 (79.6%)	434 (78.3%)
Ethnicity, n (%)		
Not reported [a]	923 (96.6%)	539 (97.3%)
Hispanic or Latino	32 (3.4%)	15 (2.7%)
Geographical region, n (%)		
North America	108 (11.3%)	76 (13.7%)
Asia Pacific	119 (12.5%)	67 (12.1%)
Rest of the World [b]	728 (76.2%)	411 (74.2%)
Body Mass Index (kg/m^2) categories, n (%)		
Missing	2 (0.2%)	3 (0.5%)
<20	16 (1.7%)	9 (1.6%)
20 to <25	217 (22.7%)	120 (21.7%)
25 to <30	414 (43.4%)	234 (42.2%)
≥30	306 (32.0%)	188 (33.9%)
Renal function, eGFR at baseline, n (%) [c]		
Normal: eGFR ≥90 mL/min	412 (43.1%)	230 (41.5%)
Mildly impaired: 60 ≤ eGFR <90 mL/min	423 (44.3%)	248 (44.8%)
Moderately impaired: 30 ≤ eGFR <60 mL/min	119 (12.5%)	76 (13.7%)
Severely impaired: 15 ≤ eGFR <30 mL/min	1 (0.1%)	0 (0.0%)
Hepatic function, n (%)		
Missing	0 (0.0%)	1 (0.2%)
Normal: total bilirubin and AST ≤ ULN	864 (90.5%)	509 (91.9%)
Mildly impaired: total bilirubin > ULN to 1.5 x ULN or total bilirubin ≤ ULN and AST > ULN	89 (9.3%)	43 (7.8%)
Moderately impaired: total bilirubin > 1.5 to 3 x ULN, any AST	2 (0.2%)	1 (0.2%)

AST = aspartate aminotransferase; BMI = body mass index; eGFR = estimated glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; N = total number of patients (100%); n = number of patients with event; SCR= Serum creatinine; StD = standard deviation; ULN = upper limit of normal.

Note: Baseline data were taken from the non-missing observation before or on the first day of study drug intake.

a: Data collection for race and ethnicity was not permitted in some countries (e.g. France). Race was not collected if ethnicity was documented as "Hispanic or Latino".

b: For countries/regions in North America, Asia Pacific, and Rest of the World.

c: eGFR was calculated according to the MDRD formula, where SCR is measured in mg/dL: eGFR (mL/min/1.73m^2) = 186 x SCR-1.154 x age 0.203 x (0.742, if female) x (1.212, if Black or African American) x (0.881, if Japanese) x (1.227, if Chinese (mainland China, Taiwan, and Hong Kong).
Source: 5.3.5.1.1 PH-39723/Table 14.1.1/19, 14.1.1/20

2.7.6.9.2.1.3.2 ベースラインの疾患特性

FAS におけるベースラインの疾患特性を表 2.7.6.9-4 に示す。いくつかの項目については、無作為割付け及び層別化のための自動音声応答システム（IVRS）のデータと症例報告書（CRF）のデータがあるが、ここでは RAVE のデータを示す。

PSADT の中央値は、ダロルタミド群で 4.39 ヵ月、プラセボ群で 4.65 ヵ月であった。ベースライン時に 6 ヵ月以下の PSADT を有する被験者は、ダロルタミド群で 669 例（70.1%）、プラセボ群で 371 例（67.0%）であった。骨粗鬆症に適応される用量で破骨細胞標的薬の投与を受けた被験者は、ダロルタミド群で 36 例（3.8%）、プラセボ群で 28 例（5.1%）であった。

ECOG-PS が 0 であった被験者数は、ダロルタミド群で 650 例（68.1%）、プラセボ群で 391 例（70.6%）であった。Gleason スコアが 7 以上であった被験者は、それぞれ 711 例（74.5%）、395 例（71.3%）であった。診断時の TNM 分類が T3 であった被験者は、それぞれ 415 例（43.5%）、216 例（39.0%）であった[2)]。大多数の被験者は、中央判定で所属リンパ節転移は認められなかった〔ダロルタミド群：792 例（82.9%）、プラセボ群：396 例（71.5%）〕。すべての被験者は、組入れ基準に基づき腫瘍転移はないと判断されていたが、有効性評価の際の中央判定で、ダロルタミド群の 50 例（5.2%）、プラセボ群の 39 例（7.0%）にベースライン時に腫瘍転移があったと判定された（5.3.5.1.1 PH-39723/Table 14.2/7s2、事後解析）。

2 つ以上のホルモン治療を受けていた被験者はダロルタミド群で 727 例（76.1%）、プラセボ群で 420 例（75.8%）であった。去勢抵抗性になってから治験薬投与開始までの期間の中央値は、ダロルタミド群で 5.54 ヵ月（範囲：0.03～170.37 ヵ月）、プラセボ群で 5.95 ヵ月（0.10～233.02 ヵ月）であり、期間の平均値はいずれの投与群においても約 12 ヵ月であった。初回診断から治験薬投与開始までの期間の中央値は、ダロルタミド群で 86.15 ヵ月、プラセボ群で 84.23 ヵ月であった。最初の ADT（GnRH アゴニスト療法又はアンタゴニスト療法、両側精巣摘除術、AR 阻害薬を含む）施行から治験薬投与開始までの時間の中央値は、ダロルタミド群で 64.16 ヵ月、プラセボ群で 61.86 ヵ月であった。

ベースライン時の血清 PSA 値の中央値は、ダロルタミド群で 9.0ng/mL、プラセボ群で 9.7ng/mL であった。その他の疾患特性に関連するベースラインの臨床検査値は、5.3.5.1.1 PH-39723/Table 14.1.1/20 を参照のこと。

2) T3、T3a 及び T3b の合計

表 2.7.6.9-4 ベースラインの疾患特性（FAS）

	Darolutamide N = 955	Placebo N = 554
PSADT (CRF) (months) [a]		
n	955	554
Mean	4.8425	4.8876
StD	2.3555	2.2755
Min	0.744	0.662
Median	4.3890	4.6500
Max	10.991	13.194
Baseline value of PSADT (CRF), n (%)		
≤ 6 months	669 (70.1%)	371 (67.0%)
>6 months	286 (29.9%)	183 (33.0%)
Baseline osteoclast-targeted therapy (CRF), n (%) [b]		
No	919 (96.2%)	526 (94.9%)
Yes	36 (3.8%)	28 (5.1%)
ECOG performance status, n (%)		
0	650 (68.1%)	391 (70.6%)
1	305 (31.9%)	163 (29.4%)
Gleason total score at initial diagnosis (factor 1 + factor 2), n (%)		
Missing	27 (2.8%)	17 (3.1%)
<7	217 (22.7%)	142 (25.6%)
≥7	711 (74.5%)	395 (71.3%)
Primary tumor classification at initial diagnosis, n (%)		
Missing [c]	26 (2.7%)	15 (2.7%)
T1 Clinically inapparent tumor neither palpable not visible by imaging	19 (2.0%)	13 (2.3%)
T1a Tumor incidental histological finding in >5% of tissue resected	5 (0.5%)	0
T1b Tumor incidental histological finding in >5% of tissue resected	9 (0.9%)	1 (0.2%)
T1c Tumor identified by needle biopsy	99 (10.4%)	53 (9.6%)
T2 Tumor confined within prostate	110 (11.5%)	58 (10.5%)
T2a Tumor involves = one-half of one lobe	32 (3.4%)	27 (4.9%)
T2b Tumor involves > one-half of one lobe but not both lobes	55 (5.8%)	38 (6.9%)
T2c Tumor involves both lobes	97 (10.2%)	72 (13.0%)
T3 Tumor extends through the prostate capsule	172 (18.0%)	87 (15.7%)
T3a Extracapsular extension (unilateral or bilateral)	113 (11.8%)	49 (8.8%)
T3b Tumor invades seminal vesicle(s)	130 (13.6%)	80 (14.4%)
T4 Tumor is fixed or invades adjacent structures other than seminal vesicles such as external	42 (4.4%)	26 (4.7%)
TX Primary tumor cannot be assessed	46 (4.8%)	35 (6.3%)
Baseline presence of regional pathological lymph nodes by central imaging review, n (%) [d]		
No	792 (82.9%)	396 (71.5%)
Yes	163 (17.1%)	158 (28.5%)
Number of prior hormonal therapies [e]		
1	177 (18.5%)	103 (18.6%)
≥2	727 (76.1%)	420 (75.8%)
Not applicable	51 (5.3%)	31 (5.6%)
Time since becoming castration-resistant to start of study treatment (months)		
n	954	553
Mean	11.7117	12.7736

表 2.7.6.9-4 ベースラインの疾患特性（FAS）（続き）

	Darolutamide N = 955	Placebo N = 554
StD	19.0278	22.8391
Min	0.033	0.099
Median	5.5355	5.9461
Max	170.368	233.016
Time since initial diagnosis to start of study treatment (months) [f]		
n	950	548
Mean	94.75	94.89
StD	55.33	59.44
Min	2.6	0.5
Median	86.15	84.23
Max	337.5	344.7
Time from start of first prior anti-androgen (AR inhibitors [g]) to start of study treatment (months)		
n	633	349
Mean	61.956	64.276
StD	45.752	48.129
Min	2.23	2.96
Median	51.150	50.820
Max	232.82	229.57
Time from start of first prior ADT [h] to start of study treatment (months)		
n	953	551
Mean	76.138	75.981
StD	56.124	54.170
Min	0.92	2.92
Median	64.160	61.860
Max	644.35	386.63

ADT = androgen deprivation therapy; AR = androgen receptor; ECOG = Eastern Cooperative Oncology Group; GnRH = gonadotropin releasing hormone; N = total number of patients (100%); n = number of patients with event; PCWG2 = Prostate cancer Clinical Trials Working Group 2; PSADT = prostate-specific antigen doubling time; SAP = Statistical analysis plan; StD = standard deviation

Note: Time variable is missing if only year was documented.

Baseline data are taken from the non-missing observation before or on the first date of study drug intake. Baseline values for PSADT and osteoclast-targeted therapy collected on CRF are based on randomization date.

a: For 14 patients, the time interval for collection of PSA samples for calculation of PSADT was between 12 and 14 months, which was slightly beyond the timelines required by PCWG2 criteria but has no meaningful impact on the results of the study.

b: For the definition (ATC codes) of osteoclast-targeted therapies (bone sparing agents). Patients receiving osteoclast-targeted therapy to prevent skeletal related events within 12 weeks before randomization were excluded per protocol. Patients receiving osteoclast-targeted therapy to prevent bone loss at a dose and schedule indicated for osteoporosis prior to study entry could continue treatment at the same dose and schedule.

c: Missing: for two patients tumor classification was not made at initial diagnosis, for one patient the classification was reported as T3c, and for all others the original records were not available to the sites (data on file).

d: Local assessment of regional lymph node classification is available in 5.3.5.1.1 PH-39723/Table 14.1.1/20.

e: Not applicable: patients who underwent surgical castration were not required to have been/being treated with hormonal drug therapy.

f: The earlier date between the clinical stage date and the Gleason assessment date was considered as the initial diagnosis date.

g: For the definitions (ATC codes) of AR inhibitors was defined in 5.3.5.1.1 PH-39723/Section 16.1.9.
h: Prior ADT is defined by GnRH agonist/antagonist, orchiectomy, anti-androgen (AR inhibitors).
Source: 5.3.5.1.1 PH-39723/Table 14.1.1/20

2.7.6.9.2.1.3.3 病歴

現在継続中ではない過去の病歴については、5.3.5.1.1 PH-39723/Table 14.1.1/22 及び Table 14.1.1/23 を参照のこと。

現在継続中の病歴は、ダロルタミド群の 940 例（98.4%）、プラセボ群の 545 例（98.4%）でみられた。いずれかの投与群で 20%以上にみられた現在継続中の病歴の器官別大分類（SOC）は、「代謝および栄養障害」〔ダロルタミド群：715 例（74.9%）、プラセボ群：420 例（75.8%）〕、「血管障害」〔685 例（71.7%）、388 例（70.0%）〕、「心臓障害」〔440 例（46.1%）、223 例（40.3%）〕、「筋骨格系および結合組織障害」〔372 例（39.0%）、220 例（39.7%）〕、「腎および尿路障害」〔323 例（33.8%）、175 例（31.6%）〕、「胃腸障害」〔261 例（27.3%）、140 例（25.3%）〕及び「生殖系および乳房障害」〔213 例（22.3%）、129 例（23.3%）〕であった（5.3.5.1.1 PH-39723/Table 14.1.1/24）。

いずれかの投与群で 10%以上にみられた現在継続中の病歴の基本語（PT）は、高血圧〔ダロルタミド群：617 例（64.6%）、プラセボ群：357 例（64.4%）〕、肥満〔568 例（59.5%）、333 例（60.1%）〕、高コレステロール血症〔125 例（13.1%）、70 例（12.6%）〕、変形性関節症〔122 例（12.8%）、65 例（11.7%）〕、良性前立腺肥大症〔103 例（10.8%）、63 例（11.4%）〕及び糖尿病〔101 例（10.6%）、68 例（12.3%）〕、であった（5.3.5.1.1 PH-39723/Table 14.1.1/25）。

痙攣発作の病歴がある患者についても組入れ可能であり、ダロルタミド群の 2 例（0.2%）は、痙攣発作の病歴があった（発現日及び回復日が組入れ前）（5.3.5.1.1 PH-39723/Table 14.1.1/23）。てんかんの病歴は、現在継続中の病歴としてダロルタミド群の 10 例（1.0%）にみられた（5.3.5.1.1 PH-39723/Table 14.1.1/25）。

骨粗鬆症は現在継続中の病歴として、ダロルタミド群の 41 例（4.3%）及びプラセボ群の 23 例（4.2%）で報告された。

2.7.6.9.2.1.3.4 前治療及び併用療法

2.7.6.9.2.1.3.4.1 前治療歴

前立腺癌の前治療として、少なくとも 1 回以上放射線療法を受けた被験者は、ダロルタミド群で 490 例（51.3%）、プラセボ群で 266 例（48.0%）であった（5.3.5.1.1 PH-39723/Table 14.1.1/37）。前立腺癌の一次治療を受けていた被験者は、ダロルタミド群で 954 例（99.9%）、プラセボ群で 554 例（100.0%）であった（5.3.5.1.1 PH-39723/Table 14.1.1/39）。最もよくみられた一次治療は、化学的去勢〔ダロルタミド群：403 例（42.2%）、プラセボ群：252 例（45.5%）〕であり、次いで前立腺除去〔239 例（25.0%）、134 例（24.2%）〕であった。精巣摘除術を受けた被験者の割合は、両投与群で同様であった〔91 例（9.5%）、50 例（9.0%）〕。

2 種類以上のホルモン治療を受けた被験者は、ダロルタミド群で 727 例（76.1%）、プラセボ群で 420 例（75.8%）であった。1 種類のホルモン治療を受けた被験者は、ダロルタミド群で 177 例（18.5%）、プラセボ群で 103 例（18.6%）であった。ホルモン治療歴が不明であった被験者は、ダロルタミド群で 51 例（5.3%）、プラセボ群で 31 例（5.6%）であり、このうち両側

精巣摘除術を受けていた被験者は、ダロルタミド群で 50 例（98.0%）、プラセボ群で 28 例（90.3%）であった（5.3.5.1.1 PH-39723/Table 14.1.1/21）。

最もよくみられた前立腺癌に対する前治療薬は、ビカルタミド〔ダロルタミド群：642 例（67.2%）、プラセボ群：358 例（64.6%）〕、リュープロレリン又はリュープロレリン酢酸塩〔483 例（50.6%）、295 例（53.2%）〕、ゴセレリン又はゴセレリン酢酸塩〔309 例（32.4%）、174 例（31.4%）〕、トリプトレリン、トリプトレリン酢酸塩又はトリプトレリンエンボン酸塩〔286 例（29.9%）、155 例（28.0%）〕及びフルタミド〔121 例（12.7%）、79 例（14.3%）〕であった（5.3.5.1.1 PH-39723/Table 14.1.1/27）。ドセタキセルは、ダロルタミド群の 1 例（0.1%）、プラセボ群の 2 例（0.4%）に前治療として使用されていた（非転移性腫瘍の用法及び期間での使用で、治験実施計画書の逸脱ではない）。

2.7.6.9.2.1.3.4.2 併用療法

FAS において、よく用いられた併用療法（いずれかの投与群で 50%以上）は、内分泌療法〔ダロルタミド群：806 例（84.4%）、プラセボ群：480 例（86.6%）〕、レニンアンジオテンシン系作用薬〔522 例（54.7%）、276 例（49.8%）〕及び鎮痛剤〔514 例（53.8%）、279 例（50.4%）〕であった（5.3.5.1.1 PH-39723/Table 14.1.1/28）。

ダロルタミド群の 245 例（25.7%）及びプラセボ群の 142 例（25.6%）は手技を併用して受けていた。ダロルタミド群でよく併用されていた手技は、「その他」（113 例、11.8%）及び外科的切除又は切除（83 例、8.7%）であり、プラセボ群ではカテーテル挿入（49 例、8.8%）、「その他」（39 例、7.0%）であった（5.3.5.1.1 PH-39723/Table 14.1.1/40）。

スタチン〔解剖治療化学分類法（ATC）分類では脂肪修飾剤〕を併用した被験者は、ダロルタミド群で 306 例（32.0%）、プラセボ群で 202 例（36.5%）であった（5.3.5.1.1 PH-39723/Table 14.1.1/29）。スタチンとして乳がん耐性タンパク（BCRP）を併用した被験者は、ダロルタミド群で 280 例（29.4%）、プラセボ群で 171 例（30.9%）であった（5.3.5.1.1 PH-39723/Table 14.3/1s3）。

試験期間中に癌性疼痛緩和のためにオピオイドを服用した被験者は、ダロルタミド群で 26 例（2.7%）、プラセボ群で 21 例（3.8%）であった（5.3.5.1.1 PH-39723/Table 14.2.3/21）。

2.7.6.9.2.2 有効性の結果

2.7.6.9.2.2.1 治験薬の投与状況

2.7.6.9.2.3.1 を参照のこと。

2.7.6.9.2.2.2 主要評価項目

FAS における MFS イベントの内訳を、表 2.7.6.9-5 に示す。

盲検下での中央診断により、データカットオフ日の時点で、ダロルタミド群の 221 例（23.1%）、プラセボ群の 216 例（39.0%）に MFS イベントが認められた（ベースライン時の転移を含む）。ベースライン後の転移は、ダロルタミド群で 130 例（58.8%）、プラセボ群で 158 例（73.1%）に認められた。いずれの群においても、転移部位は骨〔ダロルタミド群：60 例（46.2%）、プラセボ群：62 例（39.2%）〕又は遠隔リンパ節〔41 例（31.5%）、63 例（39.9%）〕が多かった。盲検下での中央診断により、ベースライン時点で既に転移があったと判断された被験者は、ダロルタミド群で 221 例中 50 例（22.6%）、プラセボ群で 216 例中 39 例（18.1%）であった。いずれの群においても、転移部位は骨〔50 例中 34 例（68.0%）、39 例中

24 例（61.5%）〕が多かった。MFS イベントが死亡であった被験者は、ダロルタミド群で 221 例中 41 例（18.6%）、プラセボ群で 216 例中 19 例（8.8%）であった。

表 2.7.6.9-5 MFS イベントの内訳（FAS）

	Darolutamide N = 955 n (%)	Placebo N = 554 n (%)
Any event [a]	221/955 (23.1%)	216/554 (39.0%)
Metastasis post baseline [b]	130/221 (58.8%)	158/216 (73.1%)
Bone [c]	60/130 (46.2%)	62/158 (39.2%)
Distant lymph nodes [c]	41/130 (31.5%)	63/158 (39.9%)
Distant lymph nodes, and bone [c]	17/130 (13.1%)	22/158 (13.9%)
Distant lymph nodes, and visceral and/or soft tissue [c]	2/130 (1.5%)	4/158 (2.5%)
Distant lymph nodes, and visceral and/or soft tissue, and bone [c]	0/130 (0.0%)	1/158 (0.6%)
Visceral and/or soft tissue [c]	9/130 (6.9%)	4/158 (2.5%)
Visceral and/or soft tissue, and bone [c]	1/130 (0.8%)	2/158 (1.3%)
Metastasis at baseline [b]	50/221 (22.6%)	39/216 (18.1%)
Bone [d]	34/ 50 (68.0%)	24/ 39 (61.5%)
Distant lymph nodes [d]	10/ 50 (20.0%)	8/ 39 (20.5%)
Distant lymph nodes, and bone [d]	3/ 50 (6.0%)	4/ 39 (10.3%)
Distant lymph nodes, and visceral and/or soft tissue [d]	1/ 50 (2.0%)	0/ 39 (0.0%)
Distant lymph nodes, and visceral and/or soft tissue, and bone [d]	0/ 50 (0.0%)	0/ 39 (0.0%)
Visceral and/or soft tissue [d]	1/ 50 (2.0%)	3/ 39 (7.7%)
Visceral and/or soft tissue, and bone [d]	1/ 50 (2.0%)	0/ 39 (0.0%)
Death [b]	41/221 (18.6%)	19/216 (8.8%)

MFS = metastasis-free survival; N = total number of patients (100%); n = number of patients with event.

a: Patients with documented metastases at baseline were considered to have an MFS event at randomization.

b: Percentages for the type of MFS event were calculated by treatment arm from the number of patients with event.

c: Percentages for the type of metastasis were calculated by treatment arm from the number of patients with metastasis.

d: Percentages for the type of baseline metastasis were calculated by treatment arm from the number of patients with baseline metastasis.

Source: 5.3.5.1.1 PH-39723/Table 14.2.1/1, 14.2.1/5, 14.2/7s2

2.7.6.9.2.2.2.1 ベースライン時の転移を無作為割付け時点でのイベントとして用いた MFS（主解析）

FAS における、MFS の主解析の結果を表 2.7.6.9-6 に、Kaplan-Meier 曲線を図 2.7.6.9-2 に示す。

MFS の主解析において、ハザード比は 0.413（95%CI：0.341～0.500、p＜0.000001）であり、ダロルタミド群のプラセボ群に対する優越性が示された。これは、プラセボ群と比較してダロル

タミド群で転移又は死亡のリスクが約 58.7%低下したことを意味する[3)]。MFS の中央値は、ダロルタミド群で 40.37 ヵ月（95%CI：34.33 ヵ月～推定不能）、プラセボ群で 18.43 ヵ月（15.51～22.34 ヵ月）であり、臨床的に意味のある差が認められた。

4、8、12、24 及び 36 ヵ月時点での非イベント発現率は、ダロルタミド群の方がプラセボ群よりも高い傾向を示し、MFS におけるダロルタミドの投与効果が長期にわたって維持されることが示唆された。

表 2.7.6.9-6 ベースライン時の転移を無作為割付け時点でのイベントとして用いた MFS：主解析（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event [a]	221 (23.1%)	216 (39.0%)
Number (%) of patients censored	734 (76.9%)	338 (61.0%)
MFS (months)		
25th percentile [95% CI]	19.97 [16.13; 22.34]	7.39 [7.16; 9.69]
Median [95% CI]	40.37 [34.33; A]	18.43 [15.51; 22.34]
75th percentile [95% CI]	A [A; A]	36.70 [30.68; 36.89]
Range (including censored values)	(0.03 - 44.28**)	(0.03 - 36.89)
Range (without censored values)	(0.03 - 40.51)	(0.03 - 36.89)
4-month event-free rate [95% CI]	0.916 [0.898; 0.934]	0.820 [0.786; 0.853]
8-month event-free rate [95% CI]	0.879 [0.858; 0.901]	0.720 [0.679; 0.761]
12-month event-free rate [95% CI]	0.825 [0.799; 0.851]	0.635 [0.588; 0.681]
24-month event-free rate [95% CI]	0.698 [0.658; 0.738]	0.415 [0.351; 0.480]
36-month event-free rate [95% CI]	0.543 [0.466; 0.620]	0.268 [0.160; 0.375]
48-month event-free rate [95% CI]	A [A; A]	0.000 [A; A]
Hazard ratio: (Darolutamide/Placebo) [95% CI] [b]	0.413 [0.341; 0.500]	
Two sided p-value from log rank test	<0.000001	

A = value cannot be estimated due to censored data; MFS = metastasis-free survival; N = total number of patients (100%); PSADT = prostate-specific antigen doubling time.

** Censored observation.

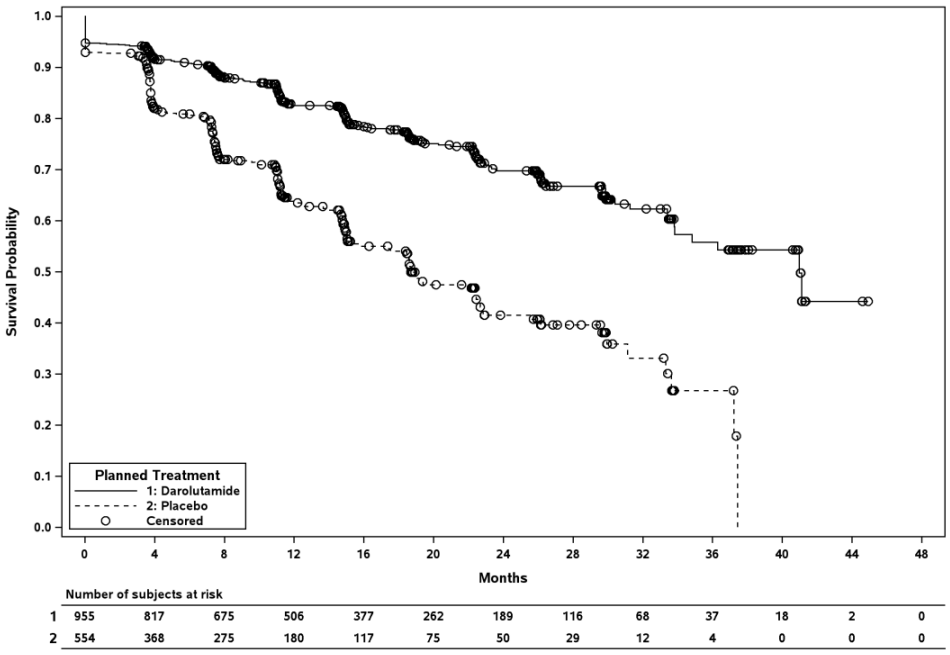
a: Patients with documented metastases at baseline (50 patients in the darolutamide arm, and 39 patients in the placebo arm) were considered to have an MFS event at randomization.

b: A hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and 95% CI was based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Note: Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.1/1, 14.2.1/2

3) リスク低下は、（1-ハザード比）×100 の式により計算した。



Source: 5.3.5.1.1 PH-39723/Figure 14.2.1/1

図 2.7.6.9-2 ベースライン時の転移を無作為割付け時点でのイベントとして用いた MFS（主解析）による Kaplan-Meier 曲線（FAS）

2.7.6.9.2.2.2.2 ベースライン時の転移を無作為割付け時点で打ち切る MFS（感度解析）

FAS における MFS の感度解析の結果を表 2.7.6.9-7 に、Kaplan-Meier 曲線を図 2.7.6.9-3 に示す。

ベースライン時の転移を打ち切りとした場合においても、主解析と同様の結果が得られた。

表 2.7.6.9-7 ベースライン時の転移を無作為割付け時点での打ち切る MFS：感度解析（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event	171 (17.9%)	177 (31.9%)
Number (%) of patients censored [a]	784 (82.1%)	377 (68.1%)
MFS (months)		
25th percentile [95% CI]	22.67 [21.91; 26.02]	10.87 [7.46; 11.07]
Median [95% CI]	40.51 [35.78; A]	22.08 [18.33; 25.76]
75th percentile [95% CI]	A [A; A]	36.70 [32.82; 36.89]
Range (including censored values)	(0.03** - 44.28**)	(0.03** - 36.89)
Range (without censored values)	(0.85 - 40.51)	(1.08 - 36.89)
4-month event-free rate [95% CI]	0.967 [0.955; 0.978]	0.882 [0.852; 0.911]
8-month event-free rate [95% CI]	0.928 [0.910; 0.946]	0.774 [0.734; 0.815]
12-month event-free rate [95% CI]	0.871 [0.847; 0.895]	0.683 [0.635; 0.730]
24-month event-free rate [95% CI]	0.737 [0.696; 0.777]	0.447 [0.378; 0.515]
36-month event-free rate [95% CI]	0.573 [0.492; 0.654]	0.288 [0.172; 0.403]
48-month event-free rate [95% CI]	A [A; A]	0.000 [A; A]
Hazard ratio: (darolutamide/placebo) [95% CI] [b]	0.356 [0.287; 0.441]	
Two sided p-value from log rank test	<0.000001	

A = value cannot be estimated due to censored data; MFS = metastasis-free survival; N = total number of patients (100%); PSADT = prostate-specific antigen doubling time.

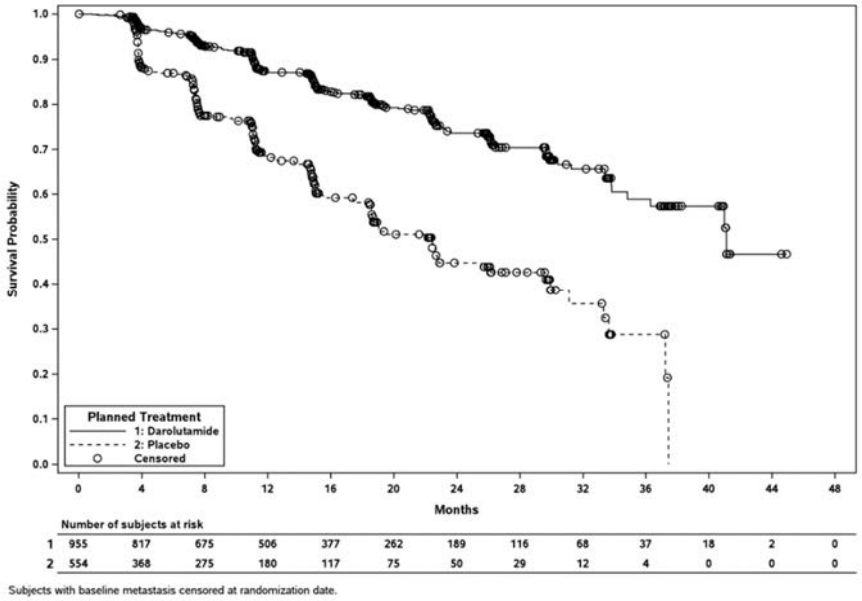
** Censored observation.

a: Patients with baseline metastasis were censored at the randomization date.

b: Hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and 95% CI was based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Note: Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.1/65, 14.2.1/66



Source: 5.3.5.1.1 PH-39723/Figure 14.2.1/32

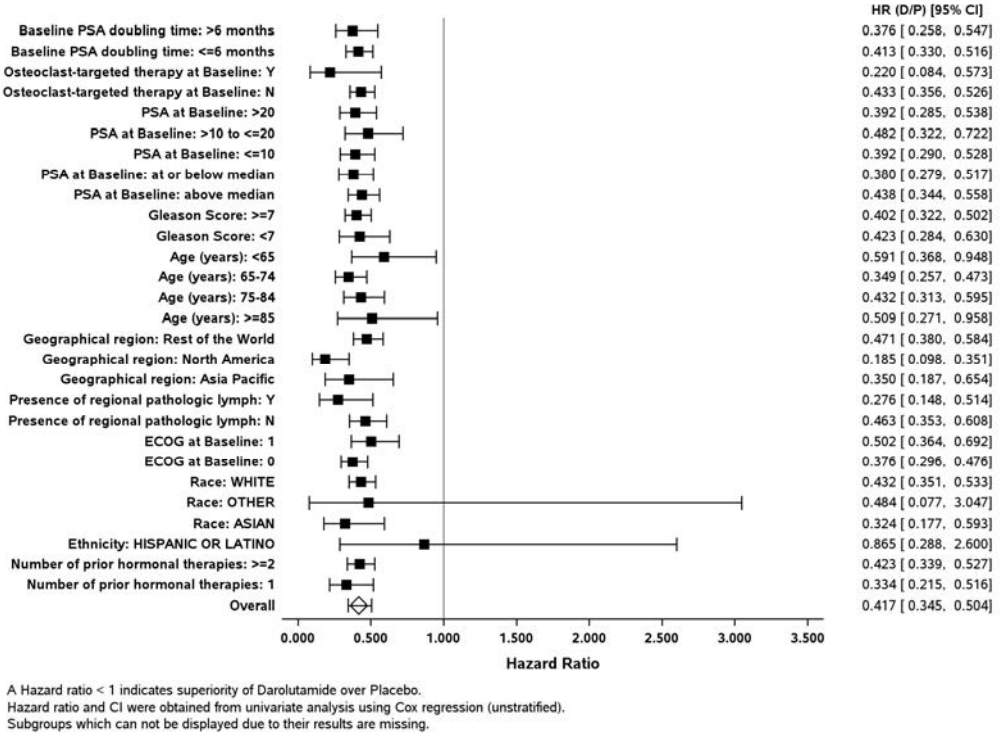
図 2.7.6.9-3 ベースライン時の転移を無作為割付け時点での打ち切る MFS（感度解析）による Kaplan-Meier 曲線（FAS）

2.7.6.9.2.2.2.3 MFS の部分集団解析

MFS に関する部分集団解析を、ベースライン時の PSADT（CRF に基づく、6 ヵ月超及び 6 ヵ月以下）、ベースライン時の破骨細胞標的薬の治療歴（CRF に基づく、有、無）、ベースライン時の中央検査機関による血清 PSA 値（ng/mL）（10 以下、10 超 20 以下、20 超)、ベースライン時の中央検査機関による血清 PSA 値（ng/mL）〔中央値以下又は中央値超（全被験者の中央値）〕、診断時の Gleason スコア（7 以上又は 7 未満）、年齢（歳）（65 歳未満、65～74 歳、75～84 歳、85 歳以上）、地域（北米、アジア太平洋、その他）、中央判定によるベースライン時の所属リンパ節転移（有、無）、ベースライン時の ECOG-PS（0、1）、人種〔白人、アジア人、黒人又はアフリカ系アメリカ人、その他（民族性「ヒスパニック系又はラテン系」）〕、過去のホルモン治療回数（1 回、2 回以上）に基づいて実施した。

MFS の部分集団解析の Forest プロットを図 2.7.6.9-4 に示す。部分集団解析の結果の詳細は、5.3.5.1.1 PH-39723/Table 14.2.1/64 を参照のこと。

全体として、いずれの部分集団においても、ほとんどの部分集団においてハザード比は 1 未満であった。被験者数及びイベント数が少ないいくつかの部分集団〔民族性：ヒスパニック系又はラテン系（47 例、イベント数 14 件）及び人種：その他（15 例、イベント数 5 件）〕では、信頼区間が広く、これらの部分集団では結果の解釈に注意が必要である（5.3.5.1.1 PH-39723/Table 14.2.1/64）。



D = darolutamide; ECOG = Eastern Cooperative Oncology Group; HR = hazard ratio; P = placebo; PSA = prostate-specific antigen
Source: 5.3.5.1.1 PH-39723/Figure 14.2.1/31

図 2.7.6.9-4 ベースライン時の転移を無作為割付け時点でのイベントとして用いた MFS（主解析）の部分集団解析の Forest プロット（FAS）

2.7.6.9.2.2.3 副次評価項目

有効性の全副次評価項目について、無作為割付け時点での PSADT（6 ヵ月以下又は 6 ヵ月超）及び破骨細胞標的薬の治療歴の有無で層別化したログランク検定を用いて、ダロルタミド群とプラセボ群を比較した。

疼痛増悪までの期間以降の副次評価項目は、MFS と OS の両方が有意である場合に、有意性を検定することが事前に規定されていた。本解析時点で OS が有意でなかったため、有効性副次評価項目である疼痛増悪までの期間、細胞傷害性薬剤による化学療法の初回開始までの期間、及び SSE の初回発現までの期間については、有意性の検定を実施しなかった。

2.7.6.9.2.2.3.1 OS

FAS における OS の結果を表 2.7.6.9-8 に、Kaplan-Meier 曲線を図 2.7.6.9-5 に示す。

FAS の 1,509 例において 136 例（9.0%）の死亡が報告された。その内訳は、ダロルタミド群 78 例（8.2%）、プラセボ群 58 例（10.5%）であった。

最終的に OS の解析は 240 イベントで計画されていたが、データカットオフ日の時点での死亡数が 136 例であった。このため、primary completion 時にイベント数が限られおり、得られた p 値は事前に規定した有意水準 0.0005 より大きかった。しかし、ダロルタミド群における OS の改善が示唆される結果、すなわちハザード比 0.706（95%CI：0.501～0.994、p＝0.045210）が観察された。

表 2.7.6.9-8 OS（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event	78 (8.2%)	58 (10.5%)
Number (%) of patients censored	877 (91.8%)	496 (89.5%)
OS (months)		
25th percentile [(95% CI]	44.45 [37.71; A]	32.56 [29.50; A]
Median [95% CI]	A [44.45; A]	A [A; A]
75th percentile [95% CI]	A [A; A]	A [A; A]
Range (including censored values)	(0.07** - 46.02**)	(0.1** - 45.57**)
Range (without censored values)	(0.85 - 44.45)	(3.15 - 34.53)
4-month survival rate [95% CI]	0.993 [0.987; 0.998]	0.994 [0.988; 1.000]
8-month survival rate [95% CI]	0.983 [0.975; 0.991]	0.985 [0.974; 0.995]
12-month survival rate [95% CI]	0.961 [0.948; 0.974]	0.966 [0.950; 0.983]
24-month survival rate [95% CI]	0.900 [0.875; 0.925]	0.855 [0.814; 0.897]
36-month survival rate [95% CI]	0.828 [0.779; 0.877]	0.728 [0.647; 0.809]
48-month survival rate [95% CI]	A [A; A]	A [A; A]
Hazard ratio: (darolutamide/placebo) [95% CI][a]	0.706 [0.501; 0.994]	
Two sided p-value from log rank test	0.045210	

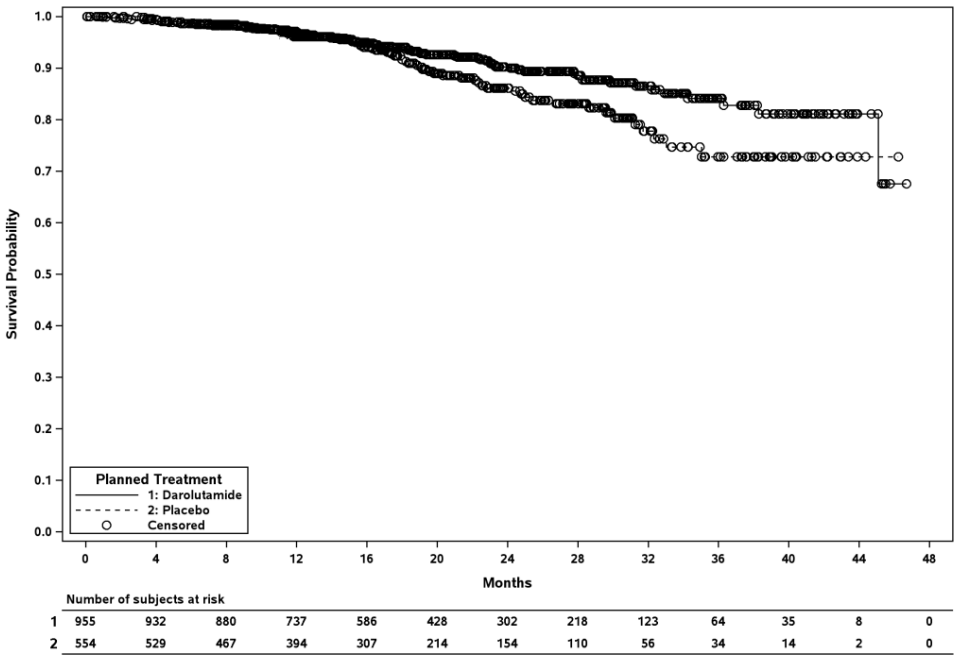
A = value cannot be estimated due to censored data; N = total number of patients (100%); OS = overall survival; PSADT = prostate-specific antigen doubling time

** Censored observation.

a: A hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and its 95% CI were based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Median, percentile and other 95% CIs were computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.2/1, 14.2.2/2



Source: 5.3.5.1.1 PH-39723/Figure 14.2.2/1

図 2.7.6.9-5 OS の Kaplan-Meier 曲線（FAS）

OS の部分集団解析については、5.3.5.1.1 PH-39723/Table 14.2.2/3～14.2.2/61、Figure 14.2.2/2～14.2.2/31 を参照のこと。

2.7.6.9.2.2.3.2 その他の副次評価項目

以下に示すその他の有効性副次評価項目は、MFS と OS の両方が有意である場合に、逐次的ゲートキーピング法を用いて、有意性を検定することが事前に規定されていた。Primary completion での解析において、OS は事前に規定した有意水準 0.0005 に達しなかった。このため、疼痛増悪までの期間、細胞傷害性薬剤による化学療法の初回開始までの期間及び SSE の初回発現までの期間については、p 値は参考としてのみ示す。

2.7.6.9.2.2.3.2.1 疼痛増悪までの期間

FAS における疼痛増悪までの期間を表 2.7.6.9-9 に示す。疼痛増悪までの期間の Kaplan-Meier 曲線は、5.3.5.1.1 PH-39723/Figure 14.2.2/32 を参照のこと。

ダロルタミド群の 251 例（26.3%）及びプラセボ群の 178 例（32.1%）に疼痛増悪が認められた。

疼痛増悪までの期間の中央値は、ダロルタミド群で 40.31 ヵ月（95%CI：33.21～41.20 ヵ月）プラセボ群で 25.36 ヵ月（19.09～29.63 ヵ月）であった。ハザード比（ダロルタミド群／プラセボ群）は 0.647（0.533～0.785、p＝0.000008）であり、疼痛増悪までの期間がダロルタミド群で延長することが示唆された。

表 2.7.6.9-9 疼痛増悪までの期間（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event	251 (26.3%)	178 (32.1%)
Number (%) of patients censored	704 (73.7%)	376 (67.9%)
Time to pain progression (months)		
25th percentile [95% CI]	14.68 [11.10; 18.43]	8.94 [7.39; 11.07]
Median [95% CI]	40.31 [33.21; 41.20]	25.36 [19.09; 29.63]
75th percentile [95% CI]	41.20 [40.80; A]	A [32.79; A]
Range (including censored values)	(0.03** - 44.32**)	(0.03** - 40.51**)
Range (without censored values)	(2.1 - 41.2)	(2.76 - 32.79)
4-month event-free rate [95% CI]	0.909 [0.889; 0.928]	0.867 [0.837; 0.898]
8-month event-free rate [95% CI]	0.821 [0.795; 0.848]	0.754 [0.714; 0.795]
12-month event-free rate [95% CI]	0.760 [0.729; 0.790]	0.686 [0.641; 0.732]
24-month event-free rate [95% CI]	0.646 [0.604; 0.687]	0.504 [0.441; 0.567]
36-month event-free rate [95% CI]	0.534 [0.468; 0.601]	0.323 [0.216; 0.430]
48-month event-free rate [95% CI]	A [A; A]	A [A; A]
Hazard ratio: (darolutamide/placebo) [95% CI] [a]	0.647 [0.533; 0.785]	
Two sided p-value from log rank test	0.000008	

A = value cannot be estimated due to censored data; N = total number of patients (100%); PSADT = prostate-specific antigen doubling time

** Censored observation

a: Hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and 95% CI was based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Note: Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.2/62, 14.2.2/63

2.7.6.9.2.2.3.2.2 細胞傷害性薬剤による化学療法の初回開始までの期間

FAS における細胞傷害性薬剤による化学療法の初回開始までの期間を表 2.7.6.9-10 に示す。細胞傷害性薬剤による化学療法の初回開始までの期間の Kaplan-Meier 曲線は、5.3.5.1.1 PH-39723/Figure 14.2.2/33 を参照のこと。

ダロルタミド群の 73 例（7.6%）及びプラセボ群の 79 例（14.3%）が、試験期間中に前立腺癌に対する細胞傷害性薬剤による化学療法を開始した。

細胞傷害性薬剤による化学療法の初回開始までの期間の中央値は、ダロルタミド群では推定できなかったが、プラセボ群では 38.21 ヵ月（95%CI：35.55～41.89 ヵ月）であった。細胞傷害性薬剤による化学療法の初回開始までの期間については、ダロルタミド群でプラセボ群よりも延長することが示唆された（ハザード比 0.433、95%CI：0.314～0.595、p＜0.000001）。

表 2.7.6.9-10 細胞傷害性薬剤による化学療法の初回開始までの期間（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event	73 (7.6%)	79 (14.3%)
Number (%) of patients censored	882 (92.4%)	475 (85.7%)
Time to initiation of first cytotoxic chemotherapy (months)		
25th percentile [95% CI]	A [A; A]	29.93 [22.44; 35.55]
Median [95% CI]	A [A; A]	38.21 [35.55; 41.89]
75th percentile [95% CI]	A [A; A]	41.89 [38.21; 41.89]
Range (including censored values)	(0.03** - 44.32**)	(0.03** - 41.89)
Range (without censored values)	(4.01 - 31.04)	(3.58 - 41.89)
4-month event-free rate [95% CI]	1.000 [1.000; 1.000]	0.996 [0.991; 1.000]
8-month event-free rate [95% CI]	0.979 [0.969; 0.988]	0.945 [0.925; 0.966]
12-month event-free rate [95% CI]	0.960 [0.947; 0.974]	0.898 [0.870; 0.927]
24-month event-free rate [95% CI]	0.887 [0.858; 0.915]	0.773 [0.720; 0.825]
36-month event-free rate [95% CI]	0.835 [0.790; 0.879]	0.629 [0.496; 0.763]
48-month event-free rate [95% CI]	A [A; A]	0.000 [A; A]
Hazard ratio: (darolutamide/placebo) [95% CI][a]	0.433 [0.314; 0.595]	
Two sided p-value from log rank test	<0.000001	

A = value cannot be estimated due to censored data; N = total number of patients (100%); PSADT = prostate-specific antigen doubling time

** Censored observation

a: A hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and its 95% CI were based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Note: Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.2/64, 14.2.2/65

2.7.6.9.2.2.3.2.3 SSE の初回発現までの期間

FAS における SSE の初回発現までの期間を表 2.7.6.9-11 に示す。SSE の初回発現までの期間の Kaplan-Meier 曲線は、5.3.5.1.1 PH-39723/Figure 14.2.2/34 を参照のこと。

SSE を有する被験者は、ダロルタミド群で 16 例（1.7%）、プラセボ群で 18 例（3.2%）と少数であった。その大部分は骨症状を緩和するための EBRT であり、ダロルタミド群で 12 例（75.0%）、プラセボ群で 11 例（61.1%）であった。

SSE の初回発現までの期間の中央値は、いずれの投与群においても推定できなかった。SSE の初回発現までの期間については、ダロルタミド群でプラセボ群よりも延長することが示唆された（ハザード比 0.428、95%CI：0.218～0.842、p＝0.011262）。

表 2.7.6.9-11 SSE の初回発現までの期間（FAS）

	Darolutamide N = 955	Placebo N = 554
Number (%) of patients with event	16/955 (1.7%)	18/554 (3.2%)
EBRT to relieve skeletal symptoms [a]	12/ 16 (75.0%)	11/ 18 (61.1%)
New symptomatic pathologic bone fracture [a]	2/ 16 (12.5%)	2/ 18 (11.1%)
Occurrence of spinal cord compression [a]	0/ 16 (0.0%)	3/ 18 (16.7%)
Tumor-related orthopedic surgical intervention [a]	2/ 16 (12.5%)	2/ 18 (11.1%)
Number (%) of patients censored	939/955 (98.3%)	536/554 (96.8%)
Time to first SSE (months)		
25th percentile [95% CI]	A [A; A]	A [38.21; A]
Median [95% CI]	A [A; A]	A [A; A]
75th percentile [95% CI]	A [A; A]	A [A; A]
Range (including censored values)	(0.03** - 44.65**)	(0.03** - 42.38**)
Range (without censored values)	(1.58 - 34.2)	(2.33 - 38.21)
4-month event-free rate [95% CI]	0.999 [0.997; 1.000]	0.996 [0.991; 1.000]
8-month event-free rate [95% CI]	0.996 [0.991; 1.000]	0.992 [0.983; 1.000]
12-month event-free rate [95% CI]	0.993 [0.987; 0.999]	0.982 [0.969; 0.994]
24-month event-free rate [95% CI]	0.980 [0.968; 0.992]	0.948 [0.920; 0.976]
36-month event-free rate [95% CI]	0.940 [0.896; 0.984]	0.904 [0.834; 0.974]
48-month event-free rate [95% CI]	A [A; A]	A [A; A]
Hazard ratio: (darolutamide/placebo) [95% CI] [b]	0.428 [0.218; 0.842]	
Two sided p-value from log rank test	0.011262	

A = value cannot be estimated due to censored data; EBRT = external beam radiation therapy; N = total number of patients (100%); PSADT = prostate-specific antigen doubling time; SSE = symptomatic skeletal event

** Censored observation

a: Percentages for the type of SSE were manually calculated by treatment arm from the number of patients with event.

b: A hazard ratio <1 indicates superiority of darolutamide over placebo. Hazard ratio and 95% CI was based on Cox Regression Model, stratified PSADT (≤ 6 months vs. > 6 months) and use of osteoclast-targeted therapy.

Note: Median, percentile and other 95% CIs computed using Kaplan-Meier estimates.

Source: 5.3.5.1.1 PH-39723/Table 14.2.2/66, 14.2.2/67, 14.2.2/70

2.7.6.9.2.3 安全性の結果

2.7.6.9.2.3.1 治験薬の曝露状況

SAF において、総投与期間（投与中断を含む）の中央値は、ダロルタミド群で 14.80 ヵ月、プラセボ群で 11.04 ヵ月であった（5.3.5.1.1 PH-39723/Table 14.1.9/1）。いずれの投与群においても、総投与期間が 6 ヵ月超 12 ヵ月以下の被験者が最も多く、ダロルタミド群で 280 例（29.4%）、プラセボ群で 187 例（33.8%）であった。総投与期間が 12 ヵ月超 30 ヵ月以下の被験者は、それぞれ 493 例（51.7%）、204 例（36.8%）であった[4)]。総投与期間が 30 ヵ月超の被験者は、それぞれ 87 例（9.1%）、18 例（3.2%）であった[5)]。データカットオフ日時点で、ダ

4) 5.3.5.1.1 PH-39723/Table 14.1.9/1 で、「>12 to =< 18 month」、「>18 to =< 24 month」及び「>24 to =<30 month」の合算により算出した。

5) 5.3.5.1.1 PH-39723/Table 14.1.9/1 で、「>30 to =< 36 month」及び「>36 month」の合算により算出した。

ロルタミド群の 615 例（64.4%）、プラセボ群の 200 例（36.1%）が投与継続中であった（表 2.7.6.9-1）。

予定投与量に対する実投与量の割合の平均値は、いずれの投与群においても約 99%であった（中央値はいずれも 100.0%）（5.3.5.1.1 PH-39723/Table 14.1.9/2）。

治験薬の用量調節は大部分の被験者で不要であった（5.3.5.1.1 PH-39723/Table 14.1.9/3）。用量調節（投与中断又は減量）を行った被験者は、ダロルタミド群で 145 例（15.2%）、プラセボ群で 54 例（9.7%）であった。被験者あたりの用量調節の回数は、いずれの投与群でも大部分の被験者で 1 回又は 2 回であり、用量調節の理由は多くが TEAE であった〔ダロルタミド群で 184／219 件（84.0%）、プラセボ群で 57／78 件（73.1%）〕。投与中断がダロルタミド群で 115／145 例（79.3%）、プラセボ群で 47／54 例（87.0%）にて行われ、減量がそれぞれ 64／145 例（44.1%）及び 19／54 例（35.2%）、再増量がそれぞれ 133／145 例（91.7%）及び 48／54 例（88.9%）で行われた。

2.7.6.9.2.3.2 有害事象の要約

TEAE の要約を表 2.7.6.9-12 に示す。

TEAE の発現割合は、ダロルタミド群で 83.2%（794／954 例）、プラセボ群で 76.9%（426／554 例）であり、治験薬と関連のある TEAE の発現割合は、それぞれ 258 例（27.0%）及び 110 例（19.9%）であった。グレード 3 以上の TEAE の発現割合はそれぞれ 273 例（28.6%）及び 126 例（22.7%）であった。

グレード 5 の TEAE の発現割合は、ダロルタミド群で 37 例（3.9%）、プラセボ群で 18 例（3.2%）であり、治験薬と関連のあるグレード 5 の TEAE はそれぞれ 1 例（0.1%）及び 2 例（0.4%）に認められた。試験期間中の死亡は、それぞれ 79 例（8.3%）及び 58 例（10.5%）に認められた。

重篤な TEAE の発現割合は、ダロルタミド群で 237 例（24.8%）、プラセボ群で 111 例（20.0%）であり、用量調節（投与中断又は減量）に至った TEAE の発現割合は、それぞれ 135 例（14.2%）及び 52 例（9.4%）、投与中止に至った TEAE の発現割合は、それぞれ 85 例（8.9%）及び 48 例（8.7%）であった。

表 2.7.6.9-12 TEAE の要約（SAF）

Number of patients (%) with:		Darolutamide N = 954 n (%)	Placebo N = 554 n (%)
Any TEAE		**794 (83.2%)**	**426 (76.9%)**
Worst CTCAE grade:	Grade 1	219 (23.0%)	134 (24.2%)
	Grade 2	302 (31.7%)	166 (30.0%)
	Grade 3	215 (22.5%)	99 (17.9%)
	Grade 4	21 (2.2%)	9 (1.6%)
	Grade 5 (death)	37 (3.9%)[c]	18 (3.2%)
	Grade 1 or 2	521 (54.6%)	300 (54.2%)
	Grade 3 or 4	236 (24.7%)	108 (19.5%)
	Grade 3, 4 or 5	273 (28.6%)	126 (22.7%)
SAE		237 (24.8%)	111 (20.0%)
TEAE leading to dose modification [a]		135 (14.2%)	52 (9.4%)
TEAE leading to permanent discontinuation of study drug		85 (8.9%)	48 (8.7%)
Any drug-related TEAE [b]		**258 (27.0%)**	**110 (19.9%)**
Worst CTCAE grade:	Grade 1	132 (13.8%)	68 (12.3%)
	Grade 2	98 (10.3%)	26 (4.7%)
	Grade 3	24 (2.5%)	14 (2.5%)
	Grade 4	3 (0.3%)	0 (0.0%)
	Grade 5 (death)	1 (0.1%)	2 (0.4%)
	Grade 1 or 2	230 (24.1%)	94 (17.0%)
	Grade 3 or 4	27 (2.8%)	14 (2.5%)
	Grade 3, 4 or 5	28 (2.9%)	16 (2.9%)
Drug-related SAE		10 (1.0%)	6 (1.1%)
Drug-related TEAE leading to dose modification [a]		49 (5.1%)	14 (2.5%)
Drug-related TEAE leading to permanent discontinuation of study drug		15 (1.6%)	13 (2.3%)
Any death		**79 (8.3%)**	**58 (10.5%)**

CTCAE = Common Terminology Criteria for Adverse Events; N = total number of patients (100%); n = number of patients with event

a: Modifications include dose interruptions and reductions.

b: Based on investigator's assessment.

c: For some of the patients in the darolutamide arm, the start of the grade 5 event was reported within 30 days after treatment discontinuation but the death occurred more than 30 days after treatment discontinuation or after the report cut-off date.

CTCAE version 4.03.

Source: 5.3.5.1.1 PH-39723/Table 14.3.1/1, 14.3.2/12, Listing 16.2.7/1

2.7.6.9.2.3.3 有害事象

2.7.6.9.2.3.3.1 TEAE

SOC 別の TEAE の発現割合を表 2.7.6.9-13 に、TEAE の発現割合及び曝露期間で調整した発現率を表 2.7.6.9-14 に示す。すべての TEAE のグレード別の集計表を付表 2.7.6.9.a.1-1 に示す。

最もよくみられた TEAE の SOC（いずれかの投与群で 20%以上）は、「胃腸障害」〔ダロルタミド群 276 例（28.9%）、プラセボ群 141 例（25.5%）〕、「筋骨格系および結合組織障害」〔270 例（28.3%）、135 例（24.4%）〕、「一般・全身障害および投与部位の状態」〔244 例（25.6%）、104 例（18.8%）〕、「感染症および寄生虫症」〔227 例（23.8%）、120 例（21.7%）〕及び「腎および尿路障害」〔198 例（20.8%）、140 例（25.3%）〕であった。

TEAE の発現割合は、ダロルタミド群で 83.2%（794／954 例）、プラセボ群で 76.9%（426／554 例）であった（表 2.7.6.9-12）。各 TEAE の発現割合は、疲労（ダロルタミド群 12.1%、プラセボ群 8.7%）を除き、10%以下であった。

ダロルタミド群でプラセボ群よりも発現割合が 1%以上高い TEAE は、疲労（ダロルタミド群 12.1%、プラセボ群 8.7%）、下痢（6.9%、5.6%）、高血圧（6.6%、5.2%）、四肢痛（5.8%、3.2%）、貧血（5.6%、4.5%）、ほてり（5.2%、4.2%）、末梢性浮腫（4.1%、3.1%）、頻尿（4.0%、2.9%）、頭痛（3.9%、2.5%）、筋骨格痛（3.9%、2.0%）、浮動性めまい（3.7%、2.5%）、体重減少（3.6%、2.2%）、咳嗽（3.0%、2.0%）、インフルエンザ（2.8%、1.6%）、上気道感染（2.6%、1.6%）及び発熱（2.0%、0.9%）であった。これらの TEAE に関し、曝露期間で調整した発現率（100 人年あたり）でみた場合、群間の差は小さくなるか、又は四肢痛（4.1、3.2）及び筋骨格痛（2.8、1.9）がダロルタミド群で発現率が高かったことを除き、プラセボ群で発現率が高かった。

プラセボ群でダロルタミド群よりも発現割合が 1%以上高い TEAE は、関節痛（ダロルタミド群 8.1%、プラセボ群 9.2%）、尿閉（3.5%、6.5%）、排尿困難（2.2%、4.7%）、上腹部痛（1.3%、2.3%）及び水腎症（1.0%、2.3%）であった。

表 2.7.6.9-13 器官別大分類別の TEAE (SAF)

MedDRA SOC Version 21.0		Darolutamide N = 954 n (%)						Placebo N = 554 n (%)					
			Worst CTCAE grade						Worst CTCAE grade				
		Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Gastrointestinal disorders	胃腸障害	276 (28.9)	173 (18.1)	81 (8.5)	16 (1.7)	4 (0.4)	2 (0.2)	141 (25.5)	85 (15.3)	45 (8.1)	11 (2.0)	0	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	270 (28.3)	150 (15.7)	102 (10.7)	18 (1.9)	0	0	135 (24.4)	79 (14.3)	50 (9.0)	6 (1.1)	0	0
General disorders and administration site conditions	一般・全身障害および投与部位の状態	244 (25.6)	151 (15.8)	72 (7.5)	13 (1.4)	0	8 (0.8)	104 (18.8)	76 (13.7)	21 (3.8)	6 (1.1)	0	1 (0.2)
Infections and infestations	感染症および寄生虫症	227 (23.8)	66 (6.9)	120 (12.6)	32 (3.4)	4 (0.4)	5 (0.5)	120 (21.7)	43 (7.8)	60 (10.8)	15 (2.7)	1 (0.2)	1 (0.2)
Renal and urinary disorders	腎および尿路障害	198 (20.8)	86 (9.0)	65 (6.8)	45 (4.7)	2 (0.2)	0	140 (25.3)	49 (8.8)	54 (9.7)	32 (5.8)	5 (0.9)	0
Vascular disorders	血管障害	152 (15.9)	76 (8.0)	39 (4.1)	36 (3.8)	0	1 (0.1)	68 (12.3)	28 (5.1)	21 (3.8)	17 (3.1)	0	2 (0.4)
Nervous system disorders	神経系障害	147 (15.4)	77 (8.1)	50 (5.2)	16 (1.7)	2 (0.2)	2 (0.2)	74 (13.4)	39 (7.0)	20 (3.6)	11 (2.0)	0	4 (0.7)
Investigations	臨床検査	144 (15.1)	70 (7.3)	55 (5.8)	18 (1.9)	1 (0.1)	0	63 (11.4)	36 (6.5)	21 (3.8)	4 (0.7)	2 (0.4)	0
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	119 (12.5)	48 (5.0)	51 (5.3)	17 (1.8)	0	3 (0.3)	46 (8.3)	15 (2.7)	21 (3.8)	10 (1.8)	0	0
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	119 (12.5)	64 (6.7)	33 (3.5)	16 (1.7)	3 (0.3)	3 (0.3)	54 (9.7)	36 (6.5)	8 (1.4)	8 (1.4)	0	2 (0.4)
Cardiac disorders	心臓障害	113 (11.8)	39 (4.1)	28 (2.9)	30 (3.1)	6 (0.6)	10 (1.0)	41 (7.4)	13 (2.3)	15 (2.7)	4 (0.7)	1 (0.2)	8 (1.4)
Metabolism and nutrition disorders	代謝および栄養障害	95 (10.0)	34 (3.6)	38 (4.0)	19 (2.0)	4 (0.4)	0	49 (8.8)	24 (4.3)	15 (2.7)	10 (1.8)	0	0
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	90 (9.4)	63 (6.6)	24 (2.5)	3 (0.3)	0	0	40 (7.2)	30 (5.4)	9 (1.6)	1 (0.2)	0	0
Blood and lymphatic system disorders	血液およびリンパ系障害	75 (7.9)	36 (3.8)	24 (2.5)	15 (1.6)	0	0	37 (6.7)	12 (2.2)	18 (3.2)	6 (1.1)	1 (0.2)	0

表 2.7.6.9-13 器官別大分類別の TEAE (SAF) (続き)

MedDRA SOC Version 21.0		Darolutamide N = 954 n (%)						Placebo N = 554 n (%)					
			Worst CTCAE grade						Worst CTCAE grade				
		Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Psychiatric disorders	精神障害	57 (6.0)	34 (3.6)	22 (2.3)	1 (0.1)	0	0	28 (5.1)	14 (2.5)	13 (2.3)	1 (0.2)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	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)	48 (5.0)	10 (1.0)	14 (1.5)	20 (2.1)	2 (0.2)	2 (0.2)	26 (4.7)	7 (1.3)	9 (1.6)	9 (1.6)	0	1 (0.2)
Reproductive system and breast disorders	生殖系および乳房障害	46 (4.8)	32 (3.4)	13 (1.4)	1 (0.1)	0	0	35 (6.3)	23 (4.2)	11 (2.0)	1 (0.2)	0	0
Hepatobiliary disorders	肝胆道系障害	31 (3.2)	21 (2.2)	4 (0.4)	4 (0.4)	1 (0.1)	1 (0.1)	10 (1.8)	6 (1.1)	1 (0.2)	3 (0.5)	0	0
Eye disorders	眼障害	20 (2.1)	11 (1.2)	4 (0.4)	5 (0.5)	0	0	19 (3.4)	8 (1.4)	6 (1.1)	5 (0.9)	0	0
Ear and labyrinth disorders	耳および迷路障害	14 (1.5)	10 (1.0)	4 (0.4)	0	0	0	11 (2.0)	8 (1.4)	3 (0.5)	0	0	0
Immune system disorders	免疫系障害	14 (1.5)	6 (0.6)	8 (0.8)	0	0	0	6 (1.1)	4 (0.7)	2 (0.4)	0	0	0
Surgical and medical procedures	外科および内科処置	10 (1.0)	1 (0.1)	1 (0.1)	8 (0.8)	0	0	5 (0.9)	0	2 (0.4)	3 (0.5)	0	0
Endocrine disorders	内分泌障害	9 (0.9)	6 (0.6)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
Product issues	製品の問題	9 (0.9)	3 (0.3)	2 (0.2)	4 (0.4)	0	0	3 (0.5)	0	2 (0.4)	1 (0.2)	0	0
Congenital, familial and genetic disorders	先天性、家族性および遺伝性障害	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events; MedDRA = Medical Dictionary for Regulatory Activities; N = total number of patients (100%); n = number of patients with event

CTCAE version 4.03.

Source: 5.3.5.1.1 PH-39723/Table 14.3.1/3

表 2.7.6.9-14 いずれかの投与群で発現割合が 2%以上の TEAE (SAF)

MedDRA PT Version 21.0		Darolutamide N = 954					Placebo N = 554				
		Total n (%)	EAIR per 100 PY [a]	Worst CTCAE grade Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Total n (%)	EAIR per 100 PY [a]	Worst CTCAE grade Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Fatigue	疲労	115 (12.1)	8.6	4 (0.4)	0	0	48 (8.7)	8.5	5 (0.9)	0	0
Back pain	背部痛	84 (8.8)	6.3	4 (0.4)	0	0	50 (9.0)	8.8	1 (0.2)	0	0
Arthralgia	関節痛	77 (8.1)	5.8	3 (0.3)	0	0	51 (9.2)	9.0	2 (0.4)	0	0
Diarrhoea	下痢	66 (6.9)	4.9	0	0	1 (0.1)	31 (5.6)	5.5	1 (0.2)	0	0
Hypertension	高血圧	63 (6.6)	4.7	30 (3.1)	0	0	29 (5.2)	5.1	12 (2.2)	0	0
Constipation	便秘	60 (6.3)	4.5	0	0	0	34 (6.1)	6.0	0	0	0
Pain in extremity	四肢痛	55 (5.8)	4.1	0	0	0	18 (3.2)	3.2	1 (0.2)	0	0
Anaemia	貧血	53 (5.6)	4.0	8 (0.8)	0	0	25 (4.5)	4.4	2 (0.4)	0	0
Hot flush	ほてり	50 (5.2)	3.7	0	0	0	23 (4.2)	4.1	0	0	0
Nausea	悪心	48 (5.0)	3.6	2 (0.2)	0	0	32 (5.8)	5.6	0	0	0
Urinary tract infection	尿路感染	47 (4.9)	3.5	6 (0.6)	0	0	28 (5.1)	4.9	3 (0.5)	0	0
Haematuria	血尿	41 (4.3)	3.1	10 (1.0)	0	0	27 (4.9)	4.8	7 (1.3)	0	0
Oedema peripheral	末梢性浮腫	39 (4.1)	2.9	0	0	0	17 (3.1)	3.0	0	0	0
Pollakiuria	頻尿	38 (4.0)	2.8	1 (0.1)	0	0	16 (2.9)	2.8	1 (0.2)	0	0
Headache	頭痛	37 (3.9)	2.8	0	0	0	14 (2.5)	2.5	1 (0.2)	0	0
Musculoskeletal pain	筋骨格痛	37 (3.9)	2.8	1 (0.1)	0	0	11 (2.0)	1.9	1 (0.2)	0	0
Asthenia	無力症	36 (3.8)	2.7	2 (0.2)	0	0	19 (3.4)	3.3	2 (0.4)	0	0
Fall	転倒	36 (3.8)	2.7	8 (0.8)	0	0	23 (4.2)	4.1	4 (0.7)	0	0
Nasopharyngitis	上咽頭炎	36 (3.8)	2.7	0	0	0	21 (3.8)	3.7	0	0	0
Dizziness	浮動性めまい	35 (3.7)	2.6	2 (0.2)	0	0	14 (2.5)	2.5	1 (0.2)	0	0
Weight decreased	体重減少	34 (3.6)	2.5	0	0	0	12 (2.2)	2.1	0	0	0
Urinary retention	尿閉	33 (3.5)	2.5	15 (1.6)	0	0	36 (6.5)	6.3	11 (2.0)	0	0
Cough	咳嗽	29 (3.0)	2.2	1 (0.1)	0	0	11 (2.0)	1.9	0	0	0
Decreased appetite	食欲減退	28 (2.9)	2.1	2 (0.2)	0	0	16 (2.9)	2.8	1 (0.2)	0	0

表 2.7.6.9-14 いずれかの投与群で発現割合が 2%以上の TEAE（SAF）（続き）

MedDRA PT Version 21.0		Darolutamide N = 954					Placebo N = 554				
		Total n (%)	EAIR per 100 PY [a]	Worst CTCAE grade			Total n (%)	EAIR per 100 PY [a]	Worst CTCAE grade		
				Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)			Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Influenza	インフルエンザ	27 (2.8)	2.0	0	1 (0.1)	1 (0.1)	9 (1.6)	1.6	0	0	0
Insomnia	不眠症	26 (2.7)	1.9	0	0	0	10 (1.8)	1.8	1 (0.2)	0	0
Upper respiratory tract infection	上気道感染	25 (2.6)	1.9	0	0	0	9 (1.6)	1.6	0	0	0
Abdominal pain	腹痛	24 (2.5)	1.8	0	1 (0.1)	0	12 (2.2)	2.1	1 (0.2)	0	0
Dyspnoea	呼吸困難	24 (2.5)	1.8	2 (0.2)	0	1 (0.1)	15 (2.7)	2.6	3 (0.5)	0	0
Atrial fibrillation	心房細動	22 (2.3)	1.6	5 (0.5)	1 (0.1)	0	8 (1.4)	1.4	1 (0.2)	1 (0.2)	0
Blood creatinine increased	血中クレアチニン増加	22 (2.3)	1.6	1 (0.1)	0	0	14 (2.5)	2.5	0	2 (0.4)	0
Dysuria	排尿困難	21 (2.2)	1.6	1 (0.1)	0	0	26 (4.7)	4.6	5 (0.9)	0	0
Gynaecomastia	女性化乳房	19 (2.0)	1.4	0	0	0	6 (1.1)	1.1	0	0	0
Pneumonia	肺炎	19 (2.0)	1.4	8 (0.8)	1 (0.1)	1 (0.1)	11 (2.0)	1.9	3 (0.5)	1 (0.2)	0
Pyrexia	発熱	19 (2.0)	1.4	1 (0.1)	0	0	5 (0.9)	0.9	0	0	0
Pruritus	そう痒症	16 (1.7)	1.2	0	0	0	11 (2.0)	1.9	0	0	0
Urinary incontinence	尿失禁	14 (1.5)	1.0	0	0	0	12 (2.2)	2.1	0	0	0
Abdominal pain upper	上腹部痛	12 (1.3)	0.9	1 (0.1)	0	0	13 (2.3)	2.3	1 (0.2)	0	0
Pelvic pain	骨盤痛	12 (1.3)	0.9	0	0	0	12 (2.2)	2.1	0	0	0
Hydronephrosis	水腎症	10 (1.0)	0.7	7 (0.7)	0	0	13 (2.3)	2.3	3 (0.5)	0	0

CTCAE = Common Terminology Criteria for Adverse Events; EAIR = exposure-adjusted incidence rate; MedDRA = Medical Dictionary for Regulatory Activities; N = total number of patients (100%); n = number of patients with event; PT = preferred term, PY = patient year.

a: EAIR of TEAEs, defined as the number of patients with a given TEAE divided by the total treatment duration of all patients in years. The rate is expressed in 100 patient years.

Note: A patient may have more than one entry.

CTCAE version 4.03.

Source: 5.3.5.1.1 PH-39723/Table 14.3.1/3, 14.3.1/7

グレード 3 及び 4 の有害事象

グレード 3 以上の TEAE の集計表を付表 2.7.6.9.a.1-3 に示す。

グレード 3 の TEAE の発現割合は、ダロルタミド群で 22.5%（215／954 例）、プラセボ群で 17.9%（99／554 例）であった（表 2.7.6.9-12）。最も発現割合の高いグレード 3 の TEAE は、高血圧（ダロルタミド群 3.1%、プラセボ群 2.2%）であり、次いで尿閉（1.6%、2.0%）及び血尿（1.0%、1.3%）であった。その他のグレード 3 の TEAE の発現割合は、いずれの投与群でも 1%未満であった（5.3.5.1.1 PH-39723/Table 14.3.1/4）。

グレード 4 の TEAE の発現割合は、ダロルタミド群で 2.2%（21／954 例）、プラセボ群で 1.6%（9／554 例）であった（表 2.7.6.9-12）。グレード 4 の TEAE として、ダロルタミド群で急性心筋梗塞、高血糖、虚血性脳卒中及び呼吸不全が各 2 例（0.2%）にみられた。これらの事象はプラセボ群ではみられなかった。プラセボ群では、腎不全が 3 例（0.5%）、血中クレアチニン増加が 2 例（0.4%）にみられた。その他のグレード 4 の TEAE の発現割合は、いずれの投与群でも 1%未満であった（5.3.5.1.1 PH-39723/Table 14.3.1/4）。

2.7.6.9.2.3.3.2 治験薬と関連のある TEAE

治験薬と関連のある TEAE のグレード別の集計表を付表 2.7.6.9.a.1-2 に示す。

治験薬と関連のある TEAE の発現割合は、ダロルタミド群で 27.0%（258／954 例）、プラセボ群で 19.9%（110／554 例）であった（表 2.7.6.9-12）。いずれかの投与群で 2%以上にみられた事象は、疲労（ダロルタミド群 7.1%、プラセボ群 4.3%）、ほてり（3.8%、2.7%）及び悪心（2.5%、3.1%）であった（5.3.5.1.1 PH-39723/Table 14.3.1/12）。

治験薬と関連のあるグレード 3 及び 4 の有害事象

治験薬と関連のあるグレード 3 以上の TEAE の集計表を付表 2.7.6.9.a.1-4 に示す。

治験薬と関連のあるグレード 3 の TEAE の発現割合は、ダロルタミド群で 2.5%（24／954 例）、プラセボ群で 2.5%（14／554 例）であった（表 2.7.6.9-12）。高血圧（ダロルタミド群 0.4%、プラセボ群 0.5%）及び疲労（0.2%、0.2%）が両投与群で認められ、ダロルタミド群にのみ 2 例以上にみられた事象は、AST 増加及び好中球数減少（各 3 例、0.3%）、ALT 増加、低ナトリウム血症及び好中球減少症（各 2 例、0.2%）であった。その他の事象はいずれかの投与群で 1 例のみに発現した（5.3.5.1.1 PH-39723/Table 14.3.1/13）。

治験薬と関連のあるグレード 4 の TEAE は、ダロルタミド群で 3 例（0.3%）に発現し、その内訳は、肝機能異常、虚血性脳卒中及び肺塞栓症が各 1 例（0.1%）であった。プラセボ群では、治験薬と関連のあるグレード 4 の TEAE はみられなかった（5.3.5.1.1 PH-39723/Table 14.3.1/13）。

2.7.6.9.2.3.4 死亡

死亡及びグレード 5 の TEAE の発現割合を、それぞれ表 2.7.6.9-15 及び表 2.7.6.9-16 に示す。

試験期間中、ダロルタミド群で 79 例（8.3%）、プラセボ群で 58 例（10.5%）の死亡がみられた（表 2.7.6.9-15）。いずれの投与群においても、前立腺癌による死亡が最も多かった〔ダロルタミド群：30 例（3.1%）、プラセボ群 25 例（4.5%）〕。

グレード 5 の TEAE はダロルタミド群で 37 例（3.9%）、プラセボ群で 18 例（3.2%）に発現した（表 2.7.6.9-16）。2 例以上にみられたグレード 5 の TEAE は、ダロルタミド群では死亡 4 例（0.4%）、心不全 3 例（0.3%）、心停止、全身健康状態低下及び肺塞栓症が各 2 例（0.2%）であり、プラセボ群では、心不全及び心停止が各 3 例（0.5%）及び急性呼吸不全 2 例（0.4%）であった。

表 2.7.6.9-15 死亡の要約（SAF）

		Darolutamide		Placebo	
		Total N = 954 n (%)	All deaths N = 79 [a] n (%)	Total N = 554 n (%)	All deaths N = 58 [a] n (%)
All deaths		79 (8.3%)	79 (100.0%)	58 (10.5%)	58 (100.0%)
Cause of death	Prostate cancer	30 (3.1%)	30 (38.0%)	25 (4.5%)	25 (43.1%)
	Other, specify	23 (2.4%)	23 (29.1%)	10 (1.8%)	10 (17.2%)
	Cardiovascular disease	18 (1.9%)	18 (22.8%)	11 (2.0%)	11 (19.0%)
	Respiratory disease	5 (0.5%)	5 (6.3%)	6 (1.1%)	6 (10.3%)
	Cerebrovascular disease	2 (0.2%)	2 (2.5%)	5 (0.9%)	5 (8.6%)
	Other cancer	1 (0.1%)	1 (1.3%)	0 (0.0%)	0 (0.0%)
	Diabetes	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (1.7%)

N = total number of patients (100%); n = number of patients with event

a: Percentages for causes of death were manually calculated by treatment arm from the total number of patients who died.

Source: 5.3.5.1.1 PH-39723/Table 14.3.2/12

表 2.7.6.9-16 グレード 5 の TEAE（SAF）

MedDRA PT Version 21.0		Darolutamide N = 954 n (%)	Placebo N = 554 n (%)
Any grade 5 TEAE		37 (3.9%)	18 (3.2%)
Death	死亡	4 (0.4%)	1 (0.2%)
Cardiac failure	心不全	3 (0.3%)	3 (0.5%)
Cardiac arrest	心停止	2 (0.2%)	3 (0.5%)
General physical health deterioration	全身健康状態低下	2 (0.2%)	0
Pulmonary embolism	肺塞栓症	2 (0.2%)	0
Acute myocardial infarction	急性心筋梗塞	1 (0.1%)	0
Alcohol poisoning	アルコール中毒	1 (0.1%)	0
Angina pectoris	狭心症	1 (0.1%)	0
Aortic dissection	大動脈解離	1 (0.1%)	0
Brain oedema	脳浮腫	1 (0.1%)	0
Cardiac disorder	心障害	1 (0.1%)	0
Cardiac failure acute	急性心不全	1 (0.1%)	0
Coronary artery disease	冠動脈疾患	1 (0.1%)	0
Diarrhoea	下痢	1 (0.1%)	0
Dyspnoea	呼吸困難	1 (0.1%)	0
Endocarditis	心内膜炎	1 (0.1%)	0
Heart injury	心臓損傷	1 (0.1%)	0
Influenza	インフルエンザ	1 (0.1%)	0
Ischaemic stroke	虚血性脳卒中	1 (0.1%)	1 (0.2%)
Liver disorder [a]	肝障害	1 (0.1%)	0
Lung infection	肺感染	1 (0.1%)	0
Meningitis bacterial	細菌性髄膜炎	1 (0.1%)	0
Multiple injuries	多発性外傷	1 (0.1%)	0
Oncologic complication	腫瘍合併症	1 (0.1%)	0
Pancreatic carcinoma	膵癌	1 (0.1%)	0
Pneumonia	肺炎	1 (0.1%)	0
Small intestinal perforation	小腸穿孔	1 (0.1%)	0
Sudden cardiac death	心突然死	1 (0.1%)	0
Sudden death	突然死	1 (0.1%)	0

表 2.7.6.9-16 グレード 5 の TEAE（SAF）（続き）

MedDRA PT Version 21.0		Darolutamide N = 954 n (%)	Placebo N = 554 n (%)
Acute respiratory failure	急性呼吸不全	0	2 (0.4%)
Arteriosclerosis	動脈硬化症	0	1 (0.2%)
Cellulitis gangrenous	壊疽性蜂巣炎	0	1 (0.2%)
Cerebral ischaemia	脳虚血	0	1 (0.2%)
Cerebrovascular accident	脳血管発作	0	1 (0.2%)
Circulatory collapse	循環虚脱	0	1 (0.2%)
Haemorrhage intracranial	頭蓋内出血	0	1 (0.2%)
Hypertensive heart disease	高血圧性心疾患	0	1 (0.2%)
Myocardial infarction	心筋梗塞	0	1 (0.2%)
Prostate cancer	前立腺癌	0	1 (0.2%)

N = total number of patients (100%); n = number of patients with event
Note: A patient may have more than one entry.
a: The reported term was liver disease progression.
Source: 5.3.5.1.1 PH-39723/Table 14.3.1/10

治験薬と関連のあるグレード 5 の TEAE は、ダロルタミド群で 1 例（小腸穿孔）、プラセボ群で 2 例（心筋梗塞、頭蓋内出血、各 1 例）に認められた（付表 2.7.6.9.a.1-2、付表 2.7.6.9.a.1-4）。

2.7.6.9.2.3.5 重篤な有害事象

いずれかの投与群で 3 例以上に発現した重篤な TEAE の発現割合及び曝露期間で調整した発現率を表 2.7.6.9-17 に示す。すべての重篤な TEAE の集計表を付表 2.7.6.9.a.1-5 に示す。

重篤な TEAE の発現割合は、ダロルタミド群で 24.8%（237／954 例）、プラセボ群で 20.0%（111／554 例）であった。いずれかの投与群で発現割合が 1%以上であった重篤な TEAE は、尿閉（ダロルタミド群 1.6%、プラセボ群 3.2%）、肺炎（1.4%、1.1%）及び血尿（1.0%、1.1%）であった。

表 2.7.6.9-17 いずれかの投与群で 3 例以上に発現した重篤な TEAE（SAF）

MedDRA PT Version 21.0		Darolutamide N = 954 n (%)	Placebo N = 554 n (%)
Any treatment-emergent SAE		237 (24.8%)	111 (20.0%)
Urinary retention	尿閉	15 (1.6%)	18 (3.2%)
Pneumonia	肺炎	13 (1.4%)	6 (1.1%)
Haematuria	血尿	10 (1.0%)	6 (1.1%)
Atrial fibrillation	心房細動	8 (0.8%)	3 (0.5%)
Cardiac failure	心不全	8 (0.8%)	4 (0.7%)
Urinary tract infection	尿路感染	7 (0.7%)	0
Urinary tract obstruction	尿路閉塞	6 (0.6%)	2 (0.4%)
Acute myocardial infarction	急性心筋梗塞	5 (0.5%)	0
Ischaemic stroke	虚血性脳卒中	5 (0.5%)	2 (0.4%)
Pulmonary embolism	肺塞栓症	5 (0.5%)	1 (0.2%)
Acute kidney injury	急性腎障害	4 (0.4%)	3 (0.5%)
Angina pectoris	狭心症	4 (0.4%)	2 (0.4%)
Death	死亡	4 (0.4%)	1 (0.2%)
Decreased appetite	食欲減退	4 (0.4%)	0
Dyspnoea	呼吸困難	4 (0.4%)	1 (0.2%)
General physical health deterioration	全身健康状態低下	4 (0.4%)	0

表 2.7.6.9-17 いずれかの投与群で 3 例以上に発現した重篤な TEAE（SAF）（続き）

MedDRA PT Version 21.0		Darolutamide N = 954 n (%)	Placebo N = 554 n (%)
Intestinal obstruction	腸閉塞	4 (0.4%)	0
Myocardial infarction	心筋梗塞	4 (0.4%)	2 (0.4%)
Bladder neoplasm	膀胱新生物	3 (0.3%)	0
Chest pain	胸痛	3 (0.3%)	0
Colon cancer	結腸癌	3 (0.3%)	0
Fall	転倒	3 (0.3%)	1 (0.2%)
Hydronephrosis	水腎症	3 (0.3%)	3 (0.5%)
Hyperglycaemia	高血糖	3 (0.3%)	1 (0.2%)
Osteoarthritis	変形性関節症	3 (0.3%)	1 (0.2%)
Pancreatic carcinoma	膵癌	3 (0.3%)	0
Pyelonephritis	腎盂腎炎	3 (0.3%)	0
Cardiac arrest	心停止	2 (0.2%)	3 (0.5%)
Cerebrovascular accident	脳血管発作	2 (0.2%)	3 (0.5%)
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	2 (0.2%)	3 (0.5%)
Dysuria	排尿困難	1 (0.1%)	3 (0.5%)
Renal failure	腎不全	1 (0.1%)	4 (0.7%)

MedDRA = Medical Dictionary for Regulatory Activities; N = total number of patients (100%); n = number of patients with event; PT = preferred term.
Note: A patient may have more than one entry.
Source: 5.3.5.1.1 PH-39723/Table 14.3.2/1, 14.3.2/2

治験薬と関連のある重篤な TEAE は、ダロルタミド群で 10 例（1.0%）、プラセボ群で 6 例（1.1%）に認められた（表 2.7.6.9-12、付表 2.7.6.9.a.1-6）。

2.7.6.9.2.3.6 その他の重要な有害事象

2.7.6.9.2.3.6.1 治験薬の投与中止に至った有害事象

治験薬の投与中止に至った TEAE の発現割合は、ダロルタミド群の 8.9%（85／954 例）、プラセボ群で 8.7%（48／554 例）であった（表 2.7.6.9-12）。

いずれかの投与群で 3 例以上にみられた治験薬の投与中止に至った TEAE は、心不全〔ダロルタミド群 4 例（0.4%）、プラセボ群 4 例（0.7%）〕及び死亡〔4 例（0.4%）、1 例（0.2%）〕であった（5.3.5.1.1 PH-39723/Table 14.3.1/18）。

治験薬の投与中止に至った治験薬と関連のある TEAE の発現割合は、ダロルタミド群で 1.6%（15／954 例）、プラセボ群で 2.3%（13／554 例）であった（5.3.5.1.1 PH-39723/Table 14.3.1/19）。

2.7.6.9.2.3.6.2 治験薬の投与中断又は減量に至った有害事象

治験薬の投与中断に至った TEAE

治験薬の投与中断に至った TEAE の発現割合は、ダロルタミド群で 12.5%（119／954 例）、プラセボ群で 8.8%（49／554 例）であった（5.3.5.1.1 PH-39723/Table 14.3.1/20）。

発現割合が 0.5%以上の治験薬の投与中断に至った TEAE は、ダロルタミド群では高血圧（ダロルタミド群 0.6%、プラセボ群 0.0%）、下痢（0.5%、0.2%）、肺炎（0.5%、0.4%）、プラセボ群では尿閉（0.1%、0.9%）、悪心（0.3%、0.5%）及び疲労（0.3%、0.5%）であった（5.3.5.1.1 PH-39723/Table 14.3.1/21）。

治験薬の投与中断に至った治験薬と関連のある TEAE の発現割合は、ダロルタミド群で 3.6%（34／954 例）、プラセボ群で 2.2%（12／554 例）であった（5.3.5.1.1 PH-39723/Table 14.3.1/22）。

治験薬の減量に至った TEAE

治験薬の減量に至った TEAE の発現割合は、ダロルタミド群で 4.8%（46／954 例）、プラセボ群で 1.6%（9／554 例）であった（5.3.5.1.1 PH-39723/Table 14.3.1/23）。よくみられた治験薬の減量に至った TEAE は、疲労（ダロルタミド群 0.7%、プラセボ群 0.4%）、高血圧（0.3%、0.2%）及び悪心（0.3%、0.4%）であった。その他の事象はいずれかの投与群で 2 例以下の発現であった。

治験薬の減量に至った治験薬と関連のある TEAE の発現割合は、ダロルタミド群で 2.9%（28／954 例）、プラセボ群で 0.9%（5／554 例）であった（5.3.5.1.1 PH-39723/Table 14.3.1/24）。

2.7.6.9.2.3.6.3 注目すべき有害事象

注目すべき有害事象の発現割合を表 2.7.6.9-18 に示す。

注目すべき有害事象には、第 2 世代アンドロゲン受容体拮抗薬又は ADT との関連が知られている事象を含めた。これらの事象のための、有害事象のグループ化には、MedDRA SOC、高位グループ語（HLGT）、高位語（HLT）及び MedDRA ラベリング分類（MLG）、データに基づくグループ化を用いた（5.3.5.1.1 PH-39723/Table 14.3.1/1s1～14.3.1/17s1）。

表 2.7.6.9-18 注目すべき有害事象（SAF）

Grouped TEAE term [a]		Darolutamide N = 954 n (%)	Darolutamide EAIR per 100 PY [b]	Placebo N = 554 n (%)	Placebo EAIR per 100 PY [b]	Incidence risk ratio for EAIR
Bone fracture	骨折	40 (4.19%)	3.0	20 (3.61%)	3.5	0.85
Fall [c]	転倒	40 (4.19%)	3.0	26 (4.69%)	4.6	0.65
Fatigue/asthenic conditions	疲労／無力症	151 (15.83%)	11.3	63 (11.37%)	11.1	1.02
Weight decreased	体重減少	34 (3.56%)	2.5	12 (2.17%)	2.1	1.21
Seizure	痙攣発作	2 (0.21%)	0.1	1 (0.18%)	0.2	0.85
Rash	発疹	28 (2.94%)	2.1	5 (0.90%)	0.9	2.38
Cardiac disorders (SOC):	心臓障害(SOC)	113 (11.80%)	N/A	41 (7.4%)	N/A	N/A
Cardiac arrhythmias	不整脈	64 (6.71%)	4.7	22 (3.97%)	3.8	1.24
Coronary artery disorders	冠動脈疾患	31 (3.25%)	2.3	14 (2.53%)	2.4	0.94
Heart failures	心不全	18 (1.89%)	1.3	5 (0.90%)	0.9	1.53
CNS vascular disorders：	中枢神経系血管障害	16 (1.68%)	1.2	10 (1.81%)	1.7	0.68
Cerebral ischaemia	脳虚血	13 (1.36%)	1.0	8 (1.44%)	1.4	0.69
Cerebral and intracranial hemorrhage	脳出血及び頭蓋内出血	2 (0.21%)	0.1	2 (0.36%)	0.4	0.43
Hypertension	高血圧	70 (7.34%)	5.2	33 (5.96%)	5.8	0.90
Vasodilatation and flushing	血管拡張術及び潮紅	54 (5.66%)	4.0	23 (4.15%)	4.1	1.00
Diabetes mellitus and hyperglycemia	糖尿病及び高血糖	22 (2.31%)	1.6	12 (2.17%)	2.1	0.78
Mental impairment disorders	精神的機能障害	16 (1.68%)	1.2	10 (1.81%)	1.7	0.68
Depressed mood disorders and disturbances	抑うつ気分	17 (1.78%)	1.3	8 (1.44%)	1.4	0.90
Breast disorders/gynaecomastia	乳房障害／女性化乳房	22 (2.31%)	1.6	9 (1.62%)	1.6	1.04

CNS = central nervous system; EAIR = exposure-adjusted incidence rate; N = total number of patients (100%); n = number of patients with event; N/A = not available; nc = not calculable; PY = patient year

Note: The table contains counts of patients. If a patient experienced more than one episode of an AE, the patient is counted only once within a grouped term.

a: The specific terms used for MedDRA searches and reported PTs for grouped TEAE terms are described separately for each special topic in the subsections below.

b: EAIR of grouped events, defined as the number of patients with events divided by treatment duration in years. The rate is expressed in 100 patient years.

c: After review of the data, the search term for “Fall” was extended to include also the MedDRA PT “Accident” by SAP supplement 1.

Source: 5.3.5.1.1 PH-39723/Table 14.3.1/3, 14.3.1/7s1, 14.3.1/8s1, 14.3.1/9s1, 14.3.1/10s1

骨折

骨折の発現割合は、ダロルタミド群で 4.19%、プラセボ群で 3.61%であり、曝露期間で調整した発現率（100 人年あたり）はダロルタミド群で 3.0、プラセボ群で 3.5 であった（リスク比 0.85）。

骨折は、ほとんどの被験者でグレード 1 又は 2 であった。グレード 3 の骨折は、ダロルタミド群で 9 例（0.9%）、プラセボ群で 5 例（0.9%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.1/29）。重篤な骨折は、ダロルタミド群で 8 例（0.8%）、プラセボ群で 6 例（1.1%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.2/11）。治験薬の投与中止に至った骨折はプラセボ群の 1 例（0.2%）にみられた（グレード 3 の顔面骨折）（5.3.5.1.1 PH-39723/Table 14.3.1/33）。

転倒

転倒の発現割合は、ダロルタミド群で 4.19%、プラセボ群で 4.69%であり、曝露期間で調整した発現率（100 人年あたり）はそれぞれ 3.0、4.6 であった（リスク比 0.65）。

転倒は、ほとんどの被験者でグレード 1 又は 2 であった。グレード 3 の転倒は、ダロルタミド群で 8 例（0.8%）、プラセボ群で 4 例（0.7%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.1/29）。重篤な転倒は、ダロルタミド群で 3 例（0.3%）、プラセボ群で 1 例（0.2%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.2/11）。治験薬の投与中止に至った転倒はなかった（5.3.5.1.1 PH-39723/Table 14.3.2/11、14.3.1/33）。

疲労／無力症

疲労／無力症の発現割合は、ダロルタミド群で 15.83%、プラセボ群で 11.37%であり、曝露期間で調整した発現率（100 人年あたり）は、それぞれ 11.3、11.1（リスク比：1.02）であった。

大部分の疲労／無力症はグレード 1 又は 2 であった。グレード 3 の疲労／無力症は、ダロルタミド群で 6 例（0.6%）、プラセボ群で 6 例（1.1%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.1/29）。重篤な疲労／無力症は、ダロルタミド群で 1 例（0.1%）（グレード 3 の無力症）にみられ（5.3.5.1.1 PH-39723/Table 14.3.2/11）、治験薬の投与中止に至った疲労／無力症は、ダロルタミド群で 3 例（0.3%）、プラセボ群で 1 例（0.2%）にみられた（5.3.5.1.1 PH-39723/Table 14.3.1/33）。

体重減少

体重減少の発現割合は、ダロルタミド群で 3.56%、プラセボ群で 2.17%であり、曝露期間で調整した発現率（100 人年あたり）は、それぞれ 2.5、2.1（リスク比：1.21）であった。

いずれの体重減少もグレード 1 又は 2 であった（5.3.5.1.1 PH-39723/Table 14.3.1/29）。重篤又は治験薬の投与中止に至った体重減少は認められなかった（5.3.5.1.1 PH-39723/Table 14.3.2/11、14.3.1/33）。

痙攣発作

痙攣発作の発現割合は、ダロルタミド群で 0.21%、プラセボ群で 0.18%であり、曝露期間で調整した発現率（100 人年あたり）は、それぞれ 0.1、0.2（リスク比：0.85）であった。

いずれの痙攣発作もグレード 1 又は 2 であった（5.3.5.1.1 PH-39723/Table 14.3.1/29）。重篤な痙攣発作はダロルタミド群で 2 例（0.2%）にみられ、治験薬の投与中止に至った痙攣発作はいずれの投与群でもみられなかった（5.3.5.1.1 PH-39723/Table 14.3.2/11、14.3.1/33）。

発疹

発疹の発現割合は、ダロルタミド群で 2.94%、プラセボ群で 0.90%であり、曝露期間で調整した発現率（100 人年あたり）は、それぞれ 2.1、0.9（リスク比：2.38）であった（5.3.5.1.1 PH-39723/Table 14.3.1/10s1）。

ダロルタミド群の 1 例でみられたグレード 3 の発疹を除き、いずれの事象もグレード 1 又は 2 であった（5.3.5.1.1 PH-39723/Table 14.3.1/3s1）。重篤な発疹は認められなかった（5.3.5.1.1 PH-39723/Table 14.3.2/11）。

心臓障害

心臓障害（SOC）の発現割合は、ダロルタミド群で 11.8%、プラセボ群で 7.4%であった（表 2.7.6.9-13）。グレード 5 の心臓障害の発現割合はダロルタミド群でプラセボ群よりも低く（ダロルタミド群 1.0%、プラセボ群 1.4%）、その他のグレードではダロルタミド群の方が高かった（付表 2.7.6.9.a.1-1）。群間の差は主に、不整脈（6.71%、3.97%）、冠動脈疾患（3.25%、2.53%）及び心不全（1.89%、0.90%）によるものであった（5.3.5.1.1 PH-39723/Table 14.3.1/7s1）。

ダロルタミド群ではプラセボ群に比べて心臓障害の病歴を有する被験者の割合が高く（ダロルタミド群 46.1%、プラセボ群 40.3%）、これが交絡因子となった可能性がある（5.3.5.1.1 PH-39723/Table 14.1.1/24）。

その他の注目すべき有害事象について、群間で特に差はみられなかった（表 2.7.6.9-18）。

2.7.6.9.2.3.7 臨床検査

2.7.6.9.2.3.7.1 血液学的検査及び血液生化学的検査

いずれかの投与群で 2%以上の頻度でみられたグレード 3 又は 4 の臨床検査値異常は、リンパ球数減少（グレード 3：ダロルタミド群 3.4%、プラセボ群 3.4%、グレード 4：0.2%、0.0%）、好中球数減少（グレード 3：2.5%、0.2%、グレード 4：0.9%、0.4%）であった（5.3.5.1.1 PH-39723/Table 14.3.4/2）。好中球数減少を除き、グレード 4 の臨床検査値異常の頻度はいずれの群でも 0.5%以下であった。

肝機能検査

グレード 3 のアラニンアミノトランスフェラーゼ（ALT）増加の頻度は、ダロルタミド群で 0.3%（3 例）、プラセボ群で 0.2%（1 例）であり、グレード 4 の ALT 増加はみられなかった（5.3.5.1.1 PH-39723/Table 14.3.4/2）。ベースラインから治験薬投与開始後に、ALT 増加が 1 グレード悪化した頻度はダロルタミド群（6.0%）でプラセボ群（4.0%）に比べてやや高かったが、2 グレード（0.3%、0.2%）及び 3 グレードの悪化（0.3%、0.2%）の頻度は両群で同様であった（5.3.5.1.1 PH-39723/Table 14.3.4/4）。4 グレードの悪化はみられなかった。

グレード 3 のアルカリホスファターゼ（ALP）増加の頻度は、ダロルタミド群で 0.1%（1 例）、プラセボ群で 0.4%（2 例）であり、グレード 4 の ALP 増加はみられなかった。ベースラインから治験薬投与開始後に、ALP 増加が 1 グレード悪化した頻度はダロルタミド群（4.0%）でプラセボ群（6.2%）に比べてやや低く、2 グレード（0.3%、0.7%）及び 3 グレードの悪化（0.1%、0.4%）は同様であった。4 グレードの悪化はみられなかった。

グレード 3 の血中ビリルビン増加の頻度は、ダロルタミド群で 0.1%（1 例）、プラセボ群で 0.0%（0 例）であり、グレード 4 の血中ビリルビン増加はみられなかった。ベースラインから

治験薬投与開始後に、血中ビリルビン増加が 1 グレード悪化した頻度はダロルタミド群（12.0%）でプラセボ群（4.2%）に比べてやや高く、2 グレード（2.8%、0.4%）及び 3 グレードの悪化（0.1%、0.0%）も同様であった。4 グレードの悪化はみられなかった。

Hy’s Law

Hy’s Law 基準〔アスパラギン酸アミノトランスフェラーゼ（AST）又は ALT が基準値上限（ULN）の 3 倍超、かつ総ビリルビンが ULN の 2 倍以上〕を満たし、ALP が ULN の 2 倍未満の被験者を、possible Hy’s Law 症例と定義した。Hy’s Law 基準を満たす被験者はいなかった（5.3.5.1.1 PH-39723/Table 14.3.4/164）。

2.7.6.9.2.3.7.2 テストステロン

ベースラインにおけるテストステロンの平均値±標準偏差は、ダロルタミド群で 0.663±1.135nmol/L（950 例）、プラセボ群で 0.632±0.412nmol/L（549 例）であった（5.3.5.1.1 PH-39723/Table 14.3.4/53）。各来院時におけるテストステロン値のベースラインからの変化は小さく、群間でも顕著な差はなかった。

2.7.6.9.2.3.8 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

血圧、心拍数、体温、体重、体格指数（BMI）及び身体所見について、試験期間を通してベースラインからの大きな変動はみられず、群間でも差はみられなかった（5.3.5.1.1 PH-39723/Table 14.3.5/1～14.3.5/8）。

心電図異常がみられた被験者の割合に、群間で差はみられなかった（5.3.5.1.1 PH-39723/Table 14.3.5/19）。また、QTcB 及び QTcF の延長（ベースラインからの変化量又は絶対値）がみられた被験者の割合に、群間で差はなかった（5.3.5.1.1 PH-39723/Table 14.3.5/9、14.3.5/10、14.3.5/16、14.3.5/17）。

2.7.6.9.3 結論

ハイリスクの非転移性去勢抵抗性前立腺癌を有する男性患者を対象とした多施設共同、無作為化、二重盲検、プラセボ対照、第Ⅲ相試験において、ダロルタミド投与により有効性主要評価項目である MFS に 21.94 ヵ月の延長が認められ、転移又は死亡のリスクが 58.7%低下した。副次評価項目である OS については、primary completion 時にイベント数が限られおり、得られた p 値は事前に規定した有意水準より大きかった。しかし、ダロルタミド群における OS の改善が示唆される結果が観察された。疼痛増悪までの期間を含むその他の副次評価項目についても、ハザード比により、ダロルタミド群のプラセボ群に対する延長傾向が示された。

ダロルタミドの忍容性は良好であった。よくみられる TEAE 及び治験薬の投与中止に至った TEAE の発現割合は、プラセボ群と同様であった。ADT 下でダロルタミドを投与しても、骨折、転倒、痙攣発作、高血圧、体重減少、精神的機能障害、糖尿病及び高血糖、脳血管障害、血管拡張術及び潮紅、抑うつ気分、及び乳房障害／女性化乳房などの、現行の nmCRPC 治療で報告されている有害事象のリスク上昇は示されなかった。

以上より、ハイリスクの非転移性去勢抵抗性前立腺癌を有する男性患者において、ダロルタミドの有用性が示された。

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2.7.6.9.a.1 付表

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=554) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		794 (83.2)	219 (23.0)	302 (31.7)	215 (22.5)	21 (2.2)	37 (3.9)	426 (76.9)	134 (24.2)	166 (30.0)	99 (17.9)	9 (1.6)	18 (3.2)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	75 (7.9)	36 (3.8)	24 (2.5)	15 (1.6)	0	0	37 (6.7)	12 (2.2)	18 (3.2)	6 (1.1)	1 (0.2)	0
	Abdominal lymphadenopathy	腹部リンパ節腫脹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Anaemia	貧血	53 (5.6)	33 (3.5)	12 (1.3)	8 (0.8)	0	0	25 (4.5)	10 (1.8)	13 (2.3)	2 (0.4)	0	0
	Basophilia	好塩基球増加症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Eosinophilia	好酸球増加症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Iron deficiency anaemia	鉄欠乏性貧血	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Leukocytosis	白血球増加症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Leukopenia	白血球減少症	7 (0.7)	1 (0.1)	5 (0.5)	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Lymphadenopathy	リンパ節症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	9 (0.9)	3 (0.3)	4 (0.4)	2 (0.2)	0	0	5 (0.9)	1 (0.2)	1 (0.2)	3 (0.5)	0	0
	Nephrogenic anaemia	腎性貧血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	13 (1.4)	2 (0.2)	7 (0.7)	4 (0.4)	0	0	5 (0.9)	1 (0.2)	3 (0.5)	0	1 (0.2)	0
	Retroperitoneal lymphadenopathy	後腹膜リンパ節腫脹	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Splenic calcification	脾臓石灰化	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Thrombocytopenia	血小板減少症	5 (0.5)	3 (0.3)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Cardiac disorders	Any	心臓障害	113 (11.8)	39 (4.1)	28 (2.9)	30 (3.1)	6 (0.6)	10 (1.0)	41 (7.4)	13 (2.3)	15 (2.7)	4 (0.7)	1 (0.2)	8 (1.4)
	Acute coronary syndrome	急性冠動脈症候群	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Acute myocardial infarction	急性心筋梗塞	5 (0.5)	0	0	2 (0.2)	2 (0.2)	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Angina pectoris	狭心症	12 (1.3)	3 (0.3)	6 (0.6)	1 (0.1)	1 (0.1)	1 (0.1)	4 (0.7)	1 (0.2)	3 (0.5)	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Aortic valve disease	大動脈弁疾患	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic valve incompetence	大動脈弁閉鎖不全症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	14 (1.5)	5 (0.5)	7 (0.7)	2 (0.2)	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Arrhythmia supraventricular	上室性不整脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Arteriosclerosis coronary artery	冠動脈硬化症	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Atrial fibrillation	心房細動	22 (2.3)	7 (0.7)	9 (0.9)	5 (0.5)	1 (0.1)	0	8 (1.4)	2 (0.4)	4 (0.7)	1 (0.2)	1 (0.2)	0
	Atrial flutter	心房粗動	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Atrioventricular block	房室ブロック	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block first degree	第一度房室ブロック	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	10 (1.0)	6 (0.6)	3 (0.3)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bundle branch block left	左脚ブロック	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bundle branch block right	右脚ブロック	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiac aneurysm	心臓瘤	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cardiac arrest	心停止	2 (0.2)	0	0	0	0	2 (0.2)	3 (0.5)	0	0	0	0	3 (0.5)
	Cardiac disorder	心障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure	心不全	13 (1.4)	3 (0.3)	5 (0.5)	1 (0.1)	1 (0.1)	3 (0.3)	5 (0.9)	0	2 (0.4)	0	0	3 (0.5)
	Cardiac failure acute	急性心不全	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure chronic	慢性心不全	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cardiac failure congestive	うっ血性心不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cardiac flutter	心粗動	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiac steatosis	心臓脂肪症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiogenic shock	心原性ショック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cardiovascular insufficiency	心血管不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Coronary artery disease	冠動脈疾患	10 (1.0)	2 (0.2)	2 (0.2)	5 (0.5)	0	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery stenosis	冠動脈狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Defect conduction intraventricular	心室内伝導障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Extrasystoles	期外収縮	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Left atrial enlargement	左房拡大	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Left ventricular dilatation	左室拡張	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mitral valve incompetence	僧帽弁閉鎖不全症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Myocardial infarction	心筋梗塞	6 (0.6)	2 (0.2)	0	3 (0.3)	1 (0.1)	0	3 (0.5)	1 (0.2)	0	1 (0.2)	0	1 (0.2)
	Myocardial ischaemia	心筋虚血	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Palpitations	動悸	7 (0.7)	6 (0.6)	0	1 (0.1)	0	0	3 (0.5)	3 (0.5)	0	0	0	0
	Sinus arrhythmia	洞性不整脈	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Sinus bradycardia	洞性徐脈	4 (0.4)	1 (0.1)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Supraventricular extrasystoles	上室性期外収縮	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Tachycardia	頻脈	5 (0.5)	3 (0.3)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Tachycardia paroxysmal	発作性頻脈	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Tricuspid valve disease	三尖弁疾患	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ventricular extrasystoles	心室性期外収縮	3 (0.3)	3 (0.3)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Ventricular fibrillation	心室細動	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ventricular tachycardia	心室性頻脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Congenital, familial and genetic disorders	Any	先天性、家族性および遺伝性障害	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Congenital renal cyst	先天性腎嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Phimosis	包茎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	14 (1.5)	10 (1.0)	4 (0.4)	0	0	0	11 (2.0)	8 (1.4)	3 (0.5)	0	0	0
	External ear disorder	外耳障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypoacusis	聴力低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Otorrhoea	耳漏	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Tinnitus	耳鳴	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	8 (0.8)	5 (0.5)	3 (0.3)	0	0	0	9 (1.6)	7 (1.3)	2 (0.4)	0	0	0
	Vertigo positional	頭位性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Endocrine disorders	Any	内分泌障害	9 (0.9)	6 (0.6)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Adrenal calcification	副腎石灰化	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Adrenomegaly	副腎肥大	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Basedow's disease	バセドウ病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyperthyroidism	甲状腺機能亢進症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hypothyroidism	甲状腺機能低下症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Thyroid calcification	甲状腺石灰化	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thyroid mass	甲状腺腫瘤	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
Eye disorders	Any	眼障害	20 (2.1)	11 (1.2)	4 (0.4)	5 (0.5)	0	0	19 (3.4)	8 (1.4)	6 (1.1)	5 (0.9)	0	0
	Age-related macular degeneration	加齢黄斑変性	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Blepharitis	眼瞼炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Blindness	失明	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Blindness unilateral	片側失明	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cataract	白内障	6 (0.6)	1 (0.1)	2 (0.2)	3 (0.3)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Conjunctival deposit	結膜沈着物	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Conjunctival haemorrhage	結膜出血	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Conjunctivitis allergic	アレルギー性結膜炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Corneal disorder	角膜障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Corneal oedema	角膜浮腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Diplopia	複視	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dry eye	眼乾燥	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Eye inflammation	眼の炎症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Eye irritation	眼刺激	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Eye pain	眼痛	0	0	0	0	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Eyelid ptosis	眼瞼下垂	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Glaucoma	緑内障	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Lacrimation increased	流涙増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Macular degeneration	黄斑変性	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Ocular hyperaemia	眼充血	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Periorbital oedema	眼窩周囲浮腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pterygium	翼状片	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Retinal artery occlusion	網膜動脈閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Retinal detachment	網膜剥離	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vision blurred	霧視	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Visual acuity reduced	視力低下	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Visual impairment	視力障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vitreous floaters	硝子体浮遊物	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Gastrointestinal disorders	Any	胃腸障害	276 (28.9)	173 (18.1)	81 (8.5)	16 (1.7)	4 (0.4)	2 (0.2)	141 (25.5)	85 (15.3)	45 (8.1)	11 (2.0)	0	0
	Abdominal discomfort	腹部不快感	6 (0.6)	3 (0.3)	3 (0.3)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Abdominal distension	腹部膨満	11 (1.2)	10 (1.0)	1 (0.1)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Abdominal hernia	腹部ヘルニア	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Abdominal pain	腹痛	24 (2.5)	11 (1.2)	12 (1.3)	0	1 (0.1)	0	12 (2.2)	7 (1.3)	4 (0.7)	1 (0.2)	0	0
	Abdominal pain lower	下腹部痛	5 (0.5)	1 (0.1)	4 (0.4)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Abdominal pain upper	上腹部痛	12 (1.3)	6 (0.6)	5 (0.5)	1 (0.1)	0	0	13 (2.3)	9 (1.6)	3 (0.5)	1 (0.2)	0	0
	Abdominal tenderness	腹部圧痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Anal haemorrhage	肛門出血	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Anal incontinence	肛門失禁	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Anorectal discomfort	肛門直腸不快感	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Ascites	腹水	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Barrett's oesophagus	バレット食道	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Bowel movement irregularity	便通不規則	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breath odour	呼気臭	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cheilitis	口唇炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Chronic gastritis	慢性胃炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colitis	大腸炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Constipation	便秘	60 (6.3)	35 (3.7)	25 (2.6)	0	0	0	34 (6.1)	25 (4.5)	9 (1.6)	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Crohn's disease	クローン病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dental caries	齲歯	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Diaphragmatic hernia	横隔膜ヘルニア	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Diarrhoea	下痢	66 (6.9)	47 (4.9)	18 (1.9)	0	0	1 (0.1)	31 (5.6)	20 (3.6)	10 (1.8)	1 (0.2)	0	0
	Diverticulum	憩室	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Diverticulum intestinal	腸憩室	10 (1.0)	9 (0.9)	1 (0.1)	0	0	0	7 (1.3)	7 (1.3)	0	0	0	0
	Diverticulum oesophageal	食道憩室	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dry mouth	口内乾燥	10 (1.0)	10 (1.0)	0	0	0	0	5 (0.9)	4 (0.7)	1 (0.2)	0	0	0
	Duodenal ulcer	十二指腸潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dyspepsia	消化不良	11 (1.2)	8 (0.8)	3 (0.3)	0	0	0	7 (1.3)	5 (0.9)	2 (0.4)	0	0	0
	Dysphagia	嚥下障害	3 (0.3)	3 (0.3)	0	0	0	0	4 (0.7)	1 (0.2)	3 (0.5)	0	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Epigastric discomfort	心窩部不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Eructation	おくび	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Faeces hard	硬便	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Flatulence	鼓腸	4 (0.4)	4 (0.4)	0	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Food poisoning	食中毒	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Frequent bowel movements	排便回数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastric disorder	胃障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastric polyps	胃ポリープ	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastric ulcer	胃潰瘍	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gastritis	胃炎	2 (0.2)	2 (0.2)	0	0	0	0	5 (0.9)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Gastritis erosive	びらん性胃炎	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Gastroduodenitis	胃十二指腸炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal angiectasia	胃腸血管拡張症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastrointestinal inflammation	胃腸の炎症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Gastrointestinal wall thickening	消化管壁肥厚	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	11 (1.2)	6 (0.6)	4 (0.4)	1 (0.1)	0	0	4 (0.7)	1 (0.2)	3 (0.5)	0	0	0
	Gingival discomfort	歯肉不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gingival pain	歯肉痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Glossitis	舌炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematochezia	血便排泄	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Haemorrhoidal haemorrhage	痔出血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haemorrhoids	痔核	6 (0.6)	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Hiatus hernia	裂孔ヘルニア	5 (0.5)	5 (0.5)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ileus	イレウス	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Impaired gastric emptying	胃排出不全	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	11 (1.2)	7 (0.7)	3 (0.3)	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4)	0	0	4 (0.4)	0	0	0	0	0	0	0	0
	Intra-abdominal haematoma	腹腔内血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Irritable bowel syndrome	過敏性腸症候群	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Jejunal stenosis	空腸狭窄	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Large intestinal stenosis	大腸狭窄	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Large intestine perforation	大腸穿孔	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lip disorder	口唇障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Lip pain	口唇痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Melaena	メレナ	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Mesenteric artery stenosis	腸間膜動脈狭窄	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mesenteric panniculitis	腸間膜脂肪織炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Nausea	悪心	48 (5.0)	40 (4.2)	6 (0.6)	2 (0.2)	0	0	32 (5.8)	22 (4.0)	10 (1.8)	0	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oesophageal pain	食道痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oesophagitis	食道炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pancreatic atrophy	膵萎縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pancreatic calcification	膵石灰化	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatic cyst	膵嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatic duct dilatation	膵管拡張	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatic steatosis	膵脂肪変性	6 (0.6)	6 (0.6)	0	0	0	0	3 (0.5)	3 (0.5)	0	0	0	0
	Pancreatitis	膵炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pancreatitis chronic	慢性膵炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Paraesthesia oral	口の錯感覚	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Parotid duct obstruction	耳下腺管閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peptic ulcer	消化性潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Periodontal disease	歯周病	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Proctalgia	肛門周囲痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Proctitis	直腸炎	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	7 (0.7)	6 (0.6)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Rectal stenosis	直腸狭窄	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Salivary gland pain	唾液腺痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Small intestinal obstruction	小腸閉塞	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Splenic artery aneurysm	脾臓動脈瘤	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Stomatitis	口内炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tongue coated	舌苔	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Tooth loss	歯の脱落	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Toothache	歯痛	7 (0.7)	4 (0.4)	3 (0.3)	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Umbilical hernia	臍ヘルニア	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Upper gastrointestinal haemorrhage	上部消化管出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Vomiting	嘔吐	15 (1.6)	10 (1.0)	4 (0.4)	1 (0.1)	0	0	10 (1.8)	4 (0.7)	5 (0.9)	1 (0.2)	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	244 (25.6)	151 (15.8)	72 (7.5)	13 (1.4)	0	8 (0.8)	104 (18.8)	76 (13.7)	21 (3.8)	6 (1.1)	0	1 (0.2)
	Asthenia	無力症	36 (3.8)	21 (2.2)	13 (1.4)	2 (0.2)	0	0	19 (3.4)	13 (2.3)	4 (0.7)	2 (0.4)	0	0
	Catheter site related reaction	カテーテル留置部位関連反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Catheter site ulcer	カテーテル留置部位潰瘍	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Chest pain	胸痛	15 (1.6)	6 (0.6)	9 (0.9)	0	0	0	8 (1.4)	6 (1.1)	2 (0.4)	0	0	0
	Chills	悪寒	8 (0.8)	7 (0.7)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Cyst	嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Death	死亡	4 (0.4)	0	0	0	0	4 (0.4)	1 (0.2)	0	0	0	0	1 (0.2)
	Discomfort	不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Exercise tolerance decreased	運動耐性低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Face oedema	顔面浮腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	115 (12.1)	80 (8.4)	31 (3.2)	4 (0.4)	0	0	48 (8.7)	36 (6.5)	7 (1.3)	5 (0.9)	0	0
	Feeling cold	冷感	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gait disturbance	歩行障害	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	General physical health deterioration	全身健康状態低下	5 (0.5)	0	1 (0.1)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0
	Granuloma	肉芽腫	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0

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	Influenza like illness	インフルエンザ様疾患	10 (1.0)	6 (0.6)	4 (0.4)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Infusion site extravasation	注入部位血管外漏出	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Injection site bruising	注射部位内出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Injection site erythema	注射部位紅斑	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Injection site pain	注射部位疼痛	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Injection site reaction	注射部位反応	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	3 (0.5)	2 (0.4)	0	1 (0.2)	0	0
	Nodule	小結節	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Non-cardiac chest pain	非心臓性胸痛	4 (0.4)	4 (0.4)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oedema	浮腫	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oedema peripheral	末梢性浮腫	39 (4.1)	33 (3.5)	6 (0.6)	0	0	0	17 (3.1)	12 (2.2)	5 (0.9)	0	0	0
	Pain	疼痛	5 (0.5)	0	5 (0.5)	0	0	0	7 (1.3)	5 (0.9)	2 (0.4)	0	0	0
	Pelvic mass	骨盤腔内腫瘤	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Performance status decreased	活動状態低下	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral swelling	末梢腫脹	13 (1.4)	8 (0.8)	4 (0.4)	1 (0.1)	0	0	7 (1.3)	4 (0.7)	3 (0.5)	0	0	0
	Pyrexia	発熱	19 (2.0)	15 (1.6)	3 (0.3)	1 (0.1)	0	0	5 (0.9)	3 (0.5)	2 (0.4)	0	0	0
	Sudden cardiac death	心突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Sudden death	突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Suprapubic pain	恥骨上痛	1 (0.1)	0	0	1 (0.1)	0	0	3 (0.5)	2 (0.4)	1 (0.2)	0	0	0
	Temperature intolerance	温度変化不耐症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thirst	口渇	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	31 (3.2)	21 (2.2)	4 (0.4)	4 (0.4)	1 (0.1)	1 (0.1)	10 (1.8)	6 (1.1)	1 (0.2)	3 (0.5)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Biliary colic	胆道仙痛	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cholangitis acute	急性胆管炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0

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	Cholecystitis chronic	慢性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholelithiasis	胆石症	7 (0.7)	6 (0.6)	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholestasis	胆汁うっ滞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Drug-induced liver injury	薬物性肝障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hepatic artery thrombosis	肝動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hepatic calcification	肝石灰化	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Hepatic cyst	肝嚢胞	7 (0.7)	7 (0.7)	0	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Hepatic function abnormal	肝機能異常	4 (0.4)	2 (0.2)	1 (0.1)	0	1 (0.1)	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hepatic steatosis	脂肪肝	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperbilirubinaemia	高ビリルビン血症	6 (0.6)	4 (0.4)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Jaundice	黄疸	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Liver disorder	肝障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Immune system disorders	Any	免疫系障害	14 (1.5)	6 (0.6)	8 (0.8)	0	0	0	6 (1.1)	4 (0.7)	2 (0.4)	0	0	0
	Allergy to arthropod sting	節足動物刺傷アレルギー	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Anaphylactic reaction	アナフィラキシー反応	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Contrast media allergy	造影剤アレルギー	3 (0.3)	3 (0.3)	0	0	0	0	3 (0.5)	2 (0.4)	1 (0.2)	0	0	0
	Contrast media reaction	造影剤反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Drug hypersensitivity	薬物過敏症	3 (0.3)	0	3 (0.3)	0	0	0	0	0	0	0	0	0
	Hypersensitivity	過敏症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Immune system disorder	免疫系障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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	Seasonal allergy	季節性アレルギー	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	227 (23.8)	66 (6.9)	120 (12.6)	32 (3.4)	4 (0.4)	5 (0.5)	120 (21.7)	43 (7.8)	60 (10.8)	15 (2.7)	1 (0.2)	1 (0.2)
	Abdominal abscess	腹部膿瘍	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Abscess	膿瘍	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Abscess intestinal	腸管膿瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Acarodermatitis	ダニ皮膚炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Acute endocarditis	急性心内膜炎	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Acute sinusitis	急性副鼻腔炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Appendicitis	虫垂炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacterial infection	細菌感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacteriuria	細菌尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Balanitis candida	カンジダ性亀頭炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balanoposthitis infective	感染性亀頭包皮炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bronchitis	気管支炎	11 (1.2)	1 (0.1)	9 (0.9)	1 (0.1)	0	0	9 (1.6)	1 (0.2)	8 (1.4)	0	0	0
	Bronchitis viral	ウイルス性気管支炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Catheter site infection	カテーテル留置部位感染	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cellulitis	蜂巣炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conjunctivitis	結膜炎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cystitis	膀胱炎	8 (0.8)	3 (0.3)	5 (0.5)	0	0	0	7 (1.3)	4 (0.7)	3 (0.5)	0	0	0
	Dermatophytosis of nail	爪の皮膚糸状菌症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Device related infection	医療機器関連感染	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ear infection	耳感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

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	Ear infection bacterial	細菌性耳感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Erysipelas	丹毒	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Eye infection bacterial	細菌性眼感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Febrile infection	熱性感染症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Folliculitis	毛包炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Fungal balanitis	真菌性亀頭炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Fungal skin infection	皮膚真菌感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gangrene	壊疽	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastroenteritis	胃腸炎	5 (0.5)	1 (0.1)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Gastroenteritis viral	ウイルス性胃腸炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gastrointestinal infection	消化管感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Genital infection fungal	真菌性性器感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gingivitis	歯肉炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Helicobacter gastritis	ヘリコバクター性胃炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Helicobacter infection	ヘリコバクター感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hepatitis C	Ｃ型肝炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Herpes zoster	帯状疱疹	4 (0.4)	0	4 (0.4)	0	0	0	4 (0.7)	2 (0.4)	2 (0.4)	0	0	0
	Infected bite	咬傷感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Infection	感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Infectious mononucleosis	伝染性単核症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Infestation	寄生	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Influenza	インフルエンザ	27 (2.8)	18 (1.9)	7 (0.7)	0	1 (0.1)	1 (0.1)	9 (1.6)	5 (0.9)	4 (0.7)	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Labyrinthitis	迷路炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Laryngitis	喉頭炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Localised infection	限局性感染	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower respiratory tract infection	下気道感染	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lung infection	肺感染	3 (0.3)	1 (0.1)	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Meningitis bacterial	細菌性髄膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Nasopharyngitis	上咽頭炎	36 (3.8)	20 (2.1)	16 (1.7)	0	0	0	21 (3.8)	16 (2.9)	5 (0.9)	0	0	0
	Oesophageal candidiasis	食道カンジダ症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Onychomycosis	爪真菌症	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Oral candidiasis	口腔カンジダ症	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Oral herpes	口腔ヘルペス	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Orchitis	精巣炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Otitis externa	外耳炎	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Otitis media	中耳炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Paronychia	爪囲炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Periodontitis	歯周炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Peritonitis	腹膜炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pharyngitis	咽頭炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pneumonia	肺炎	19 (2.0)	0	9 (0.9)	8 (0.8)	1 (0.1)	1 (0.1)	11 (2.0)	2 (0.4)	5 (0.9)	3 (0.5)	1 (0.2)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostate infection	前立腺感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pulmonary tuberculosis	肺結核	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pulpitis dental	歯髄炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pyelonephritis	腎盂腎炎	4 (0.4)	1 (0.1)	0	3 (0.3)	0	0	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pyelonephritis chronic	慢性腎盂腎炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pyuria	膿尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash pustular	膿疱性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Respiratory syncytial virus infection	ＲＳウイルス感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Respiratory tract infection	気道感染	6 (0.6)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0
	Respiratory tract infection viral	ウイルス性気道感染	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	5 (0.9)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Rhinitis	鼻炎	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	6 (1.1)	4 (0.7)	2 (0.4)	0	0	0
	Root canal infection	根管感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Sepsis	敗血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sinusitis	副鼻腔炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	4 (0.7)	2 (0.4)	2 (0.4)	0	0	0
	Skin infection	皮膚感染	4 (0.4)	0	4 (0.4)	0	0	0	0	0	0	0	0	0
	Subcutaneous abscess	皮下組織膿瘍	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tinea infection	白癬感染	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Tooth abscess	歯膿瘍	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Tooth infection	歯感染	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tracheitis	気管炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Tracheobronchitis	気管気管支炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Trichophytosis	トリコフィトン感染症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Upper respiratory tract infection	上気道感染	25 (2.6)	5 (0.5)	20 (2.1)	0	0	0	9 (1.6)	3 (0.5)	6 (1.1)	0	0	0
	Urinary tract infection	尿路感染	47 (4.9)	6 (0.6)	35 (3.7)	6 (0.6)	0	0	28 (5.1)	9 (1.6)	16 (2.9)	3 (0.5)	0	0
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urosepsis	尿路性敗血症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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	Vestibular neuronitis	前庭神経炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Viral infection	ウイルス感染	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Viral upper respiratory tract infection	ウイルス性上気道感染	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	119 (12.5)	48 (5.0)	51 (5.3)	17 (1.8)	0	3 (0.3)	46 (8.3)	15 (2.7)	21 (3.8)	10 (1.8)	0	0
	Accident	事故	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Anaemia postoperative	術後貧血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Animal bite	動物咬傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ankle fracture	足関節部骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arthropod bite	節足動物咬傷	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Auricular haematoma	耳介血腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Back injury	背部損傷	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bone contusion	骨挫傷	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cervical vertebral fracture	頚椎骨折	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Chest injury	胸部損傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Clavicle fracture	鎖骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Contusion	挫傷	12 (1.3)	9 (0.9)	3 (0.3)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cystitis radiation	放射線性膀胱炎	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Eyelid injury	眼瞼損傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Face injury	顔面損傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Facial bones fracture	顔面骨骨折	0	0	0	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Fall	転倒	36 (3.8)	10 (1.0)	18 (1.9)	8 (0.8)	0	0	23 (4.2)	9 (1.6)	10 (1.8)	4 (0.7)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fibula fracture	腓骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Foot fracture	足骨折	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Fracture	骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Frostbite	凍傷	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Haematuria traumatic	外傷性血尿	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hand fracture	手骨折	4 (0.4)	0	4 (0.4)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Head injury	頭部損傷	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Heart injury	心臓損傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Humerus fracture	上腕骨骨折	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Incision site pain	切開部位痛	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Injury	損傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Injury of conjunctiva	結膜損傷	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Joint dislocation	関節脱臼	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Joint injury	関節損傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Laceration	裂傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ligament injury	靭帯損傷	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ligament sprain	靭帯捻挫	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Limb injury	四肢損傷	7 (0.7)	5 (0.5)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Lip injury	口唇損傷	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lumbar vertebral fracture	腰椎骨折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Meniscus injury	半月板損傷	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Multiple injuries	多発性外傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Muscle strain	肉離れ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Patella fracture	膝蓋骨骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Post-traumatic pain	外傷後疼痛	5 (0.5)	3 (0.3)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Procedural pain	処置による疼痛	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Radiation proctitis	放射線性直腸炎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Radius fracture	橈骨骨折	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rib fracture	肋骨骨折	11 (1.2)	6 (0.6)	5 (0.5)	0	0	0	8 (1.4)	2 (0.4)	6 (1.1)	0	0	0
	Road traffic accident	交通事故	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Scapula fracture	肩甲骨骨折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Scratch	引っかき傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

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	Skin abrasion	皮膚擦過傷	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Soft tissue injury	軟部組織損傷	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Spinal compression fracture	脊椎圧迫骨折	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Spinal fracture	脊椎骨折	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Subarachnoid haemorrhage	くも膜下出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Subcutaneous haematoma	皮下血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Subdural haematoma	硬膜下血腫	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Sunburn	サンバーン	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thermal burn	熱傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Tooth fracture	歯牙破折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Traumatic fracture	外傷性骨折	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Traumatic haematoma	外傷性血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ulna fracture	尺骨骨折	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Upper limb fracture	上肢骨折	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Vascular graft complication	移植血管合併症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Wound complication	創合併症	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Wound dehiscence	創離開	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Wrist fracture	手首関節骨折	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	144 (15.1)	70 (7.3)	55 (5.8)	18 (1.9)	1 (0.1)	0	63 (11.4)	36 (6.5)	21 (3.8)	4 (0.7)	2 (0.4)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	7 (0.7)	4 (0.4)	0	3 (0.3)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Arteriogram coronary	冠血管造影	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	13 (1.4)	6 (0.6)	3 (0.3)	4 (0.4)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.5)	2 (0.4)	0	1 (0.2)	0	0
	Blood bilirubin increased	血中ビリルビン増加	12 (1.3)	7 (0.7)	4 (0.4)	1 (0.1)	0	0	0	0	0	0	0	0
	Blood cholesterol increased	血中コレステロール増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood chromogranin A increased	血中クロモグラニンA増加	6 (0.6)	3 (0.3)	3 (0.3)	0	0	0	6 (1.1)	4 (0.7)	1 (0.2)	1 (0.2)	0	0
	Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	22 (2.3)	9 (0.9)	12 (1.3)	1 (0.1)	0	0	14 (2.5)	5 (0.9)	7 (1.3)	0	2 (0.4)	0
	Blood glucose increased	血中ブドウ糖増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	5 (0.5)	5 (0.5)	0	0	0	0	0	0	0	0	0	0
	Blood potassium decreased	血中カリウム減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood potassium increased	血中カリウム増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Blood pressure increased	血圧上昇	4 (0.4)	0	3 (0.3)	1 (0.1)	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Blood pressure systolic increased	収縮期血圧上昇	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Blood sodium decreased	血中ナトリウム減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood testosterone increased	血中テストステロン増加	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood urea abnormal	血中尿素異常	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Blood urea increased	血中尿素増加	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Blood uric acid increased	血中尿酸増加	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Body temperature increased	体温上昇	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Breath sounds abnormal	呼吸音異常	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cardiac murmur	心雑音	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Carotid bruit	頚動脈雑音	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Chest X-ray abnormal	胸部Ｘ線異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Electrocardiogram QT prolonged	心電図ＱＴ延長	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Electrocardiogram ST segment depression	心電図ＳＴ部分下降	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastric pH decreased	胃内ｐＨ低下	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Glomerular filtration rate decreased	糸球体濾過率減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Glomerular filtration rate increased	糸球体濾過率増加	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Glucose urine present	尿中ブドウ糖陽性	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haematocrit decreased	ヘマトクリット減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematology test abnormal	血液学的検査異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haemoglobin decreased	ヘモグロビン減少	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Heart rate increased	心拍数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Heart rate irregular	心拍数不整	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Heart sounds abnormal	心音異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Lymphocyte count decreased	リンパ球数減少	9 (0.9)	3 (0.3)	6 (0.6)	0	0	0	0	0	0	0	0	0
	Lymphocyte count increased	リンパ球数増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	11 (1.2)	1 (0.1)	3 (0.3)	6 (0.6)	1 (0.1)	0	0	0	0	0	0	0
	Neutrophil count increased	好中球数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	7 (0.7)	7 (0.7)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Protein total decreased	総蛋白減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Protein urine present	尿中蛋白陽性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Red blood cell count decreased	赤血球数減少	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Transaminases increased	トランスアミナーゼ上昇	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Troponin increased	トロポニン増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urine output decreased	尿量減少	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Vitamin B12 decreased	ビタミンＢ１２減少	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Weight decreased	体重減少	34 (3.6)	22 (2.3)	12 (1.3)	0	0	0	12 (2.2)	10 (1.8)	2 (0.4)	0	0	0
	Weight increased	体重増加	14 (1.5)	11 (1.2)	3 (0.3)	0	0	0	7 (1.3)	2 (0.4)	5 (0.9)	0	0	0
	White blood cell count decreased	白血球数減少	8 (0.8)	2 (0.2)	6 (0.6)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	White blood cells urine positive	尿中白血球陽性	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	95 (10.0)	34 (3.6)	38 (4.0)	19 (2.0)	4 (0.4)	0	49 (8.8)	24 (4.3)	15 (2.7)	10 (1.8)	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cachexia	悪液質	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Decreased appetite	食欲減退	28 (2.9)	17 (1.8)	9 (0.9)	2 (0.2)	0	0	16 (2.9)	12 (2.2)	3 (0.5)	1 (0.2)	0	0
	Dehydration	脱水	6 (0.6)	0	3 (0.3)	2 (0.2)	1 (0.1)	0	4 (0.7)	1 (0.2)	2 (0.4)	1 (0.2)	0	0
	Diabetes mellitus	糖尿病	5 (0.5)	0	3 (0.3)	2 (0.2)	0	0	5 (0.9)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Diabetes mellitus inadequate control	コントロール不良の糖尿病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Diabetic metabolic decompensation	糖尿病性代謝代償不全	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dyslipidaemia	脂質異常症	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Electrolyte imbalance	電解質失調	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Folate deficiency	葉酸欠乏	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gout	痛風	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Hypercholesterolaemia	高コレステロール血症	3 (0.3)	3 (0.3)	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Hyperglycaemia	高血糖	9 (0.9)	0	5 (0.5)	2 (0.2)	2 (0.2)	0	3 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	16 (1.7)	4 (0.4)	8 (0.8)	3 (0.3)	1 (0.1)	0	9 (1.6)	2 (0.4)	4 (0.7)	3 (0.5)	0	0
	Hyperlipidaemia	高脂血症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hypernatraemia	高ナトリウム血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hypertriglyceridaemia	高トリグリセリド血症	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Hyperuricaemia	高尿酸血症	4 (0.4)	1 (0.1)	2 (0.2)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hypocalcaemia	低カルシウム血症	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Hypochloraemia	低クロール血症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hypoglycaemia	低血糖	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	9 (0.9)	3 (0.3)	4 (0.4)	2 (0.2)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Hypomagnesaemia	低マグネシウム血症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyponatraemia	低ナトリウム血症	7 (0.7)	2 (0.2)	2 (0.2)	3 (0.3)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Hypoproteinaemia	低蛋白血症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Increased appetite	食欲亢進	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Iron deficiency	鉄欠乏	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Magnesium deficiency	マグネシウム欠乏	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Malnutrition	栄養障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Metabolic alkalosis	代謝性アルカローシス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Obesity	肥満	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Type 2 diabetes mellitus	２型糖尿病	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vitamin D deficiency	ビタミンD欠乏	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	270 (28.3)	150 (15.7)	102 (10.7)	18 (1.9)	0	0	135 (24.4)	79 (14.3)	50 (9.0)	6 (1.1)	0	0
	Arthralgia	関節痛	77 (8.1)	48 (5.0)	26 (2.7)	3 (0.3)	0	0	51 (9.2)	39 (7.0)	10 (1.8)	2 (0.4)	0	0
	Arthritis	関節炎	6 (0.6)	3 (0.3)	3 (0.3)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Axillary mass	腋窩腫瘤	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Back pain	背部痛	84 (8.8)	44 (4.6)	36 (3.8)	4 (0.4)	0	0	50 (9.0)	30 (5.4)	19 (3.4)	1 (0.2)	0	0
	Bone lesion	骨病変	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bone pain	骨痛	9 (0.9)	4 (0.4)	4 (0.4)	1 (0.1)	0	0	6 (1.1)	2 (0.4)	4 (0.7)	0	0	0
	Bursitis	滑液包炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Coccydynia	尾骨痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dupuytren's contracture	デュプイトラン拘縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Exostosis	外骨腫	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Extremity contracture	四肢拘縮	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Flank pain	側腹部痛	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Groin pain	鼠径部痛	7 (0.7)	5 (0.5)	2 (0.2)	0	0	0	5 (0.9)	5 (0.9)	0	0	0	0
	Hand deformity	手変形	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Intervertebral disc protrusion	椎間板突出	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Joint range of motion decreased	関節可動域低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Joint stiffness	関節硬直	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Joint swelling	関節腫脹	4 (0.4)	4 (0.4)	0	0	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Limb discomfort	四肢不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Lumbar spinal stenosis	腰部脊柱管狭窄症	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Metatarsalgia	中足骨痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mobility decreased	運動性低下	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Muscle spasms	筋痙縮	17 (1.8)	10 (1.0)	7 (0.7)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Muscular weakness	筋力低下	10 (1.0)	8 (0.8)	2 (0.2)	0	0	0	5 (0.9)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Musculoskeletal chest pain	筋骨格系胸痛	10 (1.0)	5 (0.5)	4 (0.4)	1 (0.1)	0	0	6 (1.1)	5 (0.9)	1 (0.2)	0	0	0
	Musculoskeletal discomfort	筋骨格不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	37 (3.9)	20 (2.1)	16 (1.7)	1 (0.1)	0	0	11 (2.0)	8 (1.4)	2 (0.4)	1 (0.2)	0	0
	Musculoskeletal stiffness	筋骨格硬直	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Myalgia	筋肉痛	16 (1.7)	12 (1.3)	2 (0.2)	2 (0.2)	0	0	6 (1.1)	6 (1.1)	0	0	0	0
	Neck pain	頚部痛	9 (0.9)	6 (0.6)	3 (0.3)	0	0	0	6 (1.1)	5 (0.9)	1 (0.2)	0	0	0
	Osteitis	骨炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteitis deformans	変形性骨炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	15 (1.6)	5 (0.5)	5 (0.5)	5 (0.5)	0	0	3 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Osteochondrosis	骨端症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Osteopenia	骨減少症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Osteoporosis	骨粗鬆症	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pain in extremity	四肢痛	55 (5.8)	40 (4.2)	15 (1.6)	0	0	0	18 (3.2)	9 (1.6)	8 (1.4)	1 (0.2)	0	0
	Pathological fracture	病的骨折	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Plantar fasciitis	足底筋膜炎	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Polymyalgia rheumatica	リウマチ性多発筋痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rheumatic disorder	リウマチ性障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Spinal column stenosis	脊柱管狭窄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Spinal deformity	脊柱変形	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Spinal fusion acquired	後天性脊椎癒合	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Spinal osteoarthritis	変形性脊椎症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Spinal pain	脊椎痛	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Tendon disorder	腱障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tendonitis	腱炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Trigger finger	弾発指	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	48 (5.0)	10 (1.0)	14 (1.5)	20 (2.1)	2 (0.2)	2 (0.2)	26 (4.7)	7 (1.3)	9 (1.6)	9 (1.6)	0	1 (0.2)
	Acute leukaemia	急性白血病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Adenocarcinoma	腺癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Adrenal adenoma	副腎腺腫	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Basal cell carcinoma	基底細胞癌	5 (0.5)	2 (0.2)	3 (0.3)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Benign lung neoplasm	肺の良性新生物	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder cancer	膀胱癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Bladder neoplasm	膀胱新生物	4 (0.4)	0	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0
	Bowen's disease	ボーエン病	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Cancer pain	癌疼痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carcinoid tumour	カルチノイド腫瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Choroid melanoma	脈絡膜黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colon adenoma	大腸腺腫	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Colon cancer	結腸癌	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0
	Colon neoplasm	結腸新生物	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Gastric adenoma	胃腺腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastric cancer	胃癌	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Gastrointestinal adenocarcinoma	消化器腺癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Intestinal angioma	腸血管腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

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	Lipoma	脂肪腫	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lung adenocarcinoma stage IV	肺腺癌第４期	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Lymphangiosis carcinomatosa	癌性リンパ管症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lymphoma	リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Malignant melanoma in situ	表皮内悪性黒色腫	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Melanocytic naevus	メラノサイト性母斑	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Mesothelioma	中皮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Metastases to peritoneum	腹膜転移	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma	膵癌	3 (0.3)	0	1 (0.1)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma recurrent	再発膵癌	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pancreatic neoplasm	膵新生物	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	0	1 (0.2)
	Prostate cancer metastatic	遠隔転移を伴う前立腺癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Prostate cancer recurrent	再発前立腺癌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal adenocarcinoma	直腸腺癌	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Renal cancer	腎癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Salivary gland neoplasm	唾液腺新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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	Seborrhoeic keratosis	脂漏性角化症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin papilloma	皮膚乳頭腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Small cell lung cancer limited stage	限局型小細胞肺癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Squamous cell carcinoma of skin	皮膚有棘細胞癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Thymoma	胸腺腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Thyroid adenoma	甲状腺腺腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Tumour compression	腫瘍性圧迫	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tumour obstruction	腫瘍性閉塞	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tumour pain	腫瘍疼痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract neoplasm	尿路新生物	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Nervous system disorders	Any	神経系障害	147 (15.4)	77 (8.1)	50 (5.2)	16 (1.7)	2 (0.2)	2 (0.2)	74 (13.4)	39 (7.0)	20 (3.6)	11 (2.0)	0	4 (0.7)
	Amnesia	健忘	1 (0.1)	1 (0.1)	0	0	0	0	3 (0.5)	3 (0.5)	0	0	0	0
	Autonomic nervous system imbalance	自律神経失調	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Axonal neuropathy	軸索型ニューロパチー	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balance disorder	平衡障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Brain oedema	脳浮腫	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Bulbar palsy	球麻痺	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid arteriosclerosis	頚動脈硬化症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid artery stenosis	頚動脈狭窄	3 (0.3)	1 (0.1)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Carpal tunnel syndrome	手根管症候群	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Cerebral arteriosclerosis	脳動脈硬化症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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	Cerebral atrophy	大脳萎縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cerebrovascular accident	脳血管発作	2 (0.2)	0	0	2 (0.2)	0	0	4 (0.7)	1 (0.2)	0	2 (0.4)	0	1 (0.2)
	Cervicogenic vertigo	頚原性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cognitive disorder	認知障害	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dementia	認知症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Dementia Alzheimer's type	アルツハイマー型認知症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Depressed level of consciousness	意識レベルの低下	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Disturbance in attention	注意力障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dizziness	浮動性めまい	35 (3.7)	23 (2.4)	10 (1.0)	2 (0.2)	0	0	14 (2.5)	12 (2.2)	1 (0.2)	1 (0.2)	0	0
	Dysaesthesia	異常感覚	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Dysarthria	構語障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dysgeusia	味覚異常	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Encephalopathy	脳症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Essential tremor	本態性振戦	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Headache	頭痛	37 (3.9)	24 (2.5)	13 (1.4)	0	0	0	14 (2.5)	8 (1.4)	5 (0.9)	1 (0.2)	0	0
	Hypersomnia	過眠症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypoaesthesia	感覚鈍麻	6 (0.6)	4 (0.4)	2 (0.2)	0	0	0	5 (0.9)	3 (0.5)	1 (0.2)	1 (0.2)	0	0
	Hyposmia	嗅覚減退	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypotonia	筋緊張低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	IVth nerve paralysis	第４脳神経麻痺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Intercostal neuralgia	肋間神経痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ischaemic stroke	虚血性脳卒中	5 (0.5)	0	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Lethargy	嗜眠	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Loss of consciousness	意識消失	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Lumbar radiculopathy	腰髄神経根障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lumbosacral radiculopathy	腰仙部神経根障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Memory impairment	記憶障害	5 (0.5)	5 (0.5)	0	0	0	0	7 (1.3)	7 (1.3)	0	0	0	0
	Myelopathy	脊髄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neuralgia	神経痛	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Neuropathy peripheral	末梢性ニューロパチー	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Paraesthesia	錯感覚	6 (0.6)	5 (0.5)	1 (0.1)	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Parkinson's disease	パーキンソン病	2 (0.2)	0	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Partial seizures	部分発作	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral sensory neuropathy	末梢性感覚ニューロパチー	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Presyncope	失神寸前の状態	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Psychomotor hyperactivity	精神運動亢進	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Psychomotor skills impaired	精神運動機能障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Restless legs syndrome	下肢静止不能症候群	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Sacral radiculopathy	仙部神経根症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sciatica	坐骨神経痛	8 (0.8)	1 (0.1)	7 (0.7)	0	0	0	6 (1.1)	0	5 (0.9)	1 (0.2)	0	0
	Seizure	痙攣発作	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Senile dementia	老年認知症	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Somnolence	傾眠	8 (0.8)	7 (0.7)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Speech disorder	会話障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Syncope	失神	4 (0.4)	1 (0.1)	1 (0.1)	2 (0.2)	0	0	3 (0.5)	0	0	3 (0.5)	0	0
	Transient ischaemic attack	一過性脳虚血発作	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tremor	振戦	4 (0.4)	4 (0.4)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Vascular dementia	血管性認知症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vocal cord paresis	声帯不全麻痺	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Product issues	Any	製品の問題	9 (0.9)	3 (0.3)	2 (0.2)	4 (0.4)	0	0	3 (0.5)	0	2 (0.4)	1 (0.2)	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Device dislocation	医療機器位置異常	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device malfunction	医療機器機能不良	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Device occlusion	医療機器閉塞	5 (0.5)	2 (0.2)	1 (0.1)	2 (0.2)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Psychiatric disorders	Any	精神障害	57 (6.0)	34 (3.6)	22 (2.3)	1 (0.1)	0	0	28 (5.1)	14 (2.5)	13 (2.3)	1 (0.2)	0	0
	Agitation	激越	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Anxiety	不安	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Claustrophobia	閉所恐怖症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Delirium	譫妄	0	0	0	0	0	0	3 (0.5)	0	3 (0.5)	0	0	0
	Depressed mood	抑うつ気分	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Depression	うつ病	16 (1.7)	9 (0.9)	6 (0.6)	1 (0.1)	0	0	7 (1.3)	3 (0.5)	4 (0.7)	0	0	0
	Disorientation	失見当識	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hallucination, auditory	幻聴	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hallucination, visual	幻視	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Initial insomnia	初期不眠症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Insomnia	不眠症	26 (2.7)	14 (1.5)	12 (1.3)	0	0	0	10 (1.8)	6 (1.1)	3 (0.5)	1 (0.2)	0	0
	Irritability	易刺激性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Mental status changes	精神状態変化	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Middle insomnia	中期不眠症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Mood swings	気分動揺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nervousness	神経過敏	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nightmare	悪夢	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Panic disorder	パニック障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Restlessness	落ち着きのなさ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sleep disorder	睡眠障害	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	198 (20.8)	86 (9.0)	65 (6.8)	45 (4.7)	2 (0.2)	0	140 (25.3)	49 (8.8)	54 (9.7)	32 (5.8)	5 (0.9)	0
	Acute kidney injury	急性腎障害	9 (0.9)	1 (0.1)	3 (0.3)	4 (0.4)	1 (0.1)	0	6 (1.1)	2 (0.4)	2 (0.4)	2 (0.4)	0	0
	Anuria	無尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Azotaemia	高窒素血症	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	1 (0.2)	0
	Bladder disorder	膀胱障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Bladder diverticulum	膀胱憩室	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bladder hypertrophy	膀胱壁肥厚	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder neck obstruction	膀胱頚部閉塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Bladder obstruction	膀胱閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder outlet obstruction	膀胱出口部閉塞	0	0	0	0	0	0	4 (0.7)	0	4 (0.7)	0	0	0
	Bladder spasm	膀胱痙縮	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Calculus bladder	膀胱結石	5 (0.5)	2 (0.2)	2 (0.2)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Calculus urethral	尿道結石	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Calculus urinary	尿路結石	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Chronic kidney disease	慢性腎臓病	9 (0.9)	5 (0.5)	2 (0.2)	2 (0.2)	0	0	5 (0.9)	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	0
	Cystitis noninfective	非感染性膀胱炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dysuria	排尿困難	21 (2.2)	9 (0.9)	11 (1.2)	1 (0.1)	0	0	26 (4.7)	11 (2.0)	10 (1.8)	5 (0.9)	0	0
	Glycosuria	糖尿	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Haematuria	血尿	41 (4.3)	21 (2.2)	10 (1.0)	10 (1.0)	0	0	27 (4.9)	10 (1.8)	10 (1.8)	7 (1.3)	0	0
	Hydronephrosis	水腎症	10 (1.0)	2 (0.2)	1 (0.1)	7 (0.7)	0	0	13 (2.3)	5 (0.9)	5 (0.9)	3 (0.5)	0	0
	Hypertonic bladder	緊張性膀胱	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Incontinence	失禁	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Kidney fibrosis	腎線維症	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Leukocyturia	白血球尿	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower urinary tract symptoms	下部尿路症状	6 (0.6)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	5 (0.9)	1 (0.2)	4 (0.7)	0	0	0
	Malignant urinary tract obstruction	悪性尿路閉塞	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Micturition disorder	排尿異常	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Micturition urgency	尿意切迫	9 (0.9)	5 (0.5)	4 (0.4)	0	0	0	3 (0.5)	0	3 (0.5)	0	0	0
	Nephrocalcinosis	腎石灰沈着症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nephrolithiasis	腎結石症	14 (1.5)	10 (1.0)	4 (0.4)	0	0	0	4 (0.7)	2 (0.4)	0	2 (0.4)	0	0
	Nocturia	夜間頻尿	14 (1.5)	12 (1.3)	2 (0.2)	0	0	0	10 (1.8)	8 (1.4)	2 (0.4)	0	0	0
	Oliguria	乏尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	38 (4.0)	25 (2.6)	12 (1.3)	1 (0.1)	0	0	16 (2.9)	10 (1.8)	5 (0.9)	1 (0.2)	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

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	Polyuria	多尿	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Proteinuria	蛋白尿	9 (0.9)	5 (0.5)	4 (0.4)	0	0	0	6 (1.1)	2 (0.4)	4 (0.7)	0	0	0
	Renal aneurysm	腎動脈瘤	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Renal artery occlusion	腎動脈閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Renal artery stenosis	腎動脈狭窄症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Renal colic	腎仙痛	9 (0.9)	5 (0.5)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal cyst	腎嚢胞	9 (0.9)	9 (0.9)	0	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Renal failure	腎不全	7 (0.7)	3 (0.3)	3 (0.3)	0	1 (0.1)	0	5 (0.9)	0	1 (0.2)	1 (0.2)	3 (0.5)	0
	Renal impairment	腎機能障害	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal pain	腎臓痛	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Strangury	有痛性排尿困難	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ureteral disorder	尿管障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ureteric obstruction	尿管閉塞	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ureteric stenosis	尿管狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	6 (0.6)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Urethral discharge	尿道分泌物	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urethral meatus stenosis	外尿道口狭窄	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urethral pain	尿道痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Urethral stenosis	尿道狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Urinary hesitation	排尿躊躇	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary incontinence	尿失禁	14 (1.5)	6 (0.6)	8 (0.8)	0	0	0	12 (2.2)	7 (1.3)	5 (0.9)	0	0	0
	Urinary retention	尿閉	33 (3.5)	2 (0.2)	16 (1.7)	15 (1.6)	0	0	36 (6.5)	3 (0.5)	22 (4.0)	11 (2.0)	0	0
	Urinary tract discomfort	尿路不快感	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urinary tract disorder	尿路障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urinary tract obstruction	尿路閉塞	9 (0.9)	1 (0.1)	3 (0.3)	5 (0.5)	0	0	7 (1.3)	2 (0.4)	4 (0.7)	1 (0.2)	0	0
	Urinary tract pain	尿路痛	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Urine flow decreased	尿流量減少	2 (0.2)	0	2 (0.2)	0	0	0	3 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	46 (4.8)	32 (3.4)	13 (1.4)	1 (0.1)	0	0	35 (6.3)	23 (4.2)	11 (2.0)	1 (0.2)	0	0
	Balanoposthitis	亀頭包皮炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Benign prostatic hyperplasia	良性前立腺肥大症	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Breast discomfort	乳房不快感	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Breast induration	乳房硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast pain	乳房痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Breast tenderness	乳房圧痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Erectile dysfunction	勃起不全	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gynaecomastia	女性化乳房	19 (2.0)	14 (1.5)	5 (0.5)	0	0	0	6 (1.1)	6 (1.1)	0	0	0	0
	Nipple pain	乳頭痛	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pelvic pain	骨盤痛	12 (1.3)	10 (1.0)	2 (0.2)	0	0	0	12 (2.2)	8 (1.4)	4 (0.7)	0	0	0
	Penile pain	陰茎痛	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Penis disorder	陰茎障害	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Perineal pain	会陰痛	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Prostate induration	前立腺硬結	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostatic mass	前立腺腫瘤	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Prostatic obstruction	前立腺閉塞	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Prostatitis	前立腺炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Prostatomegaly	前立腺腫大	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Testicular pain	精巣痛	0	0	0	0	0	0	3 (0.5)	3 (0.5)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	119 (12.5)	64 (6.7)	33 (3.5)	16 (1.7)	3 (0.3)	3 (0.3)	54 (9.7)	36 (6.5)	8 (1.4)	8 (1.4)	0	2 (0.4)
	Acute respiratory failure	急性呼吸不全	2 (0.2)	0	0	2 (0.2)	0	0	2 (0.4)	0	0	0	0	2 (0.4)
	Asthma	喘息	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Atelectasis	無気肺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bronchitis chronic	慢性気管支炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Bronchospasm	気管支痙攣	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Catarrh	カタル	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	10 (1.0)	6 (0.6)	2 (0.2)	2 (0.2)	0	0	4 (0.7)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0
	Cough	咳嗽	29 (3.0)	18 (1.9)	10 (1.0)	1 (0.1)	0	0	11 (2.0)	8 (1.4)	3 (0.5)	0	0	0
	Cystic lung disease	嚢胞性肺疾患	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	24 (2.5)	11 (1.2)	10 (1.0)	2 (0.2)	0	1 (0.1)	15 (2.7)	8 (1.4)	4 (0.7)	3 (0.5)	0	0
	Dyspnoea exertional	労作性呼吸困難	6 (0.6)	4 (0.4)	1 (0.1)	1 (0.1)	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Emphysema	肺気腫	10 (1.0)	9 (0.9)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Epistaxis	鼻出血	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.5)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Haemoptysis	喀血	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Hypoxia	低酸素症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lower respiratory tract inflammation	下気道の炎症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lung disorder	肺障害	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Nasal congestion	鼻閉	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nocturnal dyspnoea	夜間呼吸困難	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Oropharyngeal pain	口腔咽頭痛	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Paranasal cyst	副鼻腔嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Paranasal sinus hypersecretion	副鼻腔分泌過多	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pleural effusion	胸水	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	4 (0.7)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Pneumonia aspiration	誤嚥性肺炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pneumonitis	肺臓炎	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumothorax	気胸	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Productive cough	湿性咳嗽	1 (0.1)	1 (0.1)	0	0	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Pulmonary calcification	肺石灰化	6 (0.6)	6 (0.6)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pulmonary congestion	肺うっ血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.5)	0	0	2 (0.2)	1 (0.1)	2 (0.2)	4 (0.7)	2 (0.4)	0	2 (0.4)	0	0
	Pulmonary fibrosis	肺線維症	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Pulmonary mass	肺腫瘤	6 (0.6)	5 (0.5)	0	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pulmonary oedema	肺水腫	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pulmonary thrombosis	肺血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Rales	ラ音	1 (0.1)	1 (0.1)	0	0	0	0	3 (0.5)	3 (0.5)	0	0	0	0
	Reflux laryngitis	逆流性喉頭炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Respiratory alkalosis	呼吸性アルカローシス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Respiratory disorder	呼吸障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Respiratory failure	呼吸不全	3 (0.3)	0	0	1 (0.1)	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Rhinalgia	鼻痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Rhinorrhoea	鼻漏	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Rhonchi	低音性連続性ラ音	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sinus disorder	副鼻腔障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Sinus polyp	副鼻腔ポリープ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sleep apnoea syndrome	睡眠時無呼吸症候群	3 (0.3)	0	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Sneezing	くしゃみ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Throat irritation	咽喉刺激感	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Throat tightness	咽喉絞扼感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Upper-airway cough syndrome	上気道咳症候群	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Wheezing	喘鳴	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	90 (9.4)	63 (6.6)	24 (2.5)	3 (0.3)	0	0	40 (7.2)	30 (5.4)	9 (1.6)	1 (0.2)	0	0
	Acne	ざ瘡	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Actinic keratosis	光線角化症	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Alopecia	脱毛症	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Blister	水疱	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Decubitus ulcer	褥瘡性潰瘍	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dermal cyst	皮膚嚢腫	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Dermatitis	皮膚炎	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dermatitis contact	接触皮膚炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Diabetic foot	糖尿病性足病変	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0

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	Dry skin	皮膚乾燥	6 (0.6)	6 (0.6)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ecchymosis	斑状出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Eczema	湿疹	6 (0.6)	4 (0.4)	2 (0.2)	0	0	0	3 (0.5)	2 (0.4)	1 (0.2)	0	0	0
	Eczema nummular	貨幣状湿疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Erythema	紅斑	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Erythema multiforme	多形紅斑	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Haemorrhage subcutaneous	皮下出血	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hyperhidrosis	多汗症	8 (0.8)	3 (0.3)	5 (0.5)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Hyperkeratosis	過角化	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hypertrichosis	多毛症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hypotrichosis	貧毛症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nail discolouration	爪変色	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Night sweats	寝汗	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Onychoclasis	爪破損	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pain of skin	皮膚疼痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pigmentation disorder	色素沈着障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pruritus	そう痒症	16 (1.7)	13 (1.4)	3 (0.3)	0	0	0	11 (2.0)	9 (1.6)	2 (0.4)	0	0	0
	Pruritus allergic	アレルギー性そう痒症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Pruritus generalised	全身性そう痒症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Psoriasis	乾癬	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Rash	発疹	17 (1.8)	10 (1.0)	6 (0.6)	1 (0.1)	0	0	4 (0.7)	4 (0.7)	0	0	0	0
	Rash macular	斑状皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash maculo-papular	斑状丘疹状皮疹	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Rash papular	丘疹性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin disorder	皮膚障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin erosion	皮膚びらん	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin exfoliation	皮膚剥脱	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin fragility	皮膚脆弱性	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin induration	皮膚硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin irritation	皮膚刺激	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin lesion	皮膚病変	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Skin mass	皮膚腫瘤	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Skin reaction	皮膚反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin ulcer	皮膚潰瘍	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Stasis dermatitis	うっ滞性皮膚炎	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Urticaria	蕁麻疹	9 (0.9)	4 (0.4)	4 (0.4)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
Surgical and medical procedures	Any	外科および内科処置	10 (1.0)	1 (0.1)	1 (0.1)	8 (0.8)	0	0	5 (0.9)	0	2 (0.4)	3 (0.5)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cataract operation	白内障手術	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cystostomy	膀胱瘻造設	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Lipoma excision	脂肪腫切除	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lymphadenectomy	リンパ節切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Orchidectomy	精巣摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostatectomy	前立腺摘除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Radiotherapy to lymph nodes	リンパ節放射線療法	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Tooth extraction	抜歯	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urethrotomy	尿道切開	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Vascular disorders	Any	血管障害	152 (15.9)	76 (8.0)	39 (4.1)	36 (3.8)	0	1 (0.1)	68 (12.3)	28 (5.1)	21 (3.8)	17 (3.1)	0	2 (0.4)
	Aortic aneurysm	大動脈瘤	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Aortic arteriosclerosis	大動脈硬化症	4 (0.4)	4 (0.4)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Aortic dissection	大動脈解離	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic thrombosis	大動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	0	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Bleeding varicose vein	出血性静脈瘤	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Circulatory collapse	循環虚脱	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Deep vein thrombosis	深部静脈血栓症	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Embolism	塞栓症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Essential hypertension	本態性高血圧症	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Flushing	潮紅	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haematoma	血腫	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Hot flush	ほてり	50 (5.2)	42 (4.4)	8 (0.8)	0	0	0	23 (4.2)	22 (4.0)	1 (0.2)	0	0	0
	Hypertension	高血圧	63 (6.6)	15 (1.6)	18 (1.9)	30 (3.1)	0	0	29 (5.2)	6 (1.1)	11 (2.0)	12 (2.2)	0	0
	Hypotension	低血圧	10 (1.0)	7 (0.7)	2 (0.2)	1 (0.1)	0	0	7 (1.3)	3 (0.5)	3 (0.5)	1 (0.2)	0	0
	Iliac artery occlusion	腸骨動脈閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Intermittent claudication	間欠性跛行	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphoedema	リンパ浮腫	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Orthostatic hypotension	起立性低血圧	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Pallor	蒼白	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	6 (0.6)	4 (0.4)	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Peripheral artery thrombosis	末梢動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Phlebitis	静脈炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thrombophlebitis	血栓性静脈炎	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Thrombophlebitis superficial	表在性血栓性静脈炎	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Thrombosis	血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Varicose vein	静脈瘤	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-1 TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=554) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Vasculitis	血管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vena cava thrombosis	大静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Venous thrombosis limb	四肢静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.1 PH-39723/Table 14.3.1/3

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		258 (27.0)	132 (13.8)	98 (10.3)	24 (2.5)	3 (0.3)	1 (0.1)	110 (19.9)	68 (12.3)	26 (4.7)	14 (2.5)	0	2 (0.4)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	17 (1.8)	6 (0.6)	8 (0.8)	3 (0.3)	0	0	4 (0.7)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Anaemia	貧血	9 (0.9)	5 (0.5)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Leukopenia	白血球減少症	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Neutropenia	好中球減少症	6 (0.6)	1 (0.1)	3 (0.3)	2 (0.2)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Cardiac disorders	Any	心臓障害	10 (1.0)	6 (0.6)	2 (0.2)	2 (0.2)	0	0	3 (0.5)	2 (0.4)	0	0	0	1 (0.2)
	Arrhythmia	不整脈	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Arrhythmia supraventricular	上室性不整脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Atrial fibrillation	心房細動	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	0	1 (0.2)
	Palpitations	動悸	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Supraventricular extrasystoles	上室性期外収縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Tinnitus	耳鳴	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
Eye disorders	Any	眼障害	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blepharitis	眼瞼炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Visual acuity reduced	視力低下	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	61 (6.4)	43 (4.5)	17 (1.8)	0	0	1 (0.1)	37 (6.7)	27 (4.9)	8 (1.4)	2 (0.4)	0	0
	Abdominal discomfort	腹部不快感	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Abdominal distension	腹部膨満	4 (0.4)	4 (0.4)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Abdominal pain	腹痛	4 (0.4)	4 (0.4)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Abdominal pain upper	上腹部痛	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	4 (0.7)	3 (0.5)	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Anal haemorrhage	肛門出血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Constipation	便秘	10 (1.0)	4 (0.4)	6 (0.6)	0	0	0	5 (0.9)	4 (0.7)	1 (0.2)	0	0	0
	Diarrhoea	下痢	15 (1.6)	11 (1.2)	4 (0.4)	0	0	0	9 (1.6)	7 (1.3)	2 (0.4)	0	0	0
	Dry mouth	口内乾燥	9 (0.9)	9 (0.9)	0	0	0	0	5 (0.9)	4 (0.7)	1 (0.2)	0	0	0
	Duodenal ulcer	十二指腸潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dyspepsia	消化不良	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Flatulence	鼓腸	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Frequent bowel movements	排便回数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Gastritis erosive	びらん性胃炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Nausea	悪心	24 (2.5)	21 (2.2)	3 (0.3)	0	0	0	17 (3.1)	12 (2.2)	5 (0.9)	0	0	0
	Oesophageal pain	食道痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Vomiting	嘔吐	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	86 (9.0)	58 (6.1)	26 (2.7)	2 (0.2)	0	0	32 (5.8)	25 (4.5)	5 (0.9)	2 (0.4)	0	0
	Asthenia	無力症	9 (0.9)	7 (0.7)	2 (0.2)	0	0	0	7 (1.3)	4 (0.7)	2 (0.4)	1 (0.2)	0	0
	Chest pain	胸痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Chills	悪寒	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Discomfort	不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Face oedema	顔面浮腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	68 (7.1)	46 (4.8)	20 (2.1)	2 (0.2)	0	0	24 (4.3)	21 (3.8)	2 (0.4)	1 (0.2)	0	0
	Gait disturbance	歩行障害	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Oedema peripheral	末梢性浮腫	5 (0.5)	3 (0.3)	2 (0.2)	0	0	0	3 (0.5)	1 (0.2)	2 (0.4)	0	0	0
	Peripheral swelling	末梢腫脹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pyrexia	発熱	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Thirst	口渇	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	6 (0.6)	4 (0.4)	1 (0.1)	0	1 (0.1)	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Hepatic function abnormal	肝機能異常	2 (0.2)	1 (0.1)	0	0	1 (0.1)	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperbilirubinaemia	高ビリルビン血症	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oral candidiasis	口腔カンジダ症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rash pustular	膿疱性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urinary tract infection	尿路感染	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Contusion	挫傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cystitis radiation	放射線性膀胱炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Spinal compression fracture	脊椎圧迫骨折	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	32 (3.4)	13 (1.4)	13 (1.4)	6 (0.6)	0	0	5 (0.9)	3 (0.5)	2 (0.4)	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	10 (1.0)	6 (0.6)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Blood bilirubin increased	血中ビリルビン増加	6 (0.6)	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	7 (0.7)	1 (0.1)	6 (0.6)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Blood urea increased	血中尿素増加	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Electrocardiogram QT prolonged	心電図ＱＴ延長	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Haemoglobin decreased	ヘモグロビン減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphocyte count decreased	リンパ球数減少	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	4 (0.4)	0	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Protein total decreased	総蛋白減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Transaminases increased	トランスアミナーゼ上昇	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Weight decreased	体重減少	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Weight increased	体重増加	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	White blood cell count decreased	白血球数減少	3 (0.3)	0	3 (0.3)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	22 (2.3)	9 (0.9)	10 (1.0)	3 (0.3)	0	0	8 (1.4)	5 (0.9)	2 (0.4)	1 (0.2)	0	0
	Decreased appetite	食欲減退	14 (1.5)	9 (0.9)	5 (0.5)	0	0	0	6 (1.1)	4 (0.7)	2 (0.4)	0	0	0
	Dehydration	脱水	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dyslipidaemia	脂質異常症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gout	痛風	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hyperglycaemia	高血糖	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Hyperlipidaemia	高脂血症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hyperuricaemia	高尿酸血症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hyponatraemia	低ナトリウム血症	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	27 (2.8)	13 (1.4)	11 (1.2)	3 (0.3)	0	0	10 (1.8)	7 (1.3)	3 (0.5)	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Arthralgia	関節痛	5 (0.5)	2 (0.2)	2 (0.2)	1 (0.1)	0	0	6 (1.1)	6 (1.1)	0	0	0	0
	Back pain	背部痛	7 (0.7)	3 (0.3)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Joint swelling	関節腫脹	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Muscle spasms	筋痙縮	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Muscular weakness	筋力低下	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Musculoskeletal pain	筋骨格痛	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Myalgia	筋肉痛	6 (0.6)	5 (0.5)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Osteoarthritis	変形性関節症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoporosis	骨粗鬆症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pain in extremity	四肢痛	5 (0.5)	3 (0.3)	2 (0.2)	0	0	0	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	31 (3.2)	22 (2.3)	7 (0.7)	1 (0.1)	1 (0.1)	0	15 (2.7)	9 (1.6)	3 (0.5)	2 (0.4)	0	1 (0.2)
	Amnesia	健忘	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balance disorder	平衡障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cognitive disorder	認知障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dizziness	浮動性めまい	11 (1.2)	8 (0.8)	2 (0.2)	1 (0.1)	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Dysgeusia	味覚異常	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Headache	頭痛	13 (1.4)	11 (1.2)	2 (0.2)	0	0	0	4 (0.7)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Hypoaesthesia	感覚鈍麻	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hyposmia	嗅覚減退	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ischaemic stroke	虚血性脳卒中	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Memory impairment	記憶障害	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Paraesthesia	錯感覚	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Psychomotor skills impaired	精神運動機能障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Somnolence	傾眠	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tremor	振戦	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	5 (0.9)	4 (0.7)	1 (0.2)	0	0	0
	Depression	うつ病	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Insomnia	不眠症	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Irritability	易刺激性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Middle insomnia	中期不眠症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Nightmare	悪夢	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Sleep disorder	睡眠障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	11 (1.2)	8 (0.8)	2 (0.2)	1 (0.1)	0	0	6 (1.1)	3 (0.5)	3 (0.5)	0	0	0
	Bladder hypertrophy	膀胱壁肥厚	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Glycosuria	糖尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematuria	血尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Nocturia	夜間頻尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Polyuria	多尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Proteinuria	蛋白尿	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Renal failure	腎不全	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Renal impairment	腎機能障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urinary incontinence	尿失禁	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urinary retention	尿閉	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Urinary tract disorder	尿路障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	16 (1.7)	11 (1.2)	5 (0.5)	0	0	0	6 (1.1)	5 (0.9)	1 (0.2)	0	0	0
	Benign prostatic hyperplasia	良性前立腺肥大症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast induration	乳房硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast pain	乳房痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Breast tenderness	乳房圧痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gynaecomastia	女性化乳房	15 (1.6)	10 (1.0)	5 (0.5)	0	0	0	3 (0.5)	3 (0.5)	0	0	0	0
	Nipple pain	乳頭痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Perineal pain	会陰痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	10 (1.0)	5 (0.5)	4 (0.4)	0	1 (0.1)	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cough	咳嗽	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Dyspnoea exertional	労作性呼吸困難	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Nasal congestion	鼻閉	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pulmonary embolism	肺塞栓症	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	34 (3.6)	24 (2.5)	9 (0.9)	1 (0.1)	0	0	10 (1.8)	7 (1.3)	3 (0.5)	0	0	0
	Alopecia	脱毛症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dry skin	皮膚乾燥	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Eczema	湿疹	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Eczema nummular	貨幣状湿疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyperhidrosis	多汗症	6 (0.6)	2 (0.2)	4 (0.4)	0	0	0	4 (0.7)	3 (0.5)	1 (0.2)	0	0	0
	Hypotrichosis	貧毛症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Night sweats	寝汗	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pruritus	そう痒症	7 (0.7)	7 (0.7)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pruritus allergic	アレルギー性そう痒症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Psoriasis	乾癬	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Rash	発疹	5 (0.5)	4 (0.4)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rash macular	斑状皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash maculo-papular	斑状丘疹状皮疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Urticaria	蕁麻疹	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Vascular disorders	Any	血管障害	59 (6.2)	36 (3.8)	18 (1.9)	5 (0.5)	0	0	20 (3.6)	13 (2.3)	3 (0.5)	4 (0.7)	0	0
	Deep vein thrombosis	深部静脈血栓症	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Flushing	潮紅	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hot flush	ほてり	36 (3.8)	29 (3.0)	7 (0.7)	0	0	0	15 (2.7)	14 (2.5)	1 (0.2)	0	0	0
	Hypertension	高血圧	11 (1.2)	1 (0.1)	6 (0.6)	4 (0.4)	0	0	4 (0.7)	0	1 (0.2)	3 (0.5)	0	0
	Hypotension	低血圧	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Orthostatic hypotension	起立性低血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral artery thrombosis	末梢動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-2 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=554) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Vasculitis	血管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.1 PH-39723/Table 14.3.1/12

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		273 (28.6%)	215 (22.5%)	21 (2.2%)	37 (3.9%)	126 (22.7%)	99 (17.9%)	9 (1.6%)	18 (3.2%)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	15 (1.6%)	15 (1.6%)	0	0	7 (1.3%)	6 (1.1%)	1 (0.2%)	0
	Anaemia	貧血	8 (0.8%)	8 (0.8%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Iron deficiency anaemia	鉄欠乏性貧血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Leukopenia	白血球減少症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphopenia	リンパ球減少症	2 (0.2%)	2 (0.2%)	0	0	3 (0.5%)	3 (0.5%)	0	0
	Neutropenia	好中球減少症	4 (0.4%)	4 (0.4%)	0	0	1 (0.2%)	0	1 (0.2%)	0
	Thrombocytopenia	血小板減少症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	46 (4.8%)	30 (3.1%)	6 (0.6%)	10 (1.0%)	13 (2.3%)	4 (0.7%)	1 (0.2%)	8 (1.4%)
	Acute myocardial infarction	急性心筋梗塞	5 (0.5%)	2 (0.2%)	2 (0.2%)	1 (0.1%)	0	0	0	0
	Angina pectoris	狭心症	3 (0.3%)	1 (0.1%)	1 (0.1%)	1 (0.1%)	0	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Aortic valve disease	大動脈弁疾患	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Arrhythmia	不整脈	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Atrial fibrillation	心房細動	6 (0.6%)	5 (0.5%)	1 (0.1%)	0	2 (0.4%)	1 (0.2%)	1 (0.2%)	0
	Atrioventricular block	房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Bradycardia	徐脈	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Cardiac arrest	心停止	2 (0.2%)	0	0	2 (0.2%)	3 (0.5%)	0	0	3 (0.5%)
	Cardiac disorder	心障害	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Cardiac failure	心不全	5 (0.5%)	1 (0.1%)	1 (0.1%)	3 (0.3%)	3 (0.5%)	0	0	3 (0.5%)
	Cardiac failure acute	急性心不全	2 (0.2%)	1 (0.1%)	0	1 (0.1%)	0	0	0	0
	Cardiac failure congestive	うっ血性心不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cardiogenic shock	心原性ショック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cardiovascular insufficiency	心血管不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Coronary artery disease	冠動脈疾患	6 (0.6%)	5 (0.5%)	0	1 (0.1%)	0	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Coronary artery stenosis	冠動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Myocardial infarction	心筋梗塞	4 (0.4%)	3 (0.3%)	1 (0.1%)	0	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Myocardial ischaemia	心筋虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Palpitations	動悸	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sinus bradycardia	洞性徐脈	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tachycardia	頻脈	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Endocrine disorders	Any	内分泌障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Eye disorders	Any	眼障害	5 (0.5%)	5 (0.5%)	0	0	5 (0.9%)	5 (0.9%)	0	0
	Blindness	失明	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blindness unilateral	片側失明	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cataract	白内障	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Eye pain	眼痛	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Macular degeneration	黄斑変性	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Retinal detachment	網膜剥離	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Visual impairment	視力障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Gastrointestinal disorders	Any	胃腸障害	22 (2.3%)	16 (1.7%)	4 (0.4%)	2 (0.2%)	11 (2.0%)	11 (2.0%)	0	0
	Abdominal pain	腹痛	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Abdominal pain upper	上腹部痛	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Anal incontinence	肛門失禁	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Colitis	大腸炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dental caries	齲歯	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Diarrhoea	下痢	1 (0.1%)	0	0	1 (0.1%)	1 (0.2%)	1 (0.2%)	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Ileus	イレウス	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4%)	4 (0.4%)	0	0	0	0	0	0
	Jejunal stenosis	空腸狭窄	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Large intestine perforation	大腸穿孔	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Melaena	メレナ	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Nausea	悪心	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Plicated tongue	ひだ舌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Small intestinal obstruction	小腸閉塞	1 (0.1%)	1 (0.1%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Vomiting	嘔吐	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	21 (2.2%)	13 (1.4%)	0	8 (0.8%)	7 (1.3%)	6 (1.1%)	0	1 (0.2%)
	Asthenia	無力症	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Death	死亡	4 (0.4%)	0	0	4 (0.4%)	1 (0.2%)	0	0	1 (0.2%)

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Fatigue	疲労	4 (0.4%)	4 (0.4%)	0	0	5 (0.9%)	5 (0.9%)	0	0
	Gait disturbance	歩行障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	General physical health deterioration	全身健康状態低下	4 (0.4%)	2 (0.2%)	0	2 (0.2%)	0	0	0	0
	Granuloma	肉芽腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Malaise	倦怠感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Peripheral swelling	末梢腫脹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pyrexia	発熱	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sudden cardiac death	心突然死	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Sudden death	突然死	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Suprapubic pain	恥骨上痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	6 (0.6%)	4 (0.4%)	1 (0.1%)	1 (0.1%)	3 (0.5%)	3 (0.5%)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cholangitis acute	急性胆管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cholecystitis chronic	慢性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cholelithiasis	胆石症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hepatic function abnormal	肝機能異常	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Liver disorder	肝障害	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	41 (4.3%)	32 (3.4%)	4 (0.4%)	5 (0.5%)	17 (3.1%)	15 (2.7%)	1 (0.2%)	1 (0.2%)
	Abscess	膿瘍	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Acute endocarditis	急性心内膜炎	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Appendicitis	虫垂炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bacterial infection	細菌感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bronchitis	気管支炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cellulitis	蜂巣炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Erysipelas	丹毒	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gastroenteritis	胃腸炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Gingivitis	歯肉炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hepatitis C	C型肝炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Influenza	インフルエンザ	2 (0.2%)	0	1 (0.1%)	1 (0.1%)	0	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lung infection	肺感染	2 (0.2%)	1 (0.1%)	0	1 (0.1%)	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Meningitis bacterial	細菌性髄膜炎	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Peritonitis	腹膜炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pneumonia	肺炎	10 (1.0%)	8 (0.8%)	1 (0.1%)	1 (0.1%)	4 (0.7%)	3 (0.5%)	1 (0.2%)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pyelonephritis	腎盂腎炎	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Respiratory tract infection	気道感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Respiratory tract infection viral	ウイルス性気道感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Sepsis	敗血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tooth abscess	歯膿瘍	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tooth infection	歯感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary tract infection	尿路感染	6 (0.6%)	6 (0.6%)	0	0	3 (0.5%)	3 (0.5%)	0	0
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urosepsis	尿路性敗血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	20 (2.1%)	17 (1.8%)	0	3 (0.3%)	10 (1.8%)	10 (1.8%)	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Ankle fracture	足関節部骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Clavicle fracture	鎖骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Facial bones fracture	顔面骨骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fall	転倒	8 (0.8%)	8 (0.8%)	0	0	4 (0.7%)	4 (0.7%)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fibula fracture	腓骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Foot fracture	足骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fracture	骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Frostbite	凍傷	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hand fracture	手骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Heart injury	心臓損傷	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Multiple injuries	多発性外傷	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Procedural pain	処置による疼痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skin abrasion	皮膚擦過傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Subdural haematoma	硬膜下血腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Thermal burn	熱傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Traumatic fracture	外傷性骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	Darolutamide (N=954) G 3 (N (%))	Darolutamide (N=954) G 4 (N (%))	Darolutamide (N=954) G 5 (N (%))	Placebo (N=554) Total (N (%))	Placebo (N=554) G 3 (N (%))	Placebo (N=554) G 4 (N (%))	Placebo (N=554) G 5 (N (%))
	Vascular graft complication	移植血管合併症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Investigations	Any	臨床検査	19 (2.0%)	18 (1.9%)	1 (0.1%)	0	6 (1.1%)	4 (0.7%)	2 (0.4%)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	4 (0.4%)	4 (0.4%)	0	0	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood bilirubin increased	血中ビリルビン増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood chromogranin A increased	血中クロモグラニンA増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood creatinine increased	血中クレアチニン増加	1 (0.1%)	1 (0.1%)	0	0	2 (0.4%)	0	2 (0.4%)	0
	Blood potassium decreased	血中カリウム減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood pressure increased	血圧上昇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood pressure systolic increased	収縮期血圧上昇	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood sodium decreased	血中ナトリウム減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood urea increased	血中尿素増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Body temperature increased	体温上昇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Electrocardiogram QT prolonged	心電図ＱＴ延長	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Glomerular filtration rate decreased	糸球体濾過率減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Neutrophil count decreased	好中球数減少	7 (0.7%)	6 (0.6%)	1 (0.1%)	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	23 (2.4%)	19 (2.0%)	4 (0.4%)	0	10 (1.8%)	10 (1.8%)	0	0
	Decreased appetite	食欲減退	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Dehydration	脱水	3 (0.3%)	2 (0.2%)	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Diabetes mellitus	糖尿病	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperglycaemia	高血糖	4 (0.4%)	2 (0.2%)	2 (0.2%)	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperkalaemia	高カリウム血症	4 (0.4%)	3 (0.3%)	1 (0.1%)	0	3 (0.5%)	3 (0.5%)	0	0
	Hypernatraemia	高ナトリウム血症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypertriglyceridaemia	高トリグリセリド血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hyperuricaemia	高尿酸血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypoglycaemia	低血糖	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyponatraemia	低ナトリウム血症	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Metabolic alkalosis	代謝性アルカローシス	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Obesity	肥満	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	18 (1.9%)	18 (1.9%)	0	0	6 (1.1%)	6 (1.1%)	0	0
	Arthralgia	関節痛	3 (0.3%)	3 (0.3%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Back pain	背部痛	4 (0.4%)	4 (0.4%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bone pain	骨痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Flank pain	側腹部痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lumbar spinal stenosis	腰部脊柱管狭窄症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Mobility decreased	運動性低下	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Muscular weakness	筋力低下	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Musculoskeletal chest pain	筋骨格系胸痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Myalgia	筋肉痛	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	5 (0.5%)	5 (0.5%)	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pain in extremity	四肢痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Spinal column stenosis	脊柱管狭窄症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Spinal fusion acquired	後天性脊椎癒合	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	24 (2.5%)	20 (2.1%)	2 (0.2%)	2 (0.2%)	10 (1.8%)	9 (1.6%)	0	1 (0.2%)
	Adenocarcinoma	腺癌	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bladder neoplasm	膀胱新生物	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Colon cancer	結腸癌	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Gastric cancer	胃癌	1 (0.1%)	1 (0.1%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Gastrointestinal adenocarcinoma	消化器腺癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphoma	リンパ腫	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Mesothelioma	中皮腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Metastases to peritoneum	腹膜転移	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Pancreatic carcinoma	膵癌	2 (0.2%)	1 (0.1%)	0	1 (0.1%)	0	0	0	0
	Pancreatic neoplasm	膵新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Rectal adenocarcinoma	直腸腺癌	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Rectal cancer	直腸癌	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Salivary gland neoplasm	唾液腺新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Thymoma	胸腺腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Tumour compression	腫瘍性圧迫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Tumour pain	腫瘍疼痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	20 (2.1%)	16 (1.7%)	2 (0.2%)	2 (0.2%)	15 (2.7%)	11 (2.0%)	0	4 (0.7%)
	Brain oedema	脳浮腫	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Carotid artery stenosis	頚動脈狭窄	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Cerebral arteriosclerosis	脳動脈硬化症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Cerebrovascular accident	脳血管発作	2 (0.2%)	2 (0.2%)	0	0	3 (0.5%)	2 (0.4%)	0	1 (0.2%)
	Dementia	認知症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dizziness	浮動性めまい	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Headache	頭痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypoaesthesia	感覚鈍麻	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ischaemic stroke	虚血性脳卒中	4 (0.4%)	1 (0.1%)	2 (0.2%)	1 (0.1%)	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Myelopathy	脊髄症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Presyncope	失神寸前の状態	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Sciatica	坐骨神経痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Senile dementia	老年認知症	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Syncope	失神	2 (0.2%)	2 (0.2%)	0	0	3 (0.5%)	3 (0.5%)	0	0
	Transient ischaemic attack	一過性脳虚血発作	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Product issues	Any	製品の問題	4 (0.4%)	4 (0.4%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Device dislocation	医療機器位置異常	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Device occlusion	医療機器閉塞	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	Darolutamide (N=954) G 3 (N (%))	Darolutamide (N=954) G 4 (N (%))	Darolutamide (N=954) G 5 (N (%))	Placebo (N=554) Total (N (%))	Placebo (N=554) G 3 (N (%))	Placebo (N=554) G 4 (N (%))	Placebo (N=554) G 5 (N (%))
	Depression	うつ病	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Insomnia	不眠症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Renal and urinary disorders	Any	腎および尿路障害	47 (4.9%)	45 (4.7%)	2 (0.2%)	0	37 (6.7%)	32 (5.8%)	5 (0.9%)	0
	Acute kidney injury	急性腎障害	5 (0.5%)	4 (0.4%)	1 (0.1%)	0	2 (0.4%)	2 (0.4%)	0	0
	Anuria	無尿	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Azotaemia	高窒素血症	0	0	0	0	1 (0.2%)	0	1 (0.2%)	0
	Bladder neck obstruction	膀胱頚部閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Calculus bladder	膀胱結石	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Chronic kidney disease	慢性腎臓病	2 (0.2%)	2 (0.2%)	0	0	3 (0.5%)	2 (0.4%)	1 (0.2%)	0
	Dysuria	排尿困難	1 (0.1%)	1 (0.1%)	0	0	5 (0.9%)	5 (0.9%)	0	0
	Haematuria	血尿	10 (1.0%)	10 (1.0%)	0	0	7 (1.3%)	7 (1.3%)	0	0
	Hydronephrosis	水腎症	7 (0.7%)	7 (0.7%)	0	0	3 (0.5%)	3 (0.5%)	0	0
	Lower urinary tract symptoms	下部尿路症状	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Nephrolithiasis	腎結石症	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Oliguria	乏尿	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pollakiuria	頻尿	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Renal colic	腎仙痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Renal failure	腎不全	1 (0.1%)	0	1 (0.1%)	0	4 (0.7%)	1 (0.2%)	3 (0.5%)	0
	Renal impairment	腎機能障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Renal pain	腎臓痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ureteric stenosis	尿管狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urethral stenosis	尿道狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary hesitation	排尿躊躇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary retention	尿閉	15 (1.6%)	15 (1.6%)	0	0	11 (2.0%)	11 (2.0%)	0	0
	Urinary tract obstruction	尿路閉塞	5 (0.5%)	5 (0.5%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urine flow decreased	尿流量減少	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Prostate induration	前立腺硬結	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Prostatic obstruction	前立腺閉塞	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	22 (2.3%)	16 (1.7%)	3 (0.3%)	3 (0.3%)	10 (1.8%)	8 (1.4%)	0	2 (0.4%)
	Acute respiratory failure	急性呼吸不全	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	0	0	2 (0.4%)
	Asthma	喘息	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	1 (0.2%)	1 (0.2%)	0
	Cough	咳嗽	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dyspnoea	呼吸困難	3 (0.3%)	2 (0.2%)	0	1 (0.1%)	3 (0.5%)	3 (0.5%)	0	0
	Dyspnoea exertional	労作性呼吸困難	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Epistaxis	鼻出血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Nocturnal dyspnoea	夜間呼吸困難	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pleural effusion	胸水	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pneumonitis	肺臓炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.5%)	2 (0.2%)	1 (0.1%)	2 (0.2%)	2 (0.4%)	2 (0.4%)	0	0
	Pulmonary mass	肺腫瘤	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pulmonary oedema	肺水腫	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Respiratory alkalosis	呼吸性アルカローシス	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Respiratory failure	呼吸不全	3 (0.3%)	1 (0.1%)	2 (0.2%)	0	1 (0.2%)	1 (0.2%)	0	0
	Rhinalgia	鼻痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Rash	発疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skin mass	皮膚腫瘤	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urticaria	蕁麻疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Surgical and medical procedures	Any	外科および内科処置	8 (0.8%)	8 (0.8%)	0	0	3 (0.5%)	3 (0.5%)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cataract operation	白内障手術	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-3 グレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cystostomy	膀胱瘻造設	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Lymphadenectomy	リンパ節切除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Orchidectomy	精巣摘除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Prostatectomy	前立腺摘除	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urethrotomy	尿道切開	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Vascular disorders	Any	血管障害	37 (3.9%)	36 (3.8%)	0	1 (0.1%)	19 (3.4%)	17 (3.1%)	0	2 (0.4%)
	Aortic dissection	大動脈解離	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Circulatory collapse	循環虚脱	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Embolism	塞栓症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Essential hypertension	本態性高血圧症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypertension	高血圧	30 (3.1%)	30 (3.1%)	0	0	12 (2.2%)	12 (2.2%)	0	0
	Hypotension	低血圧	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphoedema	リンパ浮腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Orthostatic hypotension	起立性低血圧	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Vasculitis	血管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.1 PH-39723/Table 14.3.1/4

付表 2.7.6.9.a.1-4 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		28 (2.9%)	24 (2.5%)	3 (0.3%)	1 (0.1%)	16 (2.9%)	14 (2.5%)	0	2 (0.4%)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Anaemia	貧血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Neutropenia	好中球減少症	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	0	0	1 (0.2%)
	Atrioventricular block complete	完全房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
Gastrointestinal disorders	Any	胃腸障害	1 (0.1%)	0	0	1 (0.1%)	2 (0.4%)	2 (0.4%)	0	0
	Abdominal pain upper	上腹部痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Gastritis	胃炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Asthenia	無力症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fatigue	疲労	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Hepatic function abnormal	肝機能異常	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Investigations	Any	臨床検査	6 (0.6%)	6 (0.6%)	0	0	0	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-4 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)				Placebo (N=554)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperglycaemia	高血糖	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypokalaemia	低カリウム血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hyponatraemia	低ナトリウム血症	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Arthralgia	関節痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Back pain	背部痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Myalgia	筋肉痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	2 (0.2%)	1 (0.1%)	1 (0.1%)	0	3 (0.5%)	2 (0.4%)	0	1 (0.2%)
	Dizziness	浮動性めまい	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Headache	頭痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ischaemic stroke	虚血性脳卒中	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Renal and urinary disorders	Any	腎および尿路障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary retention	尿閉	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Pulmonary embolism	肺塞栓症	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urticaria	蕁麻疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Vascular disorders	Any	血管障害	5 (0.5%)	5 (0.5%)	0	0	4 (0.7%)	4 (0.7%)	0	0
	Hypertension	高血圧	4 (0.4%)	4 (0.4%)	0	0	3 (0.5%)	3 (0.5%)	0	0

付表 2.7.6.9.a.1-4 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954) Total (N (%))	Darolutamide (N=954) G 3 (N (%))	Darolutamide (N=954) G 4 (N (%))	Darolutamide (N=954) G 5 (N (%))	Placebo (N=554) Total (N (%))	Placebo (N=554) G 3 (N (%))	Placebo (N=554) G 4 (N (%))	Placebo (N=554) G 5 (N (%))
	Peripheral ischaemia	末梢性虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Vasculitis	血管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
5.3.5.1.1 PH-39723/Table 14.3.1/13

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		237 (24.8)	7 (0.7)	42 (4.4)	132 (13.8)	19 (2.0)	37 (3.9)	111 (20.0)	1 (0.2)	22 (4.0)	61 (11.0)	9 (1.6)	18 (3.2)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	5 (0.5)	0	2 (0.2)	3 (0.3)	0	0	2 (0.4)	0	0	1 (0.2)	1 (0.2)	0
	Anaemia	貧血	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Leukopenia	白血球減少症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0
Cardiac disorders	Any	心臓障害	51 (5.3)	1 (0.1)	10 (1.0)	24 (2.5)	6 (0.6)	10 (1.0)	18 (3.2)	0	5 (0.9)	4 (0.7)	1 (0.2)	8 (1.4)
	Acute myocardial infarction	急性心筋梗塞	5 (0.5)	0	0	2 (0.2)	2 (0.2)	1 (0.1)	0	0	0	0	0	0
	Angina pectoris	狭心症	4 (0.4)	0	1 (0.1)	1 (0.1)	1 (0.1)	1 (0.1)	2 (0.4)	0	2 (0.4)	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Aortic valve disease	大動脈弁疾患	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Atrial fibrillation	心房細動	8 (0.8)	0	2 (0.2)	5 (0.5)	1 (0.1)	0	3 (0.5)	0	1 (0.2)	1 (0.2)	1 (0.2)	0
	Atrioventricular block	房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cardiac arrest	心停止	2 (0.2)	0	0	0	0	2 (0.2)	3 (0.5)	0	0	0	0	3 (0.5)
	Cardiac disorder	心障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure	心不全	8 (0.8)	0	4 (0.4)	0	1 (0.1)	3 (0.3)	4 (0.7)	0	1 (0.2)	0	0	3 (0.5)
	Cardiac failure acute	急性心不全	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure congestive	うっ血性心不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cardiovascular insufficiency	心血管不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Coronary artery disease	冠動脈疾患	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Coronary artery stenosis	冠動脈狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Myocardial infarction	心筋梗塞	4 (0.4)	0	0	3 (0.3)	1 (0.1)	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Myocardial ischaemia	心筋虚血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Palpitations	動悸	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Vertigo positional	頭位性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Eye disorders	Any	眼障害	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Retinal detachment	網膜剥離	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Visual impairment	視力障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	28 (2.9)	3 (0.3)	6 (0.6)	13 (1.4)	4 (0.4)	2 (0.2)	8 (1.4)	0	2 (0.4)	6 (1.1)	0	0
	Abdominal pain	腹痛	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Abdominal pain upper	上腹部痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bowel movement irregularity	便通不規則	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Constipation	便秘	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Diarrhoea	下痢	2 (0.2)	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Haemorrhoids	痔核	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ileus	イレウス	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼡径ヘルニア	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Inguinal hernia	鼡径ヘルニア	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4)	0	0	4 (0.4)	0	0	0	0	0	0	0	0
	Large intestine perforation	大腸穿孔	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Melaena	メレナ	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Proctitis	直腸炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Rectal stenosis	直腸狭窄	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Small intestinal obstruction	小腸閉塞	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Upper gastrointestinal haemorrhage	上部消化管出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	17 (1.8)	2 (0.2)	2 (0.2)	5 (0.5)	0	8 (0.8)	1 (0.2)	0	0	0	0	1 (0.2)
	Asthenia	無力症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Chest pain	胸痛	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Death	死亡	4 (0.4)	0	0	0	0	4 (0.4)	1 (0.2)	0	0	0	0	1 (0.2)
	Gait disturbance	歩行障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	General physical health deterioration	全身健康状態低下	4 (0.4)	0	0	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0
	Pyrexia	発熱	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sudden cardiac death	心突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Sudden death	突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	5 (0.5)	0	0	3 (0.3)	1 (0.1)	1 (0.1)	2 (0.4)	0	0	2 (0.4)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholangitis acute	急性胆管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis chronic	慢性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholelithiasis	胆石症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholestasis	胆汁うっ滞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Liver disorder	肝障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Immune system disorders	Any	免疫系障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hypersensitivity	過敏症	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Infections and infestations	Any	感染症および寄生虫症	42 (4.4)	0	9 (0.9)	24 (2.5)	4 (0.4)	5 (0.5)	19 (3.4)	0	5 (0.9)	12 (2.2)	1 (0.2)	1 (0.2)
	Abdominal abscess	腹部膿瘍	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Acute endocarditis	急性心内膜炎	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Appendicitis	虫垂炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacterial infection	細菌感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cellulitis	蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Erysipelas	丹毒	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastroenteritis	胃腸炎	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Hepatitis C	C型肝炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Herpes zoster	帯状疱疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Infectious mononucleosis	伝染性単核症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Influenza	インフルエンザ	2 (0.2)	0	0	0	1 (0.1)	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lung infection	肺感染	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Meningitis bacterial	細菌性髄膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pneumonia	肺炎	13 (1.4)	0	3 (0.3)	8 (0.8)	1 (0.1)	1 (0.1)	6 (1.1)	0	2 (0.4)	3 (0.5)	1 (0.2)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary tuberculosis	肺結核	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pyelonephritis	腎盂腎炎	3 (0.3)	0	0	3 (0.3)	0	0	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Respiratory tract infection viral	ウイルス性気道感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Sepsis	敗血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract infection	尿路感染	7 (0.7)	0	3 (0.3)	4 (0.4)	0	0	0	0	0	0	0	0
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urosepsis	尿路性敗血症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Vestibular neuronitis	前庭神経炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	19 (2.0)	0	5 (0.5)	11 (1.2)	0	3 (0.3)	10 (1.8)	0	2 (0.4)	8 (1.4)	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Ankle fracture	足関節部骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Contusion	挫傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Facial bones fracture	顔面骨骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fall	転倒	3 (0.3)	0	0	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fibula fracture	腓骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Foot fracture	足骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fracture	骨折	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hand fracture	手骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Heart injury	心臓損傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Ligament sprain	靭帯捻挫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Multiple injuries	多発性外傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Road traffic accident	交通事故	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Subarachnoid haemorrhage	くも膜下出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Subdural haematoma	硬膜下血腫	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thermal burn	熱傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Vascular graft complication	移植血管合併症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	3 (0.5)	0	2 (0.4)	0	1 (0.2)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Arteriogram coronary	冠血管造影	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	0	0	0	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0
	Body temperature increased	体温上昇	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urine output decreased	尿量減少	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	12 (1.3)	1 (0.1)	3 (0.3)	5 (0.5)	3 (0.3)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Decreased appetite	食欲減退	4 (0.4)	0	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0
	Dehydration	脱水	2 (0.2)	0	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0
	Diabetes mellitus	糖尿病	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hyperglycaemia	高血糖	3 (0.3)	0	0	1 (0.1)	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypoglycaemia	低血糖	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	8 (0.8)	0	2 (0.2)	6 (0.6)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Arthralgia	関節痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Back pain	背部痛	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Flank pain	側腹部痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	3 (0.3)	0	0	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Spinal column stenosis	脊柱管狭窄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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)	28 (2.9)	0	8 (0.8)	16 (1.7)	2 (0.2)	2 (0.2)	9 (1.6)	1 (0.2)	1 (0.2)	6 (1.1)	0	1 (0.2)
	Acute leukaemia	急性白血病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Basal cell carcinoma	基底細胞癌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder neoplasm	膀胱新生物	3 (0.3)	0	0	3 (0.3)	0	0	0	0	0	0	0	0
	Carcinoid tumour	カルチノイド腫瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Choroid melanoma	脈絡膜黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colon cancer	結腸癌	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Gastric cancer	胃癌	0	0	0	0	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lung adenocarcinoma stage IV	肺腺癌第４期	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lymphoma	リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Malignant melanoma in situ	表皮内悪性黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Mesothelioma	中皮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma	膵癌	3 (0.3)	0	1 (0.1)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Rectal adenocarcinoma	直腸腺癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Renal cancer	腎癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Salivary gland neoplasm	唾液腺新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Thymoma	胸腺腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tumour pain	腫瘍疼痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract neoplasm	尿路新生物	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Nervous system disorders	Any	神経系障害	20 (2.1)	1 (0.1)	5 (0.5)	10 (1.0)	2 (0.2)	2 (0.2)	12 (2.2)	0	1 (0.2)	7 (1.3)	0	4 (0.7)
	Brain oedema	脳浮腫	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Bulbar palsy	球麻痺	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid artery stenosis	頚動脈狭窄	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cerebrovascular accident	脳血管発作	2 (0.2)	0	0	2 (0.2)	0	0	3 (0.5)	0	0	2 (0.4)	0	1 (0.2)
	Cognitive disorder	認知障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dizziness	浮動性めまい	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Ischaemic stroke	虚血性脳卒中	5 (0.5)	0	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Myelopathy	脊髄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Partial seizures	部分発作	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Presyncope	失神寸前の状態	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Seizure	痙攣発作	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Syncope	失神	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Transient ischaemic attack	一過性脳虚血発作	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Product issues	Any	製品の問題	4 (0.4)	0	1 (0.1)	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device dislocation	医療機器位置異常	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device occlusion	医療機器閉塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Delirium	譫妄	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	43 (4.5)	2 (0.2)	5 (0.5)	34 (3.6)	2 (0.2)	0	40 (7.2)	0	9 (1.6)	26 (4.7)	5 (0.9)	0
	Acute kidney injury	急性腎障害	4 (0.4)	0	0	3 (0.3)	1 (0.1)	0	3 (0.5)	1 (0.2)	0	2 (0.4)	0	0
	Azotaemia	高窒素血症	0	0	0	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Calculus bladder	膀胱結石	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Chronic kidney disease	慢性腎臓病	0	0	0	0	0	0	2 (0.4)	0	0	1 (0.2)	1 (0.2)	0
	Dysuria	排尿困難	1 (0.1)	0	0	1 (0.1)	0	0	3 (0.5)	0	0	3 (0.5)	0	0
	Haematuria	血尿	10 (1.0)	1 (0.1)	1 (0.1)	8 (0.8)	0	0	6 (1.1)	0	1 (0.2)	5 (0.9)	0	0
	Hydronephrosis	水腎症	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	3 (0.5)	0	1 (0.2)	2 (0.4)	0	0
	Lower urinary tract symptoms	下部尿路症状	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Nephrolithiasis	腎結石症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Oliguria	乏尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Renal colic	腎仙痛	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal failure	腎不全	1 (0.1)	0	0	0	1 (0.1)	0	4 (0.7)	0	0	1 (0.2)	3 (0.5)	0
	Renal impairment	腎機能障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ureteric stenosis	尿管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urethral stenosis	尿道狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary retention	尿閉	15 (1.6)	1 (0.1)	3 (0.3)	11 (1.2)	0	0	18 (3.2)	1 (0.2)	7 (1.3)	10 (1.8)	0	0
	Urinary tract obstruction	尿路閉塞	6 (0.6)	0	1 (0.1)	5 (0.5)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Urine flow decreased	尿流量減少	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostate induration	前立腺硬結	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostatic obstruction	前立腺閉塞	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	17 (1.8)	0	3 (0.3)	8 (0.8)	3 (0.3)	3 (0.3)	9 (1.6)	0	1 (0.2)	6 (1.1)	0	2 (0.4)
	Acute respiratory failure	急性呼吸不全	2 (0.2)	0	0	2 (0.2)	0	0	2 (0.4)	0	0	0	0	2 (0.4)
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	3 (0.5)	0	1 (0.2)	1 (0.2)	1 (0.2)	0
	Cough	咳嗽	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	4 (0.4)	0	1 (0.1)	2 (0.2)	0	1 (0.1)	1 (0.2)	0	0	1 (0.2)	0	0
	Epistaxis	鼻出血	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pleural effusion	胸水	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pneumonia aspiration	誤嚥性肺炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.5)	0	0	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary mass	肺腫瘤	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pulmonary thrombosis	肺血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Respiratory failure	呼吸不全	2 (0.2)	0	0	0	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Skin mass	皮膚腫瘤	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Surgical and medical procedures	Any	外科および内科処置	5 (0.5)	0	0	5 (0.5)	0	0	3 (0.5)	0	0	3 (0.5)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Orchidectomy	精巣摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostatectomy	前立腺摘除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Vascular disorders	Any	血管障害	12 (1.3)	3 (0.3)	3 (0.3)	5 (0.5)	0	1 (0.1)	5 (0.9)	0	0	3 (0.5)	0	2 (0.4)
	Aortic aneurysm	大動脈瘤	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Aortic dissection	大動脈解離	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Circulatory collapse	循環虚脱	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Deep vein thrombosis	深部静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Embolism	塞栓症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-5 重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Hypertension	高血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypotension	低血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphoedema	リンパ浮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Orthostatic hypotension	起立性低血圧	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thrombosis	血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.1 PH-39723/Table 14.3.2/1

付表 2.7.6.9.a.1-6 治験薬と関連のある重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		10 (1.0)	0	1 (0.1)	5 (0.5)	3 (0.3)	1 (0.1)	6 (1.1)	0	0	4 (0.7)	0	2 (0.4)
Cardiac disorders	Any	心臓障害	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
Gastrointestinal disorders	Any	胃腸障害	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.2)	0	0	1 (0.2)	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
Investigations	Any	臨床検査	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	免疫系障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperglycaemia	高血糖	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Nervous system disorders	Any	神経系障害	1 (0.1)	0	0	0	1 (0.1)	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Ischaemic stroke	虚血性脳卒中	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-6 治験薬と関連のある重篤な TEAE の発現例数及び割合（CTCAE グレード別、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=954)						Placebo (N=554)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Renal and urinary disorders	Any	腎および尿路障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Urinary retention	尿閉	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	1 (0.1)	0	0	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary embolism	肺塞栓症	1 (0.1)	0	0	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
Vascular disorders	Any	血管障害	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Deep vein thrombosis	深部静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.1 PH-39723/ Table 14.3.2/7

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		53 (85.5)	11 (17.7)	24 (38.7)	16 (25.8)	1 (1.6)	1 (1.6)	21 (63.6)	8 (24.2)	9 (27.3)	3 (9.1)	1 (3.0)	0
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	5 (8.1)	1 (1.6)	1 (1.6)	3 (4.8)	0	0	0	0	0	0	0	0
	Anaemia	貧血	3 (4.8)	1 (1.6)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Iron deficiency anaemia	鉄欠乏性貧血	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	5 (8.1)	1 (1.6)	2 (3.2)	2 (3.2)	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Angina pectoris	狭心症	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Cardiac failure	心不全	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Palpitations	動悸	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Ventricular extrasystoles	心室性期外収縮	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	0	0	0	0	0	0	2 (6.1)	0	2 (6.1)	0	0	0
	Otorrhoea	耳漏	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Vertigo	回転性めまい	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Eye disorders	Any	眼障害	3 (4.8)	0	2 (3.2)	1 (1.6)	0	0	3 (9.1)	1 (3.0)	2 (6.1)	0	0	0
	Age-related macular degeneration	加齢黄斑変性	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Cataract	白内障	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Conjunctival deposit	結膜沈着物	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Corneal disorder	角膜障害	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Corneal oedema	角膜浮腫	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Dry eye	眼乾燥	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pterygium	翼状片	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Retinal artery occlusion	網膜動脈閉塞	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Gastrointestinal disorders	Any	胃腸障害	21 (33.9)	15 (24.2)	6 (9.7)	0	0	0	8 (24.2)	3 (9.1)	4 (12.1)	1 (3.0)	0	0
	Abdominal discomfort	腹部不快感	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Abdominal distension	腹部膨満	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Cheilitis	口唇炎	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Constipation	便秘	8 (12.9)	7 (11.3)	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Diarrhoea	下痢	3 (4.8)	1 (1.6)	2 (3.2)	0	0	0	4 (12.1)	1 (3.0)	2 (6.1)	1 (3.0)	0	0
	Diverticulum intestinal	腸憩室	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Dyspepsia	消化不良	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Dysphagia	嚥下障害	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Gastritis erosive	びらん性胃炎	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Haematochezia	血便排泄	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Nausea	悪心	4 (6.5)	3 (4.8)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Pancreatic cyst	膵嚢胞	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Periodontal disease	歯周病	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Tooth loss	歯の脱落	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Toothache	歯痛	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Vomiting	嘔吐	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	14 (22.6)	9 (14.5)	5 (8.1)	0	0	0	4 (12.1)	3 (9.1)	0	1 (3.0)	0	0
	Chest pain	胸痛	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Face oedema	顔面浮腫	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	1 (3.0)	0	0	1 (3.0)	0	0
	Injection site reaction	注射部位反応	2 (3.2)	0	2 (3.2)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Non-cardiac chest pain	非心臓性胸痛	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0	0
	Oedema peripheral	末梢性浮腫	1 (1.6)	1 (1.6)	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pain	疼痛	1 (1.6)	0	1 (1.6)	0	0	0	2 (6.1)	1 (3.0)	1 (3.0)	0	0	0
	Pyrexia	発熱	4 (6.5)	4 (6.5)	0	0	0	0	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	5 (8.1)	3 (4.8)	1 (1.6)	0	1 (1.6)	0	1 (3.0)	0	1 (3.0)	0	0	0
	Drug-induced liver injury	薬物性肝障害	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	4 (6.5)	2 (3.2)	1 (1.6)	0	1 (1.6)	0	1 (3.0)	0	1 (3.0)	0	0	0
Immune system disorders	Any	免疫系障害	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	2 (6.1)	1 (3.0)	1 (3.0)	0	0	0
	Contrast media allergy	造影剤アレルギー	0	0	0	0	0	0	2 (6.1)	1 (3.0)	1 (3.0)	0	0	0
	Seasonal allergy	季節性アレルギー	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	22 (35.5)	8 (12.9)	9 (14.5)	4 (6.5)	0	1 (1.6)	9 (27.3)	3 (9.1)	5 (15.2)	1 (3.0)	0	0
	Abscess	膿瘍	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Bronchitis	気管支炎	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Bronchitis viral	ウイルス性気管支炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Cystitis	膀胱炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Dermatophytosis of nail	爪の皮膚糸状菌症	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Gingivitis	歯肉炎	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Influenza	インフルエンザ	4 (6.5)	0	3 (4.8)	0	0	1 (1.6)	0	0	0	0	0	0
	Laryngitis	喉頭炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Nasopharyngitis	上咽頭炎	12 (19.4)	7 (11.3)	5 (8.1)	0	0	0	4 (12.1)	2 (6.1)	2 (6.1)	0	0	0
	Otitis externa	外耳炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Paronychia	爪囲炎	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Pneumonia	肺炎	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Pyelonephritis	腎盂腎炎	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Rhinitis	鼻炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Skin infection	皮膚感染	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Tinea infection	白癬感染	1 (1.6)	1 (1.6)	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Trichophytosis	トリコフィトン感染症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Upper respiratory tract infection	上気道感染	5 (8.1)	1 (1.6)	4 (6.5)	0	0	0	3 (9.1)	1 (3.0)	2 (6.1)	0	0	0
	Urinary tract infection	尿路感染	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	0	0	1 (3.0)	0	0
	Viral infection	ウイルス感染	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	16 (25.8)	4 (6.5)	9 (14.5)	3 (4.8)	0	0	4 (12.1)	1 (3.0)	3 (9.1)	0	0	0
	Cervical vertebral fracture	頚椎骨折	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Contusion	挫傷	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Cystitis radiation	放射線性膀胱炎	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Fall	転倒	8 (12.9)	2 (3.2)	5 (8.1)	1 (1.6)	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Foot fracture	足骨折	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Fracture	骨折	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Hand fracture	手骨折	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Joint dislocation	関節脱臼	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Lip injury	口唇損傷	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Procedural pain	処置による疼痛	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Radius fracture	橈骨骨折	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Rib fracture	肋骨骨折	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Road traffic accident	交通事故	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Subarachnoid haemorrhage	くも膜下出血	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Subdural haematoma	硬膜下血腫	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Wound complication	創合併症	0	0	0	0	0	0	2 (6.1)	0	2 (6.1)	0	0	0
Investigations	Any	臨床検査	9 (14.5)	4 (6.5)	3 (4.8)	2 (3.2)	0	0	2 (6.1)	0	1 (3.0)	0	1 (3.0)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (3.2)	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (4.8)	0	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	1 (1.6)	1 (1.6)	0	0	0	0	1 (3.0)	0	0	0	1 (3.0)	0
	Lymphocyte count decreased	リンパ球数減少	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Weight decreased	体重減少	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Weight increased	体重増加	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	White blood cell count decreased	白血球数減少	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	10 (16.1)	3 (4.8)	6 (9.7)	1 (1.6)	0	0	2 (6.1)	1 (3.0)	0	1 (3.0)	0	0
	Decreased appetite	食欲減退	7 (11.3)	3 (4.8)	3 (4.8)	1 (1.6)	0	0	1 (3.0)	0	0	1 (3.0)	0	0
	Dehydration	脱水	2 (3.2)	0	2 (3.2)	0	0	0	0	0	0	0	0	0
	Dyslipidaemia	脂質異常症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Hyperglycaemia	高血糖	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Hyperkalaemia	高カリウム血症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Hyperlipidaemia	高脂血症	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Hyperuricaemia	高尿酸血症	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	12 (19.4)	7 (11.3)	5 (8.1)	0	0	0	4 (12.1)	3 (9.1)	1 (3.0)	0	0	0
	Arthralgia	関節痛	1 (1.6)	1 (1.6)	0	0	0	0	2 (6.1)	2 (6.1)	0	0	0	0
	Arthritis	関節炎	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Back pain	背部痛	5 (8.1)	3 (4.8)	2 (3.2)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Lumbar spinal stenosis	腰部脊柱管狭窄症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Muscle spasms	筋痙縮	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Muscular weakness	筋力低下	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	2 (3.2)	0	2 (3.2)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pain in extremity	四肢痛	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	5 (8.1)	0	0	5 (8.1)	0	0	3 (9.1)	1 (3.0)	0	2 (6.1)	0	0
	Bladder neoplasm	膀胱新生物	2 (3.2)	0	0	2 (3.2)	0	0	0	0	0	0	0	0
	Colon adenoma	大腸腺腫	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Colon cancer	結腸癌	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Gastric cancer	胃癌	0	0	0	0	0	0	1 (3.0)	0	0	1 (3.0)	0	0
	Lung neoplasm malignant	肺の悪性新生物	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pancreatic carcinoma	膵癌	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (1.6)	0	0	1 (1.6)	0	0	1 (3.0)	0	0	1 (3.0)	0	0
Nervous system disorders	Any	神経系障害	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Cerebral infarction	脳梗塞	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Headache	頭痛	1 (1.6)	1 (1.6)	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Insomnia	不眠症	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	9 (14.5)	3 (4.8)	2 (3.2)	4 (6.5)	0	0	4 (12.1)	2 (6.1)	1 (3.0)	0	1 (3.0)	0
	Haematuria	血尿	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	2 (6.1)	2 (6.1)	0	0	0	0
	Hydronephrosis	水腎症	2 (3.2)	0	0	2 (3.2)	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Proteinuria	蛋白尿	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Renal failure	腎不全	0	0	0	0	0	0	1 (3.0)	0	0	0	1 (3.0)	0
	Renal impairment	腎機能障害	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Urinary retention	尿閉	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0	0
	Balanoposthitis	亀頭包皮炎	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Pelvic pain	骨盤痛	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-7 TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N(%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	6 (9.7)	2 (3.2)	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0
	Asthma	喘息	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Cough	咳嗽	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Pulmonary mass	肺腫瘤	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	9 (14.5)	5 (8.1)	4 (6.5)	0	0	0	6 (18.2)	4 (12.1)	2 (6.1)	0	0	0
	Decubitus ulcer	褥瘡性潰瘍	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Dermal cyst	皮膚嚢腫	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Dermatitis	皮膚炎	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Dry skin	皮膚乾燥	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Eczema	湿疹	0	0	0	0	0	0	2 (6.1)	1 (3.0)	1 (3.0)	0	0	0
	Erythema multiforme	多形紅斑	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Haemorrhage subcutaneous	皮下出血	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Hyperkeratosis	過角化	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pain of skin	皮膚疼痛	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Pruritus	そう痒症	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Rash	発疹	4 (6.5)	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0	0
	Skin ulcer	皮膚潰瘍	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Urticaria	蕁麻疹	1 (1.6)	0	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Vascular disorders	Any	血管障害	6 (9.7)	3 (4.8)	3 (4.8)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Deep vein thrombosis	深部静脈血栓症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Haematoma	血腫	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Hot flush	ほてり	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Hypertension	高血圧	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1 / 5

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		741 (83.1)	208 (23.3)	278 (31.2)	199 (22.3)	20 (2.2)	36 (4.0)	405 (77.7)	126 (24.2)	157 (30.1)	96 (18.4)	8 (1.5)	18 (3.5)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	70 (7.8)	35 (3.9)	23 (2.6)	12 (1.3)	0	0	37 (7.1)	12 (2.3)	18 (3.5)	6 (1.2)	1 (0.2)	0
	Abdominal lymphadenopathy	腹部リンパ節腫脹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Anaemia	貧血	50 (5.6)	32 (3.6)	11 (1.2)	7 (0.8)	0	0	25 (4.8)	10 (1.9)	13 (2.5)	2 (0.4)	0	0
	Basophilia	好塩基球増加症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Eosinophilia	好酸球増加症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Iron deficiency anaemia	鉄欠乏性貧血	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Leukocytosis	白血球増加症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Leukopenia	白血球減少症	7 (0.8)	1 (0.1)	5 (0.6)	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Lymphadenopathy	リンパ節症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	9 (1.0)	3 (0.3)	4 (0.4)	2 (0.2)	0	0	5 (1.0)	1 (0.2)	1 (0.2)	3 (0.6)	0	0
	Nephrogenic anaemia	腎性貧血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	12 (1.3)	2 (0.2)	7 (0.8)	3 (0.3)	0	0	5 (1.0)	1 (0.2)	3 (0.6)	0	1 (0.2)	0
	Retroperitoneal lymphadenopathy	後腹膜リンパ節腫脹	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Splenic calcification	脾臓石灰化	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Thrombocytopenia	血小板減少症	5 (0.6)	3 (0.3)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Cardiac disorders	Any	心臓障害	108 (12.1)	38 (4.3)	26 (2.9)	28 (3.1)	6 (0.7)	10 (1.1)	40 (7.7)	12 (2.3)	15 (2.9)	4 (0.8)	1 (0.2)	8 (1.5)
	Acute coronary syndrome	急性冠動脈症候群	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Acute myocardial infarction	急性心筋梗塞	5 (0.6)	0	0	2 (0.2)	2 (0.2)	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Angina pectoris	狭心症	10 (1.1)	3 (0.3)	5 (0.6)	0	1 (0.1)	1 (0.1)	4 (0.8)	1 (0.2)	3 (0.6)	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Aortic valve disease	大動脈弁疾患	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic valve incompetence	大動脈弁閉鎖不全症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	13 (1.5)	5 (0.6)	7 (0.8)	1 (0.1)	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Arrhythmia supraventricular	上室性不整脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Arteriosclerosis coronary artery	冠動脈硬化症	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Atrial fibrillation	心房細動	22 (2.5)	7 (0.8)	9 (1.0)	5 (0.6)	1 (0.1)	0	8 (1.5)	2 (0.4)	4 (0.8)	1 (0.2)	1 (0.2)	0
	Atrial flutter	心房粗動	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Atrioventricular block	房室ブロック	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block first degree	第一度房室ブロック	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	10 (1.1)	6 (0.7)	3 (0.3)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bundle branch block left	左脚ブロック	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bundle branch block right	右脚ブロック	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiac aneurysm	心臓瘤	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cardiac arrest	心停止	2 (0.2)	0	0	0	0	2 (0.2)	3 (0.6)	0	0	0	0	3 (0.6)
	Cardiac disorder	心障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure	心不全	12 (1.3)	3 (0.3)	4 (0.4)	1 (0.1)	1 (0.1)	3 (0.3)	5 (1.0)	0	2 (0.4)	0	0	3 (0.6)
	Cardiac failure acute	急性心不全	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure chronic	慢性心不全	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Cardiac failure congestive	うっ血性心不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cardiac flutter	心粗動	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiac steatosis	心臓脂肪症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cardiogenic shock	心原性ショック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cardiovascular insufficiency	心血管不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Coronary artery disease	冠動脈疾患	10 (1.1)	2 (0.2)	2 (0.2)	5 (0.6)	0	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery stenosis	冠動脈狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Defect conduction intraventricular	心室内伝導障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Extrasystoles	期外収縮	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Left atrial enlargement	左房拡大	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Left ventricular dilatation	左室拡張	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mitral valve incompetence	僧帽弁閉鎖不全症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Myocardial infarction	心筋梗塞	6 (0.7)	2 (0.2)	0	3 (0.3)	1 (0.1)	0	3 (0.6)	1 (0.2)	0	1 (0.2)	0	1 (0.2)
	Myocardial ischaemia	心筋虚血	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Palpitations	動悸	6 (0.7)	5 (0.6)	0	1 (0.1)	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Sinus arrhythmia	洞性不整脈	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Sinus bradycardia	洞性徐脈	4 (0.4)	1 (0.1)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Supraventricular extrasystoles	上室性期外収縮	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Tachycardia	頻脈	5 (0.6)	3 (0.3)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Tachycardia paroxysmal	発作性頻脈	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Tricuspid valve disease	三尖弁疾患	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ventricular extrasystoles	心室性期外収縮	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ventricular fibrillation	心室細動	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ventricular tachycardia	心室性頻脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Congenital, familial and genetic disorders	Any	先天性、家族性および遺伝性障害	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Congenital renal cyst	先天性腎嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Phimosis	包茎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	14 (1.6)	10 (1.1)	4 (0.4)	0	0	0	9 (1.7)	8 (1.5)	1 (0.2)	0	0	0
	External ear disorder	外耳障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypoacusis	聴力低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Otorrhoea	耳漏	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Tinnitus	耳鳴	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	8 (0.9)	5 (0.6)	3 (0.3)	0	0	0	8 (1.5)	7 (1.3)	1 (0.2)	0	0	0
	Vertigo positional	頭位性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Endocrine disorders	Any	内分泌障害	9 (1.0)	6 (0.7)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Adrenal calcification	副腎石灰化	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Adrenomegaly	副腎肥大	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Basedow's disease	バセドウ病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyperthyroidism	甲状腺機能亢進症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hypothyroidism	甲状腺機能低下症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Thyroid calcification	甲状腺石灰化	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thyroid mass	甲状腺腫瘤	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
Eye disorders	Any	眼障害	17 (1.9)	11 (1.2)	2 (0.2)	4 (0.4)	0	0	16 (3.1)	7 (1.3)	4 (0.8)	5 (1.0)	0	0
	Blepharitis	眼瞼炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Blindness	失明	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Blindness unilateral	片側失明	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cataract	白内障	4 (0.4)	1 (0.1)	1 (0.1)	2 (0.2)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Conjunctival haemorrhage	結膜出血	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Conjunctivitis allergic	アレルギー性結膜炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Diplopia	複視	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dry eye	眼乾燥	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Eye inflammation	眼の炎症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Eye irritation	眼刺激	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Eye pain	眼痛	0	0	0	0	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Eyelid ptosis	眼瞼下垂	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Glaucoma	緑内障	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Lacrimation increased	流涙増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Macular degeneration	黄斑変性	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Ocular hyperaemia	眼充血	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Periorbital oedema	眼窩周囲浮腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Retinal detachment	網膜剥離	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vision blurred	霧視	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Visual acuity reduced	視力低下	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Visual impairment	視力障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vitreous floaters	硝子体浮遊物	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Gastrointestinal disorders	Any	胃腸障害	255 (28.6)	158 (17.7)	75 (8.4)	16 (1.8)	4 (0.4)	2 (0.2)	133 (25.5)	82 (15.7)	41 (7.9)	10 (1.9)	0	0
	Abdominal discomfort	腹部不快感	5 (0.6)	3 (0.3)	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Abdominal distension	腹部膨満	11 (1.2)	10 (1.1)	1 (0.1)	0	0	0	3 (0.6)	2 (0.4)	1 (0.2)	0	0	0
	Abdominal hernia	腹部ヘルニア	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Abdominal pain	腹痛	24 (2.7)	11 (1.2)	12 (1.3)	0	1 (0.1)	0	12 (2.3)	7 (1.3)	4 (0.8)	1 (0.2)	0	0
	Abdominal pain lower	下腹部痛	5 (0.6)	1 (0.1)	4 (0.4)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Abdominal pain upper	上腹部痛	12 (1.3)	6 (0.7)	5 (0.6)	1 (0.1)	0	0	13 (2.5)	9 (1.7)	3 (0.6)	1 (0.2)	0	0
	Abdominal tenderness	腹部圧痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Anal haemorrhage	肛門出血	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Anal incontinence	肛門失禁	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Anorectal discomfort	肛門直腸不快感	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Ascites	腹水	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Barrett's oesophagus	バレット食道	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Bowel movement irregularity	便通不規則	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breath odour	呼気臭	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Chronic gastritis	慢性胃炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colitis	大腸炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Constipation	便秘	52 (5.8)	28 (3.1)	24 (2.7)	0	0	0	33 (6.3)	25 (4.8)	8 (1.5)	0	0	0
	Crohn's disease	クローン病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dental caries	齲歯	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Diaphragmatic hernia	横隔膜ヘルニア	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Diarrhoea	下痢	63 (7.1)	46 (5.2)	16 (1.8)	0	0	1 (0.1)	27 (5.2)	19 (3.6)	8 (1.5)	0	0	0
	Diverticulum	憩室	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Diverticulum intestinal	腸憩室	10 (1.1)	9 (1.0)	1 (0.1)	0	0	0	6 (1.2)	6 (1.2)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Diverticulum oesophageal	食道憩室	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dry mouth	口内乾燥	10 (1.1)	10 (1.1)	0	0	0	0	5 (1.0)	4 (0.8)	1 (0.2)	0	0	0
	Duodenal ulcer	十二指腸潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dyspepsia	消化不良	9 (1.0)	7 (0.8)	2 (0.2)	0	0	0	7 (1.3)	5 (1.0)	2 (0.4)	0	0	0
	Dysphagia	嚥下障害	3 (0.3)	3 (0.3)	0	0	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Epigastric discomfort	心窩部不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Eructation	おくび	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Faeces hard	硬便	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Flatulence	鼓腸	4 (0.4)	4 (0.4)	0	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Food poisoning	食中毒	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Frequent bowel movements	排便回数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastric disorder	胃障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastric polyps	胃ポリープ	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastric ulcer	胃潰瘍	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gastritis	胃炎	2 (0.2)	2 (0.2)	0	0	0	0	5 (1.0)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Gastritis erosive	びらん性胃炎	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Gastroduodenitis	胃十二指腸炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal angiectasia	胃腸血管拡張症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastrointestinal inflammation	胃腸の炎症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Gastrointestinal wall thickening	消化管壁肥厚	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	11 (1.2)	6 (0.7)	4 (0.4)	1 (0.1)	0	0	4 (0.8)	1 (0.2)	3 (0.6)	0	0	0
	Gingival discomfort	歯肉不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gingival pain	歯肉痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Glossitis	舌炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematochezia	血便排泄	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Haemorrhoidal haemorrhage	痔出血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haemorrhoids	痔核	6 (0.7)	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Hiatus hernia	裂孔ヘルニア	5 (0.6)	5 (0.6)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ileus	イレウス	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Impaired gastric emptying	胃排出不全	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	10 (1.1)	7 (0.8)	2 (0.2)	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4)	0	0	4 (0.4)	0	0	0	0	0	0	0	0
	Intra-abdominal haematoma	腹腔内血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Irritable bowel syndrome	過敏性腸症候群	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Jejunal stenosis	空腸狭窄	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Large intestinal stenosis	大腸狭窄	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Large intestine perforation	大腸穿孔	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lip disorder	口唇障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lip pain	口唇痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Melaena	メレナ	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Mesenteric artery stenosis	腸間膜動脈狭窄	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mesenteric panniculitis	腸間膜脂肪織炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Nausea	悪心	44 (4.9)	37 (4.1)	5 (0.6)	2 (0.2)	0	0	32 (6.1)	22 (4.2)	10 (1.9)	0	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oesophageal pain	食道痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oesophagitis	食道炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pancreatic atrophy	膵萎縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pancreatic calcification	膵石灰化	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pancreatic cyst	膵嚢胞	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatic duct dilatation	膵管拡張	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatic steatosis	膵脂肪変性	6 (0.7)	6 (0.7)	0	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Pancreatitis	膵炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pancreatitis chronic	慢性膵炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Paraesthesia oral	口の錯感覚	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Parotid duct obstruction	耳下腺管閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peptic ulcer	消化性潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Periodontal disease	歯周病	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Proctalgia	肛門周囲痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Proctitis	直腸炎	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	7 (0.8)	6 (0.7)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Rectal stenosis	直腸狭窄	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Salivary gland pain	唾液腺痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Small intestinal obstruction	小腸閉塞	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Splenic artery aneurysm	脾臓動脈瘤	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Stomatitis	口内炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tongue coated	舌苔	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Toothache	歯痛	7 (0.8)	4 (0.4)	3 (0.3)	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Umbilical hernia	臍ヘルニア	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Upper gastrointestinal haemorrhage	上部消化管出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Vomiting	嘔吐	14 (1.6)	10 (1.1)	3 (0.3)	1 (0.1)	0	0	10 (1.9)	4 (0.8)	5 (1.0)	1 (0.2)	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	230 (25.8)	142 (15.9)	67 (7.5)	13 (1.5)	0	8 (0.9)	100 (19.2)	73 (14.0)	21 (4.0)	5 (1.0)	0	1 (0.2)
	Asthenia	無力症	36 (4.0)	21 (2.4)	13 (1.5)	2 (0.2)	0	0	19 (3.6)	13 (2.5)	4 (0.8)	2 (0.4)	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Catheter site related reaction	カテーテル留置部位関連反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Catheter site ulcer	カテーテル留置部位潰瘍	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Chest pain	胸痛	14 (1.6)	6 (0.7)	8 (0.9)	0	0	0	7 (1.3)	5 (1.0)	2 (0.4)	0	0	0
	Chills	悪寒	8 (0.9)	7 (0.8)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Cyst	嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Death	死亡	4 (0.4)	0	0	0	0	4 (0.4)	1 (0.2)	0	0	0	0	1 (0.2)
	Discomfort	不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Exercise tolerance decreased	運動耐性低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	113 (12.7)	79 (8.9)	30 (3.4)	4 (0.4)	0	0	47 (9.0)	36 (6.9)	7 (1.3)	4 (0.8)	0	0
	Feeling cold	冷感	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gait disturbance	歩行障害	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	General physical health deterioration	全身健康状態低下	5 (0.6)	0	1 (0.1)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0
	Granuloma	肉芽腫	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Influenza like illness	インフルエンザ様疾患	10 (1.1)	6 (0.7)	4 (0.4)	0	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Infusion site extravasation	注入部位血管外漏出	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Injection site bruising	注射部位内出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Injection site erythema	注射部位紅斑	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Injection site pain	注射部位疼痛	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	3 (0.6)	2 (0.4)	0	1 (0.2)	0	0
	Nodule	小結節	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Non-cardiac chest pain	非心臓性胸痛	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oedema	浮腫	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oedema peripheral	末梢性浮腫	38 (4.3)	32 (3.6)	6 (0.7)	0	0	0	16 (3.1)	11 (2.1)	5 (1.0)	0	0	0
	Pain	疼痛	4 (0.4)	0	4 (0.4)	0	0	0	5 (1.0)	4 (0.8)	1 (0.2)	0	0	0
	Pelvic mass	骨盤腔内腫瘤	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Performance status decreased	活動状態低下	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral swelling	末梢腫脹	13 (1.5)	8 (0.9)	4 (0.4)	1 (0.1)	0	0	7 (1.3)	4 (0.8)	3 (0.6)	0	0	0
	Pyrexia	発熱	15 (1.7)	11 (1.2)	3 (0.3)	1 (0.1)	0	0	5 (1.0)	3 (0.6)	2 (0.4)	0	0	0
	Sudden cardiac death	心突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Sudden death	突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Suprapubic pain	恥骨上痛	1 (0.1)	0	0	1 (0.1)	0	0	3 (0.6)	2 (0.4)	1 (0.2)	0	0	0
	Temperature intolerance	温度変化不耐症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thirst	口渇	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	26 (2.9)	18 (2.0)	3 (0.3)	4 (0.4)	0	1 (0.1)	9 (1.7)	6 (1.2)	0	3 (0.6)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Biliary colic	胆道仙痛	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cholangitis acute	急性胆管炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis chronic	慢性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholelithiasis	胆石症	7 (0.8)	6 (0.7)	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholestasis	胆汁うっ滞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hepatic artery thrombosis	肝動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hepatic calcification	肝石灰化	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Hepatic cyst	肝嚢胞	7 (0.8)	7 (0.8)	0	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Hepatic steatosis	脂肪肝	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperbilirubinaemia	高ビリルビン血症	6 (0.7)	4 (0.4)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Jaundice	黄疸	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Liver disorder	肝障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Immune system disorders	Any	免疫系障害	12 (1.3)	5 (0.6)	7 (0.8)	0	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Allergy to arthropod sting	節足動物刺傷アレルギー	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Anaphylactic reaction	アナフィラキシー反応	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Contrast media allergy	造影剤アレルギー	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Contrast media reaction	造影剤反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Drug hypersensitivity	薬物過敏症	3 (0.3)	0	3 (0.3)	0	0	0	0	0	0	0	0	0
	Hypersensitivity	過敏症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Immune system disorder	免疫系障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Seasonal allergy	季節性アレルギー	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	205 (23.0)	58 (6.5)	111 (12.4)	28 (3.1)	4 (0.4)	4 (0.4)	111 (21.3)	40 (7.7)	55 (10.6)	14 (2.7)	1 (0.2)	1 (0.2)
	Abdominal abscess	腹部膿瘍	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Abscess intestinal	腸管膿瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Acarodermatitis	ダニ皮膚炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Acute endocarditis	急性心内膜炎	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Acute sinusitis	急性副鼻腔炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Appendicitis	虫垂炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacterial infection	細菌感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacteriuria	細菌尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Balanitis candida	カンジダ性亀頭炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balanoposthitis infective	感染性亀頭包皮炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bronchitis	気管支炎	10 (1.1)	1 (0.1)	9 (1.0)	0	0	0	9 (1.7)	1 (0.2)	8 (1.5)	0	0	0
	Catheter site infection	カテーテル留置部位感染	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cellulitis	蜂巣炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conjunctivitis	結膜炎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cystitis	膀胱炎	7 (0.8)	3 (0.3)	4 (0.4)	0	0	0	7 (1.3)	4 (0.8)	3 (0.6)	0	0	0
	Device related infection	医療機器関連感染	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ear infection	耳感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ear infection bacterial	細菌性耳感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Erysipelas	丹毒	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Eye infection bacterial	細菌性眼感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Febrile infection	熱性感染症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Folliculitis	毛包炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Fungal balanitis	真菌性亀頭炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Fungal skin infection	皮膚真菌感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gangrene	壊疽	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastroenteritis	胃腸炎	5 (0.6)	1 (0.1)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gastroenteritis viral	ウイルス性胃腸炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gastrointestinal infection	消化管感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Genital infection fungal	真菌性性器感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gingivitis	歯肉炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Helicobacter gastritis	ヘリコバクター性胃炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Helicobacter infection	ヘリコバクター感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hepatitis C	Ｃ型肝炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Herpes zoster	帯状疱疹	4 (0.4)	0	4 (0.4)	0	0	0	4 (0.8)	2 (0.4)	2 (0.4)	0	0	0
	Infected bite	咬傷感染	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Infection	感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Infectious mononucleosis	伝染性単核症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Infestation	寄生	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Influenza	インフルエンザ	23 (2.6)	18 (2.0)	4 (0.4)	0	1 (0.1)	0	9 (1.7)	5 (1.0)	4 (0.8)	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Labyrinthitis	迷路炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Laryngitis	喉頭炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Localised infection	限局性感染	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower respiratory tract infection	下気道感染	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lung infection	肺感染	3 (0.3)	1 (0.1)	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Meningitis bacterial	細菌性髄膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Nasopharyngitis	上咽頭炎	24 (2.7)	13 (1.5)	11 (1.2)	0	0	0	17 (3.3)	14 (2.7)	3 (0.6)	0	0	0
	Oesophageal candidiasis	食道カンジダ症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Onychomycosis	爪真菌症	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Oral candidiasis	口腔カンジダ症	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Oral herpes	口腔ヘルペス	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Orchitis	精巣炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Otitis externa	外耳炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Otitis media	中耳炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Paronychia	爪囲炎	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Periodontitis	歯周炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Peritonitis	腹膜炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pharyngitis	咽頭炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pneumonia	肺炎	18 (2.0)	0	9 (1.0)	7 (0.8)	1 (0.1)	1 (0.1)	11 (2.1)	2 (0.4)	5 (1.0)	3 (0.6)	1 (0.2)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostate infection	前立腺感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pulmonary tuberculosis	肺結核	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pulpitis dental	歯髄炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pyelonephritis	腎盂腎炎	3 (0.3)	0	0	3 (0.3)	0	0	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pyelonephritis chronic	慢性腎盂腎炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pyuria	膿尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash pustular	膿疱性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Respiratory syncytial virus infection	ＲＳウイルス感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Respiratory tract infection	気道感染	6 (0.7)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0
	Respiratory tract infection viral	ウイルス性気道感染	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	5 (1.0)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Rhinitis	鼻炎	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	6 (1.2)	4 (0.8)	2 (0.4)	0	0	0
	Root canal infection	根管感染	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Sepsis	敗血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sinusitis	副鼻腔炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	4 (0.8)	2 (0.4)	2 (0.4)	0	0	0
	Skin infection	皮膚感染	3 (0.3)	0	3 (0.3)	0	0	0	0	0	0	0	0	0
	Subcutaneous abscess	皮下組織膿瘍	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tinea infection	白癬感染	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

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System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Tooth abscess	歯膿瘍	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Tooth infection	歯感染	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tracheitis	気管炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Tracheobronchitis	気管気管支炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Upper respiratory tract infection	上気道感染	20 (2.2)	4 (0.4)	16 (1.8)	0	0	0	6 (1.2)	2 (0.4)	4 (0.8)	0	0	0
	Urinary tract infection	尿路感染	46 (5.2)	6 (0.7)	34 (3.8)	6 (0.7)	0	0	27 (5.2)	9 (1.7)	16 (3.1)	2 (0.4)	0	0
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urosepsis	尿路性敗血症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Vestibular neuronitis	前庭神経炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Viral infection	ウイルス感染	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Viral upper respiratory tract infection	ウイルス性上気道感染	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	103 (11.5)	44 (4.9)	42 (4.7)	14 (1.6)	0	3 (0.3)	42 (8.1)	14 (2.7)	18 (3.5)	10 (1.9)	0	0
	Accident	事故	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Anaemia postoperative	術後貧血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Animal bite	動物咬傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Ankle fracture	足関節部骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arthropod bite	節足動物咬傷	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Auricular haematoma	耳介血腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Back injury	背部損傷	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bone contusion	骨挫傷	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Chest injury	胸部損傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Clavicle fracture	鎖骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Contusion	挫傷	9 (1.0)	7 (0.8)	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cystitis radiation	放射線性膀胱炎	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Eyelid injury	眼瞼損傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Face injury	顔面損傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Facial bones fracture	顔面骨骨折	0	0	0	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Fall	転倒	28 (3.1)	8 (0.9)	13 (1.5)	7 (0.8)	0	0	22 (4.2)	8 (1.5)	10 (1.9)	4 (0.8)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fibula fracture	腓骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Foot fracture	足骨折	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fracture	骨折	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Frostbite	凍傷	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Haematuria traumatic	外傷性血尿	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hand fracture	手骨折	3 (0.3)	0	3 (0.3)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Head injury	頭部損傷	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Heart injury	心臓損傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Humerus fracture	上腕骨骨折	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Incision site pain	切開部位痛	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Injury	損傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Injury of conjunctiva	結膜損傷	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Joint dislocation	関節脱臼	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Joint injury	関節損傷	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Laceration	裂傷	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ligament injury	靭帯損傷	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ligament sprain	靭帯捻挫	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Limb injury	四肢損傷	7 (0.8)	5 (0.6)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Lumbar vertebral fracture	腰椎骨折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Meniscus injury	半月板損傷	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Multiple injuries	多発性外傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Muscle strain	肉離れ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Post-traumatic pain	外傷後疼痛	5 (0.6)	3 (0.3)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Procedural pain	処置による疼痛	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Radiation proctitis	放射線性直腸炎	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Radius fracture	橈骨骨折	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rib fracture	肋骨骨折	9 (1.0)	5 (0.6)	4 (0.4)	0	0	0	8 (1.5)	2 (0.4)	6 (1.2)	0	0	0
	Road traffic accident	交通事故	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Scapula fracture	肩甲骨骨折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Scratch	引っかき傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin abrasion	皮膚擦過傷	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Soft tissue injury	軟部組織損傷	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Spinal compression fracture	脊椎圧迫骨折	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Spinal fracture	脊椎骨折	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Subcutaneous haematoma	皮下血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Subdural haematoma	硬膜下血腫	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Sunburn	サンバーン	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Thermal burn	熱傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Tooth fracture	歯牙破折	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Traumatic fracture	外傷性骨折	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Traumatic haematoma	外傷性血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ulna fracture	尺骨骨折	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Upper limb fracture	上肢骨折	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Vascular graft complication	移植血管合併症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Wound dehiscence	創離開	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Wrist fracture	手首関節骨折	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	135 (15.1)	66 (7.4)	52 (5.8)	16 (1.8)	1 (0.1)	0	61 (11.7)	36 (6.9)	20 (3.8)	4 (0.8)	1 (0.2)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	5 (0.6)	3 (0.3)	0	2 (0.2)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Arteriogram coronary	冠血管造影	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	10 (1.1)	6 (0.7)	1 (0.1)	3 (0.3)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.6)	2 (0.4)	0	1 (0.2)	0	0
	Blood bilirubin increased	血中ビリルビン増加	12 (1.3)	7 (0.8)	4 (0.4)	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Blood cholesterol increased	血中コレステロール増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood chromogranin A increased	血中クロモグラニンA増加	6 (0.7)	3 (0.3)	3 (0.3)	0	0	0	6 (1.2)	4 (0.8)	1 (0.2)	1 (0.2)	0	0
	Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	21 (2.4)	8 (0.9)	12 (1.3)	1 (0.1)	0	0	13 (2.5)	5 (1.0)	7 (1.3)	0	1 (0.2)	0
	Blood glucose increased	血中ブドウ糖増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	5 (0.6)	5 (0.6)	0	0	0	0	0	0	0	0	0	0
	Blood potassium decreased	血中カリウム減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood potassium increased	血中カリウム増加	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Blood pressure increased	血圧上昇	4 (0.4)	0	3 (0.3)	1 (0.1)	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Blood pressure systolic increased	収縮期血圧上昇	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Blood sodium decreased	血中ナトリウム減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood testosterone increased	血中テストステロン増加	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blood urea abnormal	血中尿素異常	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Blood urea increased	血中尿素増加	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Blood uric acid increased	血中尿酸増加	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Body temperature increased	体温上昇	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Breath sounds abnormal	呼吸音異常	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cardiac murmur	心雑音	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Carotid bruit	頚動脈雑音	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Chest X-ray abnormal	胸部Ｘ線異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Electrocardiogram QT prolonged	心電図ＱＴ延長	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Electrocardiogram ST segment depression	心電図ＳＴ部分下降	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastric pH decreased	胃内ｐＨ低下	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Glomerular filtration rate decreased	糸球体濾過率減少	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Glomerular filtration rate increased	糸球体濾過率増加	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Glucose urine present	尿中ブドウ糖陽性	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haematocrit decreased	ヘマトクリット減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematology test abnormal	血液学的検査異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haemoglobin decreased	ヘモグロビン減少	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Heart rate increased	心拍数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Heart rate irregular	心拍数不整	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Heart sounds abnormal	心音異常	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Lymphocyte count decreased	リンパ球数減少	8 (0.9)	3 (0.3)	5 (0.6)	0	0	0	0	0	0	0	0	0
	Lymphocyte count increased	リンパ球数増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	10 (1.1)	1 (0.1)	3 (0.3)	5 (0.6)	1 (0.1)	0	0	0	0	0	0	0
	Neutrophil count increased	好中球数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	6 (0.7)	6 (0.7)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Protein total decreased	総蛋白減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Protein urine present	尿中蛋白陽性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Red blood cell count decreased	赤血球数減少	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Transaminases increased	トランスアミナーゼ上昇	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Troponin increased	トロポニン増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urine output decreased	尿量減少	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Vitamin B12 decreased	ビタミンＢ１２減少	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Weight decreased	体重減少	31 (3.5)	20 (2.2)	11 (1.2)	0	0	0	12 (2.3)	10 (1.9)	2 (0.4)	0	0	0
	Weight increased	体重増加	14 (1.6)	11 (1.2)	3 (0.3)	0	0	0	6 (1.2)	2 (0.4)	4 (0.8)	0	0	0
	White blood cell count decreased	白血球数減少	6 (0.7)	1 (0.1)	5 (0.6)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	White blood cells urine positive	尿中白血球陽性	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Metabolism and nutrition disorders	Any	筋骨格系および結合組織障害	85 (9.5)	31 (3.5)	32 (3.6)	18 (2.0)	4 (0.4)	0	47 (9.0)	23 (4.4)	15 (2.9)	9 (1.7)	0	0
	Cachexia	悪液質	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Decreased appetite	食欲減退	21 (2.4)	14 (1.6)	6 (0.7)	1 (0.1)	0	0	15 (2.9)	12 (2.3)	3 (0.6)	0	0	0
	Dehydration	脱水	4 (0.4)	0	1 (0.1)	2 (0.2)	1 (0.1)	0	4 (0.8)	1 (0.2)	2 (0.4)	1 (0.2)	0	0
	Diabetes mellitus	糖尿病	5 (0.6)	0	3 (0.3)	2 (0.2)	0	0	5 (1.0)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Diabetes mellitus inadequate control	コントロール不良の糖尿病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Diabetic metabolic decompensation	糖尿病性代謝代償不全	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dyslipidaemia	脂質異常症	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Electrolyte imbalance	電解質失調	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Folate deficiency	葉酸欠乏	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gout	痛風	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Hypercholesterolaemia	高コレステロール血症	3 (0.3)	3 (0.3)	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Hyperglycaemia	高血糖	8 (0.9)	0	4 (0.4)	2 (0.2)	2 (0.2)	0	3 (0.6)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	15 (1.7)	4 (0.4)	7 (0.8)	3 (0.3)	1 (0.1)	0	9 (1.7)	2 (0.4)	4 (0.8)	3 (0.6)	0	0
	Hyperlipidaemia	高脂血症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypernatraemia	高ナトリウム血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Hypertriglyceridaemia	高トリグリセリド血症	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Hyperuricaemia	高尿酸血症	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hypocalcaemia	低カルシウム血症	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Hypochloraemia	低クロール血症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hypoglycaemia	低血糖	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	9 (1.0)	3 (0.3)	4 (0.4)	2 (0.2)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Hypomagnesaemia	低マグネシウム血症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyponatraemia	低ナトリウム血症	7 (0.8)	2 (0.2)	2 (0.2)	3 (0.3)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Hypoproteinaemia	低蛋白血症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Increased appetite	食欲亢進	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Iron deficiency	鉄欠乏	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Magnesium deficiency	マグネシウム欠乏	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Malnutrition	栄養障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Metabolic alkalosis	代謝性アルカローシス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Obesity	肥満	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Type 2 diabetes mellitus	２型糖尿病	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vitamin D deficiency	ビタミンＤ欠乏	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	258 (28.9)	143 (16.0)	97 (10.9)	18 (2.0)	0	0	131 (25.1)	76 (14.6)	49 (9.4)	6 (1.2)	0	0
	Arthralgia	関節痛	76 (8.5)	47 (5.3)	26 (2.9)	3 (0.3)	0	0	49 (9.4)	37 (7.1)	10 (1.9)	2 (0.4)	0	0
	Arthritis	関節炎	6 (0.7)	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Axillary mass	腋窩腫瘤	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Back pain	背部痛	79 (8.9)	41 (4.6)	34 (3.8)	4 (0.4)	0	0	49 (9.4)	29 (5.6)	19 (3.6)	1 (0.2)	0	0
	Bone lesion	骨病変	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bone pain	骨痛	9 (1.0)	4 (0.4)	4 (0.4)	1 (0.1)	0	0	6 (1.2)	2 (0.4)	4 (0.8)	0	0	0
	Bursitis	滑液包炎	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Coccydynia	尾骨痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dupuytren's contracture	デュプイトラン拘縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Exostosis	外骨腫	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Extremity contracture	四肢拘縮	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Flank pain	側腹部痛	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Groin pain	鼠径部痛	7 (0.8)	5 (0.6)	2 (0.2)	0	0	0	5 (1.0)	5 (1.0)	0	0	0	0
	Hand deformity	手変形	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Intervertebral disc protrusion	椎間板突出	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Joint range of motion decreased	関節可動域低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Joint stiffness	関節硬直	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Joint swelling	関節腫脹	4 (0.4)	4 (0.4)	0	0	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Limb discomfort	四肢不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lumbar spinal stenosis	腰部脊柱管狭窄症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Metatarsalgia	中足骨痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Mobility decreased	運動性低下	3 (0.3)	0	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0
	Muscle spasms	筋痙縮	16 (1.8)	10 (1.1)	6 (0.7)	0	0	0	3 (0.6)	2 (0.4)	1 (0.2)	0	0	0
	Muscular weakness	筋力低下	9 (1.0)	7 (0.8)	2 (0.2)	0	0	0	5 (1.0)	2 (0.4)	2 (0.4)	1 (0.2)	0	0
	Musculoskeletal chest pain	筋骨格系胸痛	10 (1.1)	5 (0.6)	4 (0.4)	1 (0.1)	0	0	6 (1.2)	5 (1.0)	1 (0.2)	0	0	0
	Musculoskeletal discomfort	筋骨格不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	35 (3.9)	20 (2.2)	14 (1.6)	1 (0.1)	0	0	10 (1.9)	7 (1.3)	2 (0.4)	1 (0.2)	0	0
	Musculoskeletal stiffness	筋骨格硬直	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Myalgia	筋肉痛	16 (1.8)	12 (1.3)	2 (0.2)	2 (0.2)	0	0	6 (1.2)	6 (1.2)	0	0	0	0
	Neck pain	頚部痛	9 (1.0)	6 (0.7)	3 (0.3)	0	0	0	6 (1.2)	5 (1.0)	1 (0.2)	0	0	0
	Osteitis	骨炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteitis deformans	変形性骨炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	15 (1.7)	5 (0.6)	5 (0.6)	5 (0.6)	0	0	3 (0.6)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Osteochondrosis	骨端症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Osteopenia	骨減少症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Osteoporosis	骨粗鬆症	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pain in extremity	四肢痛	53 (5.9)	38 (4.3)	15 (1.7)	0	0	0	18 (3.5)	9 (1.7)	8 (1.5)	1 (0.2)	0	0
	Pathological fracture	病的骨折	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Plantar fasciitis	足底筋膜炎	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Polymyalgia rheumatica	リウマチ性多発筋痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rheumatic disorder	リウマチ性障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Spinal column stenosis	脊柱管狭窄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Spinal deformity	脊柱変形	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Spinal fusion acquired	後天性脊椎癒合	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Spinal osteoarthritis	変形性脊椎症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Spinal pain	脊椎痛	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Tendon disorder	腱障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tendonitis	腱炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Trigger finger	弾発指	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	43 (4.8)	10 (1.1)	14 (1.6)	15 (1.7)	2 (0.2)	2 (0.2)	23 (4.4)	6 (1.2)	9 (1.7)	7 (1.3)	0	1 (0.2)
	Acute leukaemia	急性白血病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Adenocarcinoma	腺癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Adrenal adenoma	副腎腺腫	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Basal cell carcinoma	基底細胞癌	5 (0.6)	2 (0.2)	3 (0.3)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Benign lung neoplasm	肺の良性新生物	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder cancer	膀胱癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Bladder neoplasm	膀胱新生物	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Bowen's disease	ボーエン病	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Cancer pain	癌疼痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carcinoid tumour	カルチノイド腫瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Choroid melanoma	脈絡膜黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colon cancer	結腸癌	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Colon neoplasm	結腸新生物	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Gastric adenoma	胃腺腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Gastric cancer	胃癌	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Gastrointestinal adenocarcinoma	消化器腺癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Intestinal angioma	腸血管腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lipoma	脂肪腫	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Lung adenocarcinoma stage IV	肺腺癌第４期	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lymphangiosis carcinomatosa	癌性リンパ管症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lymphoma	リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Malignant melanoma in situ	表皮内悪性黒色腫	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Melanocytic naevus	メラノサイト性母斑	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Mesothelioma	中皮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Metastases to peritoneum	腹膜転移	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma	膵癌	2 (0.2)	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma recurrent	再発膵癌	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pancreatic neoplasm	膵新生物	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	0	1 (0.2)
	Prostate cancer metastatic	遠隔転移を伴う前立腺癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Prostate cancer recurrent	再発前立腺癌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal adenocarcinoma	直腸腺癌	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Renal cancer	腎癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Salivary gland neoplasm	唾液腺新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Seborrhoeic keratosis	脂漏性角化症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin papilloma	皮膚乳頭腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Small cell lung cancer limited stage	限局型小細胞肺癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Squamous cell carcinoma of skin	皮膚有棘細胞癌	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

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	Thymoma	胸腺腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Thyroid adenoma	甲状腺腺腫	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Tumour compression	腫瘍性圧迫	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tumour obstruction	腫瘍性閉塞	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Tumour pain	腫瘍疼痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract neoplasm	尿路新生物	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Nervous system disorders	Any	神経系障害	144 (16.1)	75 (8.4)	49 (5.5)	16 (1.8)	2 (0.2)	2 (0.2)	73 (14.0)	38 (7.3)	20 (3.8)	11 (2.1)	0	4 (0.8)
	Amnesia	健忘	1 (0.1)	1 (0.1)	0	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Autonomic nervous system imbalance	自律神経失調	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Axonal neuropathy	軸索型ニューロパチー	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balance disorder	平衡障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Brain oedema	脳浮腫	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Bulbar palsy	球麻痺	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid arteriosclerosis	頚動脈硬化症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid artery stenosis	頚動脈狭窄	3 (0.3)	1 (0.1)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Carpal tunnel syndrome	手根管症候群	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Cerebral arteriosclerosis	脳動脈硬化症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cerebral atrophy	大脳萎縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cerebrovascular accident	脳血管発作	2 (0.2)	0	0	2 (0.2)	0	0	4 (0.8)	1 (0.2)	0	2 (0.4)	0	1 (0.2)
	Cervicogenic vertigo	頚原性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Cognitive disorder	認知障害	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dementia	認知症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Dementia Alzheimer's type	アルツハイマー型認知症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Depressed level of consciousness	意識レベルの低下	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0

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	Disturbance in attention	注意力障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dizziness	浮動性めまい	35 (3.9)	23 (2.6)	10 (1.1)	2 (0.2)	0	0	14 (2.7)	12 (2.3)	1 (0.2)	1 (0.2)	0	0
	Dysaesthesia	異常感覚	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Dysarthria	構語障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Dysgeusia	味覚異常	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Encephalopathy	脳症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Essential tremor	本態性振戦	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Headache	頭痛	36 (4.0)	23 (2.6)	13 (1.5)	0	0	0	13 (2.5)	7 (1.3)	5 (1.0)	1 (0.2)	0	0
	Hypersomnia	過眠症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypoaesthesia	感覚鈍麻	6 (0.7)	4 (0.4)	2 (0.2)	0	0	0	5 (1.0)	3 (0.6)	1 (0.2)	1 (0.2)	0	0
	Hyposmia	嗅覚減退	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypotonia	筋緊張低下	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	IVth nerve paralysis	第４脳神経麻痺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Intercostal neuralgia	肋間神経痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ischaemic stroke	虚血性脳卒中	5 (0.6)	0	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Lethargy	嗜眠	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Loss of consciousness	意識消失	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Lumbar radiculopathy	腰髄神経根障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lumbosacral radiculopathy	腰仙部神経根障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Memory impairment	記憶障害	5 (0.6)	5 (0.6)	0	0	0	0	7 (1.3)	7 (1.3)	0	0	0	0
	Myelopathy	脊髄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neuralgia	神経痛	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Neuropathy peripheral	末梢性ニューロパチー	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Paraesthesia	錯感覚	6 (0.7)	5 (0.6)	1 (0.1)	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Parkinson's disease	パーキンソン病	2 (0.2)	0	2 (0.2)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Partial seizures	部分発作	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral sensory neuropathy	末梢性感覚ニューロパチー	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Presyncope	失神寸前の状態	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Psychomotor hyperactivity	精神運動亢進	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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	Psychomotor skills impaired	精神運動機能障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Restless legs syndrome	下肢静止不能症候群	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Sacral radiculopathy	仙部神経根症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sciatica	坐骨神経痛	8 (0.9)	1 (0.1)	7 (0.8)	0	0	0	6 (1.2)	0	5 (1.0)	1 (0.2)	0	0
	Seizure	痙攣発作	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Senile dementia	老年認知症	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Somnolence	傾眠	8 (0.9)	7 (0.8)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Speech disorder	会話障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Syncope	失神	4 (0.4)	1 (0.1)	1 (0.1)	2 (0.2)	0	0	3 (0.6)	0	0	3 (0.6)	0	0
	Transient ischaemic attack	一過性脳虚血発作	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tremor	振戦	4 (0.4)	4 (0.4)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Vascular dementia	血管性認知症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vocal cord paresis	声帯不全麻痺	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Product issues	Any	製品の問題	9 (1.0)	3 (0.3)	2 (0.2)	4 (0.4)	0	0	3 (0.6)	0	2 (0.4)	1 (0.2)	0	0
	Device dislocation	医療機器位置異常	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device malfunction	医療機器機能不良	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Device occlusion	医療機器閉塞	5 (0.6)	2 (0.2)	1 (0.1)	2 (0.2)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
Psychiatric disorders	Any	精神障害	56 (6.3)	34 (3.8)	21 (2.4)	1 (0.1)	0	0	27 (5.2)	14 (2.7)	12 (2.3)	1 (0.2)	0	0
	Agitation	激越	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Anxiety	不安	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Claustrophobia	閉所恐怖症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Delirium	譫妄	0	0	0	0	0	0	3 (0.6)	0	3 (0.6)	0	0	0
	Depressed mood	抑うつ気分	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Depression	うつ病	16 (1.8)	9 (1.0)	6 (0.7)	1 (0.1)	0	0	7 (1.3)	3 (0.6)	4 (0.8)	0	0	0
	Disorientation	失見当識	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hallucination, auditory	幻聴	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hallucination, visual	幻視	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Initial insomnia	初期不眠症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Insomnia	不眠症	25 (2.8)	14 (1.6)	11 (1.2)	0	0	0	9 (1.7)	6 (1.2)	2 (0.4)	1 (0.2)	0	0
	Irritability	易刺激性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Mental status changes	精神状態変化	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Middle insomnia	中期不眠症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Mood swings	気分動揺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nervousness	神経過敏	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nightmare	悪夢	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Panic disorder	パニック障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Restlessness	落ち着きのなさ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sleep disorder	睡眠障害	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	189 (21.2)	83 (9.3)	63 (7.1)	41 (4.6)	2 (0.2)	0	136 (26.1)	47 (9.0)	53 (10.2)	32 (6.1)	4 (0.8)	0
	Acute kidney injury	急性腎障害	9 (1.0)	1 (0.1)	3 (0.3)	4 (0.4)	1 (0.1)	0	6 (1.2)	2 (0.4)	2 (0.4)	2 (0.4)	0	0
	Anuria	無尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Azotaemia	高窒素血症	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	1 (0.2)	0
	Bladder disorder	膀胱障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Bladder diverticulum	膀胱憩室	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bladder hypertrophy	膀胱壁肥厚	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder neck obstruction	膀胱頚部閉塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Bladder obstruction	膀胱閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder outlet obstruction	膀胱出口部閉塞	0	0	0	0	0	0	4 (0.8)	0	4 (0.8)	0	0	0
	Bladder spasm	膀胱痙縮	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Calculus bladder	膀胱結石	5 (0.6)	2 (0.2)	2 (0.2)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Calculus urethral	尿道結石	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Calculus urinary	尿路結石	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Chronic kidney disease	慢性腎臓病	9 (1.0)	5 (0.6)	2 (0.2)	2 (0.2)	0	0	5 (1.0)	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	0
	Cystitis noninfective	非感染性膀胱炎	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dysuria	排尿困難	21 (2.4)	9 (1.0)	11 (1.2)	1 (0.1)	0	0	26 (5.0)	11 (2.1)	10 (1.9)	5 (1.0)	0	0
	Glycosuria	糖尿	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Haematuria	血尿	39 (4.4)	21 (2.4)	9 (1.0)	9 (1.0)	0	0	25 (4.8)	8 (1.5)	10 (1.9)	7 (1.3)	0	0
	Hydronephrosis	水腎症	8 (0.9)	2 (0.2)	1 (0.1)	5 (0.6)	0	0	13 (2.5)	5 (1.0)	5 (1.0)	3 (0.6)	0	0
	Hypertonic bladder	緊張性膀胱	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Incontinence	失禁	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Kidney fibrosis	腎線維症	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Leukocyturia	白血球尿	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower urinary tract symptoms	下部尿路症状	6 (0.7)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	5 (1.0)	1 (0.2)	4 (0.8)	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Malignant urinary tract obstruction	悪性尿路閉塞	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Micturition disorder	排尿異常	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Micturition urgency	尿意切迫	9 (1.0)	5 (0.6)	4 (0.4)	0	0	0	3 (0.6)	0	3 (0.6)	0	0	0
	Nephrocalcinosis	腎石灰沈着症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nephrolithiasis	腎結石症	14 (1.6)	10 (1.1)	4 (0.4)	0	0	0	4 (0.8)	2 (0.4)	0	2 (0.4)	0	0
	Nocturia	夜間頻尿	14 (1.6)	12 (1.3)	2 (0.2)	0	0	0	10 (1.9)	8 (1.5)	2 (0.4)	0	0	0
	Oliguria	乏尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	35 (3.9)	23 (2.6)	11 (1.2)	1 (0.1)	0	0	16 (3.1)	10 (1.9)	5 (1.0)	1 (0.2)	0	0
	Polyuria	多尿	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Proteinuria	蛋白尿	9 (1.0)	5 (0.6)	4 (0.4)	0	0	0	5 (1.0)	2 (0.4)	3 (0.6)	0	0	0
	Renal aneurysm	腎動脈瘤	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Renal artery occlusion	腎動脈閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Renal artery stenosis	腎動脈狭窄症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Renal colic	腎仙痛	9 (1.0)	5 (0.6)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal cyst	腎嚢胞	9 (1.0)	9 (1.0)	0	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Renal failure	腎不全	7 (0.8)	3 (0.3)	3 (0.3)	0	1 (0.1)	0	4 (0.8)	0	1 (0.2)	1 (0.2)	2 (0.4)	0
	Renal impairment	腎機能障害	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal pain	腎臓痛	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Strangury	有痛性排尿困難	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ureteral disorder	尿管障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ureteric obstruction	尿管閉塞	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Ureteric stenosis	尿管狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	6 (0.7)	2 (0.2)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Urethral discharge	尿道分泌物	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urethral meatus stenosis	外尿道口狭窄	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urethral pain	尿道痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Urethral stenosis	尿道狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Urinary hesitation	排尿躊躇	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary incontinence	尿失禁	14 (1.6)	6 (0.7)	8 (0.9)	0	0	0	12 (2.3)	7 (1.3)	5 (1.0)	0	0	0
	Urinary retention	尿閉	31 (3.5)	2 (0.2)	15 (1.7)	14 (1.6)	0	0	35 (6.7)	3 (0.6)	21 (4.0)	11 (2.1)	0	0
	Urinary tract discomfort	尿路不快感	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urinary tract disorder	尿路障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Urinary tract obstruction	尿路閉塞	9 (1.0)	1 (0.1)	3 (0.3)	5 (0.6)	0	0	7 (1.3)	2 (0.4)	4 (0.8)	1 (0.2)	0	0
	Urinary tract pain	尿路痛	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Urine flow decreased	尿流量減少	2 (0.2)	0	2 (0.2)	0	0	0	3 (0.6)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	44 (4.9)	30 (3.4)	13 (1.5)	1 (0.1)	0	0	35 (6.7)	23 (4.4)	11 (2.1)	1 (0.2)	0	0
	Balanoposthitis	亀頭包皮炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Benign prostatic hyperplasia	良性前立腺肥大症	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Breast discomfort	乳房不快感	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Breast induration	乳房硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast pain	乳房痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Breast tenderness	乳房圧痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Erectile dysfunction	勃起不全	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gynaecomastia	女性化乳房	19 (2.1)	14 (1.6)	5 (0.6)	0	0	0	6 (1.2)	6 (1.2)	0	0	0	0
	Nipple pain	乳頭痛	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pelvic pain	骨盤痛	11 (1.2)	9 (1.0)	2 (0.2)	0	0	0	12 (2.3)	8 (1.5)	4 (0.8)	0	0	0
	Penile pain	陰茎痛	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Penis disorder	陰茎障害	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Perineal pain	会陰痛	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Prostate induration	前立腺硬結	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostatic mass	前立腺腫瘤	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Prostatic obstruction	前立腺閉塞	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Prostatitis	前立腺炎	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Prostatomegaly	前立腺腫大	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Testicular pain	精巣痛	0	0	0	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	113 (12.7)	62 (7.0)	31 (3.5)	14 (1.6)	3 (0.3)	3 (0.3)	54 (10.4)	36 (6.9)	8 (1.5)	8 (1.5)	0	2 (0.4)
	Acute respiratory failure	急性呼吸不全	2 (0.2)	0	0	2 (0.2)	0	0	2 (0.4)	0	0	0	0	2 (0.4)
	Asthma	喘息	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Atelectasis	無気肺	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Bronchitis chronic	慢性気管支炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Bronchospasm	気管支痙攣	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Catarrh	カタル	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	9 (1.0)	6 (0.7)	1 (0.1)	2 (0.2)	0	0	4 (0.8)	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0
	Cough	咳嗽	26 (2.9)	16 (1.8)	9 (1.0)	1 (0.1)	0	0	11 (2.1)	8 (1.5)	3 (0.6)	0	0	0
	Cystic lung disease	嚢胞性肺疾患	4 (0.4)	4 (0.4)	0	0	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	24 (2.7)	11 (1.2)	10 (1.1)	2 (0.2)	0	1 (0.1)	15 (2.9)	8 (1.5)	4 (0.8)	3 (0.6)	0	0
	Dyspnoea exertional	労作性呼吸困難	6 (0.7)	4 (0.4)	1 (0.1)	1 (0.1)	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Emphysema	肺気腫	10 (1.1)	9 (1.0)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Epistaxis	鼻出血	1 (0.1)	0	1 (0.1)	0	0	0	3 (0.6)	1 (0.2)	1 (0.2)	1 (0.2)	0	0
	Haemoptysis	喀血	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Hypoxia	低酸素症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lower respiratory tract inflammation	下気道の炎症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lung disorder	肺障害	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Nasal congestion	鼻閉	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nocturnal dyspnoea	夜間呼吸困難	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Oropharyngeal pain	口腔咽頭痛	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Paranasal cyst	副鼻腔嚢胞	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Paranasal sinus hypersecretion	副鼻腔分泌過多	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pleural effusion	胸水	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	4 (0.8)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Pneumonia aspiration	誤嚥性肺炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pneumonitis	肺臓炎	3 (0.3)	1 (0.1)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumothorax	気胸	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Productive cough	湿性咳嗽	1 (0.1)	1 (0.1)	0	0	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Pulmonary calcification	肺石灰化	6 (0.7)	6 (0.7)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pulmonary congestion	肺うっ血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.6)	0	0	2 (0.2)	1 (0.1)	2 (0.2)	4 (0.8)	2 (0.4)	0	2 (0.4)	0	0
	Pulmonary fibrosis	肺線維症	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Pulmonary mass	肺腫瘤	5 (0.6)	5 (0.6)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pulmonary oedema	肺水腫	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary thrombosis	肺血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Rales	ラ音	1 (0.1)	1 (0.1)	0	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Reflux laryngitis	逆流性喉頭炎	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Respiratory alkalosis	呼吸性アルカローシス	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-8 TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Respiratory disorder	呼吸障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Respiratory failure	呼吸不全	3 (0.3)	0	0	1 (0.1)	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Rhinalgia	鼻痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Rhinorrhoea	鼻漏	1 (0.1)	0	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Rhonchi	低音性連続性ラ音	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sinus disorder	副鼻腔障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Sinus polyp	副鼻腔ポリープ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Sleep apnoea syndrome	睡眠時無呼吸症候群	3 (0.3)	0	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Sneezing	くしゃみ	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Throat irritation	咽喉刺激感	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Throat tightness	咽喉絞扼感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Upper-airway cough syndrome	上気道咳症候群	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Wheezing	喘鳴	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	81 (9.1)	58 (6.5)	20 (2.2)	3 (0.3)	0	0	34 (6.5)	26 (5.0)	7 (1.3)	1 (0.2)	0	0
	Acne	ざ瘡	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Actinic keratosis	光線角化症	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Alopecia	脱毛症	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Blister	水疱	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dermal cyst	皮膚嚢腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dermatitis	皮膚炎	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Dermatitis contact	接触皮膚炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Diabetic foot	糖尿病性足病変	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Dry skin	皮膚乾燥	6 (0.7)	6 (0.7)	0	0	0	0	0	0	0	0	0	0
	Ecchymosis	斑状出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Eczema	湿疹	6 (0.7)	4 (0.4)	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Eczema nummular	貨幣状湿疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Erythema	紅斑	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Erythema multiforme	多形紅斑	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haemorrhage subcutaneous	皮下出血	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Hyperhidrosis	多汗症	8 (0.9)	3 (0.3)	5 (0.6)	0	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Hypertrichosis	多毛症	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Hypotrichosis	貧毛症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Nail discolouration	爪変色	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Night sweats	寝汗	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Onychoclasis	爪破損	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pigmentation disorder	色素沈着障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pruritus	そう痒症	16 (1.8)	13 (1.5)	3 (0.3)	0	0	0	10 (1.9)	8 (1.5)	2 (0.4)	0	0	0
	Pruritus allergic	アレルギー性そう痒症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Pruritus generalised	全身性そう痒症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Psoriasis	乾癬	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Rash	発疹	13 (1.5)	8 (0.9)	4 (0.4)	1 (0.1)	0	0	4 (0.8)	4 (0.8)	0	0	0	0
	Rash macular	斑状皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash maculo-papular	斑状丘疹状皮疹	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Rash papular	丘疹性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin disorder	皮膚障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin erosion	皮膚びらん	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin exfoliation	皮膚剥脱	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin fragility	皮膚脆弱性	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin induration	皮膚硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Skin irritation	皮膚刺激	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin lesion	皮膚病変	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin mass	皮膚腫瘤	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Skin reaction	皮膚反応	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Skin ulcer	皮膚潰瘍	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Stasis dermatitis	うっ滞性皮膚炎	0	0	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Urticaria	蕁麻疹	8 (0.9)	4 (0.4)	3 (0.3)	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Surgical and medical procedures	Any	外科および内科処置	10 (1.1)	1 (0.1)	1 (0.1)	8 (0.9)	0	0	5 (1.0)	0	2 (0.4)	3 (0.6)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cataract operation	白内障手術	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cystostomy	膀胱瘻造設	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Lipoma excision	脂肪腫切除	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lymphadenectomy	リンパ節切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Orchidectomy	精巣摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostatectomy	前立腺摘除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Radiotherapy to lymph nodes	リンパ節放射線療法	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Tooth extraction	抜歯	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urethrotomy	尿道切開	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Vascular disorders	Any	血管障害	146 (16.4)	73 (8.2)	36 (4.0)	36 (4.0)	0	1 (0.1)	67 (12.9)	28 (5.4)	20 (3.8)	17 (3.3)	0	2 (0.4)
	Aortic aneurysm	大動脈瘤	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Aortic arteriosclerosis	大動脈硬化症	4 (0.4)	4 (0.4)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Aortic dissection	大動脈解離	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic thrombosis	大動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	0	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Bleeding varicose vein	出血性静脈瘤	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Circulatory collapse	循環虚脱	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Deep vein thrombosis	深部静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Embolism	塞栓症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Essential hypertension	本態性高血圧症	3 (0.3)	2 (0.2)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Flushing	潮紅	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haematoma	血腫	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hot flush	ほてり	49 (5.5)	41 (4.6)	8 (0.9)	0	0	0	23 (4.4)	22 (4.2)	1 (0.2)	0	0	0
	Hypertension	高血圧	61 (6.8)	14 (1.6)	17 (1.9)	30 (3.4)	0	0	28 (5.4)	6 (1.2)	10 (1.9)	12 (2.3)	0	0
	Hypotension	低血圧	10 (1.1)	7 (0.8)	2 (0.2)	1 (0.1)	0	0	7 (1.3)	3 (0.6)	3 (0.6)	1 (0.2)	0	0
	Iliac artery occlusion	腸骨動脈閉塞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Intermittent claudication	間欠性跛行	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphoedema	リンパ浮腫	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Orthostatic hypotension	起立性低血圧	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Pallor	蒼白	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

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			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Peripheral artery thrombosis	末梢動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Phlebitis	静脈炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thrombophlebitis	血栓性静脈炎	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Thrombophlebitis superficial	表在性血栓性静脈炎	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Thrombosis	血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Varicose vein	静脈瘤	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Vasculitis	血管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Vena cava thrombosis	大静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Venous thrombosis limb	四肢静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/6

付表 2.7.6.9.a.1-9 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		14 (22.6)	7 (11.3)	4 (6.5)	2 (3.2)	1 (1.6)	0	4 (12.1)	1 (3.0)	3 (9.1)	0	0	0
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	3 (4.8)	1 (1.6)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Anaemia	貧血	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	5 (8.1)	3 (4.8)	2 (3.2)	0	0	0	0	0	0	0	0	0
	Abdominal discomfort	腹部不快感	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Constipation	便秘	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Diarrhoea	下痢	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Nausea	悪心	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	5 (8.1)	4 (6.5)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Face oedema	顔面浮腫	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Oedema peripheral	末梢性浮腫	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Pyrexia	発熱	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	2 (3.2)	1 (1.6)	0	0	1 (1.6)	0	1 (3.0)	0	1 (3.0)	0	0	0
	Hepatic function abnormal	肝機能異常	2 (3.2)	1 (1.6)	0	0	1 (1.6)	0	1 (3.0)	0	1 (3.0)	0	0	0
Investigations	Any	臨床検査	2 (3.2)	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-9 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Weight decreased	体重減少	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	White blood cell count decreased	白血球数減少	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	5 (8.1)	2 (3.2)	3 (4.8)	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Decreased appetite	食欲減退	3 (4.8)	2 (3.2)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Dehydration	脱水	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Dyslipidaemia	脂質異常症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Hyperkalaemia	高カリウム血症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Hyperlipidaemia	高脂血症	0	0	0	0	0	0	1 (3.0)	1 (3.0)	0	0	0	0
	Hyperuricaemia	高尿酸血症	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Arthralgia	関節痛	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	1 (1.6)	1 (1.6)	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Proteinuria	蛋白尿	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Renal impairment	腎機能障害	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
	Rash	発疹	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Urticaria	蕁麻疹	0	0	0	0	0	0	1 (3.0)	0	1 (3.0)	0	0	0
Vascular disorders	Any	血管障害	2 (3.2)	0	2 (3.2)	0	0	0	0	0	0	0	0	0
	Deep vein thrombosis	深部静脈血栓症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/21

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term(PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		244 (27.4)	125 (14.0)	94 (10.5)	22 (2.5)	2 (0.2)	1 (0.1)	106 (20.3)	67 (12.9)	23 (4.4)	14 (2.7)	0	2 (0.4)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	14 (1.6)	5 (0.6)	7 (0.8)	2 (0.2)	0	0	4 (0.8)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Anaemia	貧血	7 (0.8)	4 (0.4)	2 (0.2)	1 (0.1)	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Leukopenia	白血球減少症	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Neutropenia	好中球減少症	5 (0.6)	1 (0.1)	3 (0.3)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Cardiac disorders	Any	心臓障害	10 (1.1)	6 (0.7)	2 (0.2)	2 (0.2)	0	0	3 (0.6)	2 (0.4)	0	0	0	1 (0.2)
	Arrhythmia	不整脈	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Arrhythmia supraventricular	上室性不整脈	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Atrial fibrillation	心房細動	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	0	0	2 (0.4)	1 (0.2)	0	0	0	1 (0.2)
	Palpitations	動悸	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Supraventricular extrasystoles	上室性期外収縮	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Tinnitus	耳鳴	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
Eye disorders	Any	眼障害	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Blepharitis	眼瞼炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Visual acuity reduced	視力低下	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Gastrointestinal disorders	Any	胃腸障害	56 (6.3)	40 (4.5)	15 (1.7)	0	0	1 (0.1)	37 (7.1)	27 (5.2)	8 (1.5)	2 (0.4)	0	0
	Abdominal discomfort	腹部不快感	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Abdominal distension	腹部膨満	4 (0.4)	4 (0.4)	0	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Abdominal pain	腹痛	4 (0.4)	4 (0.4)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Abdominal pain upper	上腹部痛	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	4 (0.8)	3 (0.6)	0	1 (0.2)	0	0
	Anal haemorrhage	肛門出血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Constipation	便秘	9 (1.0)	3 (0.3)	6 (0.7)	0	0	0	5 (1.0)	4 (0.8)	1 (0.2)	0	0	0
	Diarrhoea	下痢	13 (1.5)	10 (1.1)	3 (0.3)	0	0	0	9 (1.7)	7 (1.3)	2 (0.4)	0	0	0
	Dry mouth	口内乾燥	9 (1.0)	9 (1.0)	0	0	0	0	5 (1.0)	4 (0.8)	1 (0.2)	0	0	0
	Duodenal ulcer	十二指腸潰瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dyspepsia	消化不良	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Flatulence	鼓腸	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Frequent bowel movements	排便回数増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Gastritis erosive	びらん性胃炎	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Nausea	悪心	21 (2.4)	19 (2.1)	2 (0.2)	0	0	0	17 (3.3)	12 (2.3)	5 (1.0)	0	0	0
	Oesophageal pain	食道痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Vomiting	嘔吐	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	81 (9.1)	54 (6.1)	25 (2.8)	2 (0.2)	0	0	32 (6.1)	25 (4.8)	5 (1.0)	2 (0.4)	0	0
	Asthenia	無力症	9 (1.0)	7 (0.8)	2 (0.2)	0	0	0	7 (1.3)	4 (0.8)	2 (0.4)	1 (0.2)	0	0
	Chest pain	胸痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Chills	悪寒	2 (0.2)	2 (0.2)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Discomfort	不快感	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Fatigue	疲労	66 (7.4)	45 (5.0)	19 (2.1)	2 (0.2)	0	0	24 (4.6)	21 (4.0)	2 (0.4)	1 (0.2)	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gait disturbance	歩行障害	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Malaise	倦怠感	0	0	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Oedema peripheral	末梢性浮腫	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	3 (0.6)	1 (0.2)	2 (0.4)	0	0	0
	Peripheral swelling	末梢腫脹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Thirst	口渇	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperbilirubinaemia	高ビリルビン血症	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Oral candidiasis	口腔カンジダ症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rash pustular	膿疱性皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Urinary tract infection	尿路感染	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Contusion	挫傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cystitis radiation	放射線性膀胱炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Spinal compression fracture	脊椎圧迫骨折	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	30 (3.4)	12 (1.3)	13 (1.5)	5 (0.6)	0	0	5 (1.0)	3 (0.6)	2 (0.4)	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	4 (0.4)	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	9 (1.0)	5 (0.6)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Blood bilirubin increased	血中ビリルビン増加	6 (0.7)	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	7 (0.8)	1 (0.1)	6 (0.7)	0	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Blood urea increased	血中尿素増加	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Electrocardiogram QT prolonged	心電図ＱＴ延長	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Haemoglobin decreased	ヘモグロビン減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphocyte count decreased	リンパ球数減少	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0
	Platelet count decreased	血小板数減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Protein total decreased	総蛋白減少	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Transaminases increased	トランスアミナーゼ上昇	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Weight decreased	体重減少	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Weight increased	体重増加	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	White blood cell count decreased	白血球数減少	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	17 (1.9)	7 (0.8)	7 (0.8)	3 (0.3)	0	0	7 (1.3)	4 (0.8)	2 (0.4)	1 (0.2)	0	0
	Decreased appetite	食欲減退	11 (1.2)	7 (0.8)	4 (0.4)	0	0	0	6 (1.2)	4 (0.8)	2 (0.4)	0	0	0
	Dehydration	脱水	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gout	痛風	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hyperglycaemia	高血糖	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	3 (0.3)	1 (0.1)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hyponatraemia	低ナトリウム血症	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

			Darolutamide (N=892)						Placebo (N=521)					
System organ class (SOC)	Preferred term (PT)		Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	26 (2.9)	12 (1.3)	11 (1.2)	3 (0.3)	0	0	10 (1.9)	7 (1.3)	3 (0.6)	0	0	0
	Arthralgia	関節痛	4 (0.4)	1 (0.1)	2 (0.2)	1 (0.1)	0	0	6 (1.2)	6 (1.2)	0	0	0	0
	Back pain	背部痛	7 (0.8)	3 (0.3)	3 (0.3)	1 (0.1)	0	0	2 (0.4)	1 (0.2)	1 (0.2)	0	0	0
	Joint swelling	関節腫脹	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Muscle spasms	筋痙縮	4 (0.4)	1 (0.1)	3 (0.3)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Muscular weakness	筋力低下	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Musculoskeletal pain	筋骨格痛	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Myalgia	筋肉痛	6 (0.7)	5 (0.6)	0	1 (0.1)	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Osteoarthritis	変形性関節症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoporosis	骨粗鬆症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pain in extremity	四肢痛	5 (0.6)	3 (0.3)	2 (0.2)	0	0	0	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	31 (3.5)	22 (2.5)	7 (0.8)	1 (0.1)	1 (0.1)	0	15 (2.9)	9 (1.7)	3 (0.6)	2 (0.4)	0	1 (0.2)
	Amnesia	健忘	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Balance disorder	平衡障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Cognitive disorder	認知障害	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dizziness	浮動性めまい	11 (1.2)	8 (0.9)	2 (0.2)	1 (0.1)	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Dysgeusia	味覚異常	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Headache	頭痛	13 (1.5)	11 (1.2)	2 (0.2)	0	0	0	4 (0.8)	2 (0.4)	1 (0.2)	1 (0.2)	0	0
	Hypoaesthesia	感覚鈍麻	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hyposmia	嗅覚減退	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Ischaemic stroke	虚血性脳卒中	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Memory impairment	記憶障害	1 (0.1)	1 (0.1)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Paraesthesia	錯感覚	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Psychomotor skills impaired	精神運動機能障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Somnolence	傾眠	4 (0.4)	3 (0.3)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tremor	振戦	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	5 (0.6)	4 (0.4)	1 (0.1)	0	0	0	5 (1.0)	4 (0.8)	1 (0.2)	0	0	0
	Depression	うつ病	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Insomnia	不眠症	2 (0.2)	2 (0.2)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Irritability	易刺激性	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Middle insomnia	中期不眠症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Nightmare	悪夢	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Sleep disorder	睡眠障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	10 (1.1)	7 (0.8)	2 (0.2)	1 (0.1)	0	0	5 (1.0)	3 (0.6)	2 (0.4)	0	0	0
	Bladder hypertrophy	膀胱壁肥厚	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Glycosuria	糖尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Haematuria	血尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Nocturia	夜間頻尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	3 (0.3)	3 (0.3)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Polyuria	多尿	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Renal failure	腎不全	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Urinary incontinence	尿失禁	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Urinary retention	尿閉	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Urinary tract disorder	尿路障害	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	16 (1.8)	11 (1.2)	5 (0.6)	0	0	0	6 (1.2)	5 (1.0)	1 (0.2)	0	0	0
	Benign prostatic hyperplasia	良性前立腺肥大症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast induration	乳房硬結	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Breast pain	乳房痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Breast tenderness	乳房圧痛	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Gynaecomastia	女性化乳房	15 (1.7)	10 (1.1)	5 (0.6)	0	0	0	3 (0.6)	3 (0.6)	0	0	0	0
	Nipple pain	乳頭痛	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Perineal pain	会陰痛	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	10 (1.1)	5 (0.6)	4 (0.4)	0	1 (0.1)	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Cough	咳嗽	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	4 (0.4)	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0
	Dyspnoea exertional	労作性呼吸困難	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Nasal congestion	鼻閉	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-10 治験薬と関連のある TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Pulmonary embolism	肺塞栓症	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	2 (0.4)	1 (0.2)	0	1 (0.2)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	32 (3.6)	23 (2.6)	8 (0.9)	1 (0.1)	0	0	9 (1.7)	7 (1.3)	2 (0.4)	0	0	0
	Alopecia	脱毛症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dry skin	皮膚乾燥	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Eczema	湿疹	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Eczema nummular	貨幣状湿疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hyperhidrosis	多汗症	6 (0.7)	2 (0.2)	4 (0.4)	0	0	0	4 (0.8)	3 (0.6)	1 (0.2)	0	0	0
	Hypotrichosis	貧毛症	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Night sweats	寝汗	1 (0.1)	1 (0.1)	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pruritus	そう痒症	7 (0.8)	7 (0.8)	0	0	0	0	2 (0.4)	2 (0.4)	0	0	0	0
	Pruritus allergic	アレルギー性そう痒症	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Psoriasis	乾癬	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0
	Rash	発疹	3 (0.3)	3 (0.3)	0	0	0	0	0	0	0	0	0	0
	Rash macular	斑状皮疹	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Rash maculo-papular	斑状丘疹状皮疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Urticaria	蕁麻疹	4 (0.4)	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
Vascular disorders	Any	血管障害	57 (6.4)	36 (4.0)	16 (1.8)	5 (0.6)	0	0	20 (3.8)	13 (2.5)	3 (0.6)	4 (0.8)	0	0
	Deep vein thrombosis	深部静脈血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Flushing	潮紅	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Hot flush	ほてり	36 (4.0)	29 (3.3)	7 (0.8)	0	0	0	15 (2.9)	14 (2.7)	1 (0.2)	0	0	0
	Hypertension	高血圧	11 (1.2)	1 (0.1)	6 (0.7)	4 (0.4)	0	0	4 (0.8)	0	1 (0.2)	3 (0.6)	0	0
	Hypotension	低血圧	3 (0.3)	2 (0.2)	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Orthostatic hypotension	起立性低血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral artery thrombosis	末梢動脈血栓症	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Vasculitis	血管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/22

付表 2.7.6.9.a.1-11 グレード3以上のTEAE（CTCAEグレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		18 (29.0%)	16 (25.8%)	1 (1.6%)	1 (1.6%)	4 (12.1%)	3 (9.1%)	1 (3.0%)	0
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	3 (4.8%)	3 (4.8%)	0	0	0	0	0	0
	Anaemia	貧血	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Iron deficiency anaemia	鉄欠乏性貧血	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	2 (3.2%)	2 (3.2%)	0	0	0	0	0	0
	Angina pectoris	狭心症	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Arrhythmia	不整脈	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Eye disorders	Any	眼障害	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Cataract	白内障	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0
	Diarrhoea	下痢	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0
	Fatigue	疲労	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (1.6%)	0	1 (1.6%)	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (1.6%)	0	1 (1.6%)	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	5 (8.1%)	4 (6.5%)	0	1 (1.6%)	1 (3.0%)	1 (3.0%)	0	0
	Abscess	膿瘍	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Bronchitis	気管支炎	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Gingivitis	歯肉炎	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Influenza	インフルエンザ	1 (1.6%)	0	0	1 (1.6%)	0	0	0	0
	Pneumonia	肺炎	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Urinary tract infection	尿路感染	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0

付表 2.7.6.9.a.1-11 グレード3以上のTEAE（CTCAEグレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	3 (4.8%)	3 (4.8%)	0	0	0	0	0	0
	Fall	転倒	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Fracture	骨折	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Investigations	Any	臨床検査	2 (3.2%)	2 (3.2%)	0	0	1 (3.0%)	0	1 (3.0%)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	0	0	0	0	1 (3.0%)	0	1 (3.0%)	0
	Neutrophil count decreased	好中球数減少	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	1 (1.6%)	1 (1.6%)	0	0	1 (3.0%)	1 (3.0%)	0	0
	Decreased appetite	食欲減退	1 (1.6%)	1 (1.6%)	0	0	1 (3.0%)	1 (3.0%)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	5 (8.1%)	5 (8.1%)	0	0	2 (6.1%)	2 (6.1%)	0	0
	Bladder neoplasm	膀胱新生物	2 (3.2%)	2 (3.2%)	0	0	0	0	0	0
	Colon cancer	結腸癌	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Gastric cancer	胃癌	0	0	0	0	1 (3.0%)	1 (3.0%)	0	0
	Pancreatic carcinoma	膵癌	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (1.6%)	1 (1.6%)	0	0	1 (3.0%)	1 (3.0%)	0	0
Renal and urinary disorders	Any	腎および尿路障害	4 (6.5%)	4 (6.5%)	0	0	1 (3.0%)	0	1 (3.0%)	0
	Haematuria	血尿	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Hydronephrosis	水腎症	2 (3.2%)	2 (3.2%)	0	0	0	0	0	0
	Renal failure	腎不全	0	0	0	0	1 (3.0%)	0	1 (3.0%)	0
	Urinary retention	尿閉	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	2 (3.2%)	2 (3.2%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-11 グレード3以上のTEAE（CTCAEグレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Asthma	喘息	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Pulmonary mass	肺腫瘤	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/7

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892) Total (N (%))	Darolutamide (N=892) G 3 (N (%))	Darolutamide (N=892) G 4 (N (%))	Darolutamide (N=892) G 5 (N (%))	Placebo (N=521) Total (N (%))	Placebo (N=521) G 3 (N (%))	Placebo (N=521) G 4 (N (%))	Placebo (N=521) G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		255 (28.6%)	199 (22.3%)	20 (2.2%)	36 (4.0%)	122 (23.4%)	96 (18.4%)	8 (1.5%)	18 (3.5%)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	12 (1.3%)	12 (1.3%)	0	0	7 (1.3%)	6 (1.2%)	1 (0.2%)	0
	Anaemia	貧血	7 (0.8%)	7 (0.8%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Leukopenia	白血球減少症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphopenia	リンパ球減少症	2 (0.2%)	2 (0.2%)	0	0	3 (0.6%)	3 (0.6%)	0	0
	Neutropenia	好中球減少症	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	0	1 (0.2%)	0
	Thrombocytopenia	血小板減少症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	44 (4.9%)	28 (3.1%)	6 (0.7%)	10 (1.1%)	13 (2.5%)	4 (0.8%)	1 (0.2%)	8 (1.5%)
	Acute myocardial infarction	急性心筋梗塞	5 (0.6%)	2 (0.2%)	2 (0.2%)	1 (0.1%)	0	0	0	0
	Angina pectoris	狭心症	2 (0.2%)	0	1 (0.1%)	1 (0.1%)	0	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Aortic valve disease	大動脈弁疾患	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Arrhythmia	不整脈	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Atrial fibrillation	心房細動	6 (0.7%)	5 (0.6%)	1 (0.1%)	0	2 (0.4%)	1 (0.2%)	1 (0.2%)	0
	Atrioventricular block	房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Bradycardia	徐脈	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Cardiac arrest	心停止	2 (0.2%)	0	0	2 (0.2%)	3 (0.6%)	0	0	3 (0.6%)
	Cardiac disorder	心障害	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Cardiac failure	心不全	5 (0.6%)	1 (0.1%)	1 (0.1%)	3 (0.3%)	3 (0.6%)	0	0	3 (0.6%)
	Cardiac failure acute	急性心不全	2 (0.2%)	1 (0.1%)	0	1 (0.1%)	0	0	0	0
	Cardiac failure congestive	うっ血性心不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cardiogenic shock	心原性ショック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cardiovascular insufficiency	心血管不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Coronary artery disease	冠動脈疾患	6 (0.7%)	5 (0.6%)	0	1 (0.1%)	0	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Coronary artery stenosis	冠動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Myocardial infarction	心筋梗塞	4 (0.4%)	3 (0.3%)	1 (0.1%)	0	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Myocardial ischaemia	心筋虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Palpitations	動悸	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sinus bradycardia	洞性徐脈	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tachycardia	頻脈	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Endocrine disorders	Any	内分泌障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Eye disorders	Any	眼障害	4 (0.4%)	4 (0.4%)	0	0	5 (1.0%)	5 (1.0%)	0	0
	Blindness	失明	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blindness unilateral	片側失明	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cataract	白内障	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Eye pain	眼痛	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Macular degeneration	黄斑変性	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Retinal detachment	網膜剥離	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Visual impairment	視力障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Gastrointestinal disorders	Any	胃腸障害	22 (2.5%)	16 (1.8%)	4 (0.4%)	2 (0.2%)	10 (1.9%)	10 (1.9%)	0	0
	Abdominal pain	腹痛	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Abdominal pain upper	上腹部痛	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Anal incontinence	肛門失禁	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Colitis	大腸炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dental caries	齲歯	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Diarrhoea	下痢	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Ileus	イレウス	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4%)	4 (0.4%)	0	0	0	0	0	0
	Jejunal stenosis	空腸狭窄	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Large intestine perforation	大腸穿孔	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Melaena	メレナ	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Nausea	悪心	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Plicated tongue	ひだ舌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Small intestinal obstruction	小腸閉塞	1 (0.1%)	1 (0.1%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Vomiting	嘔吐	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	21 (2.4%)	13 (1.5%)	0	8 (0.9%)	6 (1.2%)	5 (1.0%)	0	1 (0.2%)
	Asthenia	無力症	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Death	死亡	4 (0.4%)	0	0	4 (0.4%)	1 (0.2%)	0	0	1 (0.2%)
	Fatigue	疲労	4 (0.4%)	4 (0.4%)	0	0	4 (0.8%)	4 (0.8%)	0	0
	Gait disturbance	歩行障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	General physical health deterioration	全身健康状態低下	4 (0.4%)	2 (0.2%)	0	2 (0.2%)	0	0	0	0
	Granuloma	肉芽腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Malaise	倦怠感	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Peripheral swelling	末梢腫脹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Pyrexia	発熱	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Sudden cardiac death	心突然死	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Sudden death	突然死	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Suprapubic pain	恥骨上痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	5 (0.6%)	4 (0.4%)	0	1 (0.1%)	3 (0.6%)	3 (0.6%)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cholangitis acute	急性胆管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cholecystitis chronic	慢性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cholelithiasis	胆石症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Liver disorder	肝障害	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	36 (4.0%)	28 (3.1%)	4 (0.4%)	4 (0.4%)	16 (3.1%)	14 (2.7%)	1 (0.2%)	1 (0.2%)
	Acute endocarditis	急性心内膜炎	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Appendicitis	虫垂炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bacterial infection	細菌感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cellulitis	蜂巣炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Erysipelas	丹毒	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Gastroenteritis	胃腸炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hepatitis C	C型肝炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Influenza	インフルエンザ	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lung infection	肺感染	2 (0.2%)	1 (0.1%)	0	1 (0.1%)	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Meningitis bacterial	細菌性髄膜炎	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Peritonitis	腹膜炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pneumonia	肺炎	9 (1.0%)	7 (0.8%)	1 (0.1%)	1 (0.1%)	4 (0.8%)	3 (0.6%)	1 (0.2%)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pyelonephritis	腎盂腎炎	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Respiratory tract infection	気道感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Respiratory tract infection viral	ウイルス性気道感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Sepsis	敗血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tooth abscess	歯膿瘍	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Tooth infection	歯感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary tract infection	尿路感染	6 (0.7%)	6 (0.7%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urosepsis	尿路性敗血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	17 (1.9%)	14 (1.6%)	0	3 (0.3%)	10 (1.9%)	10 (1.9%)	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Ankle fracture	足関節部骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Clavicle fracture	鎖骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Facial bones fracture	顔面骨骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fall	転倒	7 (0.8%)	7 (0.8%)	0	0	4 (0.8%)	4 (0.8%)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fibula fracture	腓骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Foot fracture	足骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Frostbite	凍傷	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hand fracture	手骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Heart injury	心臓損傷	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Multiple injuries	多発性外傷	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Procedural pain	処置による疼痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skin abrasion	皮膚擦過傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Subdural haematoma	硬膜下血腫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Thermal burn	熱傷	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Traumatic fracture	外傷性骨折	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Vascular graft complication	移植血管合併症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Investigations	Any	臨床検査	17 (1.9%)	16 (1.8%)	1 (0.1%)	0	5 (1.0%)	4 (0.8%)	1 (0.2%)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood bilirubin increased	血中ビリルビン増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood chromogranin A increased	血中クロモグラニンA増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood creatinine increased	血中クレアチニン増加	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	0	1 (0.2%)	0
	Blood potassium decreased	血中カリウム減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Blood pressure increased	血圧上昇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood pressure systolic increased	収縮期血圧上昇	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Blood sodium decreased	血中ナトリウム減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Blood urea increased	血中尿素増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Body temperature increased	体温上昇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Electrocardiogram QT prolonged	心電図ＱＴ延長	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Glomerular filtration rate decreased	糸球体濾過率減少	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	International normalised ratio increased	国際標準比増加	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Neutrophil count decreased	好中球数減少	6 (0.7%)	5 (0.6%)	1 (0.1%)	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	22 (2.5%)	18 (2.0%)	4 (0.4%)	0	9 (1.7%)	9 (1.7%)	0	0
	Decreased appetite	食欲減退	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dehydration	脱水	3 (0.3%)	2 (0.2%)	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Diabetes mellitus	糖尿病	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperglycaemia	高血糖	4 (0.4%)	2 (0.2%)	2 (0.2%)	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperkalaemia	高カリウム血症	4 (0.4%)	3 (0.3%)	1 (0.1%)	0	3 (0.6%)	3 (0.6%)	0	0
	Hypernatraemia	高ナトリウム血症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypertriglyceridaemia	高トリグリセリド血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hyperuricaemia	高尿酸血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypoglycaemia	低血糖	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypokalaemia	低カリウム血症	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyponatraemia	低ナトリウム血症	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Metabolic alkalosis	代謝性アルカローシス	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Obesity	肥満	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	18 (2.0%)	18 (2.0%)	0	0	6 (1.2%)	6 (1.2%)	0	0
	Arthralgia	関節痛	3 (0.3%)	3 (0.3%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Back pain	背部痛	4 (0.4%)	4 (0.4%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bone pain	骨痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Flank pain	側腹部痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lumbar spinal stenosis	腰部脊柱管狭窄症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Mobility decreased	運動性低下	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Muscular weakness	筋力低下	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Musculoskeletal chest pain	筋骨格系胸痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Myalgia	筋肉痛	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	5 (0.6%)	5 (0.6%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pain in extremity	四肢痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Spinal column stenosis	脊柱管狭窄症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Spinal fusion acquired	後天性脊椎癒合	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	19 (2.1%)	15 (1.7%)	2 (0.2%)	2 (0.2%)	8 (1.5%)	7 (1.3%)	0	1 (0.2%)
	Adenocarcinoma	腺癌	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Bladder neoplasm	膀胱新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Colon cancer	結腸癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型B細胞性リンパ腫	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Gastric cancer	胃癌	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Gastrointestinal adenocarcinoma	消化器腺癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphoma	リンパ腫	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Mesothelioma	中皮腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Metastases to peritoneum	腹膜転移	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Pancreatic carcinoma	膵癌	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Pancreatic neoplasm	膵新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Rectal adenocarcinoma	直腸腺癌	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Salivary gland neoplasm	唾液腺新生物	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Thymoma	胸腺腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Tumour compression	腫瘍性圧迫	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Tumour pain	腫瘍疼痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	20 (2.2%)	16 (1.8%)	2 (0.2%)	2 (0.2%)	15 (2.9%)	11 (2.1%)	0	4 (0.8%)
	Brain oedema	脳浮腫	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Carotid artery stenosis	頚動脈狭窄	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Cerebral arteriosclerosis	脳動脈硬化症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Cerebrovascular accident	脳血管発作	2 (0.2%)	2 (0.2%)	0	0	3 (0.6%)	2 (0.4%)	0	1 (0.2%)
	Dementia	認知症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dizziness	浮動性めまい	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Headache	頭痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypoaesthesia	感覚鈍麻	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ischaemic stroke	虚血性脳卒中	4 (0.4%)	1 (0.1%)	2 (0.2%)	1 (0.1%)	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Myelopathy	脊髄症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Presyncope	失神寸前の状態	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Sciatica	坐骨神経痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Senile dementia	老年認知症	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Syncope	失神	2 (0.2%)	2 (0.2%)	0	0	3 (0.6%)	3 (0.6%)	0	0
	Transient ischaemic attack	一過性脳虚血発作	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Product issues	Any	製品の問題	4 (0.4%)	4 (0.4%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Device dislocation	医療機器位置異常	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Device occlusion	医療機器閉塞	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Depression	うつ病	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Insomnia	不眠症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Renal and urinary disorders	Any	腎および尿路障害	43 (4.8%)	41 (4.6%)	2 (0.2%)	0	36 (6.9%)	32 (6.1%)	4 (0.8%)	0
	Acute kidney injury	急性腎障害	5 (0.6%)	4 (0.4%)	1 (0.1%)	0	2 (0.4%)	2 (0.4%)	0	0
	Anuria	無尿	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Azotaemia	高窒素血症	0	0	0	0	1 (0.2%)	0	1 (0.2%)	0
	Bladder neck obstruction	膀胱頚部閉塞	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Calculus bladder	膀胱結石	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Chronic kidney disease	慢性腎臓病	2 (0.2%)	2 (0.2%)	0	0	3 (0.6%)	2 (0.4%)	1 (0.2%)	0
	Dysuria	排尿困難	1 (0.1%)	1 (0.1%)	0	0	5 (1.0%)	5 (1.0%)	0	0
	Haematuria	血尿	9 (1.0%)	9 (1.0%)	0	0	7 (1.3%)	7 (1.3%)	0	0
	Hydronephrosis	水腎症	5 (0.6%)	5 (0.6%)	0	0	3 (0.6%)	3 (0.6%)	0	0
	Lower urinary tract symptoms	下部尿路症状	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Nephrolithiasis	腎結石症	0	0	0	0	2 (0.4%)	2 (0.4%)	0	0
	Oliguria	乏尿	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pollakiuria	頻尿	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Renal colic	腎仙痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Renal failure	腎不全	1 (0.1%)	0	1 (0.1%)	0	3 (0.6%)	1 (0.2%)	2 (0.4%)	0
	Renal impairment	腎機能障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Renal pain	腎臓痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ureteric stenosis	尿管狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urethral stenosis	尿道狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary hesitation	排尿躊躇	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary retention	尿閉	14 (1.6%)	14 (1.6%)	0	0	11 (2.1%)	11 (2.1%)	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Urinary tract obstruction	尿路閉塞	5 (0.6%)	5 (0.6%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urine flow decreased	尿流量減少	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Prostate induration	前立腺硬結	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Prostatic obstruction	前立腺閉塞	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	20 (2.2%)	14 (1.6%)	3 (0.3%)	3 (0.3%)	10 (1.9%)	8 (1.5%)	0	2 (0.4%)
	Acute respiratory failure	急性呼吸不全	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	0	0	2 (0.4%)
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	1 (0.2%)	1 (0.2%)	0
	Cough	咳嗽	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Dyspnoea	呼吸困難	3 (0.3%)	2 (0.2%)	0	1 (0.1%)	3 (0.6%)	3 (0.6%)	0	0
	Dyspnoea exertional	労作性呼吸困難	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Epistaxis	鼻出血	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Nocturnal dyspnoea	夜間呼吸困難	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pleural effusion	胸水	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Pneumonitis	肺臓炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.6%)	2 (0.2%)	1 (0.1%)	2 (0.2%)	2 (0.4%)	2 (0.4%)	0	0
	Pulmonary oedema	肺水腫	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Respiratory alkalosis	呼吸性アルカローシス	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Respiratory failure	呼吸不全	3 (0.3%)	1 (0.1%)	2 (0.2%)	0	1 (0.2%)	1 (0.2%)	0	0
	Rhinalgia	鼻痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Rash	発疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Skin mass	皮膚腫瘤	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urticaria	蕁麻疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Surgical and medical procedures	Any	外科および内科処置	8 (0.9%)	8 (0.9%)	0	0	3 (0.6%)	3 (0.6%)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cataract operation	白内障手術	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-12 グレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	Darolutamide (N=62) G 3 (N (%))	Darolutamide (N=62) G 4 (N (%))	Darolutamide (N=62) G 5 (N (%))	Placebo (N=33) Total (N (%))	Placebo (N=33) G 3 (N (%))	Placebo (N=33) G 4 (N (%))	Placebo (N=33) G 5 (N (%))
	Cystostomy	膀胱瘻造設	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Lymphadenectomy	リンパ節切除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Orchidectomy	精巣摘除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Prostatectomy	前立腺摘除	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Urethrotomy	尿道切開	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Vascular disorders	Any	血管障害	37 (4.1%)	36 (4.0%)	0	1 (0.1%)	19 (3.6%)	17 (3.3%)	0	2 (0.4%)
	Aortic dissection	大動脈解離	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	2 (0.4%)	1 (0.2%)	0	1 (0.2%)
	Circulatory collapse	循環虚脱	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Embolism	塞栓症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Essential hypertension	本態性高血圧症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hypertension	高血圧	30 (3.4%)	30 (3.4%)	0	0	12 (2.3%)	12 (2.3%)	0	0
	Hypotension	低血圧	1 (0.1%)	1 (0.1%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Lymphoedema	リンパ浮腫	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Orthostatic hypotension	起立性低血圧	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Vasculitis	血管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/8

付表 2.7.6.9.a.1-13 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)				Placebo (N=33)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		3 (4.8%)	2 (3.2%)	1 (1.6%)	0	0	0	0	0
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (1.6%)	0	1 (1.6%)	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (1.6%)	0	1 (1.6%)	0	0	0	0	0
Investigations	Any	臨床検査	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	1 (1.6%)	1 (1.6%)	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/23

付表 2.7.6.9.a.1-14 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)				Placebo (N=521)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects										
All system organ classes	Any		25 (2.8%)	22 (2.5%)	2 (0.2%)	1 (0.1%)	16 (3.1%)	14 (2.7%)	0	2 (0.4%)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Anaemia	貧血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Neutropenia	好中球減少症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	0	0	1 (0.2%)
	Atrioventricular block complete	完全房室ブロック	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
Gastrointestinal disorders	Any	胃腸障害	1 (0.1%)	0	0	1 (0.1%)	2 (0.4%)	2 (0.4%)	0	0
	Abdominal pain upper	上腹部痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Gastritis	胃炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1%)	0	0	1 (0.1%)	0	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	2 (0.2%)	2 (0.2%)	0	0	2 (0.4%)	2 (0.4%)	0	0
	Asthenia	無力症	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Fatigue	疲労	2 (0.2%)	2 (0.2%)	0	0	1 (0.2%)	1 (0.2%)	0	0
Hepatobiliary disorders	Any	肝胆道系障害	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hepatobiliary disease	肝胆道系疾患	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Investigations	Any	臨床検査	5 (0.6%)	5 (0.6%)	0	0	0	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0

付表 2.7.6.9.a.1-14 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)				Placebo (N=521)			
			Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Neutrophil count decreased	好中球数減少	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	3 (0.3%)	3 (0.3%)	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hyperglycaemia	高血糖	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Hypokalaemia	低カリウム血症	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Hyponatraemia	低ナトリウム血症	2 (0.2%)	2 (0.2%)	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	3 (0.3%)	3 (0.3%)	0	0	0	0	0	0
	Arthralgia	関節痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Back pain	背部痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Musculoskeletal pain	筋骨格痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Myalgia	筋肉痛	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Nervous system disorders	Any	神経系障害	2 (0.2%)	1 (0.1%)	1 (0.1%)	0	3 (0.6%)	2 (0.4%)	0	1 (0.2%)
	Dizziness	浮動性めまい	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	1 (0.2%)	0	0	1 (0.2%)
	Headache	頭痛	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
	Ischaemic stroke	虚血性脳卒中	1 (0.1%)	0	1 (0.1%)	0	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0
Renal and urinary disorders	Any	腎および尿路障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urinary retention	尿閉	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
	Pulmonary embolism	肺塞栓症	1 (0.1%)	0	1 (0.1%)	0	1 (0.2%)	1 (0.2%)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Urticaria	蕁麻疹	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
Vascular disorders	Any	血管障害	5 (0.6%)	5 (0.6%)	0	0	4 (0.8%)	4 (0.8%)	0	0
	Hypertension	高血圧	4 (0.4%)	4 (0.4%)	0	0	3 (0.6%)	3 (0.6%)	0	0

付表 2.7.6.9.a.1-14 治験薬と関連のあるグレード3以上のTEAE（CTCAEグレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892) Total (N (%))	Darolutamide (N=892) G 3 (N (%))	Darolutamide (N=892) G 4 (N (%))	Darolutamide (N=892) G 5 (N (%))	Placebo (N=521) Total (N (%))	Placebo (N=521) G 3 (N (%))	Placebo (N=521) G 4 (N (%))	Placebo (N=521) G 5 (N (%))
	Peripheral ischaemia	末梢性虚血	1 (0.1%)	1 (0.1%)	0	0	0	0	0	0
	Vasculitis	血管炎	0	0	0	0	1 (0.2%)	1 (0.2%)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.1/24

付表 2.7.6.9.a.1-15 重篤な TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		20 (32.3)	0	7 (11.3)	11 (17.7)	1 (1.6)	1 (1.6)	3 (9.1)	0	0	2 (6.1)	1 (3.0)	0
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Anaemia	貧血	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Cardiac disorders	Any	心臓障害	4 (6.5)	0	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0
	Angina pectoris	狭心症	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Cardiac failure	心不全	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	2 (3.2)	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0
	Chest pain	胸痛	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Pyrexia	発熱	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (1.6)	0	0	0	1 (1.6)	0	0	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (1.6)	0	0	0	1 (1.6)	0	0	0	0	0	0	0
Infections and infestations	Any	感染症および寄生虫症	2 (3.2)	0	0	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0
	Influenza	インフルエンザ	1 (1.6)	0	0	0	0	1 (1.6)	0	0	0	0	0	0
	Pneumonia	肺炎	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	4 (6.5)	0	2 (3.2)	2 (3.2)	0	0	0	0	0	0	0	0
	Fracture	骨折	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Postoperative ileus	術後イレウス	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Road traffic accident	交通事故	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-15 重篤な TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62)						Placebo (N=33)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Subarachnoid haemorrhage	くも膜下出血	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Subdural haematoma	硬膜下血腫	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	2 (3.2)	0	2 (3.2)	0	0	0	0	0	0	0	0	0
	Decreased appetite	食欲減退	2 (3.2)	0	2 (3.2)	0	0	0	0	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	5 (8.1)	0	0	5 (8.1)	0	0	2 (6.1)	0	0	2 (6.1)	0	0
	Bladder neoplasm	膀胱新生物	2 (3.2)	0	0	2 (3.2)	0	0	0	0	0	0	0	0
	Colon cancer	結腸癌	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Gastric cancer	胃癌	0	0	0	0	0	0	1 (3.0)	0	0	1 (3.0)	0	0
	Pancreatic carcinoma	膵癌	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (1.6)	0	0	1 (1.6)	0	0	1 (3.0)	0	0	1 (3.0)	0	0
Nervous system disorders	Any	神経系障害	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	2 (3.2)	0	0	2 (3.2)	0	0	1 (3.0)	0	0	0	1 (3.0)	0
	Hydronephrosis	水腎症	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
	Renal failure	腎不全	0	0	0	0	0	0	1 (3.0)	0	0	0	1 (3.0)	0
	Urinary retention	尿閉	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	2 (3.2)	0	1 (1.6)	1 (1.6)	0	0	0	0	0	0	0	0
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Pulmonary mass	肺腫瘤	1 (1.6)	0	0	1 (1.6)	0	0	0	0	0	0	0	0
Vascular disorders	Any	血管障害	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-15 重篤な TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=33) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Deep vein thrombosis	深部静脈血栓症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.2/1

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=521) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		217 (24.3)	7 (0.8)	35 (3.9)	121 (13.6)	18 (2.0)	36 (4.0)	108 (20.7)	1 (0.2)	22 (4.2)	59 (11.3)	8 (1.5)	18 (3.5)
Blood and lymphatic system disorders	Any	血液およびリンパ系障害	4 (0.4)	0	2 (0.2)	2 (0.2)	0	0	2 (0.4)	0	0	1 (0.2)	1 (0.2)	0
	Anaemia	貧血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Febrile neutropenia	発熱性好中球減少症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Leukopenia	白血球減少症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Lymphopenia	リンパ球減少症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Neutropenia	好中球減少症	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0
Cardiac disorders	Any	心臓障害	47 (5.3)	1 (0.1)	8 (0.9)	22 (2.5)	6 (0.7)	10 (1.1)	18 (3.5)	0	5 (1.0)	4 (0.8)	1 (0.2)	8 (1.5)
	Acute myocardial infarction	急性心筋梗塞	5 (0.6)	0	0	2 (0.2)	2 (0.2)	1 (0.1)	0	0	0	0	0	0
	Angina pectoris	狭心症	2 (0.2)	0	0	0	1 (0.1)	1 (0.1)	2 (0.4)	0	2 (0.4)	0	0	0
	Angina unstable	不安定狭心症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Aortic valve disease	大動脈弁疾患	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aortic valve stenosis	大動脈弁狭窄	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Arrhythmia	不整脈	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrial fibrillation	心房細動	8 (0.9)	0	2 (0.2)	5 (0.6)	1 (0.1)	0	3 (0.6)	0	1 (0.2)	1 (0.2)	1 (0.2)	0
	Atrioventricular block	房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Atrioventricular block second degree	第二度房室ブロック	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Bradycardia	徐脈	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cardiac arrest	心停止	2 (0.2)	0	0	0	0	2 (0.2)	3 (0.6)	0	0	0	0	3 (0.6)
	Cardiac disorder	心障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure	心不全	7 (0.8)	0	3 (0.3)	0	1 (0.1)	3 (0.3)	4 (0.8)	0	1 (0.2)	0	0	3 (0.6)

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cardiac failure acute	急性心不全	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Cardiac failure congestive	うっ血性心不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cardiovascular insufficiency	心血管不全	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Coronary artery disease	冠動脈疾患	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	1 (0.2)	0	1 (0.2)	0	0	0
	Coronary artery occlusion	冠動脈閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Coronary artery stenosis	冠動脈狭窄	2 (0.2)	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypertensive heart disease	高血圧性心疾患	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Myocardial infarction	心筋梗塞	4 (0.4)	0	0	3 (0.3)	1 (0.1)	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Myocardial ischaemia	心筋虚血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Palpitations	動悸	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sinus node dysfunction	洞結節機能不全	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
Ear and labyrinth disorders	Any	耳および迷路障害	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0	0	0	0
	Vertigo	回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Vertigo positional	頭位性回転性めまい	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Eye disorders	Any	眼障害	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Retinal detachment	網膜剥離	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Retinal vascular disorder	網膜血管障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Visual impairment	視力障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Gastrointestinal disorders	Any	胃腸障害	27 (3.0)	2 (0.2)	6 (0.7)	13 (1.5)	4 (0.4)	2 (0.2)	8 (1.5)	0	2 (0.4)	6 (1.2)	0	0
	Abdominal pain	腹痛	2 (0.2)	0	1 (0.1)	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Abdominal pain upper	上腹部痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bowel movement irregularity	便通不規則	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Constipation	便秘	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Diarrhoea	下痢	2 (0.2)	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
	Enterovesical fistula	腸膀胱瘻	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Gastrointestinal haemorrhage	胃腸出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastrointestinal pain	消化器痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Haemorrhoids	痔核	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Ileus	イレウス	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Inguinal hernia	鼠径ヘルニア	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Intestinal obstruction	腸閉塞	4 (0.4)	0	0	4 (0.4)	0	0	0	0	0	0	0	0
	Large intestine perforation	大腸穿孔	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Large intestine polyp	大腸ポリープ	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Lower gastrointestinal haemorrhage	下部消化管出血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Melaena	メレナ	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Obstructive pancreatitis	閉塞性膵炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pancreatitis acute	急性膵炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Plicated tongue	ひだ舌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumoperitoneum	気腹	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Proctitis	直腸炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Rectal haemorrhage	直腸出血	2 (0.2)	2 (0.2)	0	0	0	0	0	0	0	0	0	0
	Rectal stenosis	直腸狭窄	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Small intestinal obstruction	小腸閉塞	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Upper gastrointestinal haemorrhage	上部消化管出血	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
General disorders and administration site conditions	Any	一般・全身障害および投与部位の状態	15 (1.7)	1 (0.1)	1 (0.1)	5 (0.6)	0	8 (0.9)	1 (0.2)	0	0	0	0	1 (0.2)
	Asthenia	無力症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Chest pain	胸痛	2 (0.2)	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0
	Death	死亡	4 (0.4)	0	0	0	0	4 (0.4)	1 (0.2)	0	0	0	0	1 (0.2)
	Gait disturbance	歩行障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	General physical health deterioration	全身健康状態低下	4 (0.4)	0	0	2 (0.2)	0	2 (0.2)	0	0	0	0	0	0
	Pyrexia	発熱	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Sudden cardiac death	心突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Sudden death	突然死	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	4 (0.4)	0	0	3 (0.3)	0	1 (0.1)	2 (0.4)	0	0	2 (0.4)	0	0
	Bile duct obstruction	胆管閉塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Bile duct stenosis	胆管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholangitis acute	急性胆管炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis acute	急性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholecystitis chronic	慢性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cholelithiasis	胆石症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cholestasis	胆汁うっ滞	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Liver disorder	肝障害	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Immune system disorders	Any	免疫系障害	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hypersensitivity	過敏症	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Infections and infestations	Any	感染症および寄生虫症	40 (4.5)	0	9 (1.0)	23 (2.6)	4 (0.4)	4 (0.4)	19 (3.6)	0	5 (1.0)	12 (2.3)	1 (0.2)	1 (0.2)
	Abdominal abscess	腹部膿瘍	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Acute endocarditis	急性心内膜炎	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Appendicitis	虫垂炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Bacterial infection	細菌感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Cellulitis	蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cholecystitis infective	感染性胆嚢炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Diverticulitis	憩室炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Endocarditis	心内膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Erysipelas	丹毒	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Gastroenteritis	胃腸炎	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Hepatitis C	Ｃ型肝炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Herpes zoster	帯状疱疹	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Infectious mononucleosis	伝染性単核症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Influenza	インフルエンザ	1 (0.1)	0	0	0	1 (0.1)	0	1 (0.2)	0	1 (0.2)	0	0	0
	Intervertebral discitis	椎間板炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lung infection	肺感染	2 (0.2)	0	0	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0
	Medical device site joint infection	医療機器使用部位関節感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Meningitis bacterial	細菌性髄膜炎	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pneumonia	肺炎	12 (1.3)	0	3 (0.3)	7 (0.8)	1 (0.1)	1 (0.1)	6 (1.2)	0	2 (0.4)	3 (0.6)	1 (0.2)	0
	Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary tuberculosis	肺結核	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Pyelonephritis	腎盂腎炎	3 (0.3)	0	0	3 (0.3)	0	0	0	0	0	0	0	0
	Pyelonephritis acute	急性腎盂腎炎	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Respiratory tract infection viral	ウイルス性気道感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Sepsis	敗血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Septic shock	敗血症性ショック	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Sialoadenitis	唾液腺炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract infection	尿路感染	7 (0.8)	0	3 (0.3)	4 (0.4)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Urinary tract infection bacterial	細菌性尿路感染	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urosepsis	尿路性敗血症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Vestibular neuronitis	前庭神経炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Wound infection	創傷感染	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Injury, poisoning and procedural complications	Any	傷害、中毒および処置合併症	15 (1.7)	0	3 (0.3)	9 (1.0)	0	3 (0.3)	10 (1.9)	0	2 (0.4)	8 (1.5)	0	0
	Alcohol poisoning	アルコール中毒	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Ankle fracture	足関節部骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Contusion	挫傷	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Craniocerebral injury	頭蓋脳損傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Facial bones fracture	顔面骨骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fall	転倒	3 (0.3)	0	0	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Femoral neck fracture	大腿骨頚部骨折	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Femur fracture	大腿骨骨折	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fibula fracture	腓骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Foot fracture	足骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Fracture	骨折	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Hand fracture	手骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Heart injury	心臓損傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Hip fracture	股関節部骨折	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Ligament sprain	靭帯捻挫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Multiple injuries	多発性外傷	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Patella fracture	膝蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Road traffic accident	交通事故	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Skull fracture	頭蓋骨骨折	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Stomal hernia	ストーマ部ヘルニア	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Subdural haematoma	硬膜下血腫	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thermal burn	熱傷	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Vascular graft complication	移植血管合併症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Investigations	Any	臨床検査	3 (0.3)	0	1 (0.1)	2 (0.2)	0	0	3 (0.6)	0	2 (0.4)	0	1 (0.2)	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Arteriogram coronary	冠血管造影	0	0	0	0	0	0	2 (0.4)	0	2 (0.4)	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Blood creatinine increased	血中クレアチニン増加	0	0	0	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0
	Body temperature increased	体温上昇	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urine output decreased	尿量減少	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	10 (1.1)	1 (0.1)	1 (0.1)	5 (0.6)	3 (0.3)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Decreased appetite	食欲減退	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Dehydration	脱水	2 (0.2)	0	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0
	Diabetes mellitus	糖尿病	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hyperglycaemia	高血糖	3 (0.3)	0	0	1 (0.1)	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperkalaemia	高カリウム血症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypoglycaemia	低血糖	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
Musculoskeletal and connective tissue disorders	Any	筋骨格系および結合組織障害	8 (0.9)	0	2 (0.2)	6 (0.7)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Arthralgia	関節痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Back pain	背部痛	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Flank pain	側腹部痛	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Osteoarthritis	変形性関節症	3 (0.3)	0	0	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Rotator cuff syndrome	肩回旋筋腱板症候群	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Spinal column stenosis	脊柱管狭窄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Any	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）	23 (2.6)	0	8 (0.9)	11 (1.2)	2 (0.2)	2 (0.2)	7 (1.3)	1 (0.2)	1 (0.2)	4 (0.8)	0	1 (0.2)
	Acute leukaemia	急性白血病	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Basal cell carcinoma	基底細胞癌	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Bladder neoplasm	膀胱新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Carcinoid tumour	カルチノイド腫瘍	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Choroid melanoma	脈絡膜黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Colon cancer	結腸癌	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Gastric cancer	胃癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Laryngeal cancer	喉頭癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lung adenocarcinoma stage IV	肺腺癌第４期	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Lung neoplasm malignant	肺の悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Lymphoma	リンパ腫	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Malignant melanoma in situ	表皮内悪性黒色腫	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Mesothelioma	中皮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Neoplasm malignant	悪性新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Oncologic complication	腫瘍合併症	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Pancreatic carcinoma	膵癌	2 (0.2)	0	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0
	Pituitary tumour	下垂体腫瘍	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostate cancer	前立腺癌	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Rectal adenocarcinoma	直腸腺癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Rectal cancer	直腸癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Renal cancer	腎癌	0	0	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Salivary gland neoplasm	唾液腺新生物	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Squamous cell carcinoma	扁平上皮癌	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Thymoma	胸腺腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Transitional cell carcinoma	移行上皮癌	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Tumour pain	腫瘍疼痛	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary tract neoplasm	尿路新生物	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Nervous system disorders	Any	神経系障害	19 (2.1)	1 (0.1)	4 (0.4)	10 (1.1)	2 (0.2)	2 (0.2)	12 (2.3)	0	1 (0.2)	7 (1.3)	0	4 (0.8)
	Brain oedema	脳浮腫	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Bulbar palsy	球麻痺	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Carotid artery stenosis	頚動脈狭窄	2 (0.2)	0	0	2 (0.2)	0	0	0	0	0	0	0	0
	Cerebral infarction	脳梗塞	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cerebral ischaemia	脳虚血	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Cerebrovascular accident	脳血管発作	2 (0.2)	0	0	2 (0.2)	0	0	3 (0.6)	0	0	2 (0.4)	0	1 (0.2)
	Cognitive disorder	認知障害	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Dizziness	浮動性めまい	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Ischaemic stroke	虚血性脳卒中	5 (0.6)	0	1 (0.1)	1 (0.1)	2 (0.2)	1 (0.1)	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Myelopathy	脊髄症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Partial seizures	部分発作	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Presyncope	失神寸前の状態	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Seizure	痙攣発作	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Syncope	失神	1 (0.1)	0	0	1 (0.1)	0	0	2 (0.4)	0	0	2 (0.4)	0	0
	Transient ischaemic attack	一過性脳虚血発作	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Product issues	Any	製品の問題	4 (0.4)	0	1 (0.1)	3 (0.3)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device dislocation	医療機器位置異常	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Device occlusion	医療機器閉塞	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
Psychiatric disorders	Any	精神障害	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Delirium	譫妄	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
Renal and urinary disorders	Any	腎および尿路障害	41 (4.6)	2 (0.2)	5 (0.6)	32 (3.6)	2 (0.2)	0	39 (7.5)	0	9 (1.7)	26 (5.0)	4 (0.8)	0
	Acute kidney injury	急性腎障害	4 (0.4)	0	0	3 (0.3)	1 (0.1)	0	3 (0.6)	1 (0.2)	0	2 (0.4)	0	0
	Azotaemia	高窒素血症	0	0	0	0	0	0	1 (0.2)	0	0	0	1 (0.2)	0
	Calculus bladder	膀胱結石	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Chronic kidney disease	慢性腎臓病	0	0	0	0	0	0	2 (0.4)	0	0	1 (0.2)	1 (0.2)	0
	Dysuria	排尿困難	1 (0.1)	0	0	1 (0.1)	0	0	3 (0.6)	0	0	3 (0.6)	0	0
	Haematuria	血尿	10 (1.1)	1 (0.1)	1 (0.1)	8 (0.9)	0	0	6 (1.2)	0	1 (0.2)	5 (1.0)	0	0
	Hydronephrosis	水腎症	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	3 (0.6)	0	1 (0.2)	2 (0.4)	0	0
	Lower urinary tract symptoms	下部尿路症状	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Nephrolithiasis	腎結石症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Oliguria	乏尿	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pollakiuria	頻尿	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Renal colic	腎仙痛	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0
	Renal failure	腎不全	1 (0.1)	0	0	0	1 (0.1)	0	3 (0.6)	0	0	1 (0.2)	2 (0.4)	0
	Renal impairment	腎機能障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ureteric stenosis	尿管狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Ureterolithiasis	尿管結石症	2 (0.2)	0	2 (0.2)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Urethral stenosis	尿道狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Urinary retention	尿閉	14 (1.6)	1 (0.1)	3 (0.3)	10 (1.1)	0	0	18 (3.5)	1 (0.2)	7 (1.3)	10 (1.9)	0	0
	Urinary tract obstruction	尿路閉塞	6 (0.7)	0	1 (0.1)	5 (0.6)	0	0	2 (0.4)	0	1 (0.2)	1 (0.2)	0	0
	Urine flow decreased	尿流量減少	1 (0.1)	0	1 (0.1)	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Reproductive system and breast disorders	Any	生殖系および乳房障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostate induration	前立腺硬結	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Prostatic obstruction	前立腺閉塞	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	15 (1.7)	0	2 (0.2)	7 (0.8)	3 (0.3)	3 (0.3)	9 (1.7)	0	1 (0.2)	6 (1.2)	0	2 (0.4)
	Acute respiratory failure	急性呼吸不全	2 (0.2)	0	0	2 (0.2)	0	0	2 (0.4)	0	0	0	0	2 (0.4)

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (0.1)	0	0	1 (0.1)	0	0	3 (0.6)	0	1 (0.2)	1 (0.2)	1 (0.2)	0
	Cough	咳嗽	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Dyspnoea	呼吸困難	4 (0.4)	0	1 (0.1)	2 (0.2)	0	1 (0.1)	1 (0.2)	0	0	1 (0.2)	0	0
	Epistaxis	鼻出血	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pleural effusion	胸水	2 (0.2)	0	1 (0.1)	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pneumonia aspiration	誤嚥性肺炎	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Pulmonary embolism	肺塞栓症	5 (0.6)	0	0	2 (0.2)	1 (0.1)	2 (0.2)	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary thrombosis	肺血栓症	0	0	0	0	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Respiratory failure	呼吸不全	2 (0.2)	0	0	0	2 (0.2)	0	1 (0.2)	0	0	1 (0.2)	0	0
Skin and subcutaneous tissue disorders	Any	皮膚および皮下組織障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Dermatitis allergic	アレルギー性皮膚炎	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Skin mass	皮膚腫瘤	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Surgical and medical procedures	Any	外科および内科処置	5 (0.6)	0	0	5 (0.6)	0	0	3 (0.6)	0	0	3 (0.6)	0	0
	Bladder catheterisation	膀胱カテーテル留置	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Cyst removal	嚢胞切除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hip arthroplasty	股関節形成	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Orchidectomy	精巣摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Prostatectomy	前立腺摘除	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Pulmonary resection	肺切除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Vascular disorders	Any	血管障害	11 (1.2)	3 (0.3)	2 (0.2)	5 (0.6)	0	1 (0.1)	5 (1.0)	0	0	3 (0.6)	0	2 (0.4)
	Aortic aneurysm	大動脈瘤	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Aortic dissection	大動脈解離	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
	Aortic stenosis	大動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Arteriosclerosis	動脈硬化症	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)

付表 2.7.6.9.a.1-16 重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
	Circulatory collapse	循環虚脱	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Embolism	塞栓症	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Hypertension	高血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Hypotension	低血圧	1 (0.1)	1 (0.1)	0	0	0	0	0	0	0	0	0	0
	Lymphoedema	リンパ浮腫	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Orthostatic hypotension	起立性低血圧	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Peripheral artery stenosis	末梢動脈狭窄	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Thrombosis	血栓症	1 (0.1)	0	1 (0.1)	0	0	0	0	0	0	0	0	0
	Venous thrombosis	静脈血栓症	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.2/2

付表 2.7.6.9.a.1-17 治験薬と関連のある重篤な TEAE の発現例数及び割合（CTCAE グレード別、日本人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=62) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Placebo (N=33) Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		2 (3.2)	0	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0
Hepatobiliary disorders	Any	肝胆道系障害	1 (1.6)	0	0	0	1 (1.6)	0	0	0	0	0	0	0
	Hepatic function abnormal	肝機能異常	1 (1.6)	0	0	0	1 (1.6)	0	0	0	0	0	0	0
Vascular disorders	Any	血管障害	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0
	Deep vein thrombosis	深部静脈血栓症	1 (1.6)	0	1 (1.6)	0	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.2/13

付表 2.7.6.9.a.1-18 治験薬と関連のある重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Number (%) of subjects														
All system organ classes	Any		8 (0.9)	0	0	5 (0.6)	2 (0.2)	1 (0.1)	6 (1.2)	0	0	4 (0.8)	0	2 (0.4)
Cardiac disorders	Any	心臓障害	2 (0.2)	0	0	2 (0.2)	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Atrioventricular block complete	完全房室ブロック	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Conduction disorder	伝導障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Myocardial infarction	心筋梗塞	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
Gastrointestinal disorders	Any	胃腸障害	1 (0.1)	0	0	0	0	1 (0.1)	1 (0.2)	0	0	1 (0.2)	0	0
	Gastritis	胃炎	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Small intestinal perforation	小腸穿孔	1 (0.1)	0	0	0	0	1 (0.1)	0	0	0	0	0	0
Investigations	Any	臨床検査	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
Metabolism and nutrition disorders	Any	代謝および栄養障害	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
	Hyperglycaemia	高血糖	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Nervous system disorders	Any	神経系障害	1 (0.1)	0	0	0	1 (0.1)	0	2 (0.4)	0	0	1 (0.2)	0	1 (0.2)
	Haemorrhage intracranial	頭蓋内出血	0	0	0	0	0	0	1 (0.2)	0	0	0	0	1 (0.2)
	Ischaemic stroke	虚血性脳卒中	1 (0.1)	0	0	0	1 (0.1)	0	0	0	0	0	0	0
	Transient ischaemic attack	一過性脳虚血発作	0	0	0	0	0	0	1 (0.2)	0	0	1 (0.2)	0	0
Renal and urinary disorders	Any	腎および尿路障害	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0
	Urinary retention	尿閉	1 (0.1)	0	0	1 (0.1)	0	0	1 (0.2)	0	1 (0.2)	0	0	0

付表 2.7.6.9.a.1-18 治験薬と関連のある重篤な TEAE の発現例数及び割合（CTCAE グレード別、外国人集団、SAF）（続き）

System organ class (SOC)	Preferred term (PT)		Darolutamide (N=892)						Placebo (N=521)					
			Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))	Total (N (%))	G 1 (N (%))	G 2 (N (%))	G 3 (N (%))	G 4 (N (%))	G 5 (N (%))
Respiratory, thoracic and mediastinal disorders	Any	呼吸器、胸郭および縦隔障害	1 (0.1)	0	0	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
	Pulmonary embolism	肺塞栓症	1 (0.1)	0	0	0	1 (0.1)	0	1 (0.2)	0	0	1 (0.2)	0	0
Vascular disorders	Any	血管障害	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0
	Peripheral ischaemia	末梢性虚血	1 (0.1)	0	0	1 (0.1)	0	0	0	0	0	0	0	0

"Worst CTCAE grade" = "Missing" includes only subjects with grade not available for all adverse events.
CTCAE version 4.03 and MedDRA version 21.0
Source: 5.3.5.1.3 17712_JP/Table 14.3.2/14

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE (SAF)

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Number of subjects (%) with at least one adverse event	Number of subjects (%) with at least one adverse event	794 (83.2%)	426 (76.9%)	258 (27.0%)	110 (19.9%)
Blood and lymphatic system disorders	血液およびリンパ系障害	75 (7.9%)	37 (6.7%)	17 (1.8%)	4 (0.7%)
Abdominal lymphadenopathy	腹部リンパ節腫脹	1 (0.1%)	0	0	0
Anaemia	貧血	53 (5.6%)	25 (4.5%)	9 (0.9%)	2 (0.4%)
Basophilia	好塩基球増加症	0	1 (0.2%)	0	0
Eosinophilia	好酸球増加症	1 (0.1%)	0	0	0
Febrile neutropenia	発熱性好中球減少症	0	1 (0.2%)	0	0
Iron deficiency anaemia	鉄欠乏性貧血	4 (0.4%)	1 (0.2%)	0	0
Leukocytosis	白血球増加症	2 (0.2%)	0	0	0
Leukopenia	白血球減少症	7 (0.7%)	2 (0.4%)	2 (0.2%)	0
Lymphadenopathy	リンパ節症	1 (0.1%)	0	0	0
Lymphopenia	リンパ球減少症	9 (0.9%)	5 (0.9%)	2 (0.2%)	1 (0.2%)
Nephrogenic anaemia	腎性貧血	1 (0.1%)	0	0	0
Neutropenia	好中球減少症	13 (1.4%)	5 (0.9%)	6 (0.6%)	1 (0.2%)
Retroperitoneal lymphadenopathy	後腹膜リンパ節腫脹	0	1 (0.2%)	0	0
Splenic calcification	脾臓石灰化	0	1 (0.2%)	0	0
Thrombocytopenia	血小板減少症	5 (0.5%)	1 (0.2%)	0	0
Cardiac disorders	心臓障害	113 (11.8%)	41 (7.4%)	10 (1.0%)	3 (0.5%)
Acute coronary syndrome	急性冠動脈症候群	0	1 (0.2%)	0	0
Acute myocardial infarction	急性心筋梗塞	5 (0.5%)	1 (0.2%)	0	0
Angina pectoris	狭心症	12 (1.3%)	4 (0.7%)	0	0
Angina unstable	不安定狭心症	0	1 (0.2%)	0	0
Aortic valve disease	大動脈弁疾患	1 (0.1%)	0	0	0
Aortic valve incompetence	大動脈弁閉鎖不全症	1 (0.1%)	0	0	0
Aortic valve stenosis	大動脈弁狭窄	3 (0.3%)	0	0	0
Arrhythmia	不整脈	14 (1.5%)	3 (0.5%)	3 (0.3%)	0
Arrhythmia supraventricular	上室性不整脈	1 (0.1%)	0	1 (0.1%)	0
Arteriosclerosis coronary artery	冠動脈硬化症	0	2 (0.4%)	0	0
Atrial fibrillation	心房細動	22 (2.3%)	8 (1.4%)	0	1 (0.2%)
Atrial flutter	心房粗動	2 (0.2%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Atrioventricular block	房室ブロック	2 (0.2%)	0	0	0
Atrioventricular block complete	完全房室ブロック	1 (0.1%)	0	1 (0.1%)	0
Atrioventricular block first degree	第一度房室ブロック	0	1 (0.2%)	0	0
Atrioventricular block second degree	第二度房室ブロック	3 (0.3%)	0	0	0
Bradycardia	徐脈	10 (1.0%)	1 (0.2%)	2 (0.2%)	0
Bundle branch block left	左脚ブロック	1 (0.1%)	1 (0.2%)	0	0
Bundle branch block right	右脚ブロック	1 (0.1%)	0	0	0
Cardiac aneurysm	心臓瘤	0	1 (0.2%)	0	0
Cardiac arrest	心停止	2 (0.2%)	3 (0.5%)	0	0
Cardiac disorder	心障害	1 (0.1%)	0	0	0
Cardiac failure	心不全	13 (1.4%)	5 (0.9%)	0	0
Cardiac failure acute	急性心不全	2 (0.2%)	0	0	0
Cardiac failure chronic	慢性心不全	2 (0.2%)	0	0	0
Cardiac failure congestive	うっ血性心不全	1 (0.1%)	0	0	0
Cardiac flutter	心粗動	1 (0.1%)	0	0	0
Cardiac steatosis	心臓脂肪症	1 (0.1%)	0	0	0
Cardiogenic shock	心原性ショック	1 (0.1%)	0	0	0
Cardiovascular insufficiency	心血管不全	1 (0.1%)	0	0	0
Conduction disorder	伝導障害	1 (0.1%)	0	1 (0.1%)	0
Coronary artery disease	冠動脈疾患	10 (1.0%)	1 (0.2%)	0	0
Coronary artery occlusion	冠動脈閉塞	1 (0.1%)	1 (0.2%)	0	0
Coronary artery stenosis	冠動脈狭窄	2 (0.2%)	0	0	0
Defect conduction intraventricular	心室内伝導障害	1 (0.1%)	0	0	0
Extrasystoles	期外収縮	2 (0.2%)	0	0	0
Hypertensive heart disease	高血圧性心疾患	0	1 (0.2%)	0	0
Left atrial enlargement	左房拡大	0	1 (0.2%)	0	0
Left ventricular dilatation	左室拡張	1 (0.1%)	0	0	0
Mitral valve incompetence	僧帽弁閉鎖不全症	1 (0.1%)	1 (0.2%)	0	0
Myocardial infarction	心筋梗塞	6 (0.6%)	3 (0.5%)	0	2 (0.4%)
Myocardial ischaemia	心筋虚血	3 (0.3%)	1 (0.2%)	0	0
Palpitations	動悸	7 (0.7%)	3 (0.5%)	1 (0.1%)	0
Sinus arrhythmia	洞性不整脈	0	1 (0.2%)	0	0
Sinus bradycardia	洞性徐脈	4 (0.4%)	0	0	0
Sinus node dysfunction	洞結節機能不全	2 (0.2%)	0	0	0
Supraventricular extrasystoles	上室性期外収縮	2 (0.2%)	0	1 (0.1%)	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Tachycardia	頻脈	5 (0.5%)	2 (0.4%)	0	0
Tachycardia paroxysmal	発作性頻脈	1 (0.1%)	0	0	0
Tricuspid valve disease	三尖弁疾患	1 (0.1%)	0	0	0
Ventricular extrasystoles	心室性期外収縮	3 (0.3%)	2 (0.4%)	0	0
Ventricular fibrillation	心室細動	0	1 (0.2%)	0	0
Ventricular tachycardia	心室性頻脈	1 (0.1%)	0	0	0
Congenital, familial and genetic disorders	先天性、家族性および遺伝性障害	5 (0.5%)	2 (0.4%)	0	0
Congenital renal cyst	先天性腎嚢胞	1 (0.1%)	0	0	0
Phimosis	包茎	4 (0.4%)	2 (0.4%)	0	0
Ear and labyrinth disorders	耳および迷路障害	14 (1.5%)	11 (2.0%)	1 (0.1%)	2 (0.4%)
External ear disorder	外耳障害	1 (0.1%)	0	0	0
Hypoacusis	聴力低下	1 (0.1%)	0	0	0
Otorrhoea	耳漏	0	2 (0.4%)	0	0
Tinnitus	耳鳴	4 (0.4%)	0	1 (0.1%)	0
Vertigo	回転性めまい	8 (0.8%)	9 (1.6%)	0	2 (0.4%)
Vertigo positional	頭位性回転性めまい	1 (0.1%)	0	0	0
Endocrine disorders	内分泌障害	9 (0.9%)	0	0	0
Adrenal calcification	副腎石灰化	2 (0.2%)	0	0	0
Adrenomegaly	副腎肥大	1 (0.1%)	0	0	0
Basedow's disease	バセドウ病	1 (0.1%)	0	0	0
Hyperthyroidism	甲状腺機能亢進症	2 (0.2%)	0	0	0
Hypothyroidism	甲状腺機能低下症	2 (0.2%)	0	0	0
Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	1 (0.1%)	0	0	0
Thyroid calcification	甲状腺石灰化	1 (0.1%)	0	0	0
Thyroid mass	甲状腺腫瘤	2 (0.2%)	0	0	0
Eye disorders	眼障害	20 (2.1%)	19 (3.4%)	1 (0.1%)	1 (0.2%)
Age-related macular degeneration	加齢黄斑変性	0	1 (0.2%)	0	0
Blepharitis	眼瞼炎	1 (0.1%)	0	1 (0.1%)	0
Blindness	失明	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Blindness unilateral	片側失明	0	1 (0.2%)	0	0
Cataract	白内障	6 (0.6%)	2 (0.4%)	0	0
Conjunctival deposit	結膜沈着物	0	1 (0.2%)	0	0
Conjunctival haemorrhage	結膜出血	1 (0.1%)	1 (0.2%)	0	0
Conjunctivitis allergic	アレルギー性結膜炎	1 (0.1%)	0	0	0
Corneal disorder	角膜障害	0	1 (0.2%)	0	0
Corneal oedema	角膜浮腫	0	1 (0.2%)	0	0
Diplopia	複視	1 (0.1%)	1 (0.2%)	0	0
Dry eye	眼乾燥	3 (0.3%)	1 (0.2%)	0	0
Eye inflammation	眼の炎症	0	1 (0.2%)	0	0
Eye irritation	眼刺激	1 (0.1%)	0	0	0
Eye pain	眼痛	0	2 (0.4%)	0	0
Eyelid ptosis	眼瞼下垂	0	1 (0.2%)	0	0
Glaucoma	緑内障	1 (0.1%)	2 (0.4%)	0	0
Lacrimation increased	流涙増加	1 (0.1%)	0	0	0
Macular degeneration	黄斑変性	0	1 (0.2%)	0	0
Ocular hyperaemia	眼充血	0	2 (0.4%)	0	0
Periorbital oedema	眼窩周囲浮腫	1 (0.1%)	0	0	0
Pterygium	翼状片	0	1 (0.2%)	0	0
Retinal artery occlusion	網膜動脈閉塞	1 (0.1%)	0	0	0
Retinal detachment	網膜剥離	1 (0.1%)	0	0	0
Retinal vascular disorder	網膜血管障害	0	1 (0.2%)	0	0
Vision blurred	霧視	1 (0.1%)	1 (0.2%)	0	0
Visual acuity reduced	視力低下	0	2 (0.4%)	0	1 (0.2%)
Visual impairment	視力障害	1 (0.1%)	1 (0.2%)	0	0
Vitreous floaters	硝子体浮遊物	0	2 (0.4%)	0	0
Gastrointestinal disorders	胃腸障害	276 (28.9%)	141 (25.5%)	61 (6.4%)	37 (6.7%)
Abdominal discomfort	腹部不快感	6 (0.6%)	1 (0.2%)	1 (0.1%)	1 (0.2%)
Abdominal distension	腹部膨満	11 (1.2%)	4 (0.7%)	4 (0.4%)	2 (0.4%)
Abdominal hernia	腹部ヘルニア	1 (0.1%)	2 (0.4%)	0	0
Abdominal pain	腹痛	24 (2.5%)	12 (2.2%)	4 (0.4%)	1 (0.2%)
Abdominal pain lower	下腹部痛	5 (0.5%)	1 (0.2%)	0	0
Abdominal pain upper	上腹部痛	12 (1.3%)	13 (2.3%)	3 (0.3%)	4 (0.7%)
Abdominal tenderness	腹部圧痛	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Anal haemorrhage	肛門出血	1 (0.1%)	1 (0.2%)	1 (0.1%)	0
Anal incontinence	肛門失禁	1 (0.1%)	0	0	0
Anorectal discomfort	肛門直腸不快感	2 (0.2%)	0	0	0
Ascites	腹水	0	1 (0.2%)	0	0
Barrett's oesophagus	バレット食道	1 (0.1%)	0	0	0
Bowel movement irregularity	便通不規則	1 (0.1%)	0	0	0
Breath odour	呼気臭	1 (0.1%)	1 (0.2%)	0	0
Cheilitis	口唇炎	0	1 (0.2%)	0	0
Chronic gastritis	慢性胃炎	2 (0.2%)	0	0	0
Colitis	大腸炎	1 (0.1%)	0	0	0
Constipation	便秘	60 (6.3%)	34 (6.1%)	10 (1.0%)	5 (0.9%)
Crohn's disease	クローン病	1 (0.1%)	0	0	0
Dental caries	齲歯	2 (0.2%)	1 (0.2%)	0	0
Diaphragmatic hernia	横隔膜ヘルニア	0	1 (0.2%)	0	0
Diarrhoea	下痢	66 (6.9%)	31 (5.6%)	15 (1.6%)	9 (1.6%)
Diverticulum	憩室	3 (0.3%)	0	0	0
Diverticulum intestinal	腸憩室	10 (1.0%)	7 (1.3%)	0	0
Diverticulum oesophageal	食道憩室	1 (0.1%)	0	0	0
Dry mouth	口内乾燥	10 (1.0%)	5 (0.9%)	9 (0.9%)	5 (0.9%)
Duodenal ulcer	十二指腸潰瘍	1 (0.1%)	0	1 (0.1%)	0
Dyspepsia	消化不良	11 (1.2%)	7 (1.3%)	3 (0.3%)	0
Dysphagia	嚥下障害	3 (0.3%)	4 (0.7%)	0	0
Enterovesical fistula	腸膀胱瘻	2 (0.2%)	0	0	0
Epigastric discomfort	心窩部不快感	1 (0.1%)	0	0	0
Eructation	おくび	1 (0.1%)	0	0	0
Faeces hard	硬便	1 (0.1%)	0	0	0
Flatulence	鼓腸	4 (0.4%)	4 (0.7%)	1 (0.1%)	1 (0.2%)
Food poisoning	食中毒	1 (0.1%)	0	0	0
Frequent bowel movements	排便回数増加	1 (0.1%)	0	1 (0.1%)	0
Gastric disorder	胃障害	1 (0.1%)	0	0	0
Gastric polyps	胃ポリープ	1 (0.1%)	0	0	0
Gastric ulcer	胃潰瘍	2 (0.2%)	1 (0.2%)	0	0
Gastritis	胃炎	2 (0.2%)	5 (0.9%)	0	1 (0.2%)
Gastritis erosive	びらん性胃炎	3 (0.3%)	0	1 (0.1%)	0
Gastroduodenitis	胃十二指腸炎	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Gastrointestinal angiectasia	胃腸血管拡張症	1 (0.1%)	0	0	0
Gastrointestinal haemorrhage	胃腸出血	1 (0.1%)	0	0	0
Gastrointestinal inflammation	胃腸の炎症	0	1 (0.2%)	0	0
Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	1 (0.1%)	0	1 (0.1%)	0
Gastrointestinal pain	消化器痛	2 (0.2%)	1 (0.2%)	0	0
Gastrointestinal wall thickening	消化管壁肥厚	1 (0.1%)	0	0	0
Gastrooesophageal reflux disease	胃食道逆流性疾患	11 (1.2%)	4 (0.7%)	1 (0.1%)	1 (0.2%)
Gingival discomfort	歯肉不快感	1 (0.1%)	0	0	0
Gingival pain	歯肉痛	1 (0.1%)	0	0	0
Glossitis	舌炎	1 (0.1%)	0	0	0
Haematochezia	血便排泄	3 (0.3%)	2 (0.4%)	0	0
Haemorrhoidal haemorrhage	痔出血	0	1 (0.2%)	0	0
Haemorrhoids	痔核	6 (0.6%)	0	0	0
Hiatus hernia	裂孔ヘルニア	5 (0.5%)	1 (0.2%)	0	0
Ileus	イレウス	2 (0.2%)	1 (0.2%)	0	0
Impaired gastric emptying	胃排出不全	1 (0.1%)	0	0	0
Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	2 (0.2%)	0	0	0
Inguinal hernia	鼠径ヘルニア	11 (1.2%)	1 (0.2%)	0	0
Intestinal obstruction	腸閉塞	4 (0.4%)	0	0	0
Intra-abdominal haematoma	腹腔内血腫	1 (0.1%)	0	0	0
Irritable bowel syndrome	過敏性腸症候群	1 (0.1%)	0	0	0
Jejunal stenosis	空腸狭窄	0	1 (0.2%)	0	0
Large intestinal stenosis	大腸狭窄	0	1 (0.2%)	0	0
Large intestine perforation	大腸穿孔	1 (0.1%)	0	0	0
Large intestine polyp	大腸ポリープ	4 (0.4%)	1 (0.2%)	0	0
Lip disorder	口唇障害	1 (0.1%)	0	0	0
Lip pain	口唇痛	0	1 (0.2%)	0	0
Lower gastrointestinal haemorrhage	下部消化管出血	2 (0.2%)	0	0	0
Melaena	メレナ	1 (0.1%)	1 (0.2%)	0	0
Mesenteric artery stenosis	腸間膜動脈狭窄	1 (0.1%)	0	0	0
Mesenteric panniculitis	腸間膜脂肪織炎	1 (0.1%)	0	0	0
Nausea	悪心	48 (5.0%)	32 (5.8%)	24 (2.5%)	17 (3.1%)
Obstructive pancreatitis	閉塞性膵炎	1 (0.1%)	0	0	0
Oesophageal pain	食道痛	0	1 (0.2%)	0	1 (0.2%)
Oesophagitis	食道炎	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Pancreatic atrophy	膵萎縮	1 (0.1%)	0	0	0
Pancreatic calcification	膵石灰化	0	1 (0.2%)	0	0
Pancreatic cyst	膵嚢胞	1 (0.1%)	1 (0.2%)	0	0
Pancreatic duct dilatation	膵管拡張	1 (0.1%)	1 (0.2%)	0	0
Pancreatic steatosis	膵脂肪変性	6 (0.6%)	3 (0.5%)	0	0
Pancreatitis	膵炎	0	1 (0.2%)	0	0
Pancreatitis acute	急性膵炎	0	1 (0.2%)	0	0
Pancreatitis chronic	慢性膵炎	1 (0.1%)	0	0	0
Paraesthesia oral	口の錯感覚	0	1 (0.2%)	0	0
Parotid duct obstruction	耳下腺管閉塞	1 (0.1%)	0	0	0
Peptic ulcer	消化性潰瘍	1 (0.1%)	1 (0.2%)	0	0
Periodontal disease	歯周病	3 (0.3%)	1 (0.2%)	0	0
Plicated tongue	ひだ舌	1 (0.1%)	0	1 (0.1%)	0
Pneumoperitoneum	気腹	1 (0.1%)	0	0	0
Proctalgia	肛門周囲痛	1 (0.1%)	0	0	0
Proctitis	直腸炎	2 (0.2%)	0	0	0
Rectal haemorrhage	直腸出血	7 (0.7%)	2 (0.4%)	1 (0.1%)	0
Rectal stenosis	直腸狭窄	1 (0.1%)	0	0	0
Salivary gland pain	唾液腺痛	1 (0.1%)	0	0	0
Small intestinal obstruction	小腸閉塞	1 (0.1%)	2 (0.4%)	0	0
Small intestinal perforation	小腸穿孔	1 (0.1%)	0	1 (0.1%)	0
Splenic artery aneurysm	脾臓動脈瘤	0	1 (0.2%)	0	0
Stomatitis	口内炎	0	1 (0.2%)	0	0
Tongue coated	舌苔	1 (0.1%)	0	0	0
Tooth loss	歯の脱落	1 (0.1%)	0	0	0
Toothache	歯痛	7 (0.7%)	4 (0.7%)	0	0
Umbilical hernia	臍ヘルニア	3 (0.3%)	1 (0.2%)	0	0
Upper gastrointestinal haemorrhage	上部消化管出血	0	1 (0.2%)	0	0
Vomiting	嘔吐	15 (1.6%)	10 (1.8%)	3 (0.3%)	2 (0.4%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	244 (25.6%)	104 (18.8%)	86 (9.0%)	32 (5.8%)
Asthenia	無力症	36 (3.8%)	19 (3.4%)	9 (0.9%)	7 (1.3%)
Catheter site related reaction	カテーテル留置部位関連反応	0	1 (0.2%)	0	0
Catheter site ulcer	カテーテル留置部位潰瘍	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Chest pain	胸痛	15 (1.6%)	8 (1.4%)	1 (0.1%)	0
Chills	悪寒	8 (0.8%)	2 (0.4%)	2 (0.2%)	2 (0.4%)
Cyst	嚢胞	1 (0.1%)	0	0	0
Death	死亡	4 (0.4%)	1 (0.2%)	0	0
Discomfort	不快感	1 (0.1%)	0	1 (0.1%)	0
Exercise tolerance decreased	運動耐性低下	1 (0.1%)	0	0	0
Face oedema	顔面浮腫	1 (0.1%)	0	1 (0.1%)	0
Fatigue	疲労	115 (12.1%)	48 (8.7%)	68 (7.1%)	24 (4.3%)
Feeling cold	冷感	2 (0.2%)	0	0	0
Gait disturbance	歩行障害	4 (0.4%)	2 (0.4%)	2 (0.2%)	0
General physical health deterioration	全身健康状態低下	5 (0.5%)	0	0	0
Granuloma	肉芽腫	2 (0.2%)	0	0	0
Influenza like illness	インフルエンザ様疾患	10 (1.0%)	4 (0.7%)	0	0
Infusion site extravasation	注入部位血管外漏出	1 (0.1%)	0	0	0
Injection site bruising	注射部位内出血	1 (0.1%)	0	0	0
Injection site erythema	注射部位紅斑	1 (0.1%)	0	0	0
Injection site pain	注射部位疼痛	2 (0.2%)	0	0	0
Injection site reaction	注射部位反応	2 (0.2%)	0	0	0
Malaise	倦怠感	4 (0.4%)	3 (0.5%)	1 (0.1%)	2 (0.4%)
Nodule	小結節	1 (0.1%)	0	0	0
Non-cardiac chest pain	非心臓性胸痛	4 (0.4%)	1 (0.2%)	0	0
Oedema	浮腫	4 (0.4%)	1 (0.2%)	0	0
Oedema peripheral	末梢性浮腫	39 (4.1%)	17 (3.1%)	5 (0.5%)	3 (0.5%)
Pain	疼痛	5 (0.5%)	7 (1.3%)	0	0
Pelvic mass	骨盤腔内腫瘤	2 (0.2%)	0	0	0
Performance status decreased	活動状態低下	1 (0.1%)	0	0	0
Peripheral swelling	末梢腫脹	13 (1.4%)	7 (1.3%)	1 (0.1%)	0
Pyrexia	発熱	19 (2.0%)	5 (0.9%)	1 (0.1%)	0
Sudden cardiac death	心突然死	1 (0.1%)	0	0	0
Sudden death	突然死	1 (0.1%)	0	0	0
Suprapubic pain	恥骨上痛	1 (0.1%)	3 (0.5%)	0	0
Temperature intolerance	温度変化不耐症	1 (0.1%)	0	0	0
Thirst	口渇	1 (0.1%)	1 (0.2%)	1 (0.1%)	1 (0.2%)

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Hepatobiliary disorders	肝胆道系障害	31 (3.2%)	10 (1.8%)	6 (0.6%)	2 (0.4%)
Bile duct obstruction	胆管閉塞	1 (0.1%)	0	0	0
Bile duct stenosis	胆管狭窄	1 (0.1%)	0	0	0
Biliary colic	胆道仙痛	1 (0.1%)	1 (0.2%)	0	0
Cholangitis acute	急性胆管炎	1 (0.1%)	1 (0.2%)	0	0
Cholecystitis acute	急性胆嚢炎	1 (0.1%)	1 (0.2%)	0	0
Cholecystitis chronic	慢性胆嚢炎	1 (0.1%)	0	0	0
Cholelithiasis	胆石症	7 (0.7%)	1 (0.2%)	0	0
Cholestasis	胆汁うっ滞	1 (0.1%)	0	0	0
Drug-induced liver injury	薬物性肝障害	1 (0.1%)	0	0	0
Hepatic artery thrombosis	肝動脈血栓症	1 (0.1%)	0	0	0
Hepatic calcification	肝石灰化	4 (0.4%)	0	0	0
Hepatic cyst	肝嚢胞	7 (0.7%)	4 (0.7%)	0	0
Hepatic function abnormal	肝機能異常	4 (0.4%)	1 (0.2%)	2 (0.2%)	1 (0.2%)
Hepatic steatosis	脂肪肝	1 (0.1%)	1 (0.2%)	0	0
Hepatobiliary disease	肝胆道系疾患	0	1 (0.2%)	0	1 (0.2%)
Hyperbilirubinaemia	高ビリルビン血症	6 (0.6%)	0	4 (0.4%)	0
Jaundice	黄疸	2 (0.2%)	0	0	0
Liver disorder	肝障害	1 (0.1%)	0	0	0
Immune system disorders	免疫系障害	14 (1.5%)	6 (1.1%)	0	0
Allergy to arthropod sting	節足動物刺傷アレルギー	1 (0.1%)	0	0	0
Anaphylactic reaction	アナフィラキシー反応	1 (0.1%)	0	0	0
Contrast media allergy	造影剤アレルギー	3 (0.3%)	3 (0.5%)	0	0
Contrast media reaction	造影剤反応	0	1 (0.2%)	0	0
Drug hypersensitivity	薬物過敏症	3 (0.3%)	0	0	0
Hypersensitivity	過敏症	2 (0.2%)	1 (0.2%)	0	0
Immune system disorder	免疫系障害	0	1 (0.2%)	0	0
Seasonal allergy	季節性アレルギー	4 (0.4%)	0	0	0
Infections and infestations	感染症および寄生虫症	227 (23.8%)	120 (21.7%)	2 (0.2%)	1 (0.2%)
Abdominal abscess	腹部膿瘍	2 (0.2%)	0	0	0
Abscess	膿瘍	1 (0.1%)	0	0	0
Abscess intestinal	腸管膿瘍	1 (0.1%)	0	0	0
Acarodermatitis	ダニ皮膚炎	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Acute endocarditis	急性心内膜炎	1 (0.1%)	0	0	0
Acute sinusitis	急性副鼻腔炎	1 (0.1%)	1 (0.2%)	0	0
Appendicitis	虫垂炎	2 (0.2%)	1 (0.2%)	0	0
Bacterial infection	細菌感染	0	1 (0.2%)	0	0
Bacteriuria	細菌尿	1 (0.1%)	0	0	0
Balanitis candida	カンジダ性亀頭炎	0	1 (0.2%)	0	0
Balanoposthitis infective	感染性亀頭包皮炎	0	1 (0.2%)	0	0
Bronchitis	気管支炎	11 (1.2%)	9 (1.6%)	0	0
Bronchitis viral	ウイルス性気管支炎	1 (0.1%)	0	0	0
Catheter site infection	カテーテル留置部位感染	0	1 (0.2%)	0	0
Cellulitis	蜂巣炎	1 (0.1%)	1 (0.2%)	0	0
Cellulitis gangrenous	壊疽性蜂巣炎	0	1 (0.2%)	0	0
Cholecystitis infective	感染性胆嚢炎	1 (0.1%)	0	0	0
Conjunctivitis	結膜炎	4 (0.4%)	0	0	0
Cystitis	膀胱炎	8 (0.8%)	7 (1.3%)	0	0
Dermatophytosis of nail	爪の皮膚糸状菌症	1 (0.1%)	0	0	0
Device related infection	医療機器関連感染	1 (0.1%)	1 (0.2%)	0	0
Diverticulitis	憩室炎	1 (0.1%)	0	0	0
Ear infection	耳感染	1 (0.1%)	0	0	0
Ear infection bacterial	細菌性耳感染	1 (0.1%)	0	0	0
Endocarditis	心内膜炎	1 (0.1%)	0	0	0
Erysipelas	丹毒	2 (0.2%)	0	0	0
Eye infection bacterial	細菌性眼感染	1 (0.1%)	0	0	0
Febrile infection	熱性感染症	1 (0.1%)	0	0	0
Folliculitis	毛包炎	1 (0.1%)	0	0	0
Fungal balanitis	真菌性亀頭炎	1 (0.1%)	0	0	0
Fungal skin infection	皮膚真菌感染	1 (0.1%)	0	0	0
Gangrene	壊疽	1 (0.1%)	0	0	0
Gastroenteritis	胃腸炎	5 (0.5%)	2 (0.4%)	0	0
Gastroenteritis viral	ウイルス性胃腸炎	0	1 (0.2%)	0	0
Gastrointestinal infection	消化管感染	0	1 (0.2%)	0	0
Genital infection fungal	真菌性性器感染	1 (0.1%)	0	0	0
Gingivitis	歯肉炎	2 (0.2%)	1 (0.2%)	0	0
Helicobacter gastritis	ヘリコバクター性胃炎	1 (0.1%)	0	0	0
Helicobacter infection	ヘリコバクター感染	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Hepatitis C	C型肝炎	0	1 (0.2%)	0	0
Herpes zoster	帯状疱疹	4 (0.4%)	4 (0.7%)	0	0
Infected bite	咬傷感染	1 (0.1%)	0	0	0
Infection	感染	0	1 (0.2%)	0	0
Infectious mononucleosis	伝染性単核症	0	1 (0.2%)	0	0
Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	2 (0.2%)	0	0	0
Infestation	寄生	0	1 (0.2%)	0	0
Influenza	インフルエンザ	27 (2.8%)	9 (1.6%)	0	0
Intervertebral discitis	椎間板炎	1 (0.1%)	0	0	0
Klebsiella bacteraemia	クレブシエラ性菌血症	0	1 (0.2%)	0	0
Labyrinthitis	迷路炎	0	1 (0.2%)	0	0
Laryngitis	喉頭炎	2 (0.2%)	0	0	0
Localised infection	限局性感染	1 (0.1%)	1 (0.2%)	0	0
Lower respiratory tract infection	下気道感染	4 (0.4%)	1 (0.2%)	0	0
Lung infection	肺感染	3 (0.3%)	0	0	0
Medical device site joint infection	医療機器使用部位関節感染	1 (0.1%)	0	0	0
Meningitis bacterial	細菌性髄膜炎	1 (0.1%)	0	0	0
Nasopharyngitis	上咽頭炎	36 (3.8%)	21 (3.8%)	0	0
Oesophageal candidiasis	食道カンジダ症	1 (0.1%)	0	0	0
Onychomycosis	爪真菌症	3 (0.3%)	2 (0.4%)	0	0
Oral candidiasis	口腔カンジダ症	3 (0.3%)	0	1 (0.1%)	0
Oral herpes	口腔ヘルペス	2 (0.2%)	0	0	0
Orchitis	精巣炎	1 (0.1%)	1 (0.2%)	0	0
Otitis externa	外耳炎	2 (0.2%)	0	0	0
Otitis media	中耳炎	1 (0.1%)	0	0	0
Paronychia	爪囲炎	1 (0.1%)	1 (0.2%)	0	0
Periodontitis	歯周炎	1 (0.1%)	1 (0.2%)	0	0
Peritonitis	腹膜炎	0	1 (0.2%)	0	0
Pharyngitis	咽頭炎	0	1 (0.2%)	0	0
Pneumonia	肺炎	19 (2.0%)	11 (2.0%)	0	0
Pneumonia pneumococcal	肺炎球菌性肺炎	1 (0.1%)	0	0	0
Pneumonia staphylococcal	ブドウ球菌性肺炎	0	1 (0.2%)	0	0
Prostate infection	前立腺感染	0	1 (0.2%)	0	0
Pulmonary tuberculosis	肺結核	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Pulpitis dental	歯髄炎	1 (0.1%)	0	0	0
Pyelonephritis	腎盂腎炎	4 (0.4%)	0	0	0
Pyelonephritis acute	急性腎盂腎炎	3 (0.3%)	1 (0.2%)	0	0
Pyelonephritis chronic	慢性腎盂腎炎	1 (0.1%)	0	0	0
Pyuria	膿尿	1 (0.1%)	0	0	0
Rash pustular	膿疱性皮疹	1 (0.1%)	0	1 (0.1%)	0
Respiratory syncytial virus infection	ＲＳウイルス感染	1 (0.1%)	0	0	0
Respiratory tract infection	気道感染	6 (0.6%)	0	0	0
Respiratory tract infection viral	ウイルス性気道感染	3 (0.3%)	5 (0.9%)	0	0
Rhinitis	鼻炎	4 (0.4%)	6 (1.1%)	0	0
Root canal infection	根管感染	0	1 (0.2%)	0	0
Sepsis	敗血症	1 (0.1%)	0	0	0
Septic shock	敗血症性ショック	1 (0.1%)	0	0	0
Sialoadenitis	唾液腺炎	1 (0.1%)	0	0	0
Sinusitis	副鼻腔炎	2 (0.2%)	4 (0.7%)	0	0
Skin infection	皮膚感染	4 (0.4%)	0	0	0
Subcutaneous abscess	皮下組織膿瘍	0	1 (0.2%)	0	0
Tinea infection	白癬感染	2 (0.2%)	1 (0.2%)	0	0
Tooth abscess	歯膿瘍	2 (0.2%)	2 (0.4%)	0	0
Tooth infection	歯感染	2 (0.2%)	1 (0.2%)	0	0
Tracheitis	気管炎	1 (0.1%)	0	0	0
Tracheobronchitis	気管気管支炎	1 (0.1%)	0	0	0
Trichophytosis	トリコフィトン感染症	1 (0.1%)	0	0	0
Upper respiratory tract infection	上気道感染	25 (2.6%)	9 (1.6%)	0	0
Urinary tract infection	尿路感染	47 (4.9%)	28 (5.1%)	0	1 (0.2%)
Urinary tract infection bacterial	細菌性尿路感染	0	1 (0.2%)	0	0
Urosepsis	尿路性敗血症	2 (0.2%)	0	0	0
Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	1 (0.1%)	0	0	0
Vestibular neuronitis	前庭神経炎	1 (0.1%)	0	0	0
Viral infection	ウイルス感染	3 (0.3%)	2 (0.4%)	0	0
Viral upper respiratory tract infection	ウイルス性上気道感染	2 (0.2%)	0	0	0
Wound infection	創傷感染	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	119 (12.5%)	46 (8.3%)	3 (0.3%)	0
Accident	事故	4 (0.4%)	3 (0.5%)	0	0
Alcohol poisoning	アルコール中毒	1 (0.1%)	0	0	0
Anaemia postoperative	術後貧血	0	1 (0.2%)	0	0
Animal bite	動物咬傷	0	1 (0.2%)	0	0
Ankle fracture	足関節部骨折	2 (0.2%)	0	0	0
Arthropod bite	節足動物咬傷	2 (0.2%)	0	0	0
Auricular haematoma	耳介血腫	0	1 (0.2%)	0	0
Back injury	背部損傷	1 (0.1%)	0	0	0
Bone contusion	骨挫傷	1 (0.1%)	1 (0.2%)	0	0
Cervical vertebral fracture	頚椎骨折	1 (0.1%)	0	0	0
Chest injury	胸部損傷	2 (0.2%)	1 (0.2%)	0	0
Clavicle fracture	鎖骨骨折	1 (0.1%)	0	0	0
Contusion	挫傷	12 (1.3%)	2 (0.4%)	1 (0.1%)	0
Craniocerebral injury	頭蓋脳損傷	1 (0.1%)	0	0	0
Cystitis radiation	放射線性膀胱炎	4 (0.4%)	0	1 (0.1%)	0
Eyelid injury	眼瞼損傷	1 (0.1%)	0	0	0
Face injury	顔面損傷	0	1 (0.2%)	0	0
Facial bones fracture	顔面骨骨折	0	2 (0.4%)	0	0
Fall	転倒	36 (3.8%)	23 (4.2%)	0	0
Femoral neck fracture	大腿骨頚部骨折	2 (0.2%)	0	0	0
Femur fracture	大腿骨骨折	2 (0.2%)	1 (0.2%)	0	0
Fibula fracture	腓骨骨折	1 (0.1%)	0	0	0
Foot fracture	足骨折	1 (0.1%)	2 (0.4%)	0	0
Fracture	骨折	2 (0.2%)	1 (0.2%)	0	0
Frostbite	凍傷	0	1 (0.2%)	0	0
Haematuria traumatic	外傷性血尿	0	1 (0.2%)	0	0
Hand fracture	手骨折	4 (0.4%)	1 (0.2%)	0	0
Head injury	頭部損傷	2 (0.2%)	0	0	0
Heart injury	心臓損傷	1 (0.1%)	0	0	0
Hip fracture	股関節部骨折	0	1 (0.2%)	0	0
Humerus fracture	上腕骨骨折	1 (0.1%)	1 (0.2%)	0	0
Incision site pain	切開部位痛	2 (0.2%)	0	0	0
Injury	損傷	2 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Injury of conjunctiva	結膜損傷	0	1 (0.2%)	0	0
Joint dislocation	関節脱臼	3 (0.3%)	0	0	0
Joint injury	関節損傷	0	1 (0.2%)	0	0
Laceration	裂傷	2 (0.2%)	1 (0.2%)	0	0
Ligament injury	靭帯損傷	0	1 (0.2%)	0	0
Ligament sprain	靭帯捻挫	3 (0.3%)	0	0	0
Limb injury	四肢損傷	7 (0.7%)	0	0	0
Lip injury	口唇損傷	1 (0.1%)	0	0	0
Lumbar vertebral fracture	腰椎骨折	0	1 (0.2%)	0	0
Meniscus injury	半月板損傷	2 (0.2%)	0	0	0
Multiple injuries	多発性外傷	1 (0.1%)	0	0	0
Muscle strain	肉離れ	1 (0.1%)	0	0	0
Patella fracture	膝蓋骨骨折	2 (0.2%)	0	0	0
Post-traumatic pain	外傷後疼痛	5 (0.5%)	0	0	0
Postoperative ileus	術後イレウス	1 (0.1%)	0	0	0
Procedural pain	処置による疼痛	3 (0.3%)	1 (0.2%)	0	0
Radiation proctitis	放射線性直腸炎	4 (0.4%)	1 (0.2%)	0	0
Radius fracture	橈骨骨折	2 (0.2%)	0	0	0
Rib fracture	肋骨骨折	11 (1.2%)	8 (1.4%)	0	0
Road traffic accident	交通事故	3 (0.3%)	1 (0.2%)	0	0
Scapula fracture	肩甲骨骨折	0	1 (0.2%)	0	0
Scratch	引っかき傷	1 (0.1%)	0	0	0
Skin abrasion	皮膚擦過傷	3 (0.3%)	1 (0.2%)	0	0
Skull fracture	頭蓋骨骨折	1 (0.1%)	0	0	0
Soft tissue injury	軟部組織損傷	2 (0.2%)	0	0	0
Spinal compression fracture	脊椎圧迫骨折	2 (0.2%)	1 (0.2%)	1 (0.1%)	0
Spinal fracture	脊椎骨折	1 (0.1%)	0	0	0
Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	2 (0.2%)	0	0	0
Stomal hernia	ストーマ部ヘルニア	0	1 (0.2%)	0	0
Subarachnoid haemorrhage	くも膜下出血	1 (0.1%)	0	0	0
Subcutaneous haematoma	皮下血腫	1 (0.1%)	0	0	0
Subdural haematoma	硬膜下血腫	1 (0.1%)	1 (0.2%)	0	0
Sunburn	サンバーン	1 (0.1%)	0	0	0
Thermal burn	熱傷	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Tooth fracture	歯牙破折	0	1 (0.2%)	0	0
Traumatic fracture	外傷性骨折	4 (0.4%)	2 (0.4%)	0	0
Traumatic haematoma	外傷性血腫	1 (0.1%)	0	0	0
Ulna fracture	尺骨骨折	1 (0.1%)	0	0	0
Upper limb fracture	上肢骨折	1 (0.1%)	1 (0.2%)	0	0
Vascular graft complication	移植血管合併症	1 (0.1%)	0	0	0
Wound complication	創合併症	0	2 (0.4%)	0	0
Wound dehiscence	創離開	1 (0.1%)	0	0	0
Wrist fracture	手首関節骨折	2 (0.2%)	0	0	0
Investigations	臨床検査	144 (15.1%)	63 (11.4%)	32 (3.4%)	5 (0.9%)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	7 (0.7%)	1 (0.2%)	4 (0.4%)	0
Arteriogram coronary	冠血管造影	0	2 (0.4%)	0	0
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	13 (1.4%)	1 (0.2%)	10 (1.0%)	0
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.1%)	3 (0.5%)	1 (0.1%)	0
Blood bilirubin increased	血中ビリルビン増加	12 (1.3%)	0	6 (0.6%)	0
Blood cholesterol increased	血中コレステロール増加	2 (0.2%)	1 (0.2%)	0	0
Blood chromogranin A increased	血中クロモグラニンＡ増加	6 (0.6%)	6 (1.1%)	0	0
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	1 (0.1%)	0	0	0
Blood creatinine increased	血中クレアチニン増加	22 (2.3%)	14 (2.5%)	7 (0.7%)	2 (0.4%)
Blood glucose increased	血中ブドウ糖増加	2 (0.2%)	0	0	0
Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	5 (0.5%)	0	2 (0.2%)	0
Blood potassium decreased	血中カリウム減少	1 (0.1%)	0	0	0
Blood potassium increased	血中カリウム増加	2 (0.2%)	2 (0.4%)	0	0
Blood pressure increased	血圧上昇	4 (0.4%)	3 (0.5%)	0	0
Blood pressure systolic increased	収縮期血圧上昇	0	1 (0.2%)	0	0
Blood sodium decreased	血中ナトリウム減少	1 (0.1%)	0	0	0
Blood testosterone increased	血中テストステロン増加	2 (0.2%)	1 (0.2%)	0	0
Blood urea abnormal	血中尿素異常	1 (0.1%)	0	0	0
Blood urea increased	血中尿素増加	3 (0.3%)	4 (0.7%)	2 (0.2%)	1 (0.2%)
Blood uric acid increased	血中尿酸増加	0	1 (0.2%)	0	0
Body temperature increased	体温上昇	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Breath sounds abnormal	呼吸音異常	2 (0.2%)	1 (0.2%)	0	0
C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.1%)	0	0	0
Cardiac murmur	心雑音	5 (0.5%)	2 (0.4%)	0	0
Carotid bruit	頚動脈雑音	1 (0.1%)	0	0	0
Chest X-ray abnormal	胸部Ｘ線異常	1 (0.1%)	0	0	0
Electrocardiogram QT prolonged	心電図ＱＴ延長	4 (0.4%)	0	1 (0.1%)	0
Electrocardiogram ST segment depression	心電図ＳＴ部分下降	1 (0.1%)	0	0	0
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.1%)	0	1 (0.1%)	0
Gastric pH decreased	胃内ｐＨ低下	0	1 (0.2%)	0	0
Glomerular filtration rate decreased	糸球体濾過率減少	1 (0.1%)	0	0	0
Glomerular filtration rate increased	糸球体濾過率増加	0	1 (0.2%)	0	0
Glucose urine present	尿中ブドウ糖陽性	1 (0.1%)	1 (0.2%)	0	0
Haematocrit decreased	ヘマトクリット減少	1 (0.1%)	0	0	0
Haematology test abnormal	血液学的検査異常	1 (0.1%)	0	0	0
Haemoglobin decreased	ヘモグロビン減少	4 (0.4%)	1 (0.2%)	1 (0.1%)	0
Heart rate increased	心拍数増加	1 (0.1%)	0	0	0
Heart rate irregular	心拍数不整	1 (0.1%)	0	0	0
Heart sounds abnormal	心音異常	1 (0.1%)	0	0	0
International normalised ratio increased	国際標準比増加	1 (0.1%)	2 (0.4%)	1 (0.1%)	0
Lymphocyte count decreased	リンパ球数減少	9 (0.9%)	0	4 (0.4%)	0
Lymphocyte count increased	リンパ球数増加	1 (0.1%)	0	0	0
Neutrophil count decreased	好中球数減少	11 (1.2%)	0	4 (0.4%)	0
Neutrophil count increased	好中球数増加	1 (0.1%)	0	0	0
Platelet count decreased	血小板数減少	7 (0.7%)	2 (0.4%)	2 (0.2%)	0
Protein total decreased	総蛋白減少	1 (0.1%)	0	1 (0.1%)	0
Protein urine present	尿中蛋白陽性	2 (0.2%)	1 (0.2%)	0	0
Red blood cell count decreased	赤血球数減少	2 (0.2%)	0	0	0
Transaminases increased	トランスアミナーゼ上昇	1 (0.1%)	0	1 (0.1%)	0
Troponin increased	トロポニン増加	1 (0.1%)	0	0	0
Urine output decreased	尿量減少	1 (0.1%)	1 (0.2%)	0	0
Vitamin B12 decreased	ビタミンＢ１２減少	0	1 (0.2%)	0	0
Weight decreased	体重減少	34 (3.6%)	12 (2.2%)	5 (0.5%)	2 (0.4%)
Weight increased	体重増加	14 (1.5%)	7 (1.3%)	1 (0.1%)	1 (0.2%)

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
White blood cell count decreased	白血球数減少	8 (0.8%)	1 (0.2%)	3 (0.3%)	0
White blood cells urine positive	尿中白血球陽性	0	1 (0.2%)	0	0
Metabolism and nutrition disorders	代謝および栄養障害	95 (10.0%)	49 (8.8%)	22 (2.3%)	8 (1.4%)
Cachexia	悪液質	1 (0.1%)	0	0	0
Decreased appetite	食欲減退	28 (2.9%)	16 (2.9%)	14 (1.5%)	6 (1.1%)
Dehydration	脱水	6 (0.6%)	4 (0.7%)	1 (0.1%)	1 (0.2%)
Diabetes mellitus	糖尿病	5 (0.5%)	5 (0.9%)	0	0
Diabetes mellitus inadequate control	コントロール不良の糖尿病	1 (0.1%)	0	0	0
Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	1 (0.2%)	0	0
Diabetic metabolic decompensation	糖尿病性代謝代償不全	0	1 (0.2%)	0	0
Dyslipidaemia	脂質異常症	4 (0.4%)	1 (0.2%)	1 (0.1%)	0
Electrolyte imbalance	電解質失調	1 (0.1%)	0	0	0
Folate deficiency	葉酸欠乏	1 (0.1%)	0	0	0
Gout	痛風	3 (0.3%)	2 (0.4%)	1 (0.1%)	0
Hypercholesterolaemia	高コレステロール血症	3 (0.3%)	2 (0.4%)	0	0
Hyperglycaemia	高血糖	9 (0.9%)	3 (0.5%)	1 (0.1%)	1 (0.2%)
Hyperkalaemia	高カリウム血症	16 (1.7%)	9 (1.6%)	4 (0.4%)	0
Hyperlipidaemia	高脂血症	1 (0.1%)	1 (0.2%)	0	1 (0.2%)
Hypernatraemia	高ナトリウム血症	0	1 (0.2%)	0	0
Hypertriglyceridaemia	高トリグリセリド血症	3 (0.3%)	0	0	0
Hyperuricaemia	高尿酸血症	4 (0.4%)	1 (0.2%)	1 (0.1%)	0
Hypocalcaemia	低カルシウム血症	1 (0.1%)	2 (0.4%)	0	0
Hypochloraemia	低クロール血症	1 (0.1%)	0	0	0
Hypoglycaemia	低血糖	3 (0.3%)	0	0	0
Hypokalaemia	低カリウム血症	9 (0.9%)	2 (0.4%)	1 (0.1%)	1 (0.2%)
Hypomagnesaemia	低マグネシウム血症	1 (0.1%)	0	0	0
Hyponatraemia	低ナトリウム血症	7 (0.7%)	2 (0.4%)	2 (0.2%)	0
Hypoproteinaemia	低蛋白血症	0	1 (0.2%)	0	0
Increased appetite	食欲亢進	1 (0.1%)	0	0	0
Iron deficiency	鉄欠乏	2 (0.2%)	1 (0.2%)	0	0
Magnesium deficiency	マグネシウム欠乏	1 (0.1%)	0	0	0
Malnutrition	栄養障害	0	1 (0.2%)	0	0
Metabolic alkalosis	代謝性アルカローシス	1 (0.1%)	0	0	0
Obesity	肥満	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Type 2 diabetes mellitus	２型糖尿病	1 (0.1%)	0	0	0
Vitamin D deficiency	ビタミンＤ欠乏	4 (0.4%)	0	0	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	270 (28.3%)	135 (24.4%)	27 (2.8%)	10 (1.8%)
Arthralgia	関節痛	77 (8.1%)	51 (9.2%)	5 (0.5%)	6 (1.1%)
Arthritis	関節炎	6 (0.6%)	1 (0.2%)	0	0
Axillary mass	腋窩腫瘤	1 (0.1%)	1 (0.2%)	0	0
Back pain	背部痛	84 (8.8%)	50 (9.0%)	7 (0.7%)	2 (0.4%)
Bone lesion	骨病変	1 (0.1%)	0	0	0
Bone pain	骨痛	9 (0.9%)	6 (1.1%)	0	0
Bursitis	滑液包炎	1 (0.1%)	1 (0.2%)	0	0
Coccydynia	尾骨痛	1 (0.1%)	0	0	0
Dupuytren's contracture	デュプイトラン拘縮	1 (0.1%)	0	0	0
Exostosis	外骨腫	2 (0.2%)	1 (0.2%)	0	0
Extremity contracture	四肢拘縮	0	1 (0.2%)	0	0
Flank pain	側腹部痛	5 (0.5%)	2 (0.4%)	0	0
Groin pain	鼠径部痛	7 (0.7%)	5 (0.9%)	0	0
Hand deformity	手変形	1 (0.1%)	0	0	0
Intervertebral disc protrusion	椎間板突出	2 (0.2%)	0	0	0
Joint range of motion decreased	関節可動域低下	1 (0.1%)	0	0	0
Joint stiffness	関節硬直	1 (0.1%)	0	0	0
Joint swelling	関節腫脹	4 (0.4%)	3 (0.5%)	0	1 (0.2%)
Limb discomfort	四肢不快感	1 (0.1%)	0	0	0
Lumbar spinal stenosis	腰部脊柱管狭窄症	1 (0.1%)	1 (0.2%)	0	0
Metatarsalgia	中足骨痛	1 (0.1%)	0	0	0
Mobility decreased	運動性低下	3 (0.3%)	0	0	0
Muscle spasms	筋痙縮	17 (1.8%)	4 (0.7%)	4 (0.4%)	1 (0.2%)
Muscular weakness	筋力低下	10 (1.0%)	5 (0.9%)	4 (0.4%)	1 (0.2%)
Musculoskeletal chest pain	筋骨格系胸痛	10 (1.0%)	6 (1.1%)	0	0
Musculoskeletal discomfort	筋骨格不快感	1 (0.1%)	0	0	0
Musculoskeletal pain	筋骨格痛	37 (3.9%)	11 (2.0%)	2 (0.2%)	1 (0.2%)
Musculoskeletal stiffness	筋骨格硬直	1 (0.1%)	0	0	0
Myalgia	筋肉痛	16 (1.7%)	6 (1.1%)	6 (0.6%)	1 (0.2%)
Neck pain	頚部痛	9 (0.9%)	6 (1.1%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Osteitis	骨炎	1 (0.1%)	0	0	0
Osteitis deformans	変形性骨炎	1 (0.1%)	0	0	0
Osteoarthritis	変形性関節症	15 (1.6%)	3 (0.5%)	1 (0.1%)	0
Osteochondrosis	骨端症	1 (0.1%)	0	0	0
Osteopenia	骨減少症	0	1 (0.2%)	0	0
Osteoporosis	骨粗鬆症	4 (0.4%)	1 (0.2%)	1 (0.1%)	0
Pain in extremity	四肢痛	55 (5.8%)	18 (3.2%)	5 (0.5%)	0
Pathological fracture	病的骨折	0	1 (0.2%)	0	0
Plantar fasciitis	足底筋膜炎	0	2 (0.4%)	0	0
Polymyalgia rheumatica	リウマチ性多発筋痛	1 (0.1%)	0	0	0
Rheumatic disorder	リウマチ性障害	1 (0.1%)	0	0	0
Rotator cuff syndrome	肩回旋筋腱板症候群	3 (0.3%)	1 (0.2%)	0	0
Spinal column stenosis	脊柱管狭窄症	1 (0.1%)	0	0	0
Spinal deformity	脊柱変形	1 (0.1%)	0	0	0
Spinal fusion acquired	後天性脊椎癒合	0	1 (0.2%)	0	0
Spinal osteoarthritis	変形性脊椎症	1 (0.1%)	0	0	0
Spinal pain	脊椎痛	3 (0.3%)	4 (0.7%)	0	0
Tendon disorder	腱障害	0	1 (0.2%)	0	0
Tendonitis	腱炎	1 (0.1%)	1 (0.2%)	0	0
Trigger finger	弾発指	1 (0.1%)	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	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）	48 (5.0%)	26 (4.7%)	0	0
Acute leukaemia	急性白血病	1 (0.1%)	0	0	0
Adenocarcinoma	腺癌	0	1 (0.2%)	0	0
Adrenal adenoma	副腎腺腫	4 (0.4%)	0	0	0
Basal cell carcinoma	基底細胞癌	5 (0.5%)	2 (0.4%)	0	0
Benign lung neoplasm	肺の良性新生物	1 (0.1%)	0	0	0
Bladder cancer	膀胱癌	0	1 (0.2%)	0	0
Bladder neoplasm	膀胱新生物	4 (0.4%)	0	0	0
Bowen's disease	ボーエン病	0	1 (0.2%)	0	0
Cancer pain	癌疼痛	0	1 (0.2%)	0	0
Carcinoid tumour	カルチノイド腫瘍	1 (0.1%)	0	0	0
Choroid melanoma	脈絡膜黒色腫	1 (0.1%)	0	0	0
Colon adenoma	大腸腺腫	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Colon cancer	結腸癌	3 (0.3%)	0	0	0
Colon neoplasm	結腸新生物	1 (0.1%)	1 (0.2%)	0	0
Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	1 (0.1%)	0	0	0
Gastric adenoma	胃腺腫	1 (0.1%)	0	0	0
Gastric cancer	胃癌	1 (0.1%)	2 (0.4%)	0	0
Gastrointestinal adenocarcinoma	消化器腺癌	1 (0.1%)	0	0	0
Intestinal angioma	腸血管腫	1 (0.1%)	0	0	0
Laryngeal cancer	喉頭癌	0	1 (0.2%)	0	0
Lipoma	脂肪腫	2 (0.2%)	1 (0.2%)	0	0
Lung adenocarcinoma stage IV	肺腺癌第４期	1 (0.1%)	0	0	0
Lung neoplasm malignant	肺の悪性新生物	1 (0.1%)	2 (0.4%)	0	0
Lymphangiosis carcinomatosa	癌性リンパ管症	1 (0.1%)	0	0	0
Lymphoma	リンパ腫	1 (0.1%)	0	0	0
Malignant melanoma in situ	表皮内悪性黒色腫	2 (0.2%)	0	0	0
Melanocytic naevus	メラノサイト性母斑	0	1 (0.2%)	0	0
Mesothelioma	中皮腫	1 (0.1%)	0	0	0
Metastases to peritoneum	腹膜転移	1 (0.1%)	0	0	0
Neoplasm malignant	悪性新生物	1 (0.1%)	0	0	0
Oncologic complication	腫瘍合併症	1 (0.1%)	0	0	0
Pancreatic carcinoma	膵癌	3 (0.3%)	0	0	0
Pancreatic carcinoma recurrent	再発膵癌	1 (0.1%)	0	0	0
Pancreatic neoplasm	膵新生物	2 (0.2%)	0	0	0
Pituitary tumour	下垂体腫瘍	1 (0.1%)	0	0	0
Prostate cancer	前立腺癌	0	2 (0.4%)	0	0
Prostate cancer metastatic	遠隔転移を伴う前立腺癌	0	1 (0.2%)	0	0
Prostate cancer recurrent	再発前立腺癌	1 (0.1%)	0	0	0
Rectal adenocarcinoma	直腸腺癌	2 (0.2%)	0	0	0
Rectal cancer	直腸癌	2 (0.2%)	1 (0.2%)	0	0
Renal cancer	腎癌	0	1 (0.2%)	0	0
Salivary gland neoplasm	唾液腺新生物	1 (0.1%)	0	0	0
Seborrhoeic keratosis	脂漏性角化症	1 (0.1%)	1 (0.2%)	0	0
Skin papilloma	皮膚乳頭腫	0	1 (0.2%)	0	0
Small cell lung cancer limited stage	限局型小細胞肺癌	0	1 (0.2%)	0	0
Squamous cell carcinoma	扁平上皮癌	1 (0.1%)	0	0	0
Squamous cell carcinoma of skin	皮膚有棘細胞癌	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Thymoma	胸腺腫	1 (0.1%)	0	0	0
Thyroid adenoma	甲状腺腺腫	0	1 (0.2%)	0	0
Transitional cell carcinoma	移行上皮癌	0	2 (0.4%)	0	0
Tumour compression	腫瘍性圧迫	0	1 (0.2%)	0	0
Tumour obstruction	腫瘍性閉塞	0	1 (0.2%)	0	0
Tumour pain	腫瘍疼痛	1 (0.1%)	0	0	0
Urinary tract neoplasm	尿路新生物	0	1 (0.2%)	0	0
Nervous system disorders	神経系障害	147 (15.4%)	74 (13.4%)	31 (3.2%)	15 (2.7%)
Amnesia	健忘	1 (0.1%)	3 (0.5%)	0	1 (0.2%)
Autonomic nervous system imbalance	自律神経失調	0	1 (0.2%)	0	0
Axonal neuropathy	軸索型ニューロパチー	0	1 (0.2%)	0	0
Balance disorder	平衡障害	1 (0.1%)	1 (0.2%)	1 (0.1%)	1 (0.2%)
Brain oedema	脳浮腫	1 (0.1%)	0	0	0
Bulbar palsy	球麻痺	0	1 (0.2%)	0	0
Carotid arteriosclerosis	頚動脈硬化症	0	1 (0.2%)	0	0
Carotid artery stenosis	頚動脈狭窄	3 (0.3%)	0	0	0
Carpal tunnel syndrome	手根管症候群	1 (0.1%)	3 (0.5%)	0	0
Cerebral arteriosclerosis	脳動脈硬化症	1 (0.1%)	0	0	0
Cerebral atrophy	大脳萎縮	1 (0.1%)	0	0	0
Cerebral infarction	脳梗塞	2 (0.2%)	0	0	0
Cerebral ischaemia	脳虚血	1 (0.1%)	1 (0.2%)	0	0
Cerebrovascular accident	脳血管発作	2 (0.2%)	4 (0.7%)	0	0
Cervicogenic vertigo	頚原性回転性めまい	1 (0.1%)	0	0	0
Cognitive disorder	認知障害	4 (0.4%)	1 (0.2%)	1 (0.1%)	0
Dementia	認知症	2 (0.2%)	0	0	0
Dementia Alzheimer's type	アルツハイマー型認知症	1 (0.1%)	0	0	0
Depressed level of consciousness	意識レベルの低下	2 (0.2%)	0	0	0
Disturbance in attention	注意力障害	0	1 (0.2%)	0	0
Dizziness	浮動性めまい	35 (3.7%)	14 (2.5%)	11 (1.2%)	4 (0.7%)
Dysaesthesia	異常感覚	1 (0.1%)	2 (0.4%)	0	0
Dysarthria	構語障害	0	1 (0.2%)	0	0
Dysgeusia	味覚異常	2 (0.2%)	4 (0.7%)	1 (0.1%)	1 (0.2%)
Encephalopathy	脳症	0	1 (0.2%)	0	0
Essential tremor	本態性振戦	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Haemorrhage intracranial	頭蓋内出血	0	1 (0.2%)	0	1 (0.2%)
Headache	頭痛	37 (3.9%)	14 (2.5%)	13 (1.4%)	4 (0.7%)
Hypersomnia	過眠症	1 (0.1%)	0	0	0
Hypoaesthesia	感覚鈍麻	6 (0.6%)	5 (0.9%)	1 (0.1%)	1 (0.2%)
Hyposmia	嗅覚減退	1 (0.1%)	0	1 (0.1%)	0
Hypotonia	筋緊張低下	1 (0.1%)	0	0	0
IVth nerve paralysis	第４脳神経麻痺	0	1 (0.2%)	0	0
Intercostal neuralgia	肋間神経痛	1 (0.1%)	0	0	0
Ischaemic stroke	虚血性脳卒中	5 (0.5%)	2 (0.4%)	1 (0.1%)	0
Lethargy	嗜眠	1 (0.1%)	1 (0.2%)	0	0
Loss of consciousness	意識消失	2 (0.2%)	0	0	0
Lumbar radiculopathy	腰髄神経根障害	0	1 (0.2%)	0	0
Lumbosacral radiculopathy	腰仙部神経根障害	1 (0.1%)	0	0	0
Memory impairment	記憶障害	5 (0.5%)	7 (1.3%)	1 (0.1%)	2 (0.4%)
Myelopathy	脊髄症	1 (0.1%)	0	0	0
Neuralgia	神経痛	2 (0.2%)	0	0	0
Neuropathy peripheral	末梢性ニューロパチー	1 (0.1%)	2 (0.4%)	0	0
Paraesthesia	錯感覚	6 (0.6%)	4 (0.7%)	1 (0.1%)	0
Parkinson's disease	パーキンソン病	2 (0.2%)	2 (0.4%)	0	0
Partial seizures	部分発作	1 (0.1%)	0	0	0
Peripheral sensory neuropathy	末梢性感覚ニューロパチー	1 (0.1%)	0	0	0
Presyncope	失神寸前の状態	4 (0.4%)	0	0	0
Psychomotor hyperactivity	精神運動亢進	0	1 (0.2%)	0	0
Psychomotor skills impaired	精神運動機能障害	0	1 (0.2%)	0	1 (0.2%)
Restless legs syndrome	下肢静止不能症候群	0	2 (0.4%)	0	0
Sacral radiculopathy	仙部神経根症	1 (0.1%)	0	0	0
Sciatica	坐骨神経痛	8 (0.8%)	6 (1.1%)	0	0
Seizure	痙攣発作	1 (0.1%)	1 (0.2%)	0	0
Senile dementia	老年認知症	2 (0.2%)	0	0	0
Somnolence	傾眠	8 (0.8%)	1 (0.2%)	4 (0.4%)	1 (0.2%)
Speech disorder	会話障害	0	1 (0.2%)	0	0
Syncope	失神	4 (0.4%)	3 (0.5%)	0	0
Transient ischaemic attack	一過性脳虚血発作	3 (0.3%)	1 (0.2%)	0	1 (0.2%)
Tremor	振戦	4 (0.4%)	2 (0.4%)	1 (0.1%)	0
Vascular dementia	血管性認知症	1 (0.1%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Vocal cord paresis	声帯不全麻痺	1 (0.1%)	0	0	0
Product issues	製品の問題	9 (0.9%)	3 (0.5%)	0	0
Device dislocation	医療機器位置異常	3 (0.3%)	1 (0.2%)	0	0
Device malfunction	医療機器機能不良	1 (0.1%)	0	0	0
Device occlusion	医療機器閉塞	5 (0.5%)	2 (0.4%)	0	0
Psychiatric disorders	精神障害	57 (6.0%)	28 (5.1%)	5 (0.5%)	5 (0.9%)
Agitation	激越	1 (0.1%)	1 (0.2%)	0	0
Anxiety	不安	5 (0.5%)	2 (0.4%)	0	0
Claustrophobia	閉所恐怖症	0	1 (0.2%)	0	0
Delirium	譫妄	0	3 (0.5%)	0	0
Depressed mood	抑うつ気分	1 (0.1%)	1 (0.2%)	0	0
Depression	うつ病	16 (1.7%)	7 (1.3%)	0	1 (0.2%)
Disorientation	失見当識	2 (0.2%)	1 (0.2%)	0	0
Hallucination, auditory	幻聴	1 (0.1%)	0	0	0
Hallucination, visual	幻視	1 (0.1%)	0	0	0
Initial insomnia	初期不眠症	0	1 (0.2%)	0	0
Insomnia	不眠症	26 (2.7%)	10 (1.8%)	2 (0.2%)	1 (0.2%)
Irritability	易刺激性	2 (0.2%)	2 (0.4%)	2 (0.2%)	1 (0.2%)
Mental status changes	精神状態変化	0	1 (0.2%)	0	0
Middle insomnia	中期不眠症	1 (0.1%)	1 (0.2%)	0	1 (0.2%)
Mood swings	気分動揺	0	1 (0.2%)	0	0
Nervousness	神経過敏	0	1 (0.2%)	0	0
Nightmare	悪夢	1 (0.1%)	0	1 (0.1%)	0
Panic disorder	パニック障害	1 (0.1%)	0	0	0
Restlessness	落ち着きのなさ	1 (0.1%)	0	0	0
Sleep disorder	睡眠障害	4 (0.4%)	1 (0.2%)	0	1 (0.2%)
Renal and urinary disorders	腎および尿路障害	198 (20.8%)	140 (25.3%)	11 (1.2%)	6 (1.1%)
Acute kidney injury	急性腎障害	9 (0.9%)	6 (1.1%)	0	0
Anuria	無尿	1 (0.1%)	0	0	0
Azotaemia	高窒素血症	0	2 (0.4%)	0	0
Bladder disorder	膀胱障害	0	1 (0.2%)	0	0
Bladder diverticulum	膀胱憩室	2 (0.2%)	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Bladder hypertrophy	膀胱壁肥厚	1 (0.1%)	0	1 (0.1%)	0
Bladder neck obstruction	膀胱頚部閉塞	2 (0.2%)	0	0	0
Bladder obstruction	膀胱閉塞	1 (0.1%)	0	0	0
Bladder outlet obstruction	膀胱出口部閉塞	0	4 (0.7%)	0	0
Bladder spasm	膀胱痙縮	0	1 (0.2%)	0	0
Calculus bladder	膀胱結石	5 (0.5%)	2 (0.4%)	0	0
Calculus urethral	尿道結石	1 (0.1%)	0	0	0
Calculus urinary	尿路結石	0	1 (0.2%)	0	0
Chronic kidney disease	慢性腎臓病	9 (0.9%)	5 (0.9%)	0	0
Cystitis noninfective	非感染性膀胱炎	1 (0.1%)	1 (0.2%)	0	0
Dysuria	排尿困難	21 (2.2%)	26 (4.7%)	0	0
Glycosuria	糖尿	4 (0.4%)	2 (0.4%)	1 (0.1%)	0
Haematuria	血尿	41 (4.3%)	27 (4.9%)	1 (0.1%)	0
Hydronephrosis	水腎症	10 (1.0%)	13 (2.3%)	0	0
Hypertonic bladder	緊張性膀胱	3 (0.3%)	2 (0.4%)	0	0
Incontinence	失禁	3 (0.3%)	1 (0.2%)	0	0
Kidney fibrosis	腎線維症	2 (0.2%)	1 (0.2%)	0	0
Leukocyturia	白血球尿	1 (0.1%)	1 (0.2%)	0	0
Lower urinary tract symptoms	下部尿路症状	6 (0.6%)	5 (0.9%)	0	0
Malignant urinary tract obstruction	悪性尿路閉塞	0	1 (0.2%)	0	0
Micturition disorder	排尿異常	1 (0.1%)	1 (0.2%)	0	0
Micturition urgency	尿意切迫	9 (0.9%)	3 (0.5%)	0	0
Nephrocalcinosis	腎石灰沈着症	0	1 (0.2%)	0	0
Nephrolithiasis	腎結石症	14 (1.5%)	4 (0.7%)	0	0
Nocturia	夜間頻尿	14 (1.5%)	10 (1.8%)	1 (0.1%)	0
Oliguria	乏尿	1 (0.1%)	0	0	0
Pollakiuria	頻尿	38 (4.0%)	16 (2.9%)	3 (0.3%)	1 (0.2%)
Polyuria	多尿	2 (0.2%)	2 (0.4%)	1 (0.1%)	0
Proteinuria	蛋白尿	9 (0.9%)	6 (1.1%)	0	1 (0.2%)
Renal aneurysm	腎動脈瘤	1 (0.1%)	1 (0.2%)	0	0
Renal artery occlusion	腎動脈閉塞	1 (0.1%)	0	0	0
Renal artery stenosis	腎動脈狭窄症	0	1 (0.2%)	0	0
Renal colic	腎仙痛	9 (0.9%)	0	0	0
Renal cyst	腎嚢胞	9 (0.9%)	4 (0.7%)	0	0
Renal failure	腎不全	7 (0.7%)	5 (0.9%)	1 (0.1%)	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Renal impairment	腎機能障害	3 (0.3%)	0	1 (0.1%)	0
Renal pain	腎臓痛	0	1 (0.2%)	0	0
Strangury	有痛性排尿困難	1 (0.1%)	0	0	0
Ureteral disorder	尿管障害	1 (0.1%)	0	0	0
Ureteric obstruction	尿管閉塞	0	1 (0.2%)	0	0
Ureteric stenosis	尿管狭窄	2 (0.2%)	0	0	0
Ureterolithiasis	尿管結石症	6 (0.6%)	2 (0.4%)	0	0
Urethral discharge	尿道分泌物	1 (0.1%)	0	0	0
Urethral meatus stenosis	外尿道口狭窄	0	1 (0.2%)	0	0
Urethral pain	尿道痛	0	1 (0.2%)	0	0
Urethral stenosis	尿道狭窄	2 (0.2%)	3 (0.5%)	0	0
Urinary hesitation	排尿躊躇	2 (0.2%)	0	0	0
Urinary incontinence	尿失禁	14 (1.5%)	12 (2.2%)	0	1 (0.2%)
Urinary retention	尿閉	33 (3.5%)	36 (6.5%)	1 (0.1%)	2 (0.4%)
Urinary tract discomfort	尿路不快感	0	1 (0.2%)	0	0
Urinary tract disorder	尿路障害	0	1 (0.2%)	0	1 (0.2%)
Urinary tract obstruction	尿路閉塞	9 (0.9%)	7 (1.3%)	0	0
Urinary tract pain	尿路痛	0	2 (0.4%)	0	0
Urine flow decreased	尿流量減少	2 (0.2%)	3 (0.5%)	0	0
Reproductive system and breast disorders	生殖系および乳房障害	46 (4.8%)	35 (6.3%)	16 (1.7%)	6 (1.1%)
Balanoposthitis	亀頭包皮炎	2 (0.2%)	0	0	0
Benign prostatic hyperplasia	良性前立腺肥大症	4 (0.4%)	2 (0.4%)	1 (0.1%)	0
Breast discomfort	乳房不快感	2 (0.2%)	0	0	0
Breast induration	乳房硬結	1 (0.1%)	0	1 (0.1%)	0
Breast pain	乳房痛	0	1 (0.2%)	0	1 (0.2%)
Breast tenderness	乳房圧痛	0	1 (0.2%)	0	1 (0.2%)
Erectile dysfunction	勃起不全	1 (0.1%)	1 (0.2%)	0	0
Gynaecomastia	女性化乳房	19 (2.0%)	6 (1.1%)	15 (1.6%)	3 (0.5%)
Nipple pain	乳頭痛	2 (0.2%)	2 (0.4%)	1 (0.1%)	0
Pelvic pain	骨盤痛	12 (1.3%)	12 (2.2%)	0	0
Penile pain	陰茎痛	4 (0.4%)	0	0	0
Penis disorder	陰茎障害	2 (0.2%)	0	0	0
Perineal pain	会陰痛	1 (0.1%)	2 (0.4%)	0	1 (0.2%)

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Prostate induration	前立腺硬結	1 (0.1%)	0	0	0
Prostatic mass	前立腺腫瘤	0	2 (0.4%)	0	0
Prostatic obstruction	前立腺閉塞	1 (0.1%)	2 (0.4%)	0	0
Prostatitis	前立腺炎	0	1 (0.2%)	0	0
Prostatomegaly	前立腺腫大	0	1 (0.2%)	0	0
Testicular pain	精巣痛	0	3 (0.5%)	0	0
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	119 (12.5%)	54 (9.7%)	10 (1.0%)	2 (0.4%)
Acute respiratory failure	急性呼吸不全	2 (0.2%)	2 (0.4%)	0	0
Asthma	喘息	1 (0.1%)	1 (0.2%)	0	0
Atelectasis	無気肺	0	1 (0.2%)	0	0
Bronchitis chronic	慢性気管支炎	1 (0.1%)	0	0	0
Bronchospasm	気管支痙攣	0	1 (0.2%)	0	0
Catarrh	カタル	1 (0.1%)	0	0	0
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	10 (1.0%)	4 (0.7%)	1 (0.1%)	0
Cough	咳嗽	29 (3.0%)	11 (2.0%)	1 (0.1%)	0
Cystic lung disease	嚢胞性肺疾患	4 (0.4%)	0	0	0
Dyspnoea	呼吸困難	24 (2.5%)	15 (2.7%)	4 (0.4%)	0
Dyspnoea exertional	労作性呼吸困難	6 (0.6%)	4 (0.7%)	2 (0.2%)	0
Emphysema	肺気腫	10 (1.0%)	2 (0.4%)	0	0
Epistaxis	鼻出血	1 (0.1%)	3 (0.5%)	0	0
Haemoptysis	喀血	0	2 (0.4%)	0	0
Hypoxia	低酸素症	1 (0.1%)	0	0	0
Lower respiratory tract inflammation	下気道の炎症	1 (0.1%)	0	0	0
Lung disorder	肺障害	2 (0.2%)	0	0	0
Nasal congestion	鼻閉	2 (0.2%)	1 (0.2%)	1 (0.1%)	0
Nocturnal dyspnoea	夜間呼吸困難	0	1 (0.2%)	0	0
Oropharyngeal pain	口腔咽頭痛	3 (0.3%)	1 (0.2%)	0	0
Paranasal cyst	副鼻腔嚢胞	1 (0.1%)	0	0	0
Paranasal sinus hypersecretion	副鼻腔分泌過多	1 (0.1%)	0	0	0
Pleural effusion	胸水	4 (0.4%)	4 (0.7%)	0	0
Pneumonia aspiration	誤嚥性肺炎	1 (0.1%)	0	0	0
Pneumonitis	肺臓炎	3 (0.3%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Pneumothorax	気胸	0	1 (0.2%)	0	0
Productive cough	湿性咳嗽	1 (0.1%)	4 (0.7%)	0	0
Pulmonary calcification	肺石灰化	6 (0.6%)	1 (0.2%)	0	0
Pulmonary congestion	肺うっ血	0	1 (0.2%)	0	0
Pulmonary embolism	肺塞栓症	5 (0.5%)	4 (0.7%)	2 (0.2%)	2 (0.4%)
Pulmonary fibrosis	肺線維症	3 (0.3%)	0	0	0
Pulmonary mass	肺腫瘤	6 (0.6%)	2 (0.4%)	0	0
Pulmonary oedema	肺水腫	1 (0.1%)	1 (0.2%)	0	0
Pulmonary thrombosis	肺血栓症	0	1 (0.2%)	0	0
Rales	ラ音	1 (0.1%)	3 (0.5%)	0	0
Reflux laryngitis	逆流性喉頭炎	2 (0.2%)	0	0	0
Respiratory alkalosis	呼吸性アルカローシス	1 (0.1%)	0	0	0
Respiratory disorder	呼吸障害	0	1 (0.2%)	0	0
Respiratory failure	呼吸不全	3 (0.3%)	1 (0.2%)	0	0
Rhinalgia	鼻痛	1 (0.1%)	0	0	0
Rhinorrhoea	鼻漏	1 (0.1%)	2 (0.4%)	0	0
Rhonchi	低音性連続性ラ音	1 (0.1%)	0	0	0
Sinus disorder	副鼻腔障害	1 (0.1%)	0	0	0
Sinus polyp	副鼻腔ポリープ	1 (0.1%)	0	0	0
Sleep apnoea syndrome	睡眠時無呼吸症候群	3 (0.3%)	1 (0.2%)	0	0
Sneezing	くしゃみ	1 (0.1%)	0	0	0
Throat irritation	咽喉刺激感	1 (0.1%)	1 (0.2%)	0	0
Throat tightness	咽喉絞扼感	1 (0.1%)	0	0	0
Upper-airway cough syndrome	上気道咳症候群	1 (0.1%)	1 (0.2%)	0	0
Wheezing	喘鳴	2 (0.2%)	2 (0.4%)	0	0
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	90 (9.4%)	40 (7.2%)	34 (3.6%)	10 (1.8%)
Acne	ざ瘡	1 (0.1%)	0	0	0
Actinic keratosis	光線角化症	2 (0.2%)	2 (0.4%)	0	0
Alopecia	脱毛症	1 (0.1%)	2 (0.4%)	1 (0.1%)	0
Blister	水疱	1 (0.1%)	0	0	0
Decubitus ulcer	褥瘡性潰瘍	0	1 (0.2%)	0	0
Dermal cyst	皮膚嚢腫	2 (0.2%)	0	0	0
Dermatitis	皮膚炎	3 (0.3%)	1 (0.2%)	0	0
Dermatitis allergic	アレルギー性皮膚炎	1 (0.1%)	1 (0.2%)	1 (0.1%)	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Dermatitis contact	接触皮膚炎	1 (0.1%)	0	0	0
Diabetic foot	糖尿病性足病変	2 (0.2%)	0	0	0
Dry skin	皮膚乾燥	6 (0.6%)	1 (0.2%)	3 (0.3%)	0
Ecchymosis	斑状出血	0	1 (0.2%)	0	0
Eczema	湿疹	6 (0.6%)	3 (0.5%)	2 (0.2%)	0
Eczema nummular	貨幣状湿疹	1 (0.1%)	0	1 (0.1%)	0
Erythema	紅斑	3 (0.3%)	1 (0.2%)	0	0
Erythema multiforme	多形紅斑	2 (0.2%)	0	0	0
Haemorrhage subcutaneous	皮下出血	1 (0.1%)	1 (0.2%)	0	0
Hyperhidrosis	多汗症	8 (0.8%)	4 (0.7%)	6 (0.6%)	4 (0.7%)
Hyperkeratosis	過角化	0	1 (0.2%)	0	0
Hypertrichosis	多毛症	0	1 (0.2%)	0	0
Hypotrichosis	貧毛症	1 (0.1%)	1 (0.2%)	1 (0.1%)	1 (0.2%)
Nail discolouration	爪変色	1 (0.1%)	0	0	0
Night sweats	寝汗	1 (0.1%)	2 (0.4%)	1 (0.1%)	1 (0.2%)
Onychoclasis	爪破損	1 (0.1%)	0	0	0
Pain of skin	皮膚疼痛	0	1 (0.2%)	0	0
Pigmentation disorder	色素沈着障害	1 (0.1%)	0	0	0
Pruritus	そう痒症	16 (1.7%)	11 (2.0%)	7 (0.7%)	2 (0.4%)
Pruritus allergic	アレルギー性そう痒症	2 (0.2%)	0	2 (0.2%)	0
Pruritus generalised	全身性そう痒症	1 (0.1%)	0	0	0
Psoriasis	乾癬	1 (0.1%)	1 (0.2%)	0	1 (0.2%)
Rash	発疹	17 (1.8%)	4 (0.7%)	5 (0.5%)	0
Rash macular	斑状皮疹	1 (0.1%)	0	1 (0.1%)	0
Rash maculo-papular	斑状丘疹状皮疹	4 (0.4%)	0	1 (0.1%)	0
Rash papular	丘疹性皮疹	1 (0.1%)	0	0	0
Skin disorder	皮膚障害	1 (0.1%)	0	0	0
Skin erosion	皮膚びらん	0	1 (0.2%)	0	0
Skin exfoliation	皮膚剥脱	1 (0.1%)	0	0	0
Skin fragility	皮膚脆弱性	1 (0.1%)	0	0	0
Skin induration	皮膚硬結	1 (0.1%)	0	0	0
Skin irritation	皮膚刺激	0	1 (0.2%)	0	0
Skin lesion	皮膚病変	3 (0.3%)	1 (0.2%)	0	0
Skin mass	皮膚腫瘤	0	1 (0.2%)	0	0
Skin reaction	皮膚反応	0	1 (0.2%)	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Skin ulcer	皮膚潰瘍	3 (0.3%)	0	0	0
Stasis dermatitis	うっ滞性皮膚炎	0	2 (0.4%)	0	0
Urticaria	蕁麻疹	9 (0.9%)	2 (0.4%)	4 (0.4%)	1 (0.2%)
Surgical and medical procedures	外科および内科処置	10 (1.0%)	5 (0.9%)	0	0
Bladder catheterisation	膀胱カテーテル留置	1 (0.1%)	0	0	0
Cataract operation	白内障手術	2 (0.2%)	0	0	0
Cyst removal	嚢胞切除	1 (0.1%)	0	0	0
Cystostomy	膀胱瘻造設	1 (0.1%)	0	0	0
Hip arthroplasty	股関節形成	1 (0.1%)	1 (0.2%)	0	0
Inguinal hernia repair	鼠径部ヘルニア修復	1 (0.1%)	0	0	0
Lipoma excision	脂肪腫切除	0	1 (0.2%)	0	0
Lymphadenectomy	リンパ節切除	0	1 (0.2%)	0	0
Orchidectomy	精巣摘除	0	1 (0.2%)	0	0
Prostatectomy	前立腺摘除	1 (0.1%)	0	0	0
Pulmonary resection	肺切除	0	1 (0.2%)	0	0
Radiotherapy to lymph nodes	リンパ節放射線療法	1 (0.1%)	0	0	0
Tooth extraction	抜歯	0	1 (0.2%)	0	0
Transurethral prostatectomy	経尿道的前立腺摘除	0	1 (0.2%)	0	0
Urethrotomy	尿道切開	1 (0.1%)	0	0	0
Vascular disorders	血管障害	152 (15.9%)	68 (12.3%)	59 (6.2%)	20 (3.6%)
Aortic aneurysm	大動脈瘤	3 (0.3%)	0	0	0
Aortic arteriosclerosis	大動脈硬化症	4 (0.4%)	1 (0.2%)	0	0
Aortic dissection	大動脈解離	1 (0.1%)	0	0	0
Aortic stenosis	大動脈狭窄	1 (0.1%)	0	0	0
Aortic thrombosis	大動脈血栓症	1 (0.1%)	0	0	0
Arteriosclerosis	動脈硬化症	0	2 (0.4%)	0	0
Bleeding varicose vein	出血性静脈瘤	0	1 (0.2%)	0	0
Circulatory collapse	循環虚脱	0	1 (0.2%)	0	0
Deep vein thrombosis	深部静脈血栓症	2 (0.2%)	0	2 (0.2%)	0
Embolism	塞栓症	1 (0.1%)	0	0	0
Essential hypertension	本態性高血圧症	3 (0.3%)	0	0	0
Flushing	潮紅	5 (0.5%)	1 (0.2%)	3 (0.3%)	0
Haematoma	血腫	2 (0.2%)	0	0	0

付表 2.7.6.9.a.1-19 TEAE 及び治験薬と関連のある TEAE（SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Treatment-emergent Darolutamide N=954 (100%)	Treatment-emergent Placebo N=554 (100%)	Study drug-related Darolutamide N=954 (100%)	Study drug-related Placebo N=554 (100%)
Hot flush	ほてり	50 (5.2%)	23 (4.2%)	36 (3.8%)	15 (2.7%)
Hypertension	高血圧	63 (6.6%)	29 (5.2%)	11 (1.2%)	4 (0.7%)
Hypotension	低血圧	10 (1.0%)	7 (1.3%)	3 (0.3%)	1 (0.2%)
Iliac artery occlusion	腸骨動脈閉塞	1 (0.1%)	0	0	0
Intermittent claudication	間欠性跛行	1 (0.1%)	0	0	0
Lymphoedema	リンパ浮腫	1 (0.1%)	1 (0.2%)	0	0
Orthostatic hypotension	起立性低血圧	2 (0.2%)	2 (0.4%)	1 (0.1%)	0
Pallor	蒼白	0	1 (0.2%)	0	0
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	6 (0.6%)	1 (0.2%)	1 (0.1%)	0
Peripheral artery stenosis	末梢動脈狭窄	1 (0.1%)	0	0	0
Peripheral artery thrombosis	末梢動脈血栓症	1 (0.1%)	0	1 (0.1%)	0
Peripheral ischaemia	末梢性虚血	1 (0.1%)	0	1 (0.1%)	0
Phlebitis	静脈炎	1 (0.1%)	0	0	0
Subclavian vein thrombosis	鎖骨下静脈血栓症	0	1 (0.2%)	0	0
Thrombophlebitis	血栓性静脈炎	0	2 (0.4%)	0	0
Thrombophlebitis superficial	表在性血栓性静脈炎	2 (0.2%)	1 (0.2%)	0	0
Thrombosis	血栓症	1 (0.1%)	0	0	0
Varicose vein	静脈瘤	2 (0.2%)	0	0	0
Vasculitis	血管炎	0	1 (0.2%)	0	1 (0.2%)
Vena cava thrombosis	大静脈血栓症	0	1 (0.2%)	0	0
Venous thrombosis	静脈血栓症	0	1 (0.2%)	0	0
Venous thrombosis limb	四肢静脈血栓症	1 (0.1%)	0	0	0

Source: 5.3.5.1.3 17712_JP/Table 1/1

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Number of subjects (%) with at least one such adverse event	Number of subjects (%) with at least one such adverse event	53 (85.5%)	21 (63.6%)	741 (83.1%)	405 (77.7%)
Blood and lymphatic system disorders	血液およびリンパ系障害	5 (8.1%)	0	70 (7.8%)	37 (7.1%)
Abdominal lymphadenopathy	腹部リンパ節腫脹	0	0	1 (0.1%)	0
Anaemia	貧血	3 (4.8%)	0	50 (5.6%)	25 (4.8%)
Basophilia	好塩基球増加症	0	0	0	1 (0.2%)
Eosinophilia	好酸球増加症	0	0	1 (0.1%)	0
Febrile neutropenia	発熱性好中球減少症	0	0	0	1 (0.2%)
Iron deficiency anaemia	鉄欠乏性貧血	1 (1.6%)	0	3 (0.3%)	1 (0.2%)
Leukocytosis	白血球増加症	0	0	2 (0.2%)	0
Leukopenia	白血球減少症	0	0	7 (0.8%)	2 (0.4%)
Lymphadenopathy	リンパ節症	0	0	1 (0.1%)	0
Lymphopenia	リンパ球減少症	0	0	9 (1.0%)	5 (1.0%)
Nephrogenic anaemia	腎性貧血	0	0	1 (0.1%)	0
Neutropenia	好中球減少症	1 (1.6%)	0	12 (1.3%)	5 (1.0%)
Retroperitoneal lymphadenopathy	後腹膜リンパ節腫脹	0	0	0	1 (0.2%)
Splenic calcification	脾臓石灰化	0	0	0	1 (0.2%)
Thrombocytopenia	血小板減少症	0	0	5 (0.6%)	1 (0.2%)
Cardiac disorders	心臓障害	5 (8.1%)	1 (3.0%)	108 (12.1%)	40 (7.7%)
Acute coronary syndrome	急性冠動脈症候群	0	0	0	1 (0.2%)
Acute myocardial infarction	急性心筋梗塞	0	0	5 (0.6%)	1 (0.2%)
Angina pectoris	狭心症	2 (3.2%)	0	10 (1.1%)	4 (0.8%)
Angina unstable	不安定狭心症	0	0	0	1 (0.2%)
Aortic valve disease	大動脈弁疾患	0	0	1 (0.1%)	0
Aortic valve incompetence	大動脈弁閉鎖不全症	0	0	1 (0.1%)	0
Aortic valve stenosis	大動脈弁狭窄	0	0	3 (0.3%)	0
Arrhythmia	不整脈	1 (1.6%)	0	13 (1.5%)	3 (0.6%)
Arrhythmia supraventricular	上室性不整脈	0	0	1 (0.1%)	0
Arteriosclerosis coronary artery	冠動脈硬化症	0	0	0	2 (0.4%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Atrial fibrillation	心房細動	0	0	22 (2.5%)	8 (1.5%)
Atrial flutter	心房粗動	0	0	2 (0.2%)	0
Atrioventricular block	房室ブロック	0	0	2 (0.2%)	0
Atrioventricular block complete	完全房室ブロック	0	0	1 (0.1%)	0
Atrioventricular block first degree	第一度房室ブロック	0	0	0	1 (0.2%)
Atrioventricular block second degree	第二度房室ブロック	0	0	3 (0.3%)	0
Bradycardia	徐脈	0	0	10 (1.1%)	1 (0.2%)
Bundle branch block left	左脚ブロック	0	0	1 (0.1%)	1 (0.2%)
Bundle branch block right	右脚ブロック	0	0	1 (0.1%)	0
Cardiac aneurysm	心臓瘤	0	0	0	1 (0.2%)
Cardiac arrest	心停止	0	0	2 (0.2%)	3 (0.6%)
Cardiac disorder	心障害	0	0	1 (0.1%)	0
Cardiac failure	心不全	1 (1.6%)	0	12 (1.3%)	5 (1.0%)
Cardiac failure acute	急性心不全	0	0	2 (0.2%)	0
Cardiac failure chronic	慢性心不全	0	0	2 (0.2%)	0
Cardiac failure congestive	うっ血性心不全	0	0	1 (0.1%)	0
Cardiac flutter	心粗動	0	0	1 (0.1%)	0
Cardiac steatosis	心臓脂肪症	0	0	1 (0.1%)	0
Cardiogenic shock	心原性ショック	0	0	1 (0.1%)	0
Cardiovascular insufficiency	心血管不全	0	0	1 (0.1%)	0
Conduction disorder	伝導障害	0	0	1 (0.1%)	0
Coronary artery disease	冠動脈疾患	0	0	10 (1.1%)	1 (0.2%)
Coronary artery occlusion	冠動脈閉塞	0	0	1 (0.1%)	1 (0.2%)
Coronary artery stenosis	冠動脈狭窄	0	0	2 (0.2%)	0
Defect conduction intraventricular	心室内伝導障害	0	0	1 (0.1%)	0
Extrasystoles	期外収縮	0	0	2 (0.2%)	0
Hypertensive heart disease	高血圧性心疾患	0	0	0	1 (0.2%)
Left atrial enlargement	左房拡大	0	0	0	1 (0.2%)
Left ventricular dilatation	左室拡張	0	0	1 (0.1%)	0
Mitral valve incompetence	僧帽弁閉鎖不全症	0	0	1 (0.1%)	1 (0.2%)
Myocardial infarction	心筋梗塞	0	0	6 (0.7%)	3 (0.6%)
Myocardial ischaemia	心筋虚血	0	0	3 (0.3%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Palpitations	動悸	1 (1.6%)	0	6 (0.7%)	3 (0.6%)
Sinus arrhythmia	洞性不整脈	0	0	0	1 (0.2%)
Sinus bradycardia	洞性徐脈	0	0	4 (0.4%)	0
Sinus node dysfunction	洞結節機能不全	0	0	2 (0.2%)	0
Supraventricular extrasystoles	上室性期外収縮	0	0	2 (0.2%)	0
Tachycardia	頻脈	0	0	5 (0.6%)	2 (0.4%)
Tachycardia paroxysmal	発作性頻脈	0	0	1 (0.1%)	0
Tricuspid valve disease	三尖弁疾患	0	0	1 (0.1%)	0
Ventricular extrasystoles	心室性期外収縮	0	1 (3.0%)	3 (0.3%)	1 (0.2%)
Ventricular fibrillation	心室細動	0	0	0	1 (0.2%)
Ventricular tachycardia	心室性頻脈	0	0	1 (0.1%)	0
Congenital, familial and genetic disorders	先天性、家族性および遺伝性障害	0	0	5 (0.6%)	2 (0.4%)
Congenital renal cyst	先天性腎嚢胞	0	0	1 (0.1%)	0
Phimosis	包茎	0	0	4 (0.4%)	2 (0.4%)
Ear and labyrinth disorders	耳および迷路障害	0	2 (6.1%)	14 (1.6%)	9 (1.7%)
External ear disorder	外耳障害	0	0	1 (0.1%)	0
Hypoacusis	聴力低下	0	0	1 (0.1%)	0
Otorrhoea	耳漏	0	1 (3.0%)	0	1 (0.2%)
Tinnitus	耳鳴	0	0	4 (0.4%)	0
Vertigo	回転性めまい	0	1 (3.0%)	8 (0.9%)	8 (1.5%)
Vertigo positional	頭位性回転性めまい	0	0	1 (0.1%)	0
Endocrine disorders	内分泌障害	0	0	9 (1.0%)	0
Adrenal calcification	副腎石灰化	0	0	2 (0.2%)	0
Adrenomegaly	副腎肥大	0	0	1 (0.1%)	0
Basedow's disease	バセドウ病	0	0	1 (0.1%)	0
Hyperthyroidism	甲状腺機能亢進症	0	0	2 (0.2%)	0
Hypothyroidism	甲状腺機能低下症	0	0	2 (0.2%)	0
Secondary adrenocortical insufficiency	続発性副腎皮質機能不全	0	0	1 (0.1%)	0
Thyroid calcification	甲状腺石灰化	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Thyroid mass	甲状腺腫瘤	0	0	2 (0.2%)	0
Eye disorders	眼障害	3 (4.8%)	3 (9.1%)	17 (1.9%)	16 (3.1%)
Age-related macular degeneration	加齢黄斑変性	0	1 (3.0%)	0	0
Blepharitis	眼瞼炎	0	0	1 (0.1%)	0
Blindness	失明	0	0	0	1 (0.2%)
Blindness unilateral	片側失明	0	0	0	1 (0.2%)
Cataract	白内障	2 (3.2%)	0	4 (0.4%)	2 (0.4%)
Conjunctival deposit	結膜沈着物	0	1 (3.0%)	0	0
Conjunctival haemorrhage	結膜出血	0	0	1 (0.1%)	1 (0.2%)
Conjunctivitis allergic	アレルギー性結膜炎	0	0	1 (0.1%)	0
Corneal disorder	角膜障害	0	1 (3.0%)	0	0
Corneal oedema	角膜浮腫	0	1 (3.0%)	0	0
Diplopia	複視	0	0	1 (0.1%)	1 (0.2%)
Dry eye	眼乾燥	0	1 (3.0%)	3 (0.3%)	0
Eye inflammation	眼の炎症	0	0	0	1 (0.2%)
Eye irritation	眼刺激	0	0	1 (0.1%)	0
Eye pain	眼痛	0	0	0	2 (0.4%)
Eyelid ptosis	眼瞼下垂	0	0	0	1 (0.2%)
Glaucoma	緑内障	0	0	1 (0.1%)	2 (0.4%)
Lacrimation increased	流涙増加	0	0	1 (0.1%)	0
Macular degeneration	黄斑変性	0	0	0	1 (0.2%)
Ocular hyperaemia	眼充血	0	0	0	2 (0.4%)
Periorbital oedema	眼窩周囲浮腫	0	0	1 (0.1%)	0
Pterygium	翼状片	0	1 (3.0%)	0	0
Retinal artery occlusion	網膜動脈閉塞	1 (1.6%)	0	0	0
Retinal detachment	網膜剥離	0	0	1 (0.1%)	0
Retinal vascular disorder	網膜血管障害	0	0	0	1 (0.2%)
Vision blurred	霧視	0	0	1 (0.1%)	1 (0.2%)
Visual acuity reduced	視力低下	0	0	0	2 (0.4%)
Visual impairment	視力障害	0	0	1 (0.1%)	1 (0.2%)
Vitreous floaters	硝子体浮遊物	0	0	0	2 (0.4%)
Gastrointestinal disorders	胃腸障害	21 (33.9%)	8 (24.2%)	255 (28.6%)	133 (25.5%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Abdominal discomfort	腹部不快感	1 (1.6%)	0	5 (0.6%)	1 (0.2%)
Abdominal distension	腹部膨満	0	1 (3.0%)	11 (1.2%)	3 (0.6%)
Abdominal hernia	腹部ヘルニア	0	0	1 (0.1%)	2 (0.4%)
Abdominal pain	腹痛	0	0	24 (2.7%)	12 (2.3%)
Abdominal pain lower	下腹部痛	0	0	5 (0.6%)	1 (0.2%)
Abdominal pain upper	上腹部痛	0	0	12 (1.3%)	13 (2.5%)
Abdominal tenderness	腹部圧痛	0	0	1 (0.1%)	0
Anal haemorrhage	肛門出血	0	0	1 (0.1%)	1 (0.2%)
Anal incontinence	肛門失禁	0	0	1 (0.1%)	0
Anorectal discomfort	肛門直腸不快感	0	0	2 (0.2%)	0
Ascites	腹水	0	0	0	1 (0.2%)
Barrett's oesophagus	バレット食道	0	0	1 (0.1%)	0
Bowel movement irregularity	便通不規則	0	0	1 (0.1%)	0
Breath odour	呼気臭	0	0	1 (0.1%)	1 (0.2%)
Cheilitis	口唇炎	0	1 (3.0%)	0	0
Chronic gastritis	慢性胃炎	0	0	2 (0.2%)	0
Colitis	大腸炎	0	0	1 (0.1%)	0
Constipation	便秘	8 (12.9%)	1 (3.0%)	52 (5.8%)	33 (6.3%)
Crohn's disease	クローン病	0	0	1 (0.1%)	0
Dental caries	齲歯	0	0	2 (0.2%)	1 (0.2%)
Diaphragmatic hernia	横隔膜ヘルニア	0	0	0	1 (0.2%)
Diarrhoea	下痢	3 (4.8%)	4 (12.1%)	63 (7.1%)	27 (5.2%)
Diverticulum	憩室	0	0	3 (0.3%)	0
Diverticulum intestinal	腸憩室	0	1 (3.0%)	10 (1.1%)	6 (1.2%)
Diverticulum oesophageal	食道憩室	0	0	1 (0.1%)	0
Dry mouth	口内乾燥	0	0	10 (1.1%)	5 (1.0%)
Duodenal ulcer	十二指腸潰瘍	0	0	1 (0.1%)	0
Dyspepsia	消化不良	2 (3.2%)	0	9 (1.0%)	7 (1.3%)
Dysphagia	嚥下障害	0	1 (3.0%)	3 (0.3%)	3 (0.6%)
Enterovesical fistula	腸膀胱瘻	0	0	2 (0.2%)	0
Epigastric discomfort	心窩部不快感	0	0	1 (0.1%)	0
Eructation	おくび	0	0	1 (0.1%)	0
Faeces hard	硬便	0	0	1 (0.1%)	0
Flatulence	鼓腸	0	0	4 (0.4%)	4 (0.8%)
Food poisoning	食中毒	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Frequent bowel movements	排便回数増加	0	0	1 (0.1%)	0
Gastric disorder	胃障害	0	0	1 (0.1%)	0
Gastric polyps	胃ポリープ	0	0	1 (0.1%)	0
Gastric ulcer	胃潰瘍	0	0	2 (0.2%)	1 (0.2%)
Gastritis	胃炎	0	0	2 (0.2%)	5 (1.0%)
Gastritis erosive	びらん性胃炎	1 (1.6%)	0	2 (0.2%)	0
Gastroduodenitis	胃十二指腸炎	0	0	1 (0.1%)	0
Gastrointestinal angiectasia	胃腸血管拡張症	0	0	1 (0.1%)	0
Gastrointestinal haemorrhage	胃腸出血	0	0	1 (0.1%)	0
Gastrointestinal inflammation	胃腸の炎症	0	0	0	1 (0.2%)
Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	0	0	1 (0.1%)	0
Gastrointestinal pain	消化器痛	0	0	2 (0.2%)	1 (0.2%)
Gastrointestinal wall thickening	消化管壁肥厚	0	0	1 (0.1%)	0
Gastrooesophageal reflux disease	胃食道逆流性疾患	0	0	11 (1.2%)	4 (0.8%)
Gingival discomfort	歯肉不快感	0	0	1 (0.1%)	0
Gingival pain	歯肉痛	0	0	1 (0.1%)	0
Glossitis	舌炎	0	0	1 (0.1%)	0
Haematochezia	血便排泄	2 (3.2%)	0	1 (0.1%)	2 (0.4%)
Haemorrhoidal haemorrhage	痔出血	0	0	0	1 (0.2%)
Haemorrhoids	痔核	0	0	6 (0.7%)	0
Hiatus hernia	裂孔ヘルニア	0	0	5 (0.6%)	1 (0.2%)
Ileus	イレウス	0	0	2 (0.2%)	1 (0.2%)
Impaired gastric emptying	胃排出不全	0	0	1 (0.1%)	0
Incarcerated inguinal hernia	嵌頓鼠径ヘルニア	0	0	2 (0.2%)	0
Inguinal hernia	鼠径ヘルニア	1 (1.6%)	0	10 (1.1%)	1 (0.2%)
Intestinal obstruction	腸閉塞	0	0	4 (0.4%)	0
Intra-abdominal haematoma	腹腔内血腫	0	0	1 (0.1%)	0
Irritable bowel syndrome	過敏性腸症候群	0	0	1 (0.1%)	0
Jejunal stenosis	空腸狭窄	0	0	0	1 (0.2%)
Large intestinal stenosis	大腸狭窄	0	0	0	1 (0.2%)
Large intestine perforation	大腸穿孔	0	0	1 (0.1%)	0
Large intestine polyp	大腸ポリープ	2 (3.2%)	0	2 (0.2%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Lip disorder	口唇障害	0	0	1 (0.1%)	0
Lip pain	口唇痛	0	0	0	1 (0.2%)
Lower gastrointestinal haemorrhage	下部消化管出血	1 (1.6%)	0	1 (0.1%)	0
Melaena	メレナ	0	0	1 (0.1%)	1 (0.2%)
Mesenteric artery stenosis	腸間膜動脈狭窄	0	0	1 (0.1%)	0
Mesenteric panniculitis	腸間膜脂肪織炎	0	0	1 (0.1%)	0
Nausea	悪心	4 (6.5%)	0	44 (4.9%)	32 (6.1%)
Obstructive pancreatitis	閉塞性膵炎	0	0	1 (0.1%)	0
Oesophageal pain	食道痛	0	0	0	1 (0.2%)
Oesophagitis	食道炎	0	0	1 (0.1%)	0
Pancreatic atrophy	膵萎縮	0	0	1 (0.1%)	0
Pancreatic calcification	膵石灰化	0	0	0	1 (0.2%)
Pancreatic cyst	膵嚢胞	1 (1.6%)	0	0	1 (0.2%)
Pancreatic duct dilatation	膵管拡張	0	0	1 (0.1%)	1 (0.2%)
Pancreatic steatosis	膵脂肪変性	0	0	6 (0.7%)	3 (0.6%)
Pancreatitis	膵炎	0	0	0	1 (0.2%)
Pancreatitis acute	急性膵炎	0	0	0	1 (0.2%)
Pancreatitis chronic	慢性膵炎	0	0	1 (0.1%)	0
Paraesthesia oral	口の錯感覚	0	0	0	1 (0.2%)
Parotid duct obstruction	耳下腺管閉塞	0	0	1 (0.1%)	0
Peptic ulcer	消化性潰瘍	0	0	1 (0.1%)	1 (0.2%)
Periodontal disease	歯周病	2 (3.2%)	0	1 (0.1%)	1 (0.2%)
Plicated tongue	ひだ舌	0	0	1 (0.1%)	0
Pneumoperitoneum	気腹	0	0	1 (0.1%)	0
Proctalgia	肛門周囲痛	0	0	1 (0.1%)	0
Proctitis	直腸炎	0	0	2 (0.2%)	0
Rectal haemorrhage	直腸出血	0	1 (3.0%)	7 (0.8%)	1 (0.2%)
Rectal stenosis	直腸狭窄	0	0	1 (0.1%)	0
Salivary gland pain	唾液腺痛	0	0	1 (0.1%)	0
Small intestinal obstruction	小腸閉塞	0	0	1 (0.1%)	2 (0.4%)
Small intestinal perforation	小腸穿孔	0	0	1 (0.1%)	0
Splenic artery aneurysm	脾臓動脈瘤	0	0	0	1 (0.2%)
Stomatitis	口内炎	0	0	0	1 (0.2%)
Tongue coated	舌苔	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Tooth loss	歯の脱落	1 (1.6%)	0	0	0
Toothache	歯痛	0	1 (3.0%)	7 (0.8%)	3 (0.6%)
Umbilical hernia	臍ヘルニア	0	0	3 (0.3%)	1 (0.2%)
Upper gastrointestinal haemorrhage	上部消化管出血	0	0	0	1 (0.2%)
Vomiting	嘔吐	1 (1.6%)	0	14 (1.6%)	10 (1.9%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	14 (22.6%)	4 (12.1%)	230 (25.8%)	100 (19.2%)
Asthenia	無力症	0	0	36 (4.0%)	19 (3.6%)
Catheter site related reaction	カテーテル留置部位関連反応	0	0	0	1 (0.2%)
Catheter site ulcer	カテーテル留置部位潰瘍	0	0	0	1 (0.2%)
Chest pain	胸痛	1 (1.6%)	1 (3.0%)	14 (1.6%)	7 (1.3%)
Chills	悪寒	0	0	8 (0.9%)	2 (0.4%)
Cyst	嚢胞	0	0	1 (0.1%)	0
Death	死亡	0	0	4 (0.4%)	1 (0.2%)
Discomfort	不快感	0	0	1 (0.1%)	0
Exercise tolerance decreased	運動耐性低下	0	0	1 (0.1%)	0
Face oedema	顔面浮腫	1 (1.6%)	0	0	0
Fatigue	疲労	2 (3.2%)	1 (3.0%)	113 (12.7%)	47 (9.0%)
Feeling cold	冷感	0	0	2 (0.2%)	0
Gait disturbance	歩行障害	0	0	4 (0.4%)	2 (0.4%)
General physical health deterioration	全身健康状態低下	0	0	5 (0.6%)	0
Granuloma	肉芽腫	0	0	2 (0.2%)	0
Influenza like illness	インフルエンザ様疾患	0	0	10 (1.1%)	4 (0.8%)
Infusion site extravasation	注入部位血管外漏出	0	0	1 (0.1%)	0
Injection site bruising	注射部位内出血	0	0	1 (0.1%)	0
Injection site erythema	注射部位紅斑	0	0	1 (0.1%)	0
Injection site pain	注射部位疼痛	0	0	2 (0.2%)	0
Injection site reaction	注射部位反応	2 (3.2%)	0	0	0
Malaise	倦怠感	2 (3.2%)	0	2 (0.2%)	3 (0.6%)
Nodule	小結節	0	0	1 (0.1%)	0
Non-cardiac chest pain	非心臓性胸痛	2 (3.2%)	0	2 (0.2%)	1 (0.2%)
Oedema	浮腫	0	0	4 (0.4%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Oedema peripheral	末梢性浮腫	1 (1.6%)	1 (3.0%)	38 (4.3%)	16 (3.1%)
Pain	疼痛	1 (1.6%)	2 (6.1%)	4 (0.4%)	5 (1.0%)
Pelvic mass	骨盤腔内腫瘤	0	0	2 (0.2%)	0
Performance status decreased	活動状態低下	0	0	1 (0.1%)	0
Peripheral swelling	末梢腫脹	0	0	13 (1.5%)	7 (1.3%)
Pyrexia	発熱	4 (6.5%)	0	15 (1.7%)	5 (1.0%)
Sudden cardiac death	心突然死	0	0	1 (0.1%)	0
Sudden death	突然死	0	0	1 (0.1%)	0
Suprapubic pain	恥骨上痛	0	0	1 (0.1%)	3 (0.6%)
Temperature intolerance	温度変化不耐症	0	0	1 (0.1%)	0
Thirst	口渇	0	0	1 (0.1%)	1 (0.2%)
Hepatobiliary disorders	肝胆道系障害	5 (8.1%)	1 (3.0%)	26 (2.9%)	9 (1.7%)
Bile duct obstruction	胆管閉塞	0	0	1 (0.1%)	0
Bile duct stenosis	胆管狭窄	0	0	1 (0.1%)	0
Biliary colic	胆道仙痛	0	0	1 (0.1%)	1 (0.2%)
Cholangitis acute	急性胆管炎	0	0	1 (0.1%)	1 (0.2%)
Cholecystitis acute	急性胆嚢炎	0	0	1 (0.1%)	1 (0.2%)
Cholecystitis chronic	慢性胆嚢炎	0	0	1 (0.1%)	0
Cholelithiasis	胆石症	0	0	7 (0.8%)	1 (0.2%)
Cholestasis	胆汁うっ滞	0	0	1 (0.1%)	0
Drug-induced liver injury	薬物性肝障害	1 (1.6%)	0	0	0
Hepatic artery thrombosis	肝動脈血栓症	0	0	1 (0.1%)	0
Hepatic calcification	肝石灰化	0	0	4 (0.4%)	0
Hepatic cyst	肝嚢胞	0	0	7 (0.8%)	4 (0.8%)
Hepatic function abnormal	肝機能異常	4 (6.5%)	1 (3.0%)	0	0
Hepatic steatosis	脂肪肝	0	0	1 (0.1%)	1 (0.2%)
Hepatobiliary disease	肝胆道系疾患	0	0	0	1 (0.2%)
Hyperbilirubinaemia	高ビリルビン血症	0	0	6 (0.7%)	0
Jaundice	黄疸	0	0	2 (0.2%)	0
Liver disorder	肝障害	0	0	1 (0.1%)	0
Immune system disorders	免疫系障害	2 (3.2%)	2 (6.1%)	12 (1.3%)	4 (0.8%)
Allergy to arthropod sting	節足動物刺傷アレルギー	0	0	1 (0.1%)	0
Anaphylactic reaction	アナフィラキシー反応	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Contrast media allergy	造影剤アレルギー	0	2 (6.1%)	3 (0.3%)	1 (0.2%)
Contrast media reaction	造影剤反応	0	0	0	1 (0.2%)
Drug hypersensitivity	薬物過敏症	0	0	3 (0.3%)	0
Hypersensitivity	過敏症	0	0	2 (0.2%)	1 (0.2%)
Immune system disorder	免疫系障害	0	0	0	1 (0.2%)
Seasonal allergy	季節性アレルギー	2 (3.2%)	0	2 (0.2%)	0
Infections and infestations	感染症および寄生虫症	22 (35.5%)	9 (27.3%)	205 (23.0%)	111 (21.3%)
Abdominal abscess	腹部膿瘍	0	0	2 (0.2%)	0
Abscess	膿瘍	1 (1.6%)	0	0	0
Abscess intestinal	腸管膿瘍	0	0	1 (0.1%)	0
Acarodermatitis	ダニ皮膚炎	0	0	1 (0.1%)	0
Acute endocarditis	急性心内膜炎	0	0	1 (0.1%)	0
Acute sinusitis	急性副鼻腔炎	0	0	1 (0.1%)	1 (0.2%)
Appendicitis	虫垂炎	0	0	2 (0.2%)	1 (0.2%)
Bacterial infection	細菌感染	0	0	0	1 (0.2%)
Bacteriuria	細菌尿	0	0	1 (0.1%)	0
Balanitis candida	カンジダ性亀頭炎	0	0	0	1 (0.2%)
Balanoposthitis infective	感染性亀頭包皮炎	0	0	0	1 (0.2%)
Bronchitis	気管支炎	1 (1.6%)	0	10 (1.1%)	9 (1.7%)
Bronchitis viral	ウイルス性気管支炎	1 (1.6%)	0	0	0
Catheter site infection	カテーテル留置部位感染	0	0	0	1 (0.2%)
Cellulitis	蜂巣炎	0	0	1 (0.1%)	1 (0.2%)
Cellulitis gangrenous	壊疽性蜂巣炎	0	0	0	1 (0.2%)
Cholecystitis infective	感染性胆嚢炎	0	0	1 (0.1%)	0
Conjunctivitis	結膜炎	0	0	4 (0.4%)	0
Cystitis	膀胱炎	1 (1.6%)	0	7 (0.8%)	7 (1.3%)
Dermatophytosis of nail	爪の皮膚糸状菌症	1 (1.6%)	0	0	0
Device related infection	医療機器関連感染	0	0	1 (0.1%)	1 (0.2%)
Diverticulitis	憩室炎	0	0	1 (0.1%)	0
Ear infection	耳感染	0	0	1 (0.1%)	0
Ear infection bacterial	細菌性耳感染	0	0	1 (0.1%)	0
Endocarditis	心内膜炎	0	0	1 (0.1%)	0
Erysipelas	丹毒	0	0	2 (0.2%)	0
Eye infection bacterial	細菌性眼感染	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Febrile infection	熱性感染症	0	0	1 (0.1%)	0
Folliculitis	毛包炎	0	0	1 (0.1%)	0
Fungal balanitis	真菌性亀頭炎	0	0	1 (0.1%)	0
Fungal skin infection	皮膚真菌感染	0	0	1 (0.1%)	0
Gangrene	壊疽	0	0	1 (0.1%)	0
Gastroenteritis	胃腸炎	0	0	5 (0.6%)	2 (0.4%)
Gastroenteritis viral	ウイルス性胃腸炎	0	0	0	1 (0.2%)
Gastrointestinal infection	消化管感染	0	0	0	1 (0.2%)
Genital infection fungal	真菌性性器感染	0	0	1 (0.1%)	0
Gingivitis	歯肉炎	1 (1.6%)	0	1 (0.1%)	1 (0.2%)
Helicobacter gastritis	ヘリコバクター性胃炎	0	0	1 (0.1%)	0
Helicobacter infection	ヘリコバクター感染	0	0	1 (0.1%)	0
Hepatitis C	Ｃ型肝炎	0	0	0	1 (0.2%)
Herpes zoster	帯状疱疹	0	0	4 (0.4%)	4 (0.8%)
Infected bite	咬傷感染	0	0	1 (0.1%)	0
Infection	感染	0	0	0	1 (0.2%)
Infectious mononucleosis	伝染性単核症	0	0	0	1 (0.2%)
Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	0	0	2 (0.2%)	0
Infestation	寄生	0	0	0	1 (0.2%)
Influenza	インフルエンザ	4 (6.5%)	0	23 (2.6%)	9 (1.7%)
Intervertebral discitis	椎間板炎	0	0	1 (0.1%)	0
Klebsiella bacteraemia	クレブシエラ性菌血症	0	0	0	1 (0.2%)
Labyrinthitis	迷路炎	0	0	0	1 (0.2%)
Laryngitis	喉頭炎	1 (1.6%)	0	1 (0.1%)	0
Localised infection	限局性感染	0	0	1 (0.1%)	1 (0.2%)
Lower respiratory tract infection	下気道感染	0	0	4 (0.4%)	1 (0.2%)
Lung infection	肺感染	0	0	3 (0.3%)	0
Medical device site joint infection	医療機器使用部位関節感染	0	0	1 (0.1%)	0
Meningitis bacterial	細菌性髄膜炎	0	0	1 (0.1%)	0
Nasopharyngitis	上咽頭炎	12 (19.4%)	4 (12.1%)	24 (2.7%)	17 (3.3%)
Oesophageal candidiasis	食道カンジダ症	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Onychomycosis	爪真菌症	0	0	3 (0.3%)	2 (0.4%)
Oral candidiasis	口腔カンジダ症	0	0	3 (0.3%)	0
Oral herpes	口腔ヘルペス	0	0	2 (0.2%)	0
Orchitis	精巣炎	0	0	1 (0.1%)	1 (0.2%)
Otitis externa	外耳炎	1 (1.6%)	0	1 (0.1%)	0
Otitis media	中耳炎	0	0	1 (0.1%)	0
Paronychia	爪囲炎	1 (1.6%)	0	0	1 (0.2%)
Periodontitis	歯周炎	0	0	1 (0.1%)	1 (0.2%)
Peritonitis	腹膜炎	0	0	0	1 (0.2%)
Pharyngitis	咽頭炎	0	0	0	1 (0.2%)
Pneumonia	肺炎	1 (1.6%)	0	18 (2.0%)	11 (2.1%)
Pneumonia pneumococcal	肺炎球菌性肺炎	0	0	1 (0.1%)	0
Pneumonia staphylococcal	ブドウ球菌性肺炎	0	0	0	1 (0.2%)
Prostate infection	前立腺感染	0	0	0	1 (0.2%)
Pulmonary tuberculosis	肺結核	0	0	0	1 (0.2%)
Pulpitis dental	歯髄炎	0	0	1 (0.1%)	0
Pyelonephritis	腎盂腎炎	1 (1.6%)	0	3 (0.3%)	0
Pyelonephritis acute	急性腎盂腎炎	1 (1.6%)	0	2 (0.2%)	1 (0.2%)
Pyelonephritis chronic	慢性腎盂腎炎	0	0	1 (0.1%)	0
Pyuria	膿尿	0	0	1 (0.1%)	0
Rash pustular	膿疱性皮疹	0	0	1 (0.1%)	0
Respiratory syncytial virus infection	ＲＳウイルス感染	0	0	1 (0.1%)	0
Respiratory tract infection	気道感染	0	0	6 (0.7%)	0
Respiratory tract infection viral	ウイルス性気道感染	0	0	3 (0.3%)	5 (1.0%)
Rhinitis	鼻炎	1 (1.6%)	0	3 (0.3%)	6 (1.2%)
Root canal infection	根管感染	0	0	0	1 (0.2%)
Sepsis	敗血症	0	0	1 (0.1%)	0
Septic shock	敗血症性ショック	0	0	1 (0.1%)	0
Sialoadenitis	唾液腺炎	0	0	1 (0.1%)	0
Sinusitis	副鼻腔炎	0	0	2 (0.2%)	4 (0.8%)
Skin infection	皮膚感染	1 (1.6%)	0	3 (0.3%)	0
Subcutaneous abscess	皮下組織膿瘍	0	0	0	1 (0.2%)
Tinea infection	白癬感染	1 (1.6%)	1 (3.0%)	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Tooth abscess	歯膿瘍	0	0	2 (0.2%)	2 (0.4%)
Tooth infection	歯感染	0	0	2 (0.2%)	1 (0.2%)
Tracheitis	気管炎	0	0	1 (0.1%)	0
Tracheobronchitis	気管気管支炎	0	0	1 (0.1%)	0
Trichophytosis	トリコフィトン感染症	1 (1.6%)	0	0	0
Upper respiratory tract infection	上気道感染	5 (8.1%)	3 (9.1%)	20 (2.2%)	6 (1.2%)
Urinary tract infection	尿路感染	1 (1.6%)	1 (3.0%)	46 (5.2%)	27 (5.2%)
Urinary tract infection bacterial	細菌性尿路感染	0	0	0	1 (0.2%)
Urosepsis	尿路性敗血症	0	0	2 (0.2%)	0
Varicella zoster virus infection	水痘帯状疱疹ウイルス感染	0	0	1 (0.1%)	0
Vestibular neuronitis	前庭神経炎	0	0	1 (0.1%)	0
Viral infection	ウイルス感染	0	1 (3.0%)	3 (0.3%)	1 (0.2%)
Viral upper respiratory tract infection	ウイルス性上気道感染	0	0	2 (0.2%)	0
Wound infection	創傷感染	0	0	1 (0.1%)	0
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	16 (25.8%)	4 (12.1%)	103 (11.5%)	42 (8.1%)
Accident	事故	0	0	4 (0.4%)	3 (0.6%)
Alcohol poisoning	アルコール中毒	0	0	1 (0.1%)	0
Anaemia postoperative	術後貧血	0	0	0	1 (0.2%)
Animal bite	動物咬傷	0	0	0	1 (0.2%)
Ankle fracture	足関節部骨折	0	0	2 (0.2%)	0
Arthropod bite	節足動物咬傷	0	0	2 (0.2%)	0
Auricular haematoma	耳介血腫	0	0	0	1 (0.2%)
Back injury	背部損傷	0	0	1 (0.1%)	0
Bone contusion	骨挫傷	0	0	1 (0.1%)	1 (0.2%)
Cervical vertebral fracture	頚椎骨折	1 (1.6%)	0	0	0
Chest injury	胸部損傷	0	0	2 (0.2%)	1 (0.2%)
Clavicle fracture	鎖骨骨折	0	0	1 (0.1%)	0
Contusion	挫傷	3 (4.8%)	0	9 (1.0%)	2 (0.4%)
Craniocerebral injury	頭蓋脳損傷	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Cystitis radiation	放射線性膀胱炎	1 (1.6%)	0	3 (0.3%)	0
Eyelid injury	眼瞼損傷	0	0	1 (0.1%)	0
Face injury	顔面損傷	0	0	0	1 (0.2%)
Facial bones fracture	顔面骨骨折	0	0	0	2 (0.4%)
Fall	転倒	8 (12.9%)	1 (3.0%)	28 (3.1%)	22 (4.2%)
Femoral neck fracture	大腿骨頚部骨折	0	0	2 (0.2%)	0
Femur fracture	大腿骨骨折	0	0	2 (0.2%)	1 (0.2%)
Fibula fracture	腓骨骨折	0	0	1 (0.1%)	0
Foot fracture	足骨折	0	1 (3.0%)	1 (0.1%)	1 (0.2%)
Fracture	骨折	2 (3.2%)	0	0	1 (0.2%)
Frostbite	凍傷	0	0	0	1 (0.2%)
Haematuria traumatic	外傷性血尿	0	0	0	1 (0.2%)
Hand fracture	手骨折	1 (1.6%)	0	3 (0.3%)	1 (0.2%)
Head injury	頭部損傷	0	0	2 (0.2%)	0
Heart injury	心臓損傷	0	0	1 (0.1%)	0
Hip fracture	股関節部骨折	0	0	0	1 (0.2%)
Humerus fracture	上腕骨骨折	0	0	1 (0.1%)	1 (0.2%)
Incision site pain	切開部位痛	0	0	2 (0.2%)	0
Injury	損傷	0	0	2 (0.2%)	1 (0.2%)
Injury of conjunctiva	結膜損傷	0	0	0	1 (0.2%)
Joint dislocation	関節脱臼	1 (1.6%)	0	2 (0.2%)	0
Joint injury	関節損傷	0	0	0	1 (0.2%)
Laceration	裂傷	0	0	2 (0.2%)	1 (0.2%)
Ligament injury	靭帯損傷	0	0	0	1 (0.2%)
Ligament sprain	靭帯捻挫	0	0	3 (0.3%)	0
Limb injury	四肢損傷	0	0	7 (0.8%)	0
Lip injury	口唇損傷	1 (1.6%)	0	0	0
Lumbar vertebral fracture	腰椎骨折	0	0	0	1 (0.2%)
Meniscus injury	半月板損傷	0	0	2 (0.2%)	0
Multiple injuries	多発性外傷	0	0	1 (0.1%)	0
Muscle strain	肉離れ	0	0	1 (0.1%)	0
Patella fracture	膝蓋骨骨折	1 (1.6%)	0	1 (0.1%)	0
Post-traumatic pain	外傷後疼痛	0	0	5 (0.6%)	0
Postoperative ileus	術後イレウス	1 (1.6%)	0	0	0
Procedural pain	処置による疼痛	1 (1.6%)	0	2 (0.2%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Radiation proctitis	放射線性直腸炎	0	0	4 (0.4%)	1 (0.2%)
Radius fracture	橈骨骨折	1 (1.6%)	0	1 (0.1%)	0
Rib fracture	肋骨骨折	2 (3.2%)	0	9 (1.0%)	8 (1.5%)
Road traffic accident	交通事故	1 (1.6%)	0	2 (0.2%)	1 (0.2%)
Scapula fracture	肩甲骨骨折	0	0	0	1 (0.2%)
Scratch	引っかき傷	0	0	1 (0.1%)	0
Skin abrasion	皮膚擦過傷	0	0	3 (0.3%)	1 (0.2%)
Skull fracture	頭蓋骨骨折	0	0	1 (0.1%)	0
Soft tissue injury	軟部組織損傷	0	0	2 (0.2%)	0
Spinal compression fracture	脊椎圧迫骨折	0	0	2 (0.2%)	1 (0.2%)
Spinal fracture	脊椎骨折	0	0	1 (0.1%)	0
Stenosis of vesicourethral anastomosis	膀胱尿道吻合部狭窄	0	0	2 (0.2%)	0
Stomal hernia	ストーマ部ヘルニア	0	0	0	1 (0.2%)
Subarachnoid haemorrhage	くも膜下出血	1 (1.6%)	0	0	0
Subcutaneous haematoma	皮下血腫	0	0	1 (0.1%)	0
Subdural haematoma	硬膜下血腫	1 (1.6%)	0	0	1 (0.2%)
Sunburn	サンバーン	0	0	1 (0.1%)	0
Thermal burn	熱傷	0	0	1 (0.1%)	0
Tooth fracture	歯牙破折	0	0	0	1 (0.2%)
Traumatic fracture	外傷性骨折	0	0	4 (0.4%)	2 (0.4%)
Traumatic haematoma	外傷性血腫	0	0	1 (0.1%)	0
Ulna fracture	尺骨骨折	0	0	1 (0.1%)	0
Upper limb fracture	上肢骨折	0	0	1 (0.1%)	1 (0.2%)
Vascular graft complication	移植血管合併症	0	0	1 (0.1%)	0
Wound complication	創合併症	0	2 (6.1%)	0	0
Wound dehiscence	創離開	0	0	1 (0.1%)	0
Wrist fracture	手首関節骨折	0	0	2 (0.2%)	0
Investigations	臨床検査	9 (14.5%)	2 (6.1%)	135 (15.1%)	61 (11.7%)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (3.2%)	0	5 (0.6%)	1 (0.2%)
Arteriogram coronary	冠血管造影	0	0	0	2 (0.4%)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (4.8%)	0	10 (1.1%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0	0	1 (0.1%)	3 (0.6%)
Blood bilirubin increased	血中ビリルビン増加	0	0	12 (1.3%)	0
Blood cholesterol increased	血中コレステロール増加	0	0	2 (0.2%)	1 (0.2%)
Blood chromogranin A increased	血中クロモグラニンＡ増加	0	0	6 (0.7%)	6 (1.2%)
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0	0	1 (0.1%)	0
Blood creatinine increased	血中クレアチニン増加	1 (1.6%)	1 (3.0%)	21 (2.4%)	13 (2.5%)
Blood glucose increased	血中ブドウ糖増加	0	0	2 (0.2%)	0
Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	0	0	5 (0.6%)	0
Blood potassium decreased	血中カリウム減少	0	0	1 (0.1%)	0
Blood potassium increased	血中カリウム増加	0	0	2 (0.2%)	2 (0.4%)
Blood pressure increased	血圧上昇	0	0	4 (0.4%)	3 (0.6%)
Blood pressure systolic increased	収縮期血圧上昇	0	0	0	1 (0.2%)
Blood sodium decreased	血中ナトリウム減少	0	0	1 (0.1%)	0
Blood testosterone increased	血中テストステロン増加	0	0	2 (0.2%)	1 (0.2%)
Blood urea abnormal	血中尿素異常	0	0	1 (0.1%)	0
Blood urea increased	血中尿素増加	0	0	3 (0.3%)	4 (0.8%)
Blood uric acid increased	血中尿酸増加	0	0	0	1 (0.2%)
Body temperature increased	体温上昇	0	0	1 (0.1%)	0
Breath sounds abnormal	呼吸音異常	0	0	2 (0.2%)	1 (0.2%)
C-reactive protein increased	Ｃ－反応性蛋白増加	0	0	1 (0.1%)	0
Cardiac murmur	心雑音	0	0	5 (0.6%)	2 (0.4%)
Carotid bruit	頚動脈雑音	0	0	1 (0.1%)	0
Chest X-ray abnormal	胸部Ｘ線異常	0	0	1 (0.1%)	0
Electrocardiogram QT prolonged	心電図ＱＴ延長	0	0	4 (0.4%)	0
Electrocardiogram ST segment depression	心電図ＳＴ部分下降	0	0	1 (0.1%)	0
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0	0	1 (0.1%)	0
Gastric pH decreased	胃内ｐＨ低下	0	0	0	1 (0.2%)
Glomerular filtration rate decreased	糸球体濾過率減少	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Glomerular filtration rate increased	糸球体濾過率増加	0	0	0	1 (0.2%)
Glucose urine present	尿中ブドウ糖陽性	0	0	1 (0.1%)	1 (0.2%)
Haematocrit decreased	ヘマトクリット減少	0	0	1 (0.1%)	0
Haematology test abnormal	血液学的検査異常	0	0	1 (0.1%)	0
Haemoglobin decreased	ヘモグロビン減少	0	0	4 (0.4%)	1 (0.2%)
Heart rate increased	心拍数増加	0	0	1 (0.1%)	0
Heart rate irregular	心拍数不整	0	0	1 (0.1%)	0
Heart sounds abnormal	心音異常	0	0	1 (0.1%)	0
International normalised ratio increased	国際標準比増加	0	0	1 (0.1%)	2 (0.4%)
Lymphocyte count decreased	リンパ球数減少	1 (1.6%)	0	8 (0.9%)	0
Lymphocyte count increased	リンパ球数増加	0	0	1 (0.1%)	0
Neutrophil count decreased	好中球数減少	1 (1.6%)	0	10 (1.1%)	0
Neutrophil count increased	好中球数増加	0	0	1 (0.1%)	0
Platelet count decreased	血小板数減少	1 (1.6%)	0	6 (0.7%)	2 (0.4%)
Protein total decreased	総蛋白減少	0	0	1 (0.1%)	0
Protein urine present	尿中蛋白陽性	0	0	2 (0.2%)	1 (0.2%)
Red blood cell count decreased	赤血球数減少	0	0	2 (0.2%)	0
Transaminases increased	トランスアミナーゼ上昇	0	0	1 (0.1%)	0
Troponin increased	トロポニン増加	0	0	1 (0.1%)	0
Urine output decreased	尿量減少	0	0	1 (0.1%)	1 (0.2%)
Vitamin B12 decreased	ビタミンＢ１２減少	0	0	0	1 (0.2%)
Weight decreased	体重減少	3 (4.8%)	0	31 (3.5%)	12 (2.3%)
Weight increased	体重増加	0	1 (3.0%)	14 (1.6%)	6 (1.2%)
White blood cell count decreased	白血球数減少	2 (3.2%)	0	6 (0.7%)	1 (0.2%)
White blood cells urine positive	尿中白血球陽性	0	0	0	1 (0.2%)
Metabolism and nutrition disorders	代謝および栄養障害	10 (16.1%)	2 (6.1%)	85 (9.5%)	47 (9.0%)
Cachexia	悪液質	0	0	1 (0.1%)	0
Decreased appetite	食欲減退	7 (11.3%)	1 (3.0%)	21 (2.4%)	15 (2.9%)
Dehydration	脱水	2 (3.2%)	0	4 (0.4%)	4 (0.8%)
Diabetes mellitus	糖尿病	0	0	5 (0.6%)	5 (1.0%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Diabetes mellitus inadequate control	コントロール不良の糖尿病	0	0	1 (0.1%)	0
Diabetic ketoacidosis	糖尿病性ケトアシドーシス	0	0	0	1 (0.2%)
Diabetic metabolic decompensation	糖尿病性代謝代償不全	0	0	0	1 (0.2%)
Dyslipidaemia	脂質異常症	1 (1.6%)	0	3 (0.3%)	1 (0.2%)
Electrolyte imbalance	電解質失調	0	0	1 (0.1%)	0
Folate deficiency	葉酸欠乏	0	0	1 (0.1%)	0
Gout	痛風	0	0	3 (0.3%)	2 (0.4%)
Hypercholesterolaemia	高コレステロール血症	0	0	3 (0.3%)	2 (0.4%)
Hyperglycaemia	高血糖	1 (1.6%)	0	8 (0.9%)	3 (0.6%)
Hyperkalaemia	高カリウム血症	1 (1.6%)	0	15 (1.7%)	9 (1.7%)
Hyperlipidaemia	高脂血症	0	1 (3.0%)	1 (0.1%)	0
Hypernatraemia	高ナトリウム血症	0	0	0	1 (0.2%)
Hypertriglyceridaemia	高トリグリセリド血症	0	0	3 (0.3%)	0
Hyperuricaemia	高尿酸血症	1 (1.6%)	0	3 (0.3%)	1 (0.2%)
Hypocalcaemia	低カルシウム血症	0	0	1 (0.1%)	2 (0.4%)
Hypochloraemia	低クロール血症	0	0	1 (0.1%)	0
Hypoglycaemia	低血糖	0	0	3 (0.3%)	0
Hypokalaemia	低カリウム血症	0	0	9 (1.0%)	2 (0.4%)
Hypomagnesaemia	低マグネシウム血症	0	0	1 (0.1%)	0
Hyponatraemia	低ナトリウム血症	0	0	7 (0.8%)	2 (0.4%)
Hypoproteinaemia	低蛋白血症	0	0	0	1 (0.2%)
Increased appetite	食欲亢進	0	0	1 (0.1%)	0
Iron deficiency	鉄欠乏	0	0	2 (0.2%)	1 (0.2%)
Magnesium deficiency	マグネシウム欠乏	0	0	1 (0.1%)	0
Malnutrition	栄養障害	0	0	0	1 (0.2%)
Metabolic alkalosis	代謝性アルカローシス	0	0	1 (0.1%)	0
Obesity	肥満	0	0	1 (0.1%)	0
Type 2 diabetes mellitus	２型糖尿病	0	0	1 (0.1%)	0
Vitamin D deficiency	ビタミンＤ欠乏	0	0	4 (0.4%)	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	12 (19.4%)	4 (12.1%)	258 (28.9%)	131 (25.1%)
Arthralgia	関節痛	1 (1.6%)	2 (6.1%)	76 (8.5%)	49 (9.4%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Arthritis	関節炎	0	1 (3.0%)	6 (0.7%)	0
Axillary mass	腋窩腫瘤	0	0	1 (0.1%)	1 (0.2%)
Back pain	背部痛	5 (8.1%)	1 (3.0%)	79 (8.9%)	49 (9.4%)
Bone lesion	骨病変	0	0	1 (0.1%)	0
Bone pain	骨痛	0	0	9 (1.0%)	6 (1.2%)
Bursitis	滑液包炎	0	0	1 (0.1%)	1 (0.2%)
Coccydynia	尾骨痛	0	0	1 (0.1%)	0
Dupuytren's contracture	デュプイトラン拘縮	0	0	1 (0.1%)	0
Exostosis	外骨腫	0	0	2 (0.2%)	1 (0.2%)
Extremity contracture	四肢拘縮	0	0	0	1 (0.2%)
Flank pain	側腹部痛	0	0	5 (0.6%)	2 (0.4%)
Groin pain	鼠径部痛	0	0	7 (0.8%)	5 (1.0%)
Hand deformity	手変形	0	0	1 (0.1%)	0
Intervertebral disc protrusion	椎間板突出	0	0	2 (0.2%)	0
Joint range of motion decreased	関節可動域低下	0	0	1 (0.1%)	0
Joint stiffness	関節硬直	0	0	1 (0.1%)	0
Joint swelling	関節腫脹	0	0	4 (0.4%)	3 (0.6%)
Limb discomfort	四肢不快感	0	0	1 (0.1%)	0
Lumbar spinal stenosis	腰部脊柱管狭窄症	1 (1.6%)	0	0	1 (0.2%)
Metatarsalgia	中足骨痛	0	0	1 (0.1%)	0
Mobility decreased	運動性低下	0	0	3 (0.3%)	0
Muscle spasms	筋痙縮	1 (1.6%)	1 (3.0%)	16 (1.8%)	3 (0.6%)
Muscular weakness	筋力低下	1 (1.6%)	0	9 (1.0%)	5 (1.0%)
Musculoskeletal chest pain	筋骨格系胸痛	0	0	10 (1.1%)	6 (1.2%)
Musculoskeletal discomfort	筋骨格不快感	0	0	1 (0.1%)	0
Musculoskeletal pain	筋骨格痛	2 (3.2%)	1 (3.0%)	35 (3.9%)	10 (1.9%)
Musculoskeletal stiffness	筋骨格硬直	0	0	1 (0.1%)	0
Myalgia	筋肉痛	0	0	16 (1.8%)	6 (1.2%)
Neck pain	頚部痛	0	0	9 (1.0%)	6 (1.2%)
Osteitis	骨炎	0	0	1 (0.1%)	0
Osteitis deformans	変形性骨炎	0	0	1 (0.1%)	0
Osteoarthritis	変形性関節症	0	0	15 (1.7%)	3 (0.6%)
Osteochondrosis	骨端症	0	0	1 (0.1%)	0
Osteopenia	骨減少症	0	0	0	1 (0.2%)
Osteoporosis	骨粗鬆症	0	0	4 (0.4%)	1 (0.2%)

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Pain in extremity	四肢痛	2 (3.2%)	0	53 (5.9%)	18 (3.5%)
Pathological fracture	病的骨折	0	0	0	1 (0.2%)
Plantar fasciitis	足底筋膜炎	0	0	0	2 (0.4%)
Polymyalgia rheumatica	リウマチ性多発筋痛	0	0	1 (0.1%)	0
Rheumatic disorder	リウマチ性障害	0	0	1 (0.1%)	0
Rotator cuff syndrome	肩回旋筋腱板症候群	0	0	3 (0.3%)	1 (0.2%)
Spinal column stenosis	脊柱管狭窄症	0	0	1 (0.1%)	0
Spinal deformity	脊柱変形	0	0	1 (0.1%)	0
Spinal fusion acquired	後天性脊椎癒合	0	0	0	1 (0.2%)
Spinal osteoarthritis	変形性脊椎症	0	0	1 (0.1%)	0
Spinal pain	脊椎痛	0	0	3 (0.3%)	4 (0.8%)
Tendon disorder	腱障害	0	0	0	1 (0.2%)
Tendonitis	腱炎	0	0	1 (0.1%)	1 (0.2%)
Trigger finger	弾発指	0	0	1 (0.1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	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）	5 (8.1%)	3 (9.1%)	43 (4.8%)	23 (4.4%)
Acute leukaemia	急性白血病	0	0	1 (0.1%)	0
Adenocarcinoma	腺癌	0	0	0	1 (0.2%)
Adrenal adenoma	副腎腺腫	0	0	4 (0.4%)	0
Basal cell carcinoma	基底細胞癌	0	0	5 (0.6%)	2 (0.4%)
Benign lung neoplasm	肺の良性新生物	0	0	1 (0.1%)	0
Bladder cancer	膀胱癌	0	0	0	1 (0.2%)
Bladder neoplasm	膀胱新生物	2 (3.2%)	0	2 (0.2%)	0
Bowen's disease	ボーエン病	0	0	0	1 (0.2%)
Cancer pain	癌疼痛	0	0	0	1 (0.2%)
Carcinoid tumour	カルチノイド腫瘍	0	0	1 (0.1%)	0
Choroid melanoma	脈絡膜黒色腫	0	0	1 (0.1%)	0
Colon adenoma	大腸腺腫	0	1 (3.0%)	0	0
Colon cancer	結腸癌	1 (1.6%)	0	2 (0.2%)	0
Colon neoplasm	結腸新生物	0	0	1 (0.1%)	1 (0.2%)
Diffuse large B-cell lymphoma	びまん性大細胞型Ｂ細胞性リンパ腫	0	0	1 (0.1%)	0
Gastric adenoma	胃腺腫	0	0	1 (0.1%)	0
Gastric cancer	胃癌	0	1 (3.0%)	1 (0.1%)	1 (0.2%)
Gastrointestinal adenocarcinoma	消化器腺癌	0	0	1 (0.1%)	0

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Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Intestinal angioma	腸血管腫	0	0	1 (0.1%)	0
Laryngeal cancer	喉頭癌	0	0	0	1 (0.2%)
Lipoma	脂肪腫	0	0	2 (0.2%)	1 (0.2%)
Lung adenocarcinoma stage IV	肺腺癌第４期	0	0	1 (0.1%)	0
Lung neoplasm malignant	肺の悪性新生物	0	1 (3.0%)	1 (0.1%)	1 (0.2%)
Lymphangiosis carcinomatosa	癌性リンパ管症	0	0	1 (0.1%)	0
Lymphoma	リンパ腫	0	0	1 (0.1%)	0
Malignant melanoma in situ	表皮内悪性黒色腫	0	0	2 (0.2%)	0
Melanocytic naevus	メラノサイト性母斑	0	0	0	1 (0.2%)
Mesothelioma	中皮腫	0	0	1 (0.1%)	0
Metastases to peritoneum	腹膜転移	0	0	1 (0.1%)	0
Neoplasm malignant	悪性新生物	0	0	1 (0.1%)	0
Oncologic complication	腫瘍合併症	0	0	1 (0.1%)	0
Pancreatic carcinoma	膵癌	1 (1.6%)	0	2 (0.2%)	0
Pancreatic carcinoma recurrent	再発膵癌	0	0	1 (0.1%)	0
Pancreatic neoplasm	膵新生物	0	0	2 (0.2%)	0
Pituitary tumour	下垂体腫瘍	0	0	1 (0.1%)	0
Prostate cancer	前立腺癌	0	0	0	2 (0.4%)
Prostate cancer metastatic	遠隔転移を伴う前立腺癌	0	0	0	1 (0.2%)
Prostate cancer recurrent	再発前立腺癌	0	0	1 (0.1%)	0
Rectal adenocarcinoma	直腸腺癌	0	0	2 (0.2%)	0
Rectal cancer	直腸癌	1 (1.6%)	1 (3.0%)	1 (0.1%)	0
Renal cancer	腎癌	0	0	0	1 (0.2%)
Salivary gland neoplasm	唾液腺新生物	0	0	1 (0.1%)	0
Seborrhoeic keratosis	脂漏性角化症	0	0	1 (0.1%)	1 (0.2%)
Skin papilloma	皮膚乳頭腫	0	0	0	1 (0.2%)
Small cell lung cancer limited stage	限局型小細胞肺癌	0	0	0	1 (0.2%)
Squamous cell carcinoma	扁平上皮癌	0	0	1 (0.1%)	0
Squamous cell carcinoma of skin	皮膚有棘細胞癌	0	0	0	1 (0.2%)
Thymoma	胸腺腫	0	0	1 (0.1%)	0
Thyroid adenoma	甲状腺腺腫	0	0	0	1 (0.2%)
Transitional cell carcinoma	移行上皮癌	0	0	0	2 (0.4%)
Tumour compression	腫瘍性圧迫	0	0	0	1 (0.2%)
Tumour obstruction	腫瘍性閉塞	0	0	0	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Tumour pain	腫瘍疼痛	0	0	1 (0.1%)	0
Urinary tract neoplasm	尿路新生物	0	0	0	1 (0.2%)
Nervous system disorders	神経系障害	3 (4.8%)	1 (3.0%)	144 (16.1%)	73 (14.0%)
Amnesia	健忘	0	0	1 (0.1%)	3 (0.6%)
Autonomic nervous system imbalance	自律神経失調	0	0	0	1 (0.2%)
Axonal neuropathy	軸索型ニューロパチー	0	0	0	1 (0.2%)
Balance disorder	平衡障害	0	0	1 (0.1%)	1 (0.2%)
Brain oedema	脳浮腫	0	0	1 (0.1%)	0
Bulbar palsy	球麻痺	0	0	0	1 (0.2%)
Carotid arteriosclerosis	頚動脈硬化症	0	0	0	1 (0.2%)
Carotid artery stenosis	頚動脈狭窄	0	0	3 (0.3%)	0
Carpal tunnel syndrome	手根管症候群	0	0	1 (0.1%)	3 (0.6%)
Cerebral arteriosclerosis	脳動脈硬化症	0	0	1 (0.1%)	0
Cerebral atrophy	大脳萎縮	0	0	1 (0.1%)	0
Cerebral infarction	脳梗塞	1 (1.6%)	0	1 (0.1%)	0
Cerebral ischaemia	脳虚血	0	0	1 (0.1%)	1 (0.2%)
Cerebrovascular accident	脳血管発作	0	0	2 (0.2%)	4 (0.8%)
Cervicogenic vertigo	頚原性回転性めまい	0	0	1 (0.1%)	0
Cognitive disorder	認知障害	0	0	4 (0.4%)	1 (0.2%)
Dementia	認知症	0	0	2 (0.2%)	0
Dementia Alzheimer's type	アルツハイマー型認知症	0	0	1 (0.1%)	0
Depressed level of consciousness	意識レベルの低下	0	0	2 (0.2%)	0
Disturbance in attention	注意力障害	0	0	0	1 (0.2%)
Dizziness	浮動性めまい	0	0	35 (3.9%)	14 (2.7%)
Dysaesthesia	異常感覚	0	0	1 (0.1%)	2 (0.4%)
Dysarthria	構語障害	0	0	0	1 (0.2%)
Dysgeusia	味覚異常	0	0	2 (0.2%)	4 (0.8%)
Encephalopathy	脳症	0	0	0	1 (0.2%)
Essential tremor	本態性振戦	0	0	1 (0.1%)	0
Haemorrhage intracranial	頭蓋内出血	0	0	0	1 (0.2%)
Headache	頭痛	1 (1.6%)	1 (3.0%)	36 (4.0%)	13 (2.5%)
Hypersomnia	過眠症	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Hypoaesthesia	感覚鈍麻	0	0	6 (0.7%)	5 (1.0%)
Hyposmia	嗅覚減退	0	0	1 (0.1%)	0
Hypotonia	筋緊張低下	0	0	1 (0.1%)	0
IVth nerve paralysis	第４脳神経麻痺	0	0	0	1 (0.2%)
Intercostal neuralgia	肋間神経痛	0	0	1 (0.1%)	0
Ischaemic stroke	虚血性脳卒中	0	0	5 (0.6%)	2 (0.4%)
Lethargy	嗜眠	0	0	1 (0.1%)	1 (0.2%)
Loss of consciousness	意識消失	0	0	2 (0.2%)	0
Lumbar radiculopathy	腰髄神経根障害	0	0	0	1 (0.2%)
Lumbosacral radiculopathy	腰仙部神経根障害	0	0	1 (0.1%)	0
Memory impairment	記憶障害	0	0	5 (0.6%)	7 (1.3%)
Myelopathy	脊髄症	0	0	1 (0.1%)	0
Neuralgia	神経痛	0	0	2 (0.2%)	0
Neuropathy peripheral	末梢性ニューロパチー	0	0	1 (0.1%)	2 (0.4%)
Paraesthesia	錯感覚	0	0	6 (0.7%)	4 (0.8%)
Parkinson's disease	パーキンソン病	0	0	2 (0.2%)	2 (0.4%)
Partial seizures	部分発作	0	0	1 (0.1%)	0
Peripheral sensory neuropathy	末梢性感覚ニューロパチー	0	0	1 (0.1%)	0
Presyncope	失神寸前の状態	0	0	4 (0.4%)	0
Psychomotor hyperactivity	精神運動亢進	0	0	0	1 (0.2%)
Psychomotor skills impaired	精神運動機能障害	0	0	0	1 (0.2%)
Restless legs syndrome	下肢静止不能症候群	0	0	0	2 (0.4%)
Sacral radiculopathy	仙部神経根症	0	0	1 (0.1%)	0
Sciatica	坐骨神経痛	0	0	8 (0.9%)	6 (1.2%)
Seizure	痙攣発作	0	0	1 (0.1%)	1 (0.2%)
Senile dementia	老年認知症	0	0	2 (0.2%)	0
Somnolence	傾眠	0	0	8 (0.9%)	1 (0.2%)
Speech disorder	会話障害	0	0	0	1 (0.2%)
Syncope	失神	0	0	4 (0.4%)	3 (0.6%)
Transient ischaemic attack	一過性脳虚血発作	1 (1.6%)	0	2 (0.2%)	1 (0.2%)
Tremor	振戦	0	0	4 (0.4%)	2 (0.4%)
Vascular dementia	血管性認知症	0	0	1 (0.1%)	0
Vocal cord paresis	声帯不全麻痺	0	0	1 (0.1%)	0
Product issues	製品の問題	0	0	9 (1.0%)	3 (0.6%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Device dislocation	医療機器位置異常	0	0	3 (0.3%)	1 (0.2%)
Device malfunction	医療機器機能不良	0	0	1 (0.1%)	0
Device occlusion	医療機器閉塞	0	0	5 (0.6%)	2 (0.4%)
Psychiatric disorders	精神障害	1 (1.6%)	1 (3.0%)	56 (6.3%)	27 (5.2%)
Agitation	激越	0	0	1 (0.1%)	1 (0.2%)
Anxiety	不安	0	0	5 (0.6%)	2 (0.4%)
Claustrophobia	閉所恐怖症	0	0	0	1 (0.2%)
Delirium	譫妄	0	0	0	3 (0.6%)
Depressed mood	抑うつ気分	0	0	1 (0.1%)	1 (0.2%)
Depression	うつ病	0	0	16 (1.8%)	7 (1.3%)
Disorientation	失見当識	0	0	2 (0.2%)	1 (0.2%)
Hallucination, auditory	幻聴	0	0	1 (0.1%)	0
Hallucination, visual	幻視	0	0	1 (0.1%)	0
Initial insomnia	初期不眠症	0	0	0	1 (0.2%)
Insomnia	不眠症	1 (1.6%)	1 (3.0%)	25 (2.8%)	9 (1.7%)
Irritability	易刺激性	0	0	2 (0.2%)	2 (0.4%)
Mental status changes	精神状態変化	0	0	0	1 (0.2%)
Middle insomnia	中期不眠症	0	0	1 (0.1%)	1 (0.2%)
Mood swings	気分動揺	0	0	0	1 (0.2%)
Nervousness	神経過敏	0	0	0	1 (0.2%)
Nightmare	悪夢	0	0	1 (0.1%)	0
Panic disorder	パニック障害	0	0	1 (0.1%)	0
Restlessness	落ち着きのなさ	0	0	1 (0.1%)	0
Sleep disorder	睡眠障害	0	0	4 (0.4%)	1 (0.2%)
Renal and urinary disorders	腎および尿路障害	9 (14.5%)	4 (12.1%)	189 (21.2%)	136 (26.1%)
Acute kidney injury	急性腎障害	0	0	9 (1.0%)	6 (1.2%)
Anuria	無尿	0	0	1 (0.1%)	0
Azotaemia	高窒素血症	0	0	0	2 (0.4%)
Bladder disorder	膀胱障害	0	0	0	1 (0.2%)
Bladder diverticulum	膀胱憩室	0	0	2 (0.2%)	1 (0.2%)
Bladder hypertrophy	膀胱壁肥厚	0	0	1 (0.1%)	0
Bladder neck obstruction	膀胱頚部閉塞	0	0	2 (0.2%)	0
Bladder obstruction	膀胱閉塞	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Bladder outlet obstruction	膀胱出口部閉塞	0	0	0	4 (0.8%)
Bladder spasm	膀胱痙縮	0	0	0	1 (0.2%)
Calculus bladder	膀胱結石	0	0	5 (0.6%)	2 (0.4%)
Calculus urethral	尿道結石	0	0	1 (0.1%)	0
Calculus urinary	尿路結石	0	0	0	1 (0.2%)
Chronic kidney disease	慢性腎臓病	0	0	9 (1.0%)	5 (1.0%)
Cystitis noninfective	非感染性膀胱炎	0	0	1 (0.1%)	1 (0.2%)
Dysuria	排尿困難	0	0	21 (2.4%)	26 (5.0%)
Glycosuria	糖尿	0	0	4 (0.4%)	2 (0.4%)
Haematuria	血尿	2 (3.2%)	2 (6.1%)	39 (4.4%)	25 (4.8%)
Hydronephrosis	水腎症	2 (3.2%)	0	8 (0.9%)	13 (2.5%)
Hypertonic bladder	緊張性膀胱	0	0	3 (0.3%)	2 (0.4%)
Incontinence	失禁	0	0	3 (0.3%)	1 (0.2%)
Kidney fibrosis	腎線維症	0	0	2 (0.2%)	1 (0.2%)
Leukocyturia	白血球尿	0	0	1 (0.1%)	1 (0.2%)
Lower urinary tract symptoms	下部尿路症状	0	0	6 (0.7%)	5 (1.0%)
Malignant urinary tract obstruction	悪性尿路閉塞	0	0	0	1 (0.2%)
Micturition disorder	排尿異常	0	0	1 (0.1%)	1 (0.2%)
Micturition urgency	尿意切迫	0	0	9 (1.0%)	3 (0.6%)
Nephrocalcinosis	腎石灰沈着症	0	0	0	1 (0.2%)
Nephrolithiasis	腎結石症	0	0	14 (1.6%)	4 (0.8%)
Nocturia	夜間頻尿	0	0	14 (1.6%)	10 (1.9%)
Oliguria	乏尿	0	0	1 (0.1%)	0
Pollakiuria	頻尿	3 (4.8%)	0	35 (3.9%)	16 (3.1%)
Polyuria	多尿	0	0	2 (0.2%)	2 (0.4%)
Proteinuria	蛋白尿	0	1 (3.0%)	9 (1.0%)	5 (1.0%)
Renal aneurysm	腎動脈瘤	0	0	1 (0.1%)	1 (0.2%)
Renal artery occlusion	腎動脈閉塞	0	0	1 (0.1%)	0
Renal artery stenosis	腎動脈狭窄症	0	0	0	1 (0.2%)
Renal colic	腎仙痛	0	0	9 (1.0%)	0
Renal cyst	腎嚢胞	0	0	9 (1.0%)	4 (0.8%)
Renal failure	腎不全	0	1 (3.0%)	7 (0.8%)	4 (0.8%)
Renal impairment	腎機能障害	1 (1.6%)	0	2 (0.2%)	0
Renal pain	腎臓痛	0	0	0	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Strangury	有痛性排尿困難	0	0	1 (0.1%)	0
Ureteral disorder	尿管障害	0	0	1 (0.1%)	0
Ureteric obstruction	尿管閉塞	0	0	0	1 (0.2%)
Ureteric stenosis	尿管狭窄	0	0	2 (0.2%)	0
Ureterolithiasis	尿管結石症	0	0	6 (0.7%)	2 (0.4%)
Urethral discharge	尿道分泌物	0	0	1 (0.1%)	0
Urethral meatus stenosis	外尿道口狭窄	0	0	0	1 (0.2%)
Urethral pain	尿道痛	0	0	0	1 (0.2%)
Urethral stenosis	尿道狭窄	0	0	2 (0.2%)	3 (0.6%)
Urinary hesitation	排尿躊躇	0	0	2 (0.2%)	0
Urinary incontinence	尿失禁	0	0	14 (1.6%)	12 (2.3%)
Urinary retention	尿閉	2 (3.2%)	1 (3.0%)	31 (3.5%)	35 (6.7%)
Urinary tract discomfort	尿路不快感	0	0	0	1 (0.2%)
Urinary tract disorder	尿路障害	0	0	0	1 (0.2%)
Urinary tract obstruction	尿路閉塞	0	0	9 (1.0%)	7 (1.3%)
Urinary tract pain	尿路痛	0	0	0	2 (0.4%)
Urine flow decreased	尿流量減少	0	0	2 (0.2%)	3 (0.6%)
Reproductive system and breast disorders	生殖系および乳房障害	2 (3.2%)	0	44 (4.9%)	35 (6.7%)
Balanoposthitis	亀頭包皮炎	1 (1.6%)	0	1 (0.1%)	0
Benign prostatic hyperplasia	良性前立腺肥大症	0	0	4 (0.4%)	2 (0.4%)
Breast discomfort	乳房不快感	0	0	2 (0.2%)	0
Breast induration	乳房硬結	0	0	1 (0.1%)	0
Breast pain	乳房痛	0	0	0	1 (0.2%)
Breast tenderness	乳房圧痛	0	0	0	1 (0.2%)
Erectile dysfunction	勃起不全	0	0	1 (0.1%)	1 (0.2%)
Gynaecomastia	女性化乳房	0	0	19 (2.1%)	6 (1.2%)
Nipple pain	乳頭痛	0	0	2 (0.2%)	2 (0.4%)
Pelvic pain	骨盤痛	1 (1.6%)	0	11 (1.2%)	12 (2.3%)
Penile pain	陰茎痛	0	0	4 (0.4%)	0
Penis disorder	陰茎障害	0	0	2 (0.2%)	0
Perineal pain	会陰痛	0	0	1 (0.1%)	2 (0.4%)
Prostate induration	前立腺硬結	0	0	1 (0.1%)	0
Prostatic mass	前立腺腫瘤	0	0	0	2 (0.4%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Prostatic obstruction	前立腺閉塞	0	0	1 (0.1%)	2 (0.4%)
Prostatitis	前立腺炎	0	0	0	1 (0.2%)
Prostatomegaly	前立腺腫大	0	0	0	1 (0.2%)
Testicular pain	精巣痛	0	0	0	3 (0.6%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	6 (9.7%)	0	113 (12.7%)	54 (10.4%)
Acute respiratory failure	急性呼吸不全	0	0	2 (0.2%)	2 (0.4%)
Asthma	喘息	1 (1.6%)	0	0	1 (0.2%)
Atelectasis	無気肺	0	0	0	1 (0.2%)
Bronchitis chronic	慢性気管支炎	0	0	1 (0.1%)	0
Bronchospasm	気管支痙攣	0	0	0	1 (0.2%)
Catarrh	カタル	0	0	1 (0.1%)	0
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	1 (1.6%)	0	9 (1.0%)	4 (0.8%)
Cough	咳嗽	3 (4.8%)	0	26 (2.9%)	11 (2.1%)
Cystic lung disease	嚢胞性肺疾患	0	0	4 (0.4%)	0
Dyspnoea	呼吸困難	0	0	24 (2.7%)	15 (2.9%)
Dyspnoea exertional	労作性呼吸困難	0	0	6 (0.7%)	4 (0.8%)
Emphysema	肺気腫	0	0	10 (1.1%)	2 (0.4%)
Epistaxis	鼻出血	0	0	1 (0.1%)	3 (0.6%)
Haemoptysis	喀血	0	0	0	2 (0.4%)
Hypoxia	低酸素症	0	0	1 (0.1%)	0
Lower respiratory tract inflammation	下気道の炎症	0	0	1 (0.1%)	0
Lung disorder	肺障害	0	0	2 (0.2%)	0
Nasal congestion	鼻閉	0	0	2 (0.2%)	1 (0.2%)
Nocturnal dyspnoea	夜間呼吸困難	0	0	0	1 (0.2%)
Oropharyngeal pain	口腔咽頭痛	0	0	3 (0.3%)	1 (0.2%)
Paranasal cyst	副鼻腔嚢胞	0	0	1 (0.1%)	0
Paranasal sinus hypersecretion	副鼻腔分泌過多	0	0	1 (0.1%)	0
Pleural effusion	胸水	0	0	4 (0.4%)	4 (0.8%)
Pneumonia aspiration	誤嚥性肺炎	0	0	1 (0.1%)	0
Pneumonitis	肺臓炎	0	0	3 (0.3%)	0
Pneumothorax	気胸	0	0	0	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

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Productive cough	湿性咳嗽	0	0	1 (0.1%)	4 (0.8%)
Pulmonary calcification	肺石灰化	0	0	6 (0.7%)	1 (0.2%)
Pulmonary congestion	肺うっ血	0	0	0	1 (0.2%)
Pulmonary embolism	肺塞栓症	0	0	5 (0.6%)	4 (0.8%)
Pulmonary fibrosis	肺線維症	0	0	3 (0.3%)	0
Pulmonary mass	肺腫瘤	1 (1.6%)	0	5 (0.6%)	2 (0.4%)
Pulmonary oedema	肺水腫	0	0	1 (0.1%)	1 (0.2%)
Pulmonary thrombosis	肺血栓症	0	0	0	1 (0.2%)
Rales	ラ音	0	0	1 (0.1%)	3 (0.6%)
Reflux laryngitis	逆流性喉頭炎	0	0	2 (0.2%)	0
Respiratory alkalosis	呼吸性アルカローシス	0	0	1 (0.1%)	0
Respiratory disorder	呼吸障害	0	0	0	1 (0.2%)
Respiratory failure	呼吸不全	0	0	3 (0.3%)	1 (0.2%)
Rhinalgia	鼻痛	0	0	1 (0.1%)	0
Rhinorrhoea	鼻漏	0	0	1 (0.1%)	2 (0.4%)
Rhonchi	低音性連続性ラ音	0	0	1 (0.1%)	0
Sinus disorder	副鼻腔障害	0	0	1 (0.1%)	0
Sinus polyp	副鼻腔ポリープ	0	0	1 (0.1%)	0
Sleep apnoea syndrome	睡眠時無呼吸症候群	0	0	3 (0.3%)	1 (0.2%)
Sneezing	くしゃみ	0	0	1 (0.1%)	0
Throat irritation	咽喉刺激感	0	0	1 (0.1%)	1 (0.2%)
Throat tightness	咽喉絞扼感	0	0	1 (0.1%)	0
Upper-airway cough syndrome	上気道咳症候群	0	0	1 (0.1%)	1 (0.2%)
Wheezing	喘鳴	0	0	2 (0.2%)	2 (0.4%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	9 (14.5%)	6 (18.2%)	81 (9.1%)	34 (6.5%)
Acne	ざ瘡	0	0	1 (0.1%)	0
Actinic keratosis	光線角化症	0	0	2 (0.2%)	2 (0.4%)
Alopecia	脱毛症	0	0	1 (0.1%)	2 (0.4%)
Blister	水疱	0	0	1 (0.1%)	0
Decubitus ulcer	褥瘡性潰瘍	0	1 (3.0%)	0	0
Dermal cyst	皮膚嚢腫	1 (1.6%)	0	1 (0.1%)	0
Dermatitis	皮膚炎	0	1 (3.0%)	3 (0.3%)	0
Dermatitis allergic	アレルギー性皮膚炎	0	0	1 (0.1%)	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Dermatitis contact	接触皮膚炎	0	0	1 (0.1%)	0
Diabetic foot	糖尿病性足病変	0	0	2 (0.2%)	0
Dry skin	皮膚乾燥	0	1 (3.0%)	6 (0.7%)	0
Ecchymosis	斑状出血	0	0	0	1 (0.2%)
Eczema	湿疹	0	2 (6.1%)	6 (0.7%)	1 (0.2%)
Eczema nummular	貨幣状湿疹	0	0	1 (0.1%)	0
Erythema	紅斑	0	0	3 (0.3%)	1 (0.2%)
Erythema multiforme	多形紅斑	1 (1.6%)	0	1 (0.1%)	0
Haemorrhage subcutaneous	皮下出血	1 (1.6%)	0	0	1 (0.2%)
Hyperhidrosis	多汗症	0	0	8 (0.9%)	4 (0.8%)
Hyperkeratosis	過角化	0	1 (3.0%)	0	0
Hypertrichosis	多毛症	0	0	0	1 (0.2%)
Hypotrichosis	貧毛症	0	0	1 (0.1%)	1 (0.2%)
Nail discolouration	爪変色	0	0	1 (0.1%)	0
Night sweats	寝汗	0	0	1 (0.1%)	2 (0.4%)
Onychoclasis	爪破損	0	0	1 (0.1%)	0
Pain of skin	皮膚疼痛	0	1 (3.0%)	0	0
Pigmentation disorder	色素沈着障害	0	0	1 (0.1%)	0
Pruritus	そう痒症	0	1 (3.0%)	16 (1.8%)	10 (1.9%)
Pruritus allergic	アレルギー性そう痒症	0	0	2 (0.2%)	0
Pruritus generalised	全身性そう痒症	0	0	1 (0.1%)	0
Psoriasis	乾癬	0	0	1 (0.1%)	1 (0.2%)
Rash	発疹	4 (6.5%)	0	13 (1.5%)	4 (0.8%)
Rash macular	斑状皮疹	0	0	1 (0.1%)	0
Rash maculo-papular	斑状丘疹状皮疹	0	0	4 (0.4%)	0
Rash papular	丘疹性皮疹	0	0	1 (0.1%)	0
Skin disorder	皮膚障害	0	0	1 (0.1%)	0
Skin erosion	皮膚びらん	0	0	0	1 (0.2%)
Skin exfoliation	皮膚剥脱	0	0	1 (0.1%)	0
Skin fragility	皮膚脆弱性	0	0	1 (0.1%)	0
Skin induration	皮膚硬結	0	0	1 (0.1%)	0
Skin irritation	皮膚刺激	0	0	0	1 (0.2%)
Skin lesion	皮膚病変	0	0	3 (0.3%)	1 (0.2%)
Skin mass	皮膚腫瘤	0	0	0	1 (0.2%)
Skin reaction	皮膚反応	0	0	0	1 (0.2%)

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Skin ulcer	皮膚潰瘍	1 (1.6%)	0	2 (0.2%)	0
Stasis dermatitis	うっ滞性皮膚炎	0	0	0	2 (0.4%)
Urticaria	蕁麻疹	1 (1.6%)	1 (3.0%)	8 (0.9%)	1 (0.2%)
Surgical and medical procedures	外科および内科処置	0	0	10 (1.1%)	5 (1.0%)
Bladder catheterisation	膀胱カテーテル留置	0	0	1 (0.1%)	0
Cataract operation	白内障手術	0	0	2 (0.2%)	0
Cyst removal	嚢胞切除	0	0	1 (0.1%)	0
Cystostomy	膀胱瘻造設	0	0	1 (0.1%)	0
Hip arthroplasty	股関節形成	0	0	1 (0.1%)	1 (0.2%)
Inguinal hernia repair	鼠径部ヘルニア修復	0	0	1 (0.1%)	0
Lipoma excision	脂肪腫切除	0	0	0	1 (0.2%)
Lymphadenectomy	リンパ節切除	0	0	0	1 (0.2%)
Orchidectomy	精巣摘除	0	0	0	1 (0.2%)
Prostatectomy	前立腺摘除	0	0	1 (0.1%)	0
Pulmonary resection	肺切除	0	0	0	1 (0.2%)
Radiotherapy to lymph nodes	リンパ節放射線療法	0	0	1 (0.1%)	0
Tooth extraction	抜歯	0	0	0	1 (0.2%)
Transurethral prostatectomy	経尿道的前立腺摘除	0	0	0	1 (0.2%)
Urethrotomy	尿道切開	0	0	1 (0.1%)	0
Vascular disorders	血管障害	6 (9.7%)	1 (3.0%)	146 (16.4%)	67 (12.9%)
Aortic aneurysm	大動脈瘤	0	0	3 (0.3%)	0
Aortic arteriosclerosis	大動脈硬化症	0	0	4 (0.4%)	1 (0.2%)
Aortic dissection	大動脈解離	0	0	1 (0.1%)	0
Aortic stenosis	大動脈狭窄	0	0	1 (0.1%)	0
Aortic thrombosis	大動脈血栓症	0	0	1 (0.1%)	0
Arteriosclerosis	動脈硬化症	0	0	0	2 (0.4%)
Bleeding varicose vein	出血性静脈瘤	0	0	0	1 (0.2%)
Circulatory collapse	循環虚脱	0	0	0	1 (0.2%)
Deep vein thrombosis	深部静脈血栓症	1 (1.6%)	0	1 (0.1%)	0
Embolism	塞栓症	0	0	1 (0.1%)	0
Essential hypertension	本態性高血圧症	0	0	3 (0.3%)	0
Flushing	潮紅	0	0	5 (0.6%)	1 (0.2%)
Haematoma	血腫	1 (1.6%)	0	1 (0.1%)	0

付表 2.7.6.9.a.1-20 TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Hot flush	ほてり	1 (1.6%)	0	49 (5.5%)	23 (4.4%)
Hypertension	高血圧	2 (3.2%)	1 (3.0%)	61 (6.8%)	28 (5.4%)
Hypotension	低血圧	0	0	10 (1.1%)	7 (1.3%)
Iliac artery occlusion	腸骨動脈閉塞	0	0	1 (0.1%)	0
Intermittent claudication	間欠性跛行	0	0	1 (0.1%)	0
Lymphoedema	リンパ浮腫	0	0	1 (0.1%)	1 (0.2%)
Orthostatic hypotension	起立性低血圧	0	0	2 (0.2%)	2 (0.4%)
Pallor	蒼白	0	0	0	1 (0.2%)
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (1.6%)	0	5 (0.6%)	1 (0.2%)
Peripheral artery stenosis	末梢動脈狭窄	0	0	1 (0.1%)	0
Peripheral artery thrombosis	末梢動脈血栓症	0	0	1 (0.1%)	0
Peripheral ischaemia	末梢性虚血	0	0	1 (0.1%)	0
Phlebitis	静脈炎	0	0	1 (0.1%)	0
Subclavian vein thrombosis	鎖骨下静脈血栓症	0	0	0	1 (0.2%)
Thrombophlebitis	血栓性静脈炎	0	0	0	2 (0.4%)
Thrombophlebitis superficial	表在性血栓性静脈炎	0	0	2 (0.2%)	1 (0.2%)
Thrombosis	血栓症	0	0	1 (0.1%)	0
Varicose vein	静脈瘤	0	0	2 (0.2%)	0
Vasculitis	血管炎	0	0	0	1 (0.2%)
Vena cava thrombosis	大静脈血栓症	0	0	0	1 (0.2%)
Venous thrombosis	静脈血栓症	0	0	0	1 (0.2%)
Venous thrombosis limb	四肢静脈血栓症	0	0	1 (0.1%)	0

Source : 5.3.5.1.3 17712_JP/Table 1/2

付表 2.7.6.9.a.1-21 治験薬と関連のある TEAE（日本人集団及び外国人集団、SAF）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Number of subjects (%) with at least one such adverse event	Number of subjects (%) with at least one such adverse event	14 (22.6%)	4 (12.1%)	244 (27.4%)	106 (20.3%)
Blood and lymphatic system disorders	血液およびリンパ系障害	3 (4.8%)	0	14 (1.6%)	4 (0.8%)
Anaemia	貧血	2 (3.2%)	0	7 (0.8%)	2 (0.4%)
Leukopenia	白血球減少症	0	0	2 (0.2%)	0
Lymphopenia	リンパ球減少症	0	0	2 (0.2%)	1 (0.2%)
Neutropenia	好中球減少症	1 (1.6%)	0	5 (0.6%)	1 (0.2%)
Cardiac disorders	心臓障害	0	0	10 (1.1%)	3 (0.6%)
Arrhythmia	不整脈	0	0	3 (0.3%)	0
Arrhythmia supraventricular	上室性不整脈	0	0	1 (0.1%)	0
Atrial fibrillation	心房細動	0	0	0	1 (0.2%)
Atrioventricular block complete	完全房室ブロック	0	0	1 (0.1%)	0
Bradycardia	徐脈	0	0	2 (0.2%)	0
Conduction disorder	伝導障害	0	0	1 (0.1%)	0
Myocardial infarction	心筋梗塞	0	0	0	2 (0.4%)
Palpitations	動悸	0	0	1 (0.1%)	0
Supraventricular extrasystoles	上室性期外収縮	0	0	1 (0.1%)	0
Ear and labyrinth disorders	耳および迷路障害	0	0	1 (0.1%)	2 (0.4%)
Tinnitus	耳鳴	0	0	1 (0.1%)	0
Vertigo	回転性めまい	0	0	0	2 (0.4%)
Eye disorders	眼障害	0	0	1 (0.1%)	1 (0.2%)
Blepharitis	眼瞼炎	0	0	1 (0.1%)	0
Visual acuity reduced	視力低下	0	0	0	1 (0.2%)
Gastrointestinal disorders	胃腸障害	5 (8.1%)	0	56 (6.3%)	37 (7.1%)
Abdominal discomfort	腹部不快感	1 (1.6%)	0	0	1 (0.2%)
Abdominal distension	腹部膨満	0	0	4 (0.4%)	2 (0.4%)
Abdominal pain	腹痛	0	0	4 (0.4%)	1 (0.2%)

付表 2.7.6.9.a.1-21 治験薬と関連のある TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Abdominal pain upper	上腹部痛	0	0	3 (0.3%)	4 (0.8%)
Anal haemorrhage	肛門出血	0	0	1 (0.1%)	0
Constipation	便秘	1 (1.6%)	0	9 (1.0%)	5 (1.0%)
Diarrhoea	下痢	2 (3.2%)	0	13 (1.5%)	9 (1.7%)
Dry mouth	口内乾燥	0	0	9 (1.0%)	5 (1.0%)
Duodenal ulcer	十二指腸潰瘍	0	0	1 (0.1%)	0
Dyspepsia	消化不良	0	0	3 (0.3%)	0
Flatulence	鼓腸	0	0	1 (0.1%)	1 (0.2%)
Frequent bowel movements	排便回数増加	0	0	1 (0.1%)	0
Gastritis	胃炎	0	0	0	1 (0.2%)
Gastritis erosive	びらん性胃炎	0	0	1 (0.1%)	0
Gastrointestinal mucosa hyperaemia	胃腸粘膜充血	0	0	1 (0.1%)	0
Gastrooesophageal reflux disease	胃食道逆流性疾患	0	0	1 (0.1%)	1 (0.2%)
Nausea	悪心	3 (4.8%)	0	21 (2.4%)	17 (3.3%)
Oesophageal pain	食道痛	0	0	0	1 (0.2%)
Plicated tongue	ひだ舌	0	0	1 (0.1%)	0
Rectal haemorrhage	直腸出血	0	0	1 (0.1%)	0
Small intestinal perforation	小腸穿孔	0	0	1 (0.1%)	0
Vomiting	嘔吐	0	0	3 (0.3%)	2 (0.4%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	5 (8.1%)	0	81 (9.1%)	32 (6.1%)
Asthenia	無力症	0	0	9 (1.0%)	7 (1.3%)
Chest pain	胸痛	0	0	1 (0.1%)	0
Chills	悪寒	0	0	2 (0.2%)	2 (0.4%)
Discomfort	不快感	0	0	1 (0.1%)	0
Face oedema	顔面浮腫	1 (1.6%)	0	0	0
Fatigue	疲労	2 (3.2%)	0	66 (7.4%)	24 (4.6%)
Gait disturbance	歩行障害	0	0	2 (0.2%)	0
Malaise	倦怠感	1 (1.6%)	0	0	2 (0.4%)
Oedema peripheral	末梢性浮腫	1 (1.6%)	0	4 (0.4%)	3 (0.6%)
Peripheral swelling	末梢腫脹	0	0	1 (0.1%)	0
Pyrexia	発熱	1 (1.6%)	0	0	0
Thirst	口渇	0	0	1 (0.1%)	1 (0.2%)

付表 2.7.6.9.a.1-21 治験薬と関連のある TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Hepatobiliary disorders	肝胆道系障害	2 (3.2%)	1 (3.0%)	4 (0.4%)	1 (0.2%)
Hepatic function abnormal	肝機能異常	2 (3.2%)	1 (3.0%)	0	0
Hepatobiliary disease	肝胆道系疾患	0	0	0	1 (0.2%)
Hyperbilirubinaemia	高ビリルビン血症	0	0	4 (0.4%)	0
Infections and infestations	感染症および寄生虫症	0	0	2 (0.2%)	1 (0.2%)
Oral candidiasis	口腔カンジダ症	0	0	1 (0.1%)	0
Rash pustular	膿疱性皮疹	0	0	1 (0.1%)	0
Urinary tract infection	尿路感染	0	0	0	1 (0.2%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	0	0	3 (0.3%)	0
Contusion	挫傷	0	0	1 (0.1%)	0
Cystitis radiation	放射線性膀胱炎	0	0	1 (0.1%)	0
Spinal compression fracture	脊椎圧迫骨折	0	0	1 (0.1%)	0
Investigations	臨床検査	2 (3.2%)	0	30 (3.4%)	5 (1.0%)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0	0	4 (0.4%)	0
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (1.6%)	0	9 (1.0%)	0
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0	0	1 (0.1%)	0
Blood bilirubin increased	血中ビリルビン増加	0	0	6 (0.7%)	0
Blood creatinine increased	血中クレアチニン増加	0	0	7 (0.8%)	2 (0.4%)
Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	0	0	2 (0.2%)	0
Blood urea increased	血中尿素増加	0	0	2 (0.2%)	1 (0.2%)
Electrocardiogram QT prolonged	心電図ＱＴ延長	0	0	1 (0.1%)	0
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0	0	1 (0.1%)	0
Haemoglobin decreased	ヘモグロビン減少	0	0	1 (0.1%)	0
International normalised ratio increased	国際標準比増加	0	0	1 (0.1%)	0
Lymphocyte count decreased	リンパ球数減少	0	0	4 (0.4%)	0
Neutrophil count decreased	好中球数減少	1 (1.6%)	0	3 (0.3%)	0
Platelet count decreased	血小板数減少	1 (1.6%)	0	1 (0.1%)	0
Protein total decreased	総蛋白減少	0	0	1 (0.1%)	0
Transaminases increased	トランスアミナーゼ上昇	0	0	1 (0.1%)	0
Weight decreased	体重減少	1 (1.6%)	0	4 (0.4%)	2 (0.4%)
Weight increased	体重増加	0	0	1 (0.1%)	1 (0.2%)

付表 2.7.6.9.a.1-21 治験薬と関連のあるTEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
White blood cell count decreased	白血球数減少	1 (1.6%)	0	2 (0.2%)	0
Metabolism and nutrition disorders	代謝および栄養障害	5 (8.1%)	1 (3.0%)	17 (1.9%)	7 (1.3%)
Decreased appetite	食欲減退	3 (4.8%)	0	11 (1.2%)	6 (1.2%)
Dehydration	脱水	1 (1.6%)	0	0	1 (0.2%)
Dyslipidaemia	脂質異常症	1 (1.6%)	0	0	0
Gout	痛風	0	0	1 (0.1%)	0
Hyperglycaemia	高血糖	0	0	1 (0.1%)	1 (0.2%)
Hyperkalaemia	高カリウム血症	1 (1.6%)	0	3 (0.3%)	0
Hyperlipidaemia	高脂血症	0	1 (3.0%)	0	0
Hyperuricaemia	高尿酸血症	1 (1.6%)	0	0	0
Hypokalaemia	低カリウム血症	0	0	1 (0.1%)	1 (0.2%)
Hyponatraemia	低ナトリウム血症	0	0	2 (0.2%)	0
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	1 (1.6%)	0	26 (2.9%)	10 (1.9%)
Arthralgia	関節痛	1 (1.6%)	0	4 (0.4%)	6 (1.2%)
Back pain	背部痛	0	0	7 (0.8%)	2 (0.4%)
Joint swelling	関節腫脹	0	0	0	1 (0.2%)
Muscle spasms	筋痙縮	0	0	4 (0.4%)	1 (0.2%)
Muscular weakness	筋力低下	0	0	4 (0.4%)	1 (0.2%)
Musculoskeletal pain	筋骨格痛	0	0	2 (0.2%)	1 (0.2%)
Myalgia	筋肉痛	0	0	6 (0.7%)	1 (0.2%)
Osteoarthritis	変形性関節症	0	0	1 (0.1%)	0
Osteoporosis	骨粗鬆症	0	0	1 (0.1%)	0
Pain in extremity	四肢痛	0	0	5 (0.6%)	0
Nervous system disorders	神経系障害	0	0	31 (3.5%)	15 (2.9%)
Amnesia	健忘	0	0	0	1 (0.2%)
Balance disorder	平衡障害	0	0	1 (0.1%)	1 (0.2%)
Cognitive disorder	認知障害	0	0	1 (0.1%)	0
Dizziness	浮動性めまい	0	0	11 (1.2%)	4 (0.8%)
Dysgeusia	味覚異常	0	0	1 (0.1%)	1 (0.2%)
Haemorrhage intracranial	頭蓋内出血	0	0	0	1 (0.2%)
Headache	頭痛	0	0	13 (1.5%)	4 (0.8%)

付表 2.7.6.9.a.1-21 治験薬と関連のある TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Hypoaesthesia	感覚鈍麻	0	0	1 (0.1%)	1 (0.2%)
Hyposmia	嗅覚減退	0	0	1 (0.1%)	0
Ischaemic stroke	虚血性脳卒中	0	0	1 (0.1%)	0
Memory impairment	記憶障害	0	0	1 (0.1%)	2 (0.4%)
Paraesthesia	錯感覚	0	0	1 (0.1%)	0
Psychomotor skills impaired	精神運動機能障害	0	0	0	1 (0.2%)
Somnolence	傾眠	0	0	4 (0.4%)	1 (0.2%)
Transient ischaemic attack	一過性脳虚血発作	0	0	0	1 (0.2%)
Tremor	振戦	0	0	1 (0.1%)	0
Psychiatric disorders	精神障害	0	0	5 (0.6%)	5 (1.0%)
Depression	うつ病	0	0	0	1 (0.2%)
Insomnia	不眠症	0	0	2 (0.2%)	1 (0.2%)
Irritability	易刺激性	0	0	2 (0.2%)	1 (0.2%)
Middle insomnia	中期不眠症	0	0	0	1 (0.2%)
Nightmare	悪夢	0	0	1 (0.1%)	0
Sleep disorder	睡眠障害	0	0	0	1 (0.2%)
Renal and urinary disorders	腎および尿路障害	1 (1.6%)	1 (3.0%)	10 (1.1%)	5 (1.0%)
Bladder hypertrophy	膀胱壁肥厚	0	0	1 (0.1%)	0
Glycosuria	糖尿	0	0	1 (0.1%)	0
Haematuria	血尿	0	0	1 (0.1%)	0
Nocturia	夜間頻尿	0	0	1 (0.1%)	0
Pollakiuria	頻尿	0	0	3 (0.3%)	1 (0.2%)
Polyuria	多尿	0	0	1 (0.1%)	0
Proteinuria	蛋白尿	0	1 (3.0%)	0	0
Renal failure	腎不全	0	0	1 (0.1%)	0
Renal impairment	腎機能障害	1 (1.6%)	0	0	0
Urinary incontinence	尿失禁	0	0	0	1 (0.2%)
Urinary retention	尿閉	0	0	1 (0.1%)	2 (0.4%)
Urinary tract disorder	尿路障害	0	0	0	1 (0.2%)
Reproductive system and breast disorders	生殖系および乳房障害	0	0	16 (1.8%)	6 (1.2%)
Benign prostatic hyperplasia	良性前立腺肥大症	0	0	1 (0.1%)	0
Breast induration	乳房硬結	0	0	1 (0.1%)	0

付表 2.7.6.9.a.1-21 治験薬と関連のあるTEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Breast pain	乳房痛	0	0	0	1 (0.2%)
Breast tenderness	乳房圧痛	0	0	0	1 (0.2%)
Gynaecomastia	女性化乳房	0	0	15 (1.7%)	3 (0.6%)
Nipple pain	乳頭痛	0	0	1 (0.1%)	0
Perineal pain	会陰痛	0	0	0	1 (0.2%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	0	0	10 (1.1%)	2 (0.4%)
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	0	0	1 (0.1%)	0
Cough	咳嗽	0	0	1 (0.1%)	0
Dyspnoea	呼吸困難	0	0	4 (0.4%)	0
Dyspnoea exertional	労作性呼吸困難	0	0	2 (0.2%)	0
Nasal congestion	鼻閉	0	0	1 (0.1%)	0
Pulmonary embolism	肺塞栓症	0	0	2 (0.2%)	2 (0.4%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	2 (3.2%)	1 (3.0%)	32 (3.6%)	9 (1.7%)
Alopecia	脱毛症	0	0	1 (0.1%)	0
Dermatitis allergic	アレルギー性皮膚炎	0	0	1 (0.1%)	0
Dry skin	皮膚乾燥	0	0	3 (0.3%)	0
Eczema	湿疹	0	0	2 (0.2%)	0
Eczema nummular	貨幣状湿疹	0	0	1 (0.1%)	0
Hyperhidrosis	多汗症	0	0	6 (0.7%)	4 (0.8%)
Hypotrichosis	貧毛症	0	0	1 (0.1%)	1 (0.2%)
Night sweats	寝汗	0	0	1 (0.1%)	1 (0.2%)
Pruritus	そう痒症	0	0	7 (0.8%)	2 (0.4%)
Pruritus allergic	アレルギー性そう痒症	0	0	2 (0.2%)	0
Psoriasis	乾癬	0	0	0	1 (0.2%)
Rash	発疹	2 (3.2%)	0	3 (0.3%)	0
Rash macular	斑状皮疹	0	0	1 (0.1%)	0
Rash maculo-papular	斑状丘疹状皮疹	0	0	1 (0.1%)	0
Urticaria	蕁麻疹	0	1 (3.0%)	4 (0.4%)	0
Vascular disorders	血管障害	2 (3.2%)	0	57 (6.4%)	20 (3.8%)
Deep vein thrombosis	深部静脈血栓症	1 (1.6%)	0	1 (0.1%)	0
Flushing	潮紅	0	0	3 (0.3%)	0

付表 2.7.6.9.a.1-21 治験薬と関連のある TEAE（日本人集団及び外国人集団、SAF）（続き）

Primary system organ class Preferred term MedDRA version 21.0	Primary system organ class Preferred term MedDRA version 21.0	Japanese Darolutamide N=62 (100%)	Japanese Placebo N=33 (100%)	Non-Japanese Darolutamide N=892 (100%)	Non-Japanese Placebo N=521 (100%)
Hot flush	ほてり	0	0	36 (4.0%)	15 (2.9%)
Hypertension	高血圧	0	0	11 (1.2%)	4 (0.8%)
Hypotension	低血圧	0	0	3 (0.3%)	1 (0.2%)
Orthostatic hypotension	起立性低血圧	0	0	1 (0.1%)	0
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	1 (1.6%)	0	0	0
Peripheral artery thrombosis	末梢動脈血栓症	0	0	1 (0.1%)	0
Peripheral ischaemia	末梢性虚血	0	0	1 (0.1%)	0
Vasculitis	血管炎	0	0	0	1 (0.2%)

Source：5.3.5.1.3 17712_JP/Table 1/3

2.7.6.9.a.2 試験スケジュール

付表 2.7.6.9.a.2-1 治験薬投与期間中の試験スケジュール

Protocol activities	Screening period	Double-blind study treatment period (darolutamide or placebo)					
		Visit 1	Visit 2	Visit 3	Visit 4 and subsequent visits	Start of open-label treatment visit *	End-of-study treatment visit **
	Within 28 days before randomisation	Day 1[1]	Day 15 (±3 days)	Day 29 (±5 days)	Week 16 (±7 days) and every subsequent 16 weeks	and subsequent visits every 16 weeks (±7 days)	28 days (+7 days) after last dose
IC	x						
Demography	x						
Medical history	x						
Prostate cancer history, incl. treatments and procedures	x						
Eligibility criteria and randomisation		x					
BPI-SF		x			x	x	x
EORTC-QLQ-PR25	x	x			x	x	x
FACT-P or PCS of FACT-P	x (FACT-P)	x (FACT-P)			x[2]	x[2]	x (FACT-P)
EQ-5D-3L	x	x			x[3]	x[3]	x[3]
Physical examination, weight	x[4]	x		x	x	x	x
12-lead ECG and vital signs	x[5]	x[5]	x[5]	x[5]	x[5]	x[17]	x
Laboratory safety assessments	x	x	x	x	x	x	x
Serum PSA[14]	x	x			x	x	x
Testosterone	x	x			x		
PK samples at participating centres[6]			x[5, 6]	x[5, 6]	x[5, 6]		
PK diary dispensing[6]		x	x	x			
PK diary collection			x	x	x		
ECOG performance status	x				x	x	x
Pain diary dispensing	x			x	x	x	x
Pain diary collection[7]		x			x	x	x
Chest, abdomen and pelvic CT/MRI	x[8]				x[8]	x[8]	
Bone scan[9]	x[8]				x[8]	x[8]	
First SSE			x	x	x	x	x
First prostate cancer-related invasive procedure			x	x	x	x	x
Survival status[18]			x	x	x	x	x
Adverse events[10]	x	x	x	x	x	x	x

Concomitant treatments[11]	x	x	x	x	x	x	x
Study drug dispensing and accountability		x		x	x	x	x[15]
PG IC	x[12]						
PG sample		x[16]					
Tumour-related biomarker blood sample[13]		x				x[13]	x

Abbreviations: IC = informed consent; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; OS = overall survival; PG = pharmacogenomics; HR = heart rate; PK = pharmacokinetic; PSA = prostate-specific antigen; SSE = symptomatic skeletal event

* Under the conditions, patients who choose to receive open-label darolutamide will have a start of open-label treatment visit at the time of study treatment code unblinding.
Patients in the darolutamide arm continuing open-label darolutamide treatment will have subsequent visits every 16 weeks until metastasis is seen by local reading.
Patients in the placebo arm crossing over to open-label darolutamide treatment will have subsequent visits every 16 weeks until metastasis is seen by local reading.
Those patients who do not choose to continue with open-label darolutamide treatment, will have an end-of-study treatment visit at the time of unblinding (*added by amendment 3*).

** The end-of-study treatment visit procedures for placebo patients crossing over to open-label darolutamide treatment are described (*added by amendment 3*).

[1] In case the start of study treatment is not logistically feasible on the same day as randomisation, randomisation can be performed 1 day before the initiation of study treatment.

[2] FACT-P will be assessed at the week 16 visit only, and PCS subscale of FACT-P will be assessed at the subsequent 16-week visits thereafter. For placebo patients crossing over to open-label darolutamide, FACT-P will be assessed at the start of open-label treatment visit; whereas for patients in the darolutamide arm continuing open-label treatment, PCS subscale of FACT-P will continue to be assessed at this visit and at subsequent 16-week visits thereafter (*modified by amendment 3*).

[3] EQ-5D-3L will be assessed at the week 16 visit only, and end-of-study treatment visit. For placebo patients crossing over to open-label darolutamide, EQ-5D-3L will be assessed at the start of open-label treatment instead of end-of-study treatment visit. If the end of the double-blind treatment period occurs less than 16 weeks from the start of study treatment, the EQ-5D-3L assessment is required in the first 16 weeks of open-label darolutamide treatment (*modified by amendment 2 and 3*).

[4] Also height will be recorded at the screening visit.

[5] A triplicate 12-lead ECG including HR in a supine position after at least 10 minutes rest will be performed at screening and on day 1 for all patients. For patients participating to PK sampling, a triplicate 12-lead ECG will be also performed before PK samplings. The 3 consecutive recordings will be performed within approximately 5 minutes. BP and HR (unless recorded by ECG) in a supine position after at least 10 minutes rest. The assessments will be done in the following order: ECGs and vital signs before any type of blood draw. For those patients who do not participate to PK sampling, 12-lead ECG will be obtained once on visits after day 1. (*modified by amendment 2 and 3*).

[6] If PK sampling is not feasible during these visits, later visits may be used for PK procedures (*modified by amendment 2*).

[7] Patients will be instructed to complete the diary for 6 days (-6 to -1 day) before day 1 and every 16-week visits until documented pain progression.

[8] CT/MRI and bone scans are acceptable if performed within 42 days prior to start of study treatment. A local qualified site physician (e.g. site radiologist or PI, at the PI's discretion) must first review the screening scans and confirm the patient is non-metastatic before submitting the scans to central review to confirm eligibility. If the local qualified site physician detects metastasis, the scans should not be submitted to central review. For guidance on CT/MRI and bone scans performed at Week 16 and subsequent visits during double-blind treatment. Scans are acceptable if performed within 42 days prior to the start of open-label treatment visit. Imaging will be conducted every 16 weeks (±7 days) during the open-label darolutamide treatment after the start of open-label treatment visit. Patients continuing open-label darolutamide will only have local imaging, central confirmation is not required (*modified by amendment 2 and 3*).

[9] New lesion(s) in bone scan must be confirmed by CT/MRI (whichever imaging was conducted at screening for soft tissue) or x-ray. If confirmatory scan is negative (does not confirm progression), the patient will continue study treatment and visit study centre as specified in the study event table.

[10] All AEs including SAEs will be recorded from the date of signing IC and continuing until the end-of-study treatment visit (including open-label darolutamide treatment phase). Any AEs or SAEs that occur after the end-of-study treatment visit and which are considered to be related to the study treatment or any study procedures have to be reported and entered into the eCRF. When the eCRF is not available anymore, all SAEs considered study treatment related should be reported to Bayer using a paper SAE form. AEs related to study procedures and all SAEs will be recorded for screening failures (*modified by amendment 2 and 3*).

[11] Once the patient has been withdrawn from study treatment, concomitant treatments will be recorded if used to treat new related or unresolved related AEs or if it is an antineoplastic therapy.

[12] An optional PG IC for pharmacogenetic research study will be obtained at screening visit (or later during the study if feasible) unless precluded by local guidelines, e.g. IEC/IRB or regulatory authorities (*modified by amendment 2*).

[13] Blood (plasma) sampling for tumour-related biomarker evaluation will be collected on day 1 visit before study treatment administration, at the start of open-label treatment visit, and at the end-of-study treatment visit unless precluded by local guidelines, e.g. IEC/IRB or regulatory authorities. For placebo patients crossing over to open-label darolutamide treatment, sampling will not be performed at the end-of-study treatment visit (*modified by amendment 3*).

[14] The local PSA result taken at screening should be used to confirm the patient has CRPC (inclusion criterion 4) and meets inclusion criterion 6 (*added by amendment 2*).

[15] Only study drug accountability performed at the end-of-study treatment visit (*added by amendment 2*).

[16] A blood sample for DNA extraction will be taken at day 1 visit (or later during the study if feasible) only from patients who have signed the PG IC unless precluded by local guidelines, e.g. IEC/IRB or regulatory authorities (*added by amendment 2*).

[17] 12-lead ECG will be performed only at the start of open-label visit. ECG is not required on subsequent visits during the open-label darolutamide treatment (*added by amendment 3*).

[18] Survival data will also be collected through an additional survival sweep. All patients considered alive shortly after the database cut-off date for the MFS analysis and prior to any subsequent analysis of OS will be contacted for survival status (*added by amendment 3*).

Source: 5.3.5.1.1 PH-39723/Section 16.1.1

付表 2.7.6.9.a.2-2 盲検下の治験薬投与中止後又は追跡調査期間中の試験スケジュール

Protocol activities	For patients discontinuing study drug during double-blind period before confirmed metastasis and not initiating any prohibited treatment	For patients after confirmed metastasis, or receiving subsequent treatment after unblinding	For placebo patients crossing over to open-label darolutamide	
	Visits Every 16 weeks (±7 days) from end-of-study treatment visit[1]	Visits or phone contacts Every 16 weeks (±7 days) from end-of-study treatment visit[2]	Visits Every 16 weeks (±7 days) from start of open-label treatment visit[1]	End-of-study treatment visit 28 days (+7 days) after last dose
BPI-SF	X	X	X	X
Dispensing of pain diary	X	X	X	X
Collection of pain diary and pain medications	X[3]	X[3]	X[3]	X
PCS subscale of FACT-P	X	X	X	X
ECOG performance status	X	X	X	X
Use of subsequent antineoplastic therapies	X	X	X	X
Laboratory safety assessments			X	X
Collection of AEs and SAEs considered to be related to study treatment or procedures	X	X	X[5]	X[5]
Collection of concomitant treatments used to treat new related or unresolved related AEs	X	X	X	X
Darolutamide dispensing and accountability			X	X[7]
First SSE	X	X	X	X
First prostate cancer-related invasive procedure for prostate cancer	X	X	X	X
Survival status[8]	X	X	X	X
Serum PSA	X		X[6]	
Chest, abdomen, and pelvic CT/MRI	X		X[6]	
Bone scan[4]	X		X[6]	

[1] Until confirmed metastasis, death or the end of the study (*modified by amendment 2*)

[2] Until death or the end of the study

[3] Patients will be instructed to complete the diary for 6 days before each 16-week visit until documented pain progression. Pain medications will be recorded on CRFs at each 16-week visit until documented pain progression.

[4] New lesion(s) in bone scan must be confirmed by CT/MRI (whichever imaging was conducted at screening for soft tissue) or x-ray. If confirmatory scan is negative (does not confirm progression), the patient will continue to visit study centre as specified in the study event table.

[5] For placebo patients crossing over to open-label darolutamide, all AEs and SAEs irrespective of relatedness will be captured (*added by amendment 3*).

[6] Placebo patients crossing over to open-label darolutamide will only have local PSA testing and imaging, central confirmation is not required (*added by amendment 3*).

[7] Only drug accountability performed at the end-of-study treatment visit (*added by amendment 3*).

[8] Survival data will also be collected through an additional survival sweep. All patients considered alive shortly after the database cut-off date for the MFS analysis and prior to any subsequent analysis of OS will be contacted for survival status (*added by amendment 3*).

Source: 5.3.5.1.1 PH-39723/Section 16.1.1

2.7.6.10 【国外試験】去勢抵抗性前立腺癌患者を対象とした第Ⅱ相試験：試験 18035（報告書番号 R-11102）

参照項目：5.3.5.2.1 R-11102

2.7.6.10.1 試験計画の概要

試験の標題：

去勢抵抗性前立腺癌（CRPC）患者を対象としたダロルタミドの安全性及び忍容性を検討する非盲検、非無作為化、非対照、多施設共同試験（試験 17829 の長期継続試験）

実施医療機関：17 施設（チェコ、エストニア、フィンランド、フランス、英国、米国）

試験期間：

最初の被験者の組入れ日：2011 年 6 月 30 日

最後の被験者の完了日：2015 年 10 月 21 日

開発のフェーズ：第Ⅱ相

目的：

主要目的

ダロルタミドの長期的な安全性及び忍容性を検討する。

副次目的

ダロルタミドの抗腫瘍効果を、前立腺特異抗原（PSA）の奏効、軟組織及び骨病変の変化、米国東海岸がん臨床試験グループの全身状態（ECOG-PS）及び投与期間により評価する。

試験方法：

本試験は、非盲検、非無作為化、非対照、多施設共同試験であり、試験 17829 の長期継続試験である。試験 17829 の第 12 週来院時に被験者から本試験への参加について文書による同意を得た。被験者は試験開始から 6 ヵ月までは月に 1 回来院し、以降は 3 ヵ月おき（フランスのみ第 19 回の来院以後は 4 ヵ月おき）に来院することとした。完全奏効（CR）、部分奏効（PR）又は安定（SD）が認められた被験者では、治験責任（分担）医師により病勢進行と評価されるまで、又は忍容できない有害事象が認められるまで、治験責任（分担）医師の判断で投与を継続できることとした。治験薬投与終了後の 4 週間を追跡観察期間とした。

被験薬：

ダロルタミドカプセル 100mg（[redacted]年[redacted]月[redacted]日よりダロルタミドフィルムコーティング錠 300mg に変更）

用法・用量

ダロルタミドを 1 日 2 回食後に経口投与した。各被験者の開始用量は、試験 17829 の第 12 週と同じ用量とした。1 回あたりの最高用量は 700mg（試験 17829 の第Ⅱ相パートでの最高用量）とし、増量を 1 回のみ認めた。

投与期間

試験 17829 の治験薬初回投与日から、治験責任（分担）医師により病勢進行と評価されるまで、又は忍容できない有害事象が認められるまで。

対照薬：なし

選択基準：

(1) 試験 17829 で、治験薬と関連のある重篤な有害事象や用量制限毒性（DLT）を認めず、治験実施計画書に従って 12 週間の投与を完了した被験者

(2) 試験 17829 の第 12 週において、奏効又は SD が認められた被験者

有効性の評価項目：

- 血清 PSA 値：採血し、血清中 PSA 濃度を測定した。
- PSA 増悪までの期間（TTPP）：試験 17829 の治験薬投与開始から PSA 増悪までの期間と定義した。
- 軟部組織及び骨病変の評価：

  - 軟部組織：胸部、腹部及び骨盤のコンピュータ断層撮影（CT）又は磁気共鳴画像（MRI）を実施し、標的病変及び非標的病変の変化を固形がんの治療効果判定のための新ガイドライン（RECIST）Ver. 1.1[1]に従い評価した。

  - 骨：骨シンチグラフィを実施し、治験責任（分担）医師が前立腺がんワーキンググループ 2（PCWG2）の基準[2]に従い、骨病変の変化を評価した。
- ECOG-PS：試験 17829 のベースラインからの変化を評価した。
- 画像診断に基づく無増悪期間（TTP）：試験 17829 の治験薬投与開始から、画像診断（CT/MRI 又は骨シンチグラフィ）に基づく軟部組織又は骨における初回増悪までの期間と定義した。
- 画像診断に基づく無増悪生存期間（rPFS）：試験 17829 の治験薬投与開始から、画像診断に基づく軟部組織又は骨における初回増悪、又は死亡までの期間と定義した。
- 臨床的病勢進行：臨床的病勢進行は、食欲減退、体重減少、骨痛の変化又は骨痛の悪化、鎮痛薬使用の増加、悪液質又は ECOG-PS の低下（ECOG スコアの増加）及び進行性 CRPC の他の症状に基づいて判断した。
- 投与期間：試験 17829 の治験薬投与開始から本試験の投与中止までの期間を算出した。

安全性の評価項目：

有害事象、バイタルサイン（心拍数、血圧）、12 誘導心電図（ECG）、理学的検査及び臨床検査

被験者数：

目標被験者数

最大で約 130 例

設定根拠

本試験は試験 17829 に参加した被験者を対象に、ダロルタミドの長期的な安全性及び忍容性を検討するために実施した。したがって、必要被験者数の検討は行っていない。

解析方法：

解析対象集団

安全性解析対象集団（SAF）：本試験で少なくとも 1 回の治験薬投与を受けた被験者。

TTPP、TTP、rPFS、臨床的病勢進行及び投与期間の解析は、本試験への参加の有無を問わず、試験 17829 で少なくとも 1 回の治験薬投与を受け、それぞれの評価項目について評価可能な被験者を対象とした。その他の有効性及び安全性の解析には SAF を用いた。

有効性の解析

- PSA 値の評価：試験 17829 のベースライン（治験薬初回投与前 14 日以内）からの PSA 値の変化率及び投与後のいずれかの評価時点におけるベースラインからの最大変化率を、記述統計量を用いて要約した。
- TTPP の評価：PCWG2 の基準に基づいた TTPP の中央値及びその両側 95%信頼区間（CI）を

Kaplan-Meier 法により推定した。用量群別及び化学療法又は CYP17 阻害剤（CYP17i）による前治療歴の有無別（以下、部分集団別）に解析を行った。

- 軟部組織における効果の評価：RECIST Ver.1.1 に基づき、奏効例の割合を用量群別及び部分集団別に評価した。
- 骨における効果の評価：骨病変数のベースラインからの変化を用量群別及び部分集団別に「新病変なし」又は「新病変あり」として集計した。
- ECOG-PS の評価：ECOG-PS 及びベースラインからの変化を、用量群別及び部分集団別に集計した。
- TTP の評価：TTP の中央値を Kaplan-Meier 法より推定した。用量群別及び部分集団別に解析を行った。
- rPFS：rPFS の中央値を Kaplan-Meier 法より推定した。用量群別及び部分集団別に解析を行った。
- 臨床的病勢進行の評価：臨床的病勢進行を用量群別及び部分集団別に記述統計量を用いて要約した。
- 投与期間の評価：投与期間の中央値を用量群別及び部分集団別に算出した。

安全性の解析

本試験期間中に報告された有害事象は、ICH 国際医薬用語集（MedDRA）Ver.18.0 を用いてコーディングし、各有害事象の発現例数及び発現割合を集計した。有害事象のグレードは、NCI-CTCAE Ver.4.03 を用いて評価した。CTCAE に示されていない有害事象は、重症度を軽度、中等度及び高度で評価した。治験薬との関連性は、治験責任（分担）医師の判断により、「関連あり」又は「関連なし」とした。試験 17829 での治験薬投与開始後から本試験終了来院時までに発現した有害事象の発現例数及び発現割合を用量群別に集計した。

心拍数、血圧及び 12 誘導 ECG パラメータの絶対値並びにベースラインからの変化量を記述統計量で要約した。補正 QT（QTc）間隔延長が認められた被験者数を集計した。臨床検査値の絶対値及びベースラインからの変化量を記述統計量で要約した。

2.7.6.10.1.1 試験スケジュール

試験スケジュールを表 2.7.6.10-1 に示す。

表 2.7.6.10-1 試験スケジュール

Protocol activities	Visit 7[a]	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	Visit 13	Visit 14	Visits 15, 16, 17 etc.	End-of-study/ discontinued visit
	Month 3 (week 12)	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 12	Month 15, 18, 21, etc[g]	
Informed Consent	x									
Eligibility criteria and decision of entry	x									
Study treatment	x									
Weight	x[b]									x
Heart Rate and Blood Pressure[f]	x[b]	x	x	x	x	x	x	x	x	x
Centrally read 12-lead ECG[f]	x[b]	x	x	x	x	x	x	x	x	x
Physical examination	x[b]	x	x	x	x	x	x	x	x	x
Blood sample for haematology and clinical chemistry	x[b]	x	x	x	x	x	x	x	x	x
Urine sample for urinalysis	x[b]	x	x	x	x	x	x	x	x	x
Blood sample for PSA	x[b, e]	x	x	x	x	x	x	x	x	x
Chest, abdomen and pelvic CT (or magnetic resonance imaging)	x[b, e]			x[c, e]			x[c, e]	x[c, e]	x[c, e]	
Radionuclide bone scan	x[b, e]			x[d, e]			x[d, e]	x[d, e]	x[d, e]	
ECOG performance status	x[b]			x			x	x	x	
Dispense study treatment	x	x	x	x	x	x	x	x	x	
Return study treatment	x[b]	x	x	x	x	x	x	x	x	
AEs and serious AEs	x									
Medical history and current medical conditions	x									
Concomitant treatments	x									

a: Visit numbering was continued from study 17829
b: As a part of study 17829 week 12 procedures
c: Every 3 months and every 4 months after Visit 19 in France
d: Every 3 months, and every 4 months after Visit 19 in France, except every 6 months for patients with no bone metastasis or bone pain at week 12
e: To be performed within 1 week prior to the visit date
f: Measured after 10 minutes resting in the supine position
g: Every 3 months and every 4 months after Visit 19 in France

2.7.6.10.2 成績

特に断らない限り、試験 17829 及び本試験（試験 18035）を通しての結果を以下に示す。また、ベースラインとして試験 17829 のベースラインのデータを用いた。

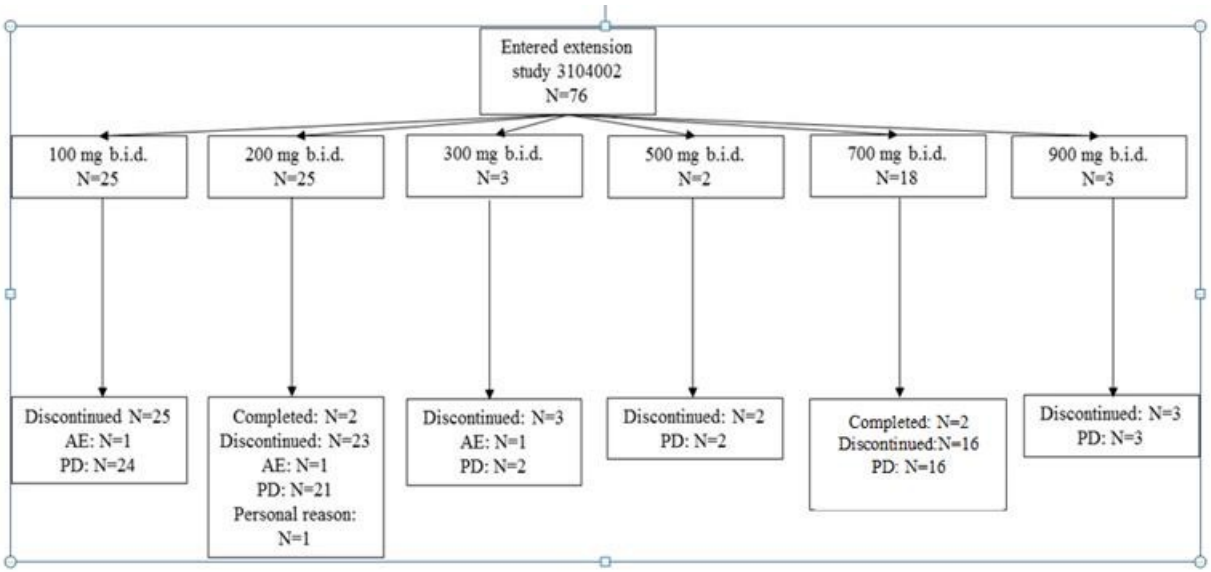
2.7.6.10.2.1 試験対象集団

2.7.6.10.2.1.1 被験者の内訳

被験者の内訳を図 2.7.6.10-1 及び表 2.7.6.10-2 に示す。

計 76 例の被験者が試験 17829 の第 I 相パート又は第Ⅱ相パートから本試験に移行し、少なくとも 1 回の治験薬投与を受けた。そのうち、化学療法歴なし／CYP17i 投与歴なしの被験者は 32 例（42.1%）、化学療法歴あり／CYP17i 投与歴なしの被験者は 21 例（27.6%）、CYP17i 投与歴ありの被験者は 23 例（30.3%）であった。

本試験の主な中止理由は病勢進行（89.5%）であり、その他は有害事象（3.9%）及び同意撤回（1.3%）であった。



AE = adverse event, PD = progressive disease, Study 3104002 = Study 18035
Completed patients started compassionate use of darolutamide after the study
Source：5.3.5.2.1 R-11102/Table 14.1.1.3, Listing 16.2.1.1

図 2.7.6.10-1 被験者の内訳

表 2.7.6.10-2 被験者の内訳

	100mg b.i.d.	200mg b.i.d.	300mg b.i.d.	500mg b.i.d.	700mg b.i.d.[b]	900mg b.i.d.	Total
Safety population	25 (100.0)	25 (100.0)	3 (100.0)	2 (100.0)	18 (100.0)	3 (100.0)	76 (100.0)
Chemo-/CYP17i-naïve patients	10 (40.0)	11 (44.0)	2 (66.7)	1 (50.0)	6 (33.3)	2 (66.7)	32 (42.1)
Post-chemo/CYP17i-naïve patients	8 (32.0)	4 (16.0)	1 (33.3)	0	7 (38.9)	1 (33.3)	21 (27.6)
Post-CYP17i patients	7 (28.0)	10 (40.0)	0	1 (50.0)	5 (27.8)	0	23 (30.3)
Discontinued study	25 (100.0)	23 (92.0)	3 (100.0)	2 (100.0)	16 (88.9)	3 (100.0)	72 (94.7)
due to disease progression	24 (96.0)	21 (84.0)	2 (66.7)	2 (100.0)	16 (88.9)	3 (100.0)	68 (89.5)
due to personal reasons	0	1 (4.0)	0	0	0	0	1 (1.3)
due to AE	1 (4.0)	1 (4.0)	1 (33.3)	0	0	0	3 (3.9)
Completed study[a]	0	2 (8.0)	0	0	2 (11.1)	0	4 (5.3)

a: Started compassionate use of darolutamide after the study
b: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation
Source : 5.3.5.2.1 R-11102/Table 14.1.1.3

2.7.6.10.2.1.2 解析対象集団

76 例全例が SAF に採用された（表 2.7.6.10-2）。なお、治験実施計画書からの重大な逸脱を認めた 2 例（被験者番号：[redacted]、[redacted] いずれも禁止された放射線療法の実施）も SAF に含めた。

2.7.6.10.2.1.3 人口統計学的及びベースラインの特性

2.7.6.10.2.1.3.1 人口統計学的及びベースラインの特性

SAF での人口統計学的特性及びその他の特性を表 2.7.6.10-3 に示す。

被験者の年齢の中央値は 68.0 歳（範囲：55～83 歳）であった。黒人及びアジア人の各 1 例以外はすべて白人であった。ベースラインの ECOG-PS が 0 であった被験者は 67.1%であり、1 であった被験者は 32.9%であった。血液 7.5mL あたりの循環腫瘍細胞（CTC）数が 5 個未満の被験者の割合（47 例、61.8%）は、5 個以上の被験者の割合（23 例、30.3%）より高かった。ベースラインの PSA 値の中央値は 69.1ng/mL（3～1294ng/mL）であった。

表 2.7.6.10-3 人口統計学的特性及びその他の特性（SAF）

	100 mg b.i.d. (N=25)	200 mg b.i.d. (N=25)	300 mg b.i.d. (N=3)	500 mg b.i.d. (N=2)	700 mg b.i.d.[a] (N=18)	900 mg b.i.d. (N=3)	Total (N=76)
Age (years), n	25	25	3	2	18	3	76
Mean±SD	67.2±6.5	69.4±8.3	65.3±3.5	62.0±2.8	74.1±6.1	67.7±3.2	69.4±7.3
Median	67.0	67.0	65.0	62.0	76.0	69.0	68.0
(range)	(55-82)	(55-83)	(62-69)	(60-64)	(63-82)	(64-70)	(55-83)
<65 years, n (%)	8 (32.0)	8 (32.0)	1 (33.3)	2 (100.0)	3 (16.7)	1 (33.3)	23 (30.3)
65-74 years, n (%)	13 (52.0)	8 (32.0)	2 (66.7)	0	5 (27.8)	2 (66.7)	30 (39.5)
≥75 years, n (%)	4 (16.0)	9 (36.0)	0	0	10 (55.6)	0	23 (30.3)
Race, n	25	25	3	2	18	3	76
Caucasian, n (%)	24 (96.0)	24 (96.0)	3 (100.0)	2 (100.0)	18 (100.0)	3 (100.0)	74 (97.4)
Black, n (%)	0	1 (4.0)	0	0	0	0	1 (1.3)
Asian, n (%)	1 (4.0)	0	0	0	0	0	1 (1.3)
BMI (kg/m^2), n	25	25	3	2	18	3	76
Mean±SD	27.5±4.4	28.5±5.6	27.2±2.1	29.2±4.7	28.7±5.4	28.6±1.5	28.2±4.9
ECOG, n	25	25	3	2	18	3	76
0, n (%)	17 (68.0)	15 (60.0)	3 (100.0)	2 (100.0)	11 (61.1)	3 (100.0)	51 (67.1)
1, n (%)	8 (32.0)	10 (40.0)	0	0	7 (38.9)	0	25 (32.9)
PSA (ng/mL), n	25	25	3	2	18	3	76
Mean±SD	207.3±267.4	201.8±315.6	82.3±119.1	21.0±16.8	274.8±327.1	20.8±8.1	204.3±288.8
Median	96.0	59.1	22.0	21.0	150.9	16.2	69.1
(range)	(4-899)	(3-1207)	(5-219)	(9-33)	(9-1294)	(16-30)	(3-1294)
CTC count per 7.5mL blood, n	24	23	3	2	15	3	70
<5 cells, n (%)	18 (72.0)	14 (56.0)	2 (66.7)	2 (100.0)	9 (50.0)	2 (66.7)	47 (61.8)
≥5 cells, n (%)	6 (24.0)	9 (36.0)	1 (33.3)	0	6 (33.3)	1 (33.3)	23 (30.3)
Haemoglobin (g/L), n	25	25	3	2	18	3	76
Mean±SD	132.6±11.1	128.2±10.9	138.0±10.6	135.5±9.2	124.0±11.6	130.7±4.9	129.3±11.3
Median	134.0	129.0	142.0	135.5	126.0	133.0	128.0
(range)	(109-151)	(108-152)	(126-146)	(129-142)	(100-145)	(125-134)	(100-152)
Serum ALP (U/L), n	25	25	3	2	18	3	76
Mean±SD	93.1±46.2	98.3±47.7	134.7±91.2	60.0±29.7	157.9±144.3	279.0±310.6	118.3±103.9
Median	73.0	71.0	105.0	60.0	107.0	139.0	83.0
(range)	(46-269)	(46-198)	(62-237)	(39-81)	(40-559)	(63-635)	(39-635)
LDH (U/L), n	25	25	3	2	16	1	72
Mean±SD	239.0±74.1	267.0±107.9	271.0±124.2	196.0±24.0	244.0±75.3	326.0	251.2±88.1
Median	218.0	225.0	209.0	196.0	216.0	326.0	217.0
(range)	(148-472)	(147-491)	(190-414)	(179-213)	(161-428)	(326-326)	(147-491)
Albumin (g/L), n	25	25	3	2	18	3	76
Mean±SD	38.5±4.6	39.4±4.1	42.7±5.1	39.5±0.7	39.3±4.8	41.7±10.1	39.3±4.7
Median	37.5	39.0	44.0	39.5	40.9	47.0	39.0
(range)	(31-51)	(33-46)	(37-47)	(39-40)	(28-45)	(30-48)	(28-51)

a: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Source：5.3.5.2.1 R-11102/Table 14.1.3.1.3

2.7.6.10.2.1.3.2 ベースラインの疾患特性

SAF における試験 17829 のベースラインの疾患特性を表 2.7.6.10-4 に示す。

前立腺癌と診断されてから試験 17829 における治験薬投与開始までの期間の平均値は 78.9 ヵ月（範囲：10～228 ヵ月）であった。初回治療として、被験者の多くは薬物による去勢（39 例、51.3%）、放射線治療（15 例、19.7%）又は前立腺切除術（11 例、14.5%）を受けていた（5.3.5.2.1 R-11102/Table 14.1.3.2.3）。

表 2.7.6.10-4 試験 17829 のベースラインの疾患特性（SAF）

	100mg b.i.d. (N=25)	200mg b.i.d. (N=25)	300mg b.i.d. (N=3)	500mg b.i.d. (N=2)	700mg b.i.d.[e] (N=18)	900mg b.i.d. (N=3)	Total (N=76)
Time from initial diagnosis (months)[a]							
Mean±SD	72.5±52.0	88.1±54.2	41.7±47.4	127.7±50.2	75.5±54.1	80.7±12.4	78.9±52.3
Initial treatment of primary tumour							
Prostatectomy, n (%)	4 (16.0)	5 (20.0)	0	1 (50.0)	0	1 (33.3)	11 (14.5)
Orchiectomy, n (%)	3 (12.0)	1 (4.0)	0	0	1 (5.6)	0	5 (6.6)
Chemical castration, n (%)	16 (64.0)	8 (32.0)	2 (66.7)	1 (50.0)	12 (66.7)	0	39 (51.3)
Radiotherapy, n (%)	1 (4.0)	8 (32.0)	0	0	4 (22.2)	2 (66.7)	15 (19.7)
Ablathermia, n (%)	0	1 (4.0)	0	0	0	0	1 (1.3)
Brachytherapy, n (%)	0	0	1 (33.3)	0	0	0	1 (1.3)
Hormonal therapy, n (%)	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Gleason score at diagnosis							
2-6, n (%)	1 (4.0)	6 (26.1)	0	1 (50.0)	2 (11.8)	0	10 (13.9)
7, n (%)	9 (36.0)	9 (39.1)	1 (50.0)	1 (50.0)	8 (47.1)	1 (33.3)	29 (40.3)
8-10, n (%)	15 (60.0)	8 (34.8)	1 (50.0)	0	7 (41.2)	2 (66.7)	33 (45.8)
Type of progression at study entry							
PSA only	4 (16.0)	5 (20.0)	0	2 (100.0)	6 (33.3)	1 (33.3)	18 (23.7)
Radiographic with PSA	19 (76.0)	16 (64.0)	3 (100.0)	0	11 (61.1)	2 (66.7)	51 (67.1)
Radiographic without PSA	2 (8.0)	4 (16.0)	0	0	1 (5.6)	0	7 (9.2)
Disease localisation at screening							
Bone only, n (%)	7 (28.0)	8 (32.0)	1 (33.3)	2 (100.0)	8 (44.4)	0	26 (34.2)
Soft tissue only, n (%)	4 (16.0)	5 (20.0)	2 (66.7)	0	3 (16.7)	2 (66.7)	16 (21.1)
Both bone and soft tissue, n (%)	14 (56.0)	11 (44.0)	0	0	7 (38.9)	1 (33.3)	33 (43.4)
None	0	1 (4.0)[b]	0	0	0	0	1 (1.3)

表 2.7.6.10-4 試験 17829 のベースラインの疾患特性（SAF）（続き）

	100mg b.i.d. (N=25)	200mg b.i.d. (N=25)	300mg b.i.d. (N=3)	500mg b.i.d. (N=2)	700mg b.i.d.[e] (N=18)	900mg b.i.d. (N=3)	Total (N=76)
Soft tissue disease metastasis site at screening							
No metastases	7 (28.0)	9 (36.0)	1 (33.3)	2 (100.0)	8 (44.4)	0	27 (35.5)
Other	14 (56.0)	13 (52.0)	2 (66.7)	0	3 (16.7)	3 (100.0)	35 (46.1)
Visceral[c]	3 (12.0)	0	0	0	5 (27.8)	0	8 (10.5)
Visceral[c] and Other	1 (4.0)	3 (12.0)	0	0	2 (11.1)	0	6 (7.9)
Previous chemotherapy							
Yes, n (%)	14 (56.0)	13 (52.0)	1 (33.3)	1 (50.0)	9 (50.0)	1 (33.3)	39 (51.3)
1 line	12 (48.0)	13 (52.0)	1 (33.3)	1 (50.0)	9 (50.0)	1 (33.3)	37 (48.7)
2 lines	2 (8.0)	0	0	0	0	0	2 (2.6)
LHRH therapy							
Yes, n (%)[d]	22 (88.0)	22 (88.0)	3 (100.0)	2 (100.0)	15 (83.3)	3 (100.0)	67 (88.2)
Previous first generation antiandrogen therapy							
Yes, n (%)	25 (100.0)	25 (100.0)	3 (100.0)	2 (100.0)	18 (100.0)	3 (100.0)	76 (100.0)
Previous ketoconazole therapy							
Yes, n (%)	2 (8.0)	0	0	1 (50.0)	0	0	3 (3.9)

a: Time from initial diagnosis is the time from the initial diagnosis of prostate cancer to the first dose of study medication in study 17829

b: Metastatic disease was recorded in this patient's medical history

c: Visceral included metastases in one or more of the following organs: liver, lung, kidney

d: The patients who did not receive LHRH therapy had prior bilateral orchiectomy

e: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Source : 5.3.5.2.1 R-11102/Table 14.1.3.2.3

2.7.6.10.2.1.3.3 病歴及び合併症

76 例中最もよくみられた病歴又は合併症は高血圧（45 例、59.2%）であり、次いで高コレステロール血症（17 例、22.4%）及び背部痛（11 例、14.5%）であった（5.3.5.2.1 R-11102/Table 14.1.4.3）。

2.7.6.10.2.1.3.4 前治療及び併用療法

76 例全例が前治療歴として少なくとも 1 つの第 1 世代抗アンドロゲン療法を受けており、そのうち 74 例（97.4%）がビカルタミド、10 例（13.2%）が Cyproterone、5 例（6.6%）がフルタミドの投与を受けていた。また、19 例（25.0%）がアビラテロン、6 例（7.9%）がエストラムスチンの投与を、7 例（9.2%）がグルココルチコイドの全身投与を受けていた（5.3.5.2.1 R-11102/Table 14.1.5.1.3）。

本試験では、被験者が外科的に去勢されていない場合、黄体形成ホルモン放出ホルモン（LHRH）による治療の継続を必須とした。よく用いられた LHRH 薬は、ゴセレリン（35 例、46.1%）及びリュープロレリン（28 例、36.8%）であった。その他のよく用いられた併用薬は、パラセタモール（27 例、35.5%）、アセチルサリチル酸（21 例、27.6%）、オメプラゾール及びシンバスタチン（各 16 例、21.1%）であった（5.3.5.2.1 R-11102/Table 14.1.5.2.3）。

2.7.6.10.2.2 有効性の結果

2.7.6.10.2.2.1 血清 PSA 値

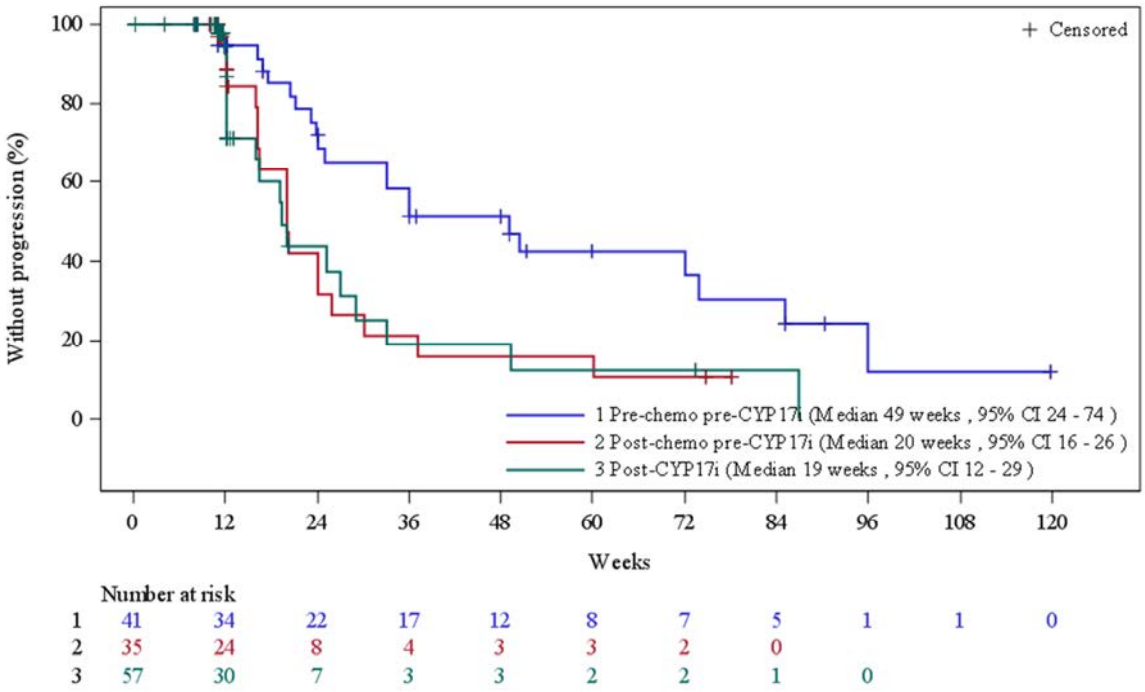
SAF の 76 例全例において、試験期間中に臨床的に意味のある血清 PSA 値の減少が認められた。血清 PSA 値は、化学療法歴なし／CYP17i 投与歴なしの被験者で最も減少した。また、この部分集団では最高用量である 700mg 群で血清 PSA 値が最も減少した（5.3.5.2.1 R-11102/Table 14.2.1.1.3、14.2.1.1.3.1-3）。

2.7.6.10.2.2.2 TTPP

TTPP の解析は評価可能な 133 例を対象とした。TTPP の Kaplan-Meier 曲線を前治療別に図 2.7.6.10-2 に、用量群別に図 2.7.6.10-3 に示す。

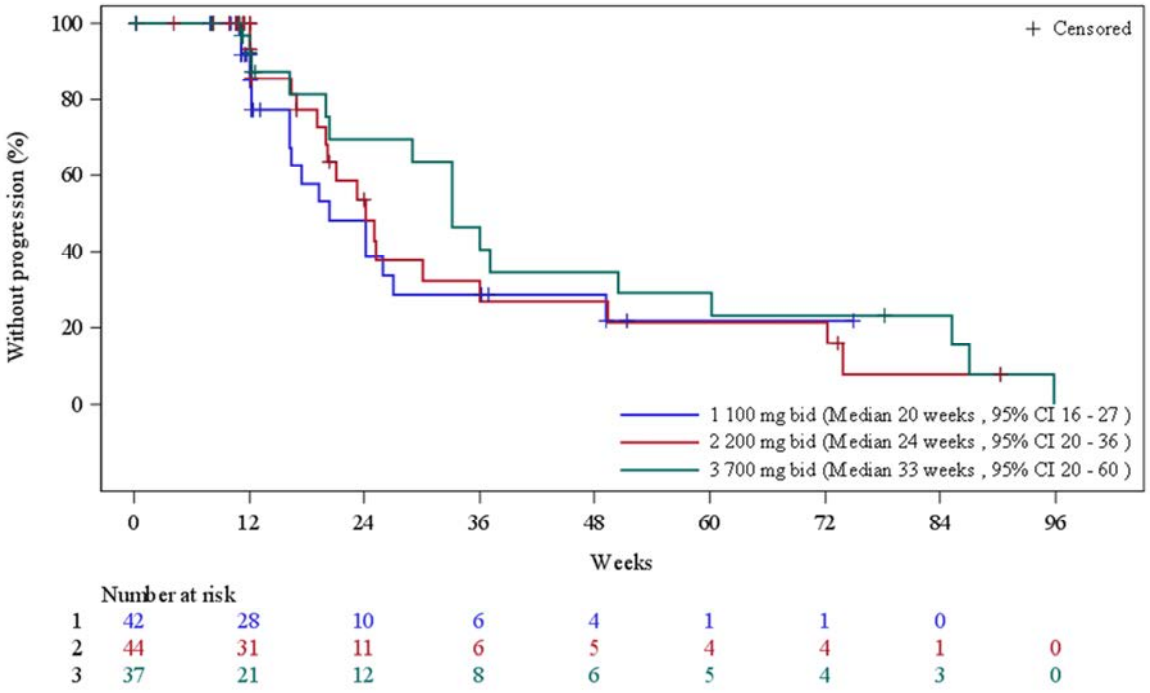
TTPP の中央値は、化学療法歴なし／CYP17i 投与歴なしの被験者（41 例）で治験薬初回投与開始から 49.1 週間（95%CI：24.1～73.9 週間）、化学療法歴あり／CYP17i 投与歴なしの被験者（35 例）で 20.1 週間（16.1～26.0 週間）、CYP17i 投与歴ありの被験者（57 例）で 19.3 週間（12.3～29.0 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.2）。

TTPP の中央値は 100mg と 200mg 群が同程度〔100mg 群で 20.4 週間（95%CI：16.1～27.0 週間）、200mg 群で 24.1 週間（20.0～36.0 週間）〕であり、700mg 群が顕著に長かった〔33.1 週間（20.0～60.1 週間）〕（5.3.5.2.1 R-11102/Table 14.2.1.2.1）。



Source：5.3.5.2.1 R-11102/Figure 14.4.4.1.1

図 2.7.6.10-2 前治療別 TTPP の Kaplan-Meier 曲線（評価可能例、N＝133）



Source：5.3.5.2.1 R-11102/Figure 14.4.4.1.2

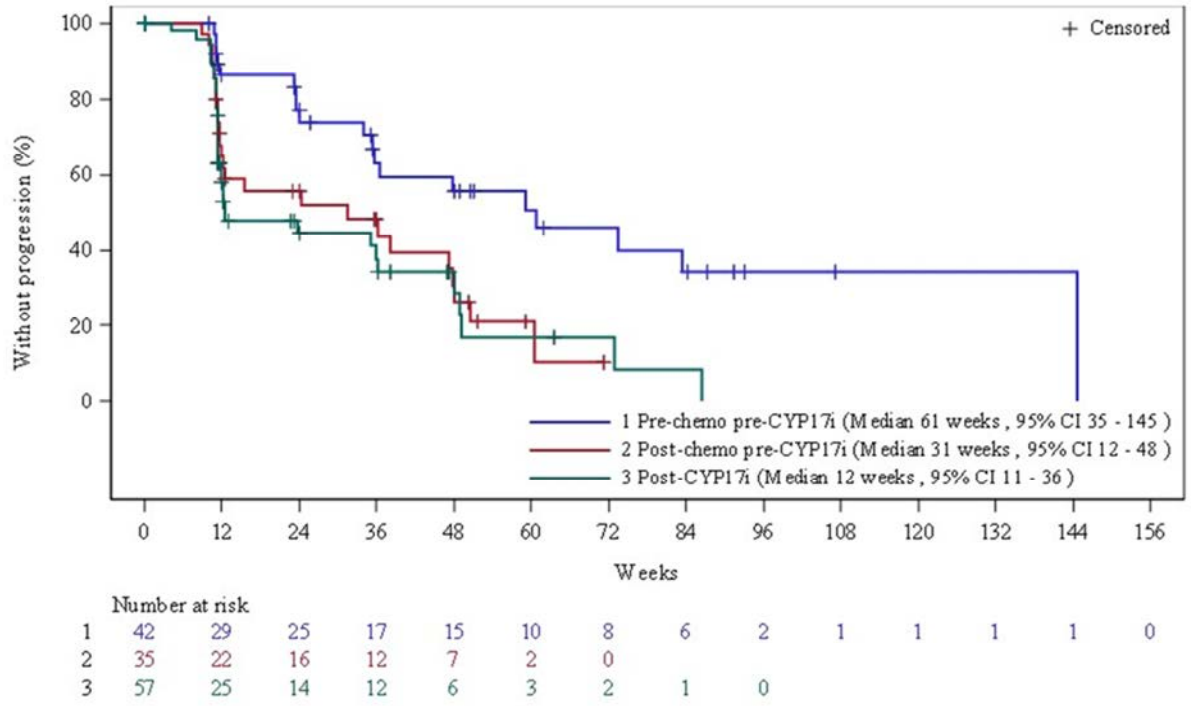
図 2.7.6.10-3 用量群別 TTPP の Kaplan-Meier 曲線（評価可能例、選択された用量群、N＝123）

2.7.6.10.2.2.3 TTP

TTP の解析は 134 例を対象とした。TTP の Kaplan-Meier 曲線を前治療別に図 2.7.6.10-4、用量群別に図 2.7.6.10-5 に示す。

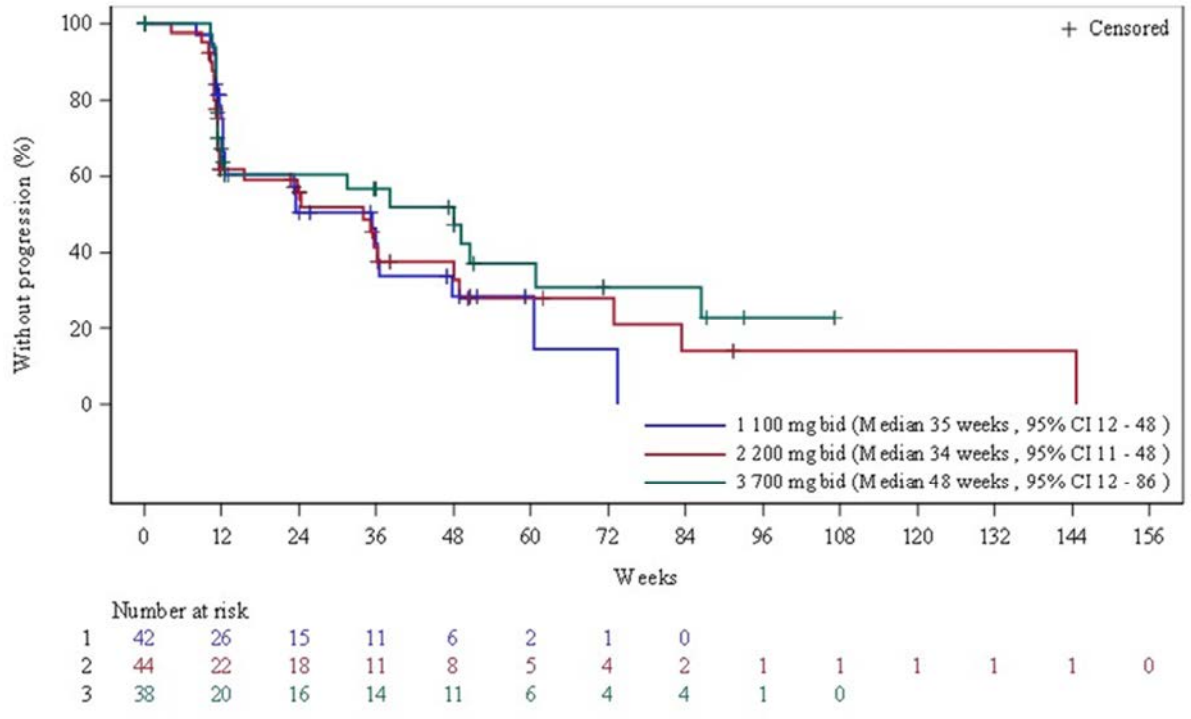
TTP の中央値は、化学療法歴なし／CYP17i 投与歴なしの被験者（42 例）で治験薬投与開始から 60.7 週間（95%CI：35.4～144.7 週間）、化学療法歴あり／CYP17i 投与歴なしの被験者（35 例）で 31.4 週間（11.7～47.7 週間）、CYP17i 投与歴ありの被験者（57 例）で 12.4 週間（11.4～36.1 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.9）。

TTP の中央値は 100mg と 200mg 群が同程度〔100mg 群で 35.4 週間（95%CI：12.1～47.7 週間）、200mg 群で 34.0 週間（11.4～48.0 週間）〕であり、700mg 群が特に長かった〔48.0 週間（11.9～86.4 週間）〕（5.3.5.2.1 R-11102/Table 14.2.1.9.1）。



Source：5.3.5.2.1 R-11102/Figure 14.4.4.3.1

図 2.7.6.10-4 前治療別 TTP の Kaplan-Meier 曲線（N＝134）



Source：5.3.5.2.1 R-11102/Figure 14.4.4.3.2

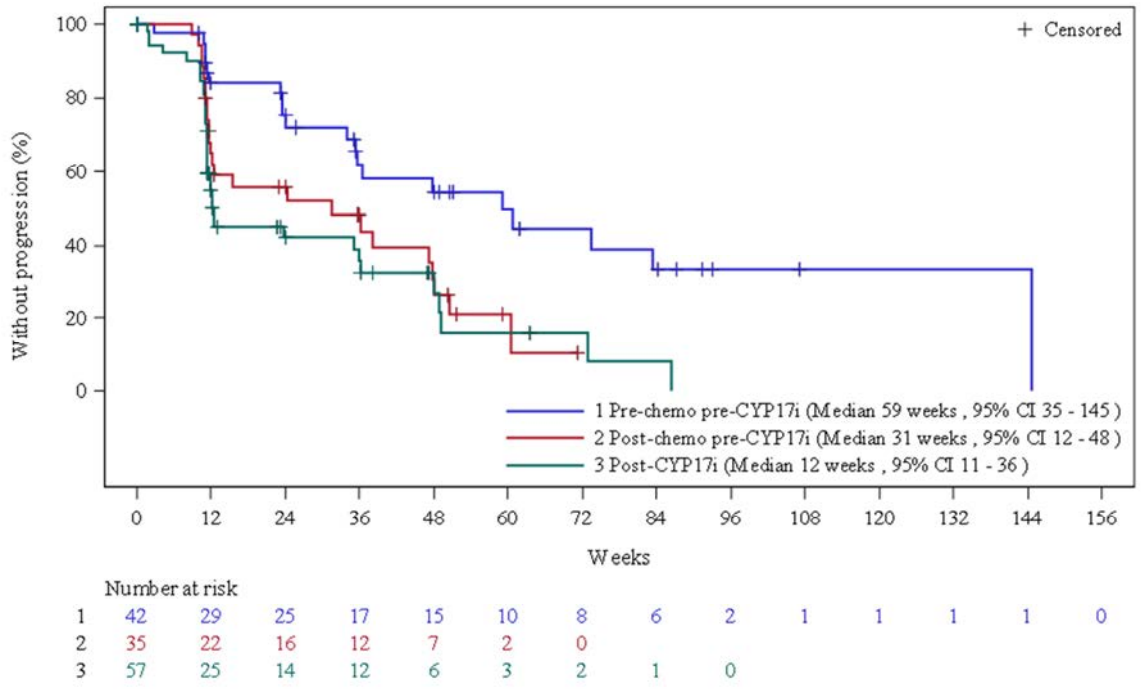
図 2.7.6.10-5　用量群別 TTP の Kaplan-Meier 曲線（選択された用量群、N＝124）

2.7.6.10.2.2.4　rPFS

rPFS の解析は 134 例を対象とした。rPFS の Kaplan-Meier 曲線を前治療別に図 2.7.6.10-6、用量群別に図 2.7.6.10-7 に示す。

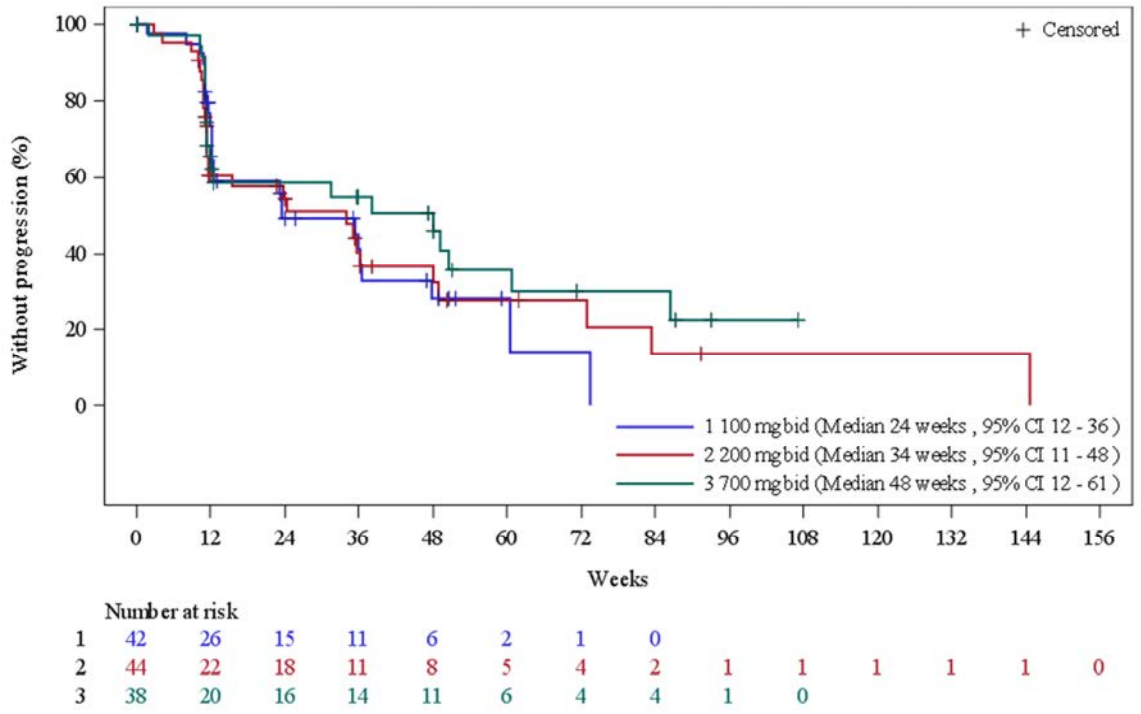
rPFS の中央値は、化学療法歴なし／CYP17i 投与歴なしの被験者（42 例）で 59.0 週間（95% CI：35.4～144.7 週間）、化学療法歴あり／CYP17i 投与歴なしの被験者（35 例）で 31.4 週間（11.7～47.7 週間）、CYP17i 投与歴ありの被験者（57 例）で 12.1 週間（11.4～36.1 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.10）。

rPFS の中央値は、100mg 群で 23.6 週間（95%CI：12.1～36.4 週間）、200mg 群で 34.0 週間（11.4～48.0 週間）、700mg 群で 48.0 週間（11.9～60.7 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.10.1）。



Source：5.3.5.2.1 R-11102/Figure 14.4.4.4.1

図 2.7.6.10-6 前治療別 rPFS の Kaplan-Meier 曲線（N＝134）



Source：5.3.5.2.1 R-11102/Figure 14.4.4.4.2

図 2.7.6.10-7 用量群別 rPFS の Kaplan-Meier 曲線（選択された用量群、N＝124）

2.7.6.10.2.2.5 投与期間

投与期間の解析は 134 例を対象とした。投与期間の中央値は 23.6 週間（95%CI：12.6～32.0 週間）であり、治験薬投与開始から試験終了来院時までの中央値は 28.7 週間（17.7～39.3 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.8、14.2.1.13）。

投与期間の中央値は、化学療法歴なし／CYP17i 投与歴なしの被験者（42 例）で 40.6 週間（95%CI：29.9～56.4 週間）、化学療法歴あり／CYP17i 投与歴なしの被験者（35 例）で 26.0 週間（12.4～36.4 週間）、CYP17i 投与歴ありの被験者（57 例）で 12.3 週間（12.1～16.3 週間）であった。治験薬投与開始から試験終了来院時までの中央値は、化学療法歴なし／CYP17i 投与歴なしの被験者で 48.1 週間（30.4～62.9 週間）、化学療法歴あり／CYP17i 投与歴なしの被験者で 30.0 週間（16.3～40.1 週間）、CYP17i 投与歴ありの被験者で 16.4 週間（16.1～23.1 週間）であった（5.3.5.2.1 R-11102/Table 14.2.1.8、14.2.1.13）。

2.7.6.10.2.2.6 軟部組織及び骨病変における効果

軟部組織の標的病変及び非標的病変を SAF の 76 例で評価した結果、第 12 週に 9 例（18.0%）に PR が認められた（化学療法歴なし／CYP17i 投与歴なしが 5 例、化学療法歴あり／CYP17i 投与歴なしが 2 例、CYP17i 投与歴ありが 2 例、5.3.5.2.1 R-11102/Table 14.2.1.3.1.3、14.2.1.3.1.3.1-3）。大部分の奏効は標的病変で認められた〔第 12 週の標的病変における PR 9 例（25.7％）、SD 24 例（68.6％）、PD 2 例（5.7％）、5.3.5.2.1 R-11102/Table 14.2.1.3.2.3〕。

骨病変を SAF の 76 例で評価した結果、第 12 週に 67 例（88.2%）で新たな骨病変は認められなかった。新たな骨病変が認められた 9 例（11.8%）のうち、化学療法歴なし／CYP17i 投与歴なしは 2 例、化学療法歴あり／CYP17i 投与歴なしは 1 例、CYP17i 投与歴ありは 6 例であった。CYP17i 投与歴ありの 1 例では 20 個超の新たな骨病変が認められた。第 12 週以降の各評価時点を通して、ほとんどの被験者で新たな骨病変は認められなかった（5.3.5.2.1 R-11102/Table 14.2.1.4.3.3、14.2.1.4.3.3.1-3）。

2.7.6.10.2.2.7 ECOG-PS

大部分の被験者は各評価時点を通して ECOG-PS が安定していた。ほとんどの変化は－1 又は＋1であった（5.3.5.2.1 R-11102/Table 14.2.1.7.3、14.2.1.7.3.1-14.2.1.7.3.3）。

2.7.6.10.2.2.8 臨床的病勢進行

治験薬投与期間中に 76 例中 18 例（23.7%）に臨床的病勢進行が認められた。最も多かった臨床症状は疼痛の悪化又は鎮痛薬の使用増加（4 例、18.4%）であった。臨床的病勢進行と判断された症状及びその割合は、用量群間及び部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で概して同様であった（5.3.5.2.1 R-11102/Table 14.2.1.11.3、14.2.1.11.3.1-3）。

2.7.6.10.2.3 安全性の結果

本項には、本試験に移行した 76 例を対象に、試験 17829 の開始時から本試験終了時までの安全性データを示す。

2.7.6.10.2.3.1 治験薬の曝露状況

試験 17829 初回投与からの治験薬の曝露状況を表 2.7.6.10-5 に示す。病勢進行後の治験薬の増量状況を用量群別に表 2.7.6.10-6 に示す。

投与日数の平均値は 366.9 日であり、中央値は 335.0 日であった。

病勢進行後に増量された被験者は 100mg 群で 14 例（56.0%）、200mg 群で 10 例（40.0%）であった。700mg 群の 1 例は、剤形変更〔ダロルタミドカプセル 100mg からダロルタミドフィルムコーティング錠 300mg へ変更〕のため、第 28 ヵ月に 600mg に減量された。

表 2.7.6.10-5 試験 17829 初回投与からの治験薬の曝露状況（SAF）

	100mg b.i.d. (N=25)	200mg b.i.d. (N=25)	300mg b.i.d. (N=3)	500mg b.i.d. (N=2)	700mg b.i.d.[a] (N=18)	900mg b.i.d. (N=3)	Total (N=76)
Days on treatment							
N	25	25	3	2	18	3	76
Mean±SD	302.8±129.5	358.6±235.7	522.7±362.7	548.0±134.4	432.4±214.8	300.3±79.9	366.9±204.9
Median	259.0	294.0	482.0	548.0	408.0	335.0	335.0
(range)	(104-593)	(114-1076)	(182-904)	(453-643)	(121-938)	(209-357)	(104-1076)

a: Dose changed for patient [redacted] from 700mg to 600mg b.i.d. at month 28 due to change from the capsule to tablet formulation
Source：5.3.5.2.1 R-11102/Table 14.1.6

表 2.7.6.10-6 病勢進行後の増量の状況（SAF）

	100mg b.i.d. (N=25)	200mg b.i.d. (N=25)	300mg b.i.d. (N=3)	500mg b.i.d. (N=2)	700mg b.i.d.[a] (N=18)	900mg b.i.d. (N=3)	Total (N=76)
Treatment dose changed, n (%)	14 (56.0)	10 (40.0)	0	0	0	0	24[a] (31.6)
Dose changed to:							
200 mg b.i.d.	8 (32.0)	0	0	0	0	0	8 (10.5)
300 mg b.i.d.	1 (4.0)	2 (8.0)	0	0	0	0	3 (3.9)
400 mg b.i.d.	0	1 (4.0)	0	0	0	0	1 (1.3)
700 mg b.i.d.	5 (20.0)	7 (28.0)	0	0	0	0	12 (15.8)

a: Dose changed for 1 additional patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation used in phase III
Source：5.3.5.2.1 R-11102/Table 14.2.1.12

2.7.6.10.2.3.2 有害事象の要約

試験 17829 の治験薬投与開始から本試験の終了来院時までの期間中に発現した有害事象の要約を表 2.7.6.10-7 に示す。

試験 17829 で治験薬投与を開始した後、76 例全例に有害事象が認められた。治験薬と関連のある有害事象は 33 例（43.4%）に発現した。重篤な有害事象は 19 例（25.0%）に発現し、そのうち 1 例は病勢進行による死亡であった。この死亡例を含む 3 例が有害事象により試験を中止した。有害事象による減量はなかった。大部分の有害事象の重症度はグレード 1 であった。有害事象の発現状況に用量依存的な傾向はみられなかった。有害事象の発現状況は、部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で同様であった（5.3.5.2.1 R-11102/Table 14.3.1.1.3.1-3）。

表 2.7.6.10-7 治験薬投与開始から本試験の終了来院時までに発現した有害事象の要約（SAF）

	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patient count							
AEs	25 (100.0)	25 (100.0)	3 (100.0)	2 (100.0)	18 (100.0)	3 (100.0)	76 (100.0)
Related AEs	10 (40.0)	10 (40.0)	1 (33.3)	2 (100.0)	8 (44.4)	2 (66.7)	33 (43.4)
SAEs	8 (32.0)	4 (16.0)	2 (66.7)	0	5 (27.8)	0	19 (25.0)
Other significant AEs	2 (8.0)	3 (12.0)	1 (33.3)	0	2 (11.1)	1 (33.3)	9 (11.8)
Grade 5 AEs	1 (4.0)	0	0	0	0	0	1 (1.3)
Grade 4 AEs	0	0	1 (33.3)	0	0	0	1 (1.3)
Grade 3 AEs	6 (24.0)	6 (24.0)	2 (66.7)	0	5 (27.8)	0	19 (25.0)
Grade 2 AEs	20 (80.0)	23 (92.0)	2 (66.7)	0	16 (88.9)	3 (100.0)	64 (84.2)
Grade 1 AEs	25 (100.0)	25 (100.0)	3 (100.0)	2 (100.0)	17 (94.4)	3 (100.0)	75 (98.7)
Grade ≥3 AEs	6 (24.0)	6 (24.0)	2 (66.7)	0	5 (27.8)	0	19 (25.0)
AEs leading to death	1 (4.0)	0	0	0	0	0	1 (1.3)
AEs leading to study discontinuation	1 (4.0)	1 (4.0)	1 (33.3)	0	0	0	3 (3.9)

a : Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Data source: 5.3.5.2.1 R-11102/Table 14.3.1.1.3

2.7.6.10.2.3.3 有害事象

2.7.6.10.2.3.3.1 治験薬投与開始から本試験の終了来院時までに発現した有害事象

試験 17829 の治験薬投与開始から本試験の終了来院時までに発現した有害事象を表 2.7.6.10-8 に示す。すべての有害事象の集計表を 2.7.6.10.a.1 に示す。

最も多く認められた有害事象は、背部痛（23 例、30.3%）、疲労（22 例、28.9%）、関節痛（19 例、25.0%）及び疼痛（16 例、21.1%）であり、ほとんどはグレード 1 又は 2 であった。有害事象の発現状況に用量依存的な傾向はみられなかった。有害事象の発現状況は、部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で同様であった（5.3.5.2.1 R-11102/Table 14.3.1.2.1.3.1-3）。

グレード 3 以上の有害事象を表 2.7.6.10-9 に示す。

グレード 3 以上の有害事象は 19 例（25.0%）で認められた。そのうちグレード 4 の有害事象が 1 例、グレード 5 の有害事象が 1 例で認められた。

2 例以上で認められたグレード 3 以上の有害事象は、背部痛（3 例、3.9%）、尿路性敗血症、急性腎不全、貧血、麻痺性イレウス、疲労、疼痛、血中アルカリホスファターゼ増加、尿閉及びリンパ浮腫（各 2 例、2.6%）であった。グレード 3 以上の有害事象の発現割合は部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で同程度であった（5.3.5.2.1 R-11102/Table 14.3.1.2.2.3.1-3、14.3.1.2.5.3.1-3）。

表 2.7.6.10-8 治験薬投与開始から本試験の終了来院時までに発現した有害事象（全体の 5%以上、SAF）

PT (Ver.18.0)	基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patients		**25 (100.0)**	**25 (100.0)**	**3 (100.0)**	**2 (100.0)**	**18 (100.0)**	**3 (100.0)**	**76 (100.0)**
Back pain	背部痛	4 (16.0)	9 (36.0)	2 (66.7)	0	7 (38.9)	1 (33.3)	23 (30.3)
Fatigue	疲労	3 (12.0)	6 (24.0)	1 (33.3)	1 (50.0)	9 (50.0)	2 (66.7)	22 (28.9)
Arthralgia	関節痛	9 (36.0)	4 (16.0)	2 (66.7)	0	3 (16.7)	1 (33.3)	19 (25.0)
Pain	疼痛	8 (32.0)	3 (12.0)	1 (33.3)	1 (50.0)	3 (16.7)	0	16 (21.1)
Constipation	便秘	5 (20.0)	5 (20.0)	0	0	2 (11.1)	1 (33.3)	13 (17.1)
Diarrhoea	下痢	4 (16.0)	3 (12.0)	2 (66.7)	0	2 (11.1)	2 (66.7)	13 (17.1)
Nausea	悪心	3 (12.0)	5 (20.0)	1 (33.3)	0	3 (16.7)	1 (33.3)	13 (17.1)
Decreased appetite	食欲減退	4 (16.0)	6 (24.0)	0	0	2 (11.1)	0	12 (15.8)
Oedema peripheral	末梢性浮腫	4 (16.0)	1 (4.0)	0	0	6 (33.3)	0	11 (14.5)
Hypertension	高血圧	3 (12.0)	2 (8.0)	1 (33.3)	0	3 (16.7)	0	9 (11.8)
Asthenia	無力症	4 (16.0)	4 (16.0)	0	0	0	0	8 (10.5)
Nasopharyngitis	鼻咽頭炎	2 (8.0)	2 (8.0)	0	1 (50.0)	1 (5.6)	2 (66.7)	8 (10.5)
Insomnia	不眠症	3 (12.0)	4 (16.0)	0	0	1 (5.6)	0	8 (10.5)
Vomiting	嘔吐	1 (4.0)	2 (8.0)	0	0	3 (16.7)	1 (33.3)	7 (9.2)
Headache	頭痛	2 (8.0)	3 (12.0)	0	0	1 (5.6)	1 (33.3)	7 (9.2)
Haematuria	血尿	4 (16.0)	1 (4.0)	0	0	2 (11.1)	0	7 (9.2)
Gynaecomastia	女性化乳房	1 (4.0)	2 (8.0)	0	1 (50.0)	2 (11.1)	1 (33.3)	7 (9.2)
Hot flush	ほてり	1 (4.0)	3 (12.0)	0	0	2 (11.1)	1 (33.3)	7 (9.2)
Urinary tract infection	尿路感染	2 (8.0)	2 (8.0)	0	0	1 (5.6)	1 (33.3)	6 (7.9)
Fall	転倒	3 (12.0)	1 (4.0)	0	0	2 (11.1)	0	6 (7.9)
Muscular weakness	筋力低下	2 (8.0)	0	0	1 (50.0)	3 (16.7)	0	6 (7.9)
Dizziness	浮動性めまい	1 (4.0)	3 (12.0)	1 (33.3)	0	0	1 (33.3)	6 (7.9)
Dyspnoea	呼吸困難	4 (16.0)	1 (4.0)	0	1 (50.0)	0	0	6 (7.9)
Dyspepsia	消化不良	0	2 (8.0)	0	0	3 (16.7)	0	5 (6.6)
Contusion	挫傷	2 (8.0)	0	0	0	3 (16.7)	0	5 (6.6)
Pain in extremity	四肢痛	2 (8.0)	2 (8.0)	0	0	0	1 (33.3)	5 (6.6)
Urinary incontinence	尿失禁	0	1 (4.0)	0	1 (50.0)	3 (16.7)	0	5 (6.6)
Rash	発疹	1 (4.0)	0	1 (33.3)	0	2 (11.1)	1 (33.3)	5 (6.6)

表 2.7.6.10-8 治験薬投与開始から本試験の終了来院時までに発現した有害事象（全体の 5%以上、SAF）（続き）

PT (Ver.18.0)	基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Anaemia	貧血	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Abdominal distension	腹部膨満	1 (4.0)	1 (4.0)	1 (33.3)	0	1 (5.6)	0	4 (5.3)
Flatulence	放屁	0	1 (4.0)	1 (33.3)	0	1 (5.6)	1 (33.3)	4 (5.3)
Peripheral swelling	末梢腫脹	2 (8.0)	0	1 (33.3)	0	1 (5.6)	0	4 (5.3)
Pyrexia	発熱	2 (8.0)	1 (4.0)	0	0	1 (5.6)	0	4 (5.3)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Bone pain	骨痛	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Muscle spasms	筋痙縮	0	1 (4.0)	1 (33.3)	0	2 (11.1)	0	4 (5.3)
Musculoskeletal pain	筋骨格痛	3 (12.0)	0	0	0	1 (5.6)	0	4 (5.3)
Hydronephrosis	水腎症	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Pelvic pain	骨盤痛	2 (8.0)	1 (4.0)	0	0	1 (5.6)	0	4 (5.3)
Cough	咳嗽	1 (4.0)	1 (4.0)	0	1 (50.0)	1 (5.6)	0	4 (5.3)
Epistaxis	鼻出血	1 (4.0)	1 (4.0)	0	0	1 (5.6)	1 (33.3)	4 (5.3)

a: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Source : 5.3.5.2.1 R-11102/Table 14.3.1.1.3, 14.3.1.2.1.3

表 2.7.6.10-9 治験薬投与開始から本試験の終了来院時までに発現したグレード3以上の有害事象（SAF）

Grade ≥3 AEs by PT (Ver.18.0)	基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patients		**6 (24.0)**	**6 (24.0)**	**2 (66.7)**	**0**	**5 (27.8)**	**0**	**19 (25.0)**
Back pain	背部痛	0	1 (4.0)	0	0	2 (11.1)	0	3 (3.9)
Urosepsis	尿路性敗血症	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Acute kidney injury	急性腎不全	2 (8.0)	0	0	0	0	0	2 (2.6)
Anaemia	貧血	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Ileus paralytic	麻痺性イレウス	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Fatigue	疲労	0	2 (8.0)	0	0	0	0	2 (2.6)
Pain	疼痛	0	1 (4.0)	1 (33.3)	0	0	0	2 (2.6)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Urinary retention	尿閉	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Lymphoedema	リンパ浮腫	0	1 (4.0)	1 (33.3)	0	0	0	2 (2.6)
Atrial fibrillation	心房細動	1 (4.0)	0	0	0	0	0	1 (1.3)
Liver abscess	肝膿瘍	1 (4.0)	0	0	0	0	0	1 (1.3)
Cervical vertebral fracture	頚椎骨折	1 (4.0)	0	0	0	0	0	1 (1.3)
Metastases to liver	肝転移	1 (4.0)	0	0	0	0	0	1 (1.3)
Prostate cancer	前立腺癌	1 (4.0)	0	0	0	0	0	1 (1.3)
Monoparesis	不全単麻痺	1 (4.0)	0	0	0	0	0	1 (1.3)
Syncope	失神	1 (4.0)	0	0	0	0	0	1 (1.3)
Orthostatic hypotension	起立性低血圧	1 (4.0)	0	0	0	0	0	1 (1.3)
Abdominal pain	腹痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Diverticulitis	憩室炎	0	1 (4.0)	0	0	0	0	1 (1.3)
Infection	感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Hyponatraemia	低ナトリウム血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Arthralgia	関節痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Pathological fracture	病的骨折	0	1 (4.0)	0	0	0	0	1 (1.3)
Paraplegia	対麻痺	0	1 (4.0)	0	0	0	0	1 (1.3)
Insomnia	不眠症	0	1 (4.0)	0	0	0	0	1 (1.3)
Sleep apnoea syndrome	睡眠時無呼吸症候群	0	1 (4.0)	0	0	0	0	1 (1.3)

表 2.7.6.10-9 治験薬投与開始から本試験の終了来院時までに発現したグレード3以上の有害事象（SAF）（続き）

Grade ≥3 AEs by PT (Ver.18.0)	基本語	100mg b.i.d. (N=25)	200mg b.i.d. (N=25)	300mg b.i.d. (N=3)	500mg b.i.d. (N=2)	700mg b.i.d.[a] (N=18)	900mg b.i.d. (N=3)	Total (N=76)
Hypertension	高血圧	0	1 (4.0)	0	0	0	0	1 (1.3)
Rectal adenocarcinoma	直腸腺癌	0	0	1 (33.3)	0	0	0	1 (1.3)
Presyncope	失神寸前の状態	0	0	1 (33.3)	0	0	0	1 (1.3)
Vomiting	嘔吐	0	0	0	0	1 (5.6)	0	1 (1.3)
Enterobacter test positive	エンテロバクター検査陽性	0	0	0	0	1 (5.6)	0	1 (1.3)
Muscular weakness	筋力低下	0	0	0	0	1 (5.6)	0	1 (1.3)
Angioedema	血管浮腫	0	0	0	0	1 (5.6)	0	1 (1.3)

a: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Source : 5.3.5.2.1 R-11102/Table 14.3.1.1.3, 14.3.1.2.5.3

2.7.6.10.2.3.3.2 治験薬と関連のある有害事象

試験 17829 の治験薬投与開始から本試験の終了来院時までに発現した治験薬と関連のある有害事象を表 2.7.6.10-10 に示す。

治験薬と関連のある有害事象は 33 例（43.3%）で認められた。最も多く認められた治験薬と関連のある有害事象は疲労（9 例、11.8%）、ほてり及び下痢（各 4 例、5.3%）であった。治験薬と関連のある有害事象の発現状況に用量依存的な傾向はみられなかった。有害事象のプロファイルに部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で顕著な違いはみられなかった（5.3.5.2.1 R-11102/Table 14.3.1.2.3.3.1-3）。

治験薬と関連のある有害事象の重症度は 1 例（グレード 3 の疲労）を除いてすべてグレード 1 又は 2 であった（5.3.5.2.1 R-11102/14.3.1.2.4.3）。

表 2.7.6.10-10 治験薬投与開始から本試験の終了来院時までに発現した治験薬と関連のある有害事象（SAF）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patients		**10 (40.0)**	**10 (40.0)**	**1 (33.3)**	**2 (100.0)**	**8 (44.4)**	**2 (66.7)**	**33 (43.4)**
Eye disorders	**眼障害**	**2 (8.0)**	**0**	**0**	**0**	**0**	**0**	**2 (2.6)**
Eyelid oedema	眼瞼浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Periorbital oedema	眼窩周囲浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Gastrointestinal disorders	**胃腸障害**	**3 (12.0)**	**3 (12.0)**	**1 (33.3)**	**1 (50.0)**	**2 (11.1)**	**2 (66.7)**	**12 (15.8)**
Abdominal distension	腹部膨満	0	0	1 (33.3)	0	1 (5.6)	0	2 (2.6)
Abnormal faeces	異常便	1 (4.0)	0	0	0	0	0	1 (1.3)
Cheilitis	口唇炎	0	0	0	1 (50.0)	0	0	1 (1.3)
Constipation	便秘	0	0	0	0	1 (5.6)	1 (33.3)	2 (2.6)
Diarrhoea	下痢	1 (4.0)	1 (4.0)	1 (33.3)	0	0	1 (33.3)	4 (5.3)
Dry mouth	口内乾燥	1 (4.0)	0	0	0	0	0	1 (1.3)
Dyspepsia	消化不良	0	0	0	0	1 (5.6)	0	1 (1.3)
Flatulence	放屁	0	1 (4.0)	1 (33.3)	0	0	1 (33.3)	3 (3.9)
Nausea	悪心	0	1 (4.0)	0	0	0	1 (33.3)	2 (2.6)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**3 (12.0)**	**3 (12.0)**	**0**	**0**	**4 (22.2)**	**2 (66.7)**	**12 (15.8)**
Asthenia	無力症	1 (4.0)	2 (8.0)	0	0	0	0	3 (3.9)
Face oedema	顔面浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Fatigue	疲労	1 (4.0)	2 (8.0)	0	0	4 (22.2)	2 (66.7)	9 (11.8)
Malaise	倦怠感	0	1 (4.0)	0	0	0	0	1 (1.3)
Infections and infestations	**感染症および寄生虫症**	**0**	**0**	**0**	**0**	**0**	**1 (33.3)**	**1 (1.3)**
Nasopharyngitis	鼻咽頭炎	0	0	0	0	0	1 (33.3)	1 (1.3)
Investigations	**臨床検査**	**0**	**0**	**0**	**0**	**1 (5.6)**	**0**	**1 (1.3)**
Weight increased	体重増加	0	0	0	0	1 (5.6)	0	1 (1.3)
Metabolism and nutrition disorders	**代謝および栄養障害**	**0**	**2 (8.0)**	**0**	**0**	**0**	**0**	**2 (2.6)**
Decreased appetite	食欲減退	0	2 (8.0)	0	0	0	0	2 (2.6)

表 2.7.6.10-10 治験薬投与開始から本試験の終了来院時までに発現した治験薬と関連のある有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**2 (8.0)**	**1 (4.0)**	**0**	**0**	**1 (5.6)**	**0**	**4 (5.3)**
Arthralgia	関節痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Back pain	背部痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Muscle spasms	筋痙縮	0	0	0	0	1 (5.6)	0	1 (1.3)
Myalgia	筋肉痛	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Pain in jaw	顎痛	1 (4.0)	0	0	0	0	0	1 (1.3)
Nervous system disorders	**神経系障害**	**0**	**2 (8.0)**	**0**	**0**	**2 (11.1)**	**1 (33.3)**	**5 (6.6)**
Ageusia	味覚消失	0	1 (4.0)	0	0	0	0	1 (1.3)
Dizziness	浮動性めまい	0	0	0	0	0	1 (33.3)	1 (1.3)
Headache	頭痛	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Somnolence	傾眠	0	0	0	0	1 (5.6)	0	1 (1.3)
Renal and urinary disorders	**腎および尿路障害**	**0**	**2 (8.0)**	**0**	**0**	**1 (5.6)**	**0**	**3 (3.9)**
Pollakiuria	頻尿	0	2 (8.0)	0	0	0	0	2 (2.6)
Urinary incontinence	尿失禁	0	0	0	0	1 (5.6)	0	1 (1.3)
Reproductive system and breast disorders	**生殖系および乳房障害**	**0**	**0**	**0**	**1 (50.0)**	**1 (5.6)**	**0**	**2 (2.6)**
Gynaecomastia	女性化乳房	0	0	0	1 (50.0)	1 (5.6)	0	2 (2.6)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**2 (8.0)**	**1 (4.0)**	**0**	**0**	**1 (5.6)**	**0**	**4 (5.3)**
Dry skin	皮膚乾燥	1 (4.0)	0	0	0	0	0	1 (1.3)
Erythema	紅斑	1 (4.0)	0	0	0	0	0	1 (1.3)
Night sweats	寝汗	0	1 (4.0)	0	0	0	0	1 (1.3)
Skin atrophy	皮膚萎縮	0	0	0	0	1 (5.6)	0	1 (1.3)
Vascular disorders	**血管障害**	**0**	**2 (8.0)**	**0**	**0**	**1 (5.6)**	**1 (33.3)**	**4 (5.3)**
Hot flush	ほてり	0	2 (8.0)	0	0	1 (5.6)	1 (33.3)	4 (5.3)
Hypertension	高血圧	0	1 (4.0)	0	0	0	0	1 (1.3)
Poor peripheral circulation	末梢循環不良	0	0	0	0	1 (5.6)	0	1 (1.3)

a: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation
Source：5.3.5.2.1 R-11102/Table 14.3.1.1.3, 14.3.1.2.3.3

2.7.6.10.2.3.4 死亡

本試験期間中に 100mg 群の 1 例に死亡（被験者番号[redacted]）が認められた（表 2.7.6.10-11）。当該被験者では、病勢進行が、投与中止及び死亡に至った重篤な有害事象として報告された。治験責任（分担）医師により、当該死亡は治験薬と関連なしと判断された。

表 2.7.6.10-11 治験薬投与開始から本試験終了来院時までに発現した死亡の一覧

Patient Age	Study drug start/stop date	AE Start date	Cause of death	MedDRA PT (Ver.18.0)	Causality	Action taken
Phase II Cohort expansion, Pre-chemo pre-CYP17i, 100mg b.i.d.[a]						
[redacted]	Day 1* / Day 351*	Day 333*	Progression of prostate cancer	Prostate 前立腺癌	No	Discontinued permanently

a：病勢進行により 200mg b.i.d.に増量

Source：5.3.5.2.1 R-11102/Table 14.3.2.2, 14.3.3 Narratives

2.7.6.10.2.3.5 重篤な有害事象

試験 17829 の治験薬投与開始から本試験の終了来院時までに発現した重篤な有害事象を表 2.7.6.10-12 に示す。

重篤な有害事象（病勢進行により死亡した 1 例を含む）が 19 例（25.0%）で認められた。治験薬と関連のある重篤な有害事象は認められなかった（5.3.5.2.1 R-11102/14.3.1.4.3.3）。

重篤な有害事象は、背部痛（3 例、3.9%）、便秘、麻痺性イレウス、発熱、腎盂腎炎、尿路性敗血症、水腎症、急性腎不全及び深部静脈血栓症（各 2 例、2.6%）を除いて各 1 例で認められた。

表 2.7.6.10-12 治験薬投与開始から本試験の終了来院時までに発現した重篤な有害事象（SAF）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patients, n (%)		**8 (32.0)**	**4 (16.0)**	**2 (66.7)**	**0**	**5 (27.8)**	**0**	**19 (25.0)**
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**0**	**1 (4.0)**	**0**	**0**	**0**	**0**	**1 (1.3)**
Anaemia	貧血	0	1 (4.0)	0	0	0	0	1 (1.3)
Cardiac disorders	**心臓障害**	**2 (8.0)**	**0**	**0**	**0**	**0**	**0**	**2 (2.6)**
Atrial fibrillation	心房細動	1 (4.0)	0	0	0	0	0	1 (1.3)
Cardiac failure	心不全	1 (4.0)	0	0	0	0	0	1 (1.3)
Gastrointestinal disorders	**胃腸障害**	**2 (8.0)**	**2 (8.0)**	**0**	**0**	**2 (11.1)**	**0**	**6 (7.9)**
Abdominal pain	腹痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Constipation	便秘	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Diarrhoea	下痢	1 (4.0)	0	0	0	0	0	1 (1.3)
Ileus paralytic	麻痺性イレウス	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Nausea	悪心	0	0	0	0	1 (5.6)	0	1 (1.3)
Vomiting	嘔吐	1 (4.0)	0	0	0	0	0	1 (1.3)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**1 (4.0)**	**1 (4.0)**	**0**	**0**	**1 (5.6)**	**0**	**3 (3.9)**
Chills	悪寒	0	0	0	0	1 (5.6)	0	1 (1.3)
Fatigue	疲労	0	1 (4.0)	0	0	0	0	1 (1.3)
Pain	疼痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Pyrexia	発熱	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Infections and infestations	**感染症および寄生虫症**	**4 (16.0)**	**1 (4.0)**	**0**	**0**	**2 (11.1)**	**0**	**7 (9.2)**
Diverticulitis	憩室炎	0	1 (4.0)	0	0	0	0	1 (1.3)
Enterobacter infection	エンテロバクター感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Gastroenteritis	胃腸炎	1 (4.0)	0	0	0	0	0	1 (1.3)
Infection	感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Liver abscess	肝膿瘍	1 (4.0)	0	0	0	0	0	1 (1.3)
Lung infection	肺感染	1 (4.0)	0	0	0	0	0	1 (1.3)

表 2.7.6.10-12 治験薬投与開始から本試験の終了来院時までに発現した重篤な有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Pneumonia	肺炎	0	0	0	0	1 (5.6)	0	1 (1.3)
Pyelonephritis	腎盂腎炎	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Stenotrophomonas infection	ステノトロフォモナス感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Urinary tract infection	尿路感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Urosepsis	尿路性敗血症	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**2 (8.0)**	**0**	**0**	**0**	**0**	**0**	**2 (2.6)**
Cervical vertebral fracture	頚椎骨折	1 (4.0)	0	0	0	0	0	1 (1.3)
Contusion	挫傷	1 (4.0)	0	0	0	0	0	1 (1.3)
Facial bones fracture	顔面骨骨折	1 (4.0)	0	0	0	0	0	1 (1.3)
Fall	転倒	1 (4.0)	0	0	0	0	0	1 (1.3)
Laceration	裂傷	1 (4.0)	0	0	0	0	0	1 (1.3)
Investigations	**臨床検査**	**0**	**0**	**0**	**0**	**1 (5.6)**	**0**	**1 (1.3)**
Enterobacter test positive	エンテロバクター検査陽性	0	0	0	0	1 (5.6)	0	1 (1.3)
Metabolism and nutrition disorders	**代謝および栄養障害**	**0**	**1 (4.0)**	**0**	**0**	**0**	**0**	**1 (1.3)**
Decreased appetite	食欲減退	0	1 (4.0)	0	0	0	0	1 (1.3)
Hyperkalaemia	高カリウム血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Hyponatraemia	低ナトリウム血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**0**	**1 (4.0)**	**0**	**0**	**2 (11.1)**	**0**	**3 (3.9)**
Back pain	背部痛	0	1 (4.0)	0	0	2 (11.1)	0	3 (3.9)
Muscular weakness	筋力低下	0	0	0	0	1 (5.6)	0	1 (1.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**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**	**1 (33.3)**	**0**	**0**	**0**	**2 (2.6)**
Prostate cancer	前立腺癌	1 (4.0)	0	0	0	0	0	1 (1.3)
Rectal adenocarcinoma	直腸腺癌	0	0	1 (33.3)	0	0	0	1 (1.3)

表 2.7.6.10-12 治験薬投与開始から本試験の終了来院時までに発現した重篤な有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Nervous system disorders	**神経系障害**	**1 (4.0)**	**1 (4.0)**	**0**	**0**	**0**	**0**	**2 (2.6)**
Cerebral ischaemia	脳虚血	0	1 (4.0)	0	0	0	0	1 (1.3)
Syncope	失神	1 (4.0)	0	0	0	0	0	1 (1.3)
Psychiatric disorders	**精神障害**	**0**	**1 (4.0)**	**0**	**0**	**0**	**0**	**1 (1.3)**
Confusional state	錯乱状態	0	1 (4.0)	0	0	0	0	1 (1.3)
Insomnia	不眠症	0	1 (4.0)	0	0	0	0	1 (1.3)
Renal and urinary disorders	**腎および尿路障害**	**2 (8.0)**	**1 (4.0)**	**0**	**0**	**2 (11.1)**	**0**	**5 (6.6)**
Acute kidney injury	急性腎不全	2 (8.0)	0	0	0	0	0	2 (2.6)
Calculus urinary	尿路結石	0	1 (4.0)	0	0	0	0	1 (1.3)
Hydronephrosis	水腎症	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Urethral stenosis	尿道狭窄	0	0	0	0	1 (5.6)	0	1 (1.3)
Urinary incontinence	尿失禁	0	0	0	0	1 (5.6)	0	1 (1.3)
Urinary retention	尿閉	0	0	0	0	1 (5.6)	0	1 (1.3)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**0**	**1 (4.0)**	**0**	**0**	**0**	**0**	**1 (1.3)**
Dyspnoea	呼吸困難	0	1 (4.0)	0	0	0	0	1 (1.3)
Sleep apnoea syndrome	睡眠時無呼吸症候群	0	1 (4.0)	0	0	0	0	1 (1.3)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**0**	**0**	**0**	**0**	**1 (5.6)**	**0**	**1 (1.3)**
Angioedema	血管浮腫	0	0	0	0	1 (5.6)	0	1 (1.3)
Vascular disorders	**血管障害**	**2 (8.0)**	**1 (4.0)**	**1 (33.3)**	**0**	**0**	**0**	**4 (5.3)**
Deep vein thrombosis	深部静脈血栓症	1 (4.0)	0	1 (33.3)	0	0	0	2 (2.6)
Lymphoedema	リンパ浮腫	0	1 (4.0)	0	0	0	0	1 (1.3)
Orthostatic hypotension	起立性低血圧	1 (4.0)	0	0	0	0	0	1 (1.3)

a : Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation

Source : 5.3.5.2.1 R-11102/Table 14.3.1.1.3, 14.3.1.4.1.3

2.7.6.10.2.3.6 その他の重要な有害事象

重篤な有害事象以外の治験薬の投与中断又は投与中止に至った有害事象、治験責任（分担）医師により特定されたその他の重要な有害事象、グレード 4 の非重篤な有害事象（例えば、病勢進行によるもの）及び二次性悪性腫瘍を、その他の重要な有害事象とした。

その他の重要な有害事象の一覧を表 2.7.6.10-13 に示す。

その他の重要な有害事象は 9 例（11.8%）で認められた。1 例で認められた疲労、筋肉痛及び倦怠感を除いて、すべて治験薬と関連なしと判定された。

表 2.7.6.10-13 治験薬投与開始から本試験終了来院時までに発現したその他の重要な有害事象の一覧（SAF）

Patient	MedDRA PT (Ver.18.0)	基本語	Time from first study treatment start (days)	Duration (days)	Severity	Causality	Action taken with study treatment	Final outcome
[redacted]	Lymphoedema	リンパ浮腫	481	-	Grade 4	Not related	None	Unchanged
	Vomiting	嘔吐	89	0	Grade 1	Not related	Interrupted	Resolved
	Bowen's disease	ボーエン病	Unknown	-	Grade 1	Not related	None	Unchanged
	Infection	感染	111	8	Grade 2	Not related	Interrupted	Resolved
	Anaemia [a]	貧血	8	1	Grade 3	Not related	Interrupted	Resolved
	Fatigue	疲労	182	15	Grade 3	Related	Interrupted	Improved
	Myalgia	筋肉痛	182	48	Grade 2	Related	Interrupted	Improved
	Malaise	倦怠感	182	48	Grade 2	Related	Interrupted	Improved
	Fatigue	疲労	197	33	Grade 2	Related	Discontinued permanently	Improved
	Supraventricular extrasystoles [a]	上室性期外収縮	0	1	Grade 1	Not related	Interrupted	Resolved
	Ventricular extrasystoles [a]	心室性期外収縮	5	1	Grade 1	Not related	Interrupted	Resolved
	Heart rate increased [a]	心拍数増加	5	1	Grade 1	Not related	Interrupted	Resolved
	Arthralgia [a]	関節痛	30	17	Grade 2	Not related	None	Resolved
	Chest pain [a]	胸痛	47	0	Grade 2	Not related	None	Resolved
	Arthralgia	関節痛	145	-	Grade 3	Not related	None	Unchanged
	Exposed bone in jaw [a]	顎骨露出	48	-	Grade 2	Not related	None	Unchanged

a: Events reported in 17829 study report (R-9584)

Source : 5.3.5.2.1 R-11102/Table 14.3.2.4, 14.3.2.5

2.7.6.10.2.3.7 臨床検査

ベースラインから、臨床的に意味のある急性又は慢性の臨床検査値の変化は認められなかった。また、用量群間で臨床的に意味のある違いも認められなかった（5.3.5.2.1 R-11102/Table 14.3.5.1.2.3、14.3.5.2.2.3、14.3.5.3.2.3、Figure 14.4.2.1.1、14.4.2.1.2）。

有害事象として報告された最も多かった臨床検査値異常は、血尿（7 例、9.2%）であり、次いで血中アルカリホスファターゼ増加及び貧血（各 4 例、5.3%）であった（表 2.7.6.10-8）。

2.7.6.10.2.3.8 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

2.7.6.10.2.3.8.1 バイタルサイン

ベースラインからの心拍数又は血圧の顕著な変化はみられず、用量依存的な傾向も認められなかった（5.3.5.2.1 R-11102/Table 14.3.6.1.2.3、14.3.6.2.2.3、14.3.6.3.2.3、Figure 14.4.3.1.2、14.4.3.2.2、14.4.3.3.2）。

2.7.6.10.2.3.8.2 12 誘導 ECG

いずれの ECG パラメータにおいても、ベースラインからの急性又は慢性の顕著な変化はみられなかった。ECG パラメータの変化には、用量群間で大きな違いはなかった（5.3.5.2.1 R-11102/Table 14.3.8.2.2.3、14.3.8.3.2.3、14.3.8.4.2.3、14.3.8.5.2.3、14.3.8.6.2.3、14.3.8.7.3.1）。

治験責任（分担）医師により臨床的に意味があると判断された ECG 異常は 5 例に認められ、いずれも治験薬と関連のない有害事象と判定された。重症度はすべてグレード 1 であった（5.3.5.2.1 R-11102/Listing 16.2.7.2-3、16.2.9.3.1）。

QTcF 間隔のカテゴリカル解析を表 2.7.6.10-14 に示す。

QTcF 間隔が 450ms を超えた被験者は 13 例（17.1%）であり、480ms を超えた被験者はなかった。QTcF 間隔のベースラインからの変化が 30ms を超えた被験者は 6 例（8.3%）で、ベースラインからの変化が 60ms を超えた被験者はなかった。

QTcF 間隔の変化に用量依存的な傾向はみられず、部分集団間（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）で顕著な違いはみられなかった（5.3.5.2.1 R-11102/Table 14.3.8.10.2.3.1-3）。

表 2.7.6.10-14 QTcF 間隔のカテゴリカル解析（SAF）

QTc interval categories	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d. (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
QTcF interval							
＞450ms	2 (8.0)	6 (24.0)	2 (66.7)	0	3 (16.7)	0	13 (17.1)
＞480ms	0	0	0	0	0	0	0
QTcF categorical change from pre-dose							
＞30ms	2 (8.3)	1 (4.3)	1 (33.3)	0	2 (11.8)	0	6 (8.3)
＞60ms	0	0	0	0	0	0	0

Source：5.3.5.2.1 R-11102/Table 14.3.8.10.2.3, 14.3.8.10.4.3

2.7.6.10.3 結論

本試験でみられた有害事象プロファイルは、試験 17829 の 12 週間のデータの解析結果及び進行性前立腺癌の患者集団で予想される有害事象プロファイルを反映したものであった。有害事象の大部分は、重症度がグレード 1 又は 2 であり、治験責任（分担）医師により治験薬と関連なしと判定された。有害事象の発現プロファイルに用量依存的な傾向は示されなかった。臨床検査値、バイタルサイン及び ECG パラメータに臨床的に意味のある変化は認められなかった。

ダロルタミドの抗腫瘍効果は、いずれの用量群又は部分集団（化学療法歴なし／CYP17i 投与歴なし、化学療法歴あり／CYP17i 投与歴なし、CYP17i 投与歴あり）でも認められた。化学療法歴なし／CYP17i 投与歴なしの部分集団で最もよく奏効が認められ、そのうち 700mg 群で最もよく奏効が認められた。

本試験の結果から、ダロルタミドは CRPC 患者において安全かつ有効な治療法であることが示され、長期的な有用性が示唆された。また、ダロルタミド 700mg の 1 日 2 回投与は、100 又は 200mg の 1 日 2 回と同様に忍容性が良好であり、化学療法歴なし／CYP17i 投与歴なしの被験者集団において低用量よりも優れた抗腫瘍効果を有することが示唆された。

参考文献

1) Eisenhauer EA et al., Eur J Cancer 45(2):228-247

2) Scher HI et al., J Clin Oncol 2008:26(7):1148-1159

2.7.6.10.a 付録

2.7.6.10.a.1 付表..... 2

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）..... 2

2.7.6.10.a.1 付表

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Patients		**25 (100.0)**	**25 (100.0)**	**3 (100.0)**	**2 (100.0)**	**18 (100.0)**	**3 (100.0)**	**76 (100.0)**
Blood and lymphatic system disorders	**血液およびリンパ系障害**	**2 (8.0)**	**2 (8.0)**	**0**	**0**	**1 (5.6)**	**0**	**5 (6.6)**
Anaemia	貧血	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Lymphadenopathy	リンパ節症	1 (4.0)	0	0	0	0	0	1 (1.3)
Cardiac disorders	**心臓障害**	**5 (20.0)**	**1 (4.0)**	**0**	**0**	**3 (16.7)**	**0**	**9 (11.8)**
Atrial fibrillation	心房細動	1 (4.0)	0	0	0	0	0	1 (1.3)
Cardiac failure	心不全	1 (4.0)	0	0	0	0	0	1 (1.3)
Coronary artery disease	冠動脈疾患	1 (4.0)	0	0	0	0	0	1 (1.3)
Mitral valve incompetence	僧帽弁閉鎖不全症	1 (4.0)	0	0	0	0	0	1 (1.3)
Palpitations	動悸	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Supraventricular extrasystoles	上室性期外収縮	1 (4.0)	0	0	0	0	0	1 (1.3)
Supraventricular tachycardia	上室性頻脈	0	0	0	0	1 (5.6)	0	1 (1.3)
Tachycardia	頻脈	0	0	0	0	1 (5.6)	0	1 (1.3)
Ventricular extrasystoles	心室性期外収縮	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Ear and labyrinth disorders	**耳および迷路障害**	**0**	**0**	**0**	**0**	**2 (11.1)**	**0**	**2 (2.6)**
Ear pain	耳痛	0	0	0	0	1 (5.6)	0	1 (1.3)
Motion sickness	乗物酔い	0	0	0	0	1 (5.6)	0	1 (1.3)
Eye disorders	**眼障害**	**4 (16.0)**	**0**	**1 (33.3)**	**0**	**1 (5.6)**	**0**	**6 (7.9)**
Eye pain	眼痛	1 (4.0)	0	0	0	0	0	1 (1.3)
Eye pruritus	眼そう痒症	0	0	0	0	1 (5.6)	0	1 (1.3)
Eyelid oedema	眼瞼浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Ocular hyperaemia	眼充血	0	0	1 (33.3)	0	0	0	1 (1.3)
Periorbital oedema	眼窩周囲浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Visual acuity reduced	視力低下	1 (4.0)	0	0	0	0	0	1 (1.3)

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Gastrointestinal disorders	**胃腸障害**	**12 (48.0)**	**15 (60.0)**	**2 (66.7)**	**1 (50.0)**	**8 (44.4)**	**2 (66.7)**	**40 (52.6)**
Abdominal distension	腹部膨満	1 (4.0)	1 (4.0)	1 (33.3)	0	1 (5.6)	0	4 (5.3)
Abdominal pain	腹痛	0	2 (8.0)	0	0	1 (5.6)	0	3 (3.9)
Abdominal pain upper	上腹部痛	0	0	0	0	1 (5.6)	0	1 (1.3)
Abnormal faeces	異常便	1 (4.0)	0	0	0	0	0	1 (1.3)
Anal fissure	裂肛	0	1 (4.0)	0	0	0	0	1 (1.3)
Aphthous stomatitis	アフタ性口内炎	1 (4.0)	0	0	0	0	0	1 (1.3)
Cheilitis	口唇炎	0	0	0	1 (50.0)	0	0	1 (1.3)
Constipation	便秘	5 (20.0)	5 (20.0)	0	0	2 (11.1)	1 (33.3)	13 (17.1)
Diarrhoea	下痢	4 (16.0)	3 (12.0)	2 (66.7)	0	2 (11.1)	2 (66.7)	13 (17.1)
Dry mouth	口内乾燥	2 (8.0)	0	0	0	1 (5.6)	0	3 (3.9)
Dyspepsia	消化不良	0	2 (8.0)	0	0	3 (16.7)	0	5 (6.6)
Flatulence	放屁	0	1 (4.0)	1 (33.3)	0	1 (5.6)	1 (33.3)	4 (5.3)
Gastritis	胃炎	1 (4.0)	0	0	0	0	0	1 (1.3)
Gingival pain	歯肉痛	0	0	0	0	1 (5.6)	0	1 (1.3)
Haemorrhoidal haemorrhage	痔出血	0	0	1 (33.3)	0	0	0	1 (1.3)
Ileus paralytic	麻痺性イレウス	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Nausea	悪心	3 (12.0)	5 (20.0)	1 (33.3)	0	3 (16.7)	1 (33.3)	13 (17.1)
Oesophagitis	食道炎	0	0	0	0	1 (5.6)	0	1 (1.3)
Rectal haemorrhage	直腸出血	0	1 (4.0)	0	0	0	1 (33.3)	2 (2.6)
Stomatitis	口内炎	3 (12.0)	0	0	0	0	0	3 (3.9)
Tongue discolouration	舌変色	0	0	0	0	1 (5.6)	0	1 (1.3)
Vomiting	嘔吐	1 (4.0)	2 (8.0)	0	0	3 (16.7)	1 (33.3)	7 (9.2)
General disorders and administration site conditions	**一般・全身障害および投与部位の状態**	**16 (64.0)**	**14 (56.0)**	**2 (66.7)**	**2 (100.0)**	**16 (88.9)**	**2 (66.7)**	**52 (68.4)**
Asthenia	無力症	4 (16.0)	4 (16.0)	0	0	0	0	8 (10.5)
Chest pain	胸痛	1 (4.0)	2 (8.0)	0	0	0	0	3 (3.9)
Chills	悪寒	0	0	0	0	1 (5.6)	0	1 (1.3)
Face oedema	顔面浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Fatigue	疲労	3 (12.0)	6 (24.0)	1 (33.3)	1 (50.0)	9 (50.0)	2 (66.7)	22 (28.9)

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Influenza like illness	インフルエンザ様疾患	1 (4.0)	0	0	0	0	0	1 (1.3)
Localised oedema	限局性浮腫	0	0	0	0	1 (5.6)	0	1 (1.3)
Malaise	倦怠感	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Oedema peripheral	末梢性浮腫	4 (16.0)	1 (4.0)	0	0	6 (33.3)	0	11 (14.5)
Pain	疼痛	8 (32.0)	3 (12.0)	1 (33.3)	1 (50.0)	3 (16.7)	0	16 (21.1)
Peripheral swelling	末梢腫脹	2 (8.0)	0	1 (33.3)	0	1 (5.6)	0	4 (5.3)
Pyrexia	発熱	2 (8.0)	1 (4.0)	0	0	1 (5.6)	0	4 (5.3)
Immune system disorders	**免疫系障害**	**0**	**0**	**1 (33.3)**	**0**	**0**	**0**	**1 (1.3)**
Hypersensitivity	過敏症	0	0	1 (33.3)	0	0	0	1 (1.3)
Infections and infestations	**感染症および寄生虫症**	**12 (48.0)**	**11 (44.0)**	**1 (33.3)**	**2 (100.0)**	**9 (50.0)**	**2 (66.7)**	**37 (48.7)**
Bronchitis	気管支炎	0	0	0	1 (50.0)	1 (5.6)	0	2 (2.6)
Cellulitis	蜂巣炎	0	0	0	0	1 (5.6)	0	1 (1.3)
Diverticulitis	憩室炎	0	1 (4.0)	0	0	0	0	1 (1.3)
Enterobacter infection	エンテロバクター感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Eye infection	眼感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Gastroenteritis	胃腸炎	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Herpes zoster	帯状疱疹	0	1 (4.0)	0	0	0	0	1 (1.3)
Infection	感染	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Influenza	インフルエンザ	1 (4.0)	1 (4.0)	0	0	1 (5.6)	0	3 (3.9)
Liver abscess	肝膿瘍	1 (4.0)	0	0	0	0	0	1 (1.3)
Lower respiratory tract infection	下気道感染	1 (4.0)	0	0	0	2 (11.1)	0	3 (3.9)
Lung infection	肺感染	1 (4.0)	0	0	0	0	0	1 (1.3)
Nasopharyngitis	鼻咽頭炎	2 (8.0)	2 (8.0)	0	1 (50.0)	1 (5.6)	2 (66.7)	8 (10.5)
Onychomycosis	爪真菌症	0	1 (4.0)	0	0	0	0	1 (1.3)
Oral herpes	口腔ヘルペス	0	0	0	0	1 (5.6)	1 (33.3)	2 (2.6)
Pneumonia	肺炎	0	0	0	0	1 (5.6)	0	1 (1.3)
Pyelonephritis	腎盂腎炎	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Pyelonephritis acute	急性腎盂腎炎	0	1 (4.0)	0	0	0	0	1 (1.3)
Rhinitis	鼻炎	0	0	0	1 (50.0)	0	0	1 (1.3)

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Sinusitis	副鼻腔炎	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Stenotrophomonas infection	ステノトロフォモナス感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Tinea cruris	股部白癬	0	0	0	0	1 (5.6)	0	1 (1.3)
Tooth abscess	歯膿瘍	0	1 (4.0)	0	0	0	0	1 (1.3)
Tooth infection	歯感染	0	1 (4.0)	0	0	0	0	1 (1.3)
Upper respiratory tract infection	上気道感染	2 (8.0)	0	0	0	0	0	2 (2.6)
Urinary tract infection	尿路感染	2 (8.0)	2 (8.0)	0	0	1 (5.6)	1 (33.3)	6 (7.9)
Urosepsis	尿路性敗血症	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Viral infection	ウイルス感染	1 (4.0)	0	1 (33.3)	0	0	0	2 (2.6)
Injury, poisoning and procedural complications	**傷害、中毒および処置合併症**	**5 (20.0)**	**3 (12.0)**	**0**	**0**	**6 (33.3)**	**2 (66.7)**	**16 (21.1)**
Cervical vertebral fracture	頚椎骨折	1 (4.0)	0	0	0	0	0	1 (1.3)
Contusion	挫傷	2 (8.0)	0	0	0	3 (16.7)	0	5 (6.6)
Facial bones fracture	顔面骨骨折	1 (4.0)	0	0	0	0	0	1 (1.3)
Fall	転倒	3 (12.0)	1 (4.0)	0	0	2 (11.1)	0	6 (7.9)
Foot fracture	足骨折	0	0	0	0	0	1 (33.3)	1 (1.3)
Infusion related reaction	注入に伴う反応	0	1 (4.0)	0	0	0	0	1 (1.3)
Laceration	裂傷	1 (4.0)	0	0	0	2 (11.1)	0	3 (3.9)
Ligament sprain	靭帯捻挫	0	1 (4.0)	0	0	0	0	1 (1.3)
Muscle strain	肉離れ	0	0	0	0	1 (5.6)	0	1 (1.3)
Rib fracture	肋骨骨折	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Sunburn	サンバーン	0	0	0	0	0	1 (33.3)	1 (1.3)
Investigations	**臨床検査**	**7 (28.0)**	**7 (28.0)**	**0**	**1 (50.0)**	**3 (16.7)**	**0**	**18 (23.7)**
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Blood creatinine increased	血中クレアチニン増加	1 (4.0)	0	0	0	0	0	1 (1.3)
Blood lactate dehydrogenase increased	血中乳酸脱水素酵素増加	0	2 (8.0)	0	0	0	0	2 (2.6)

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Blood pressure increased	血圧上昇	1 (4.0)	0	0	0	0	0	1 (1.3)
Blood urine present	尿中血陽性	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Cardiac murmur	心雑音	0	0	0	1 (50.0)	0	0	1 (1.3)
Electrocardiogram PR prolongation	心電図ＰＲ延長	1 (4.0)	0	0	0	0	0	1 (1.3)
Electrocardiogram QT prolonged	心電図ＱＴ延長	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Enterobacter test positive	エンテロバクター検査陽性	0	0	0	0	1 (5.6)	0	1 (1.3)
Heart rate increased	心拍数増加	1 (4.0)	0	0	0	0	0	1 (1.3)
Liver palpable	肝触知	0	1 (4.0)	0	0	0	0	1 (1.3)
Urine output increased	尿量増加	0	1 (4.0)	0	0	0	0	1 (1.3)
Weight decreased	体重減少	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Weight increased	体重増加	0	0	0	0	1 (5.6)	0	1 (1.3)
Metabolism and nutrition disorders	**代謝および栄養障害**	**4 (16.0)**	**6 (24.0)**	**0**	**0**	**3 (16.7)**	**0**	**13 (17.1)**
Cachexia	悪液質	0	1 (4.0)	0	0	0	0	1 (1.3)
Decreased appetite	食欲減退	4 (16.0)	6 (24.0)	0	0	2 (11.1)	0	12 (15.8)
Hyperkalaemia	高カリウム血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Hyperuricaemia	高尿酸血症	0	0	0	0	1 (5.6)	0	1 (1.3)
Hypoalbuminaemia	低アルブミン血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Hypocalcaemia	低カルシウム血症	0	0	0	0	1 (5.6)	0	1 (1.3)
Hypoglycaemia	低血糖症	0	0	0	0	1 (5.6)	0	1 (1.3)
Hyponatraemia	低ナトリウム血症	0	1 (4.0)	0	0	0	0	1 (1.3)
Musculoskeletal and connective tissue disorders	**筋骨格系および結合組織障害**	**18 (72.0)**	**15 (60.0)**	**3 (100.0)**	**1 (50.0)**	**12 (66.7)**	**1 (33.3)**	**50 (65.8)**
Arthralgia	関節痛	9 (36.0)	4 (16.0)	2 (66.7)	0	3 (16.7)	1 (33.3)	19 (25.0)
Arthritis	関節炎	0	1 (4.0)	0	0	0	0	1 (1.3)
Back pain	背部痛	4 (16.0)	9 (36.0)	2 (66.7)	0	7 (38.9)	1 (33.3)	23 (30.3)
Bone pain	骨痛	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)

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Bursitis	滑液包炎	1 (4.0)	0	0	0	0	0	1 (1.3)
Dupuytren's contracture	デュプイトラン拘縮	0	0	1 (33.3)	0	0	0	1 (1.3)
Exposed bone in jaw	顎骨露出	0	0	0	0	1 (5.6)	0	1 (1.3)
Flank pain	側腹部痛	3 (12.0)	0	0	0	0	0	3 (3.9)
Groin pain	鼠径部痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Joint lock	関節ロック	0	0	0	0	1 (5.6)	0	1 (1.3)
Joint stiffness	関節硬直	0	0	1 (33.3)	0	0	0	1 (1.3)
Joint swelling	関節腫脹	0	0	0	0	2 (11.1)	0	2 (2.6)
Muscle spasms	筋痙縮	0	1 (4.0)	1 (33.3)	0	2 (11.1)	0	4 (5.3)
Muscular weakness	筋力低下	2 (8.0)	0	0	1 (50.0)	3 (16.7)	0	6 (7.9)
Musculoskeletal chest pain	筋骨格系胸痛	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Musculoskeletal pain	筋骨格痛	3 (12.0)	0	0	0	1 (5.6)	0	4 (5.3)
Myalgia	筋肉痛	2 (8.0)	1 (4.0)	0	0	0	0	3 (3.9)
Neck pain	頚部痛	0	1 (4.0)	0	0	2 (11.1)	0	3 (3.9)
Osteoarthritis	変形性関節症	0	0	0	0	1 (5.6)	0	1 (1.3)
Pain in extremity	四肢痛	2 (8.0)	2 (8.0)	0	0	0	1 (33.3)	5 (6.6)
Pain in jaw	顎痛	1 (4.0)	0	0	0	0	0	1 (1.3)
Pathological fracture	病的骨折	0	1 (4.0)	0	0	0	0	1 (1.3)
Spinal pain	脊椎痛	0	0	1 (33.3)	0	0	1 (33.3)	2 (2.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**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)**	**2 (8.0)**	**1 (33.3)**	**0**	**1 (5.6)**	**0**	**5 (6.6)**
Bowen's disease	ボーエン病	0	0	0	0	1 (5.6)	0	1 (1.3)
Cancer pain	癌疼痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Meningioma	髄膜腫	0	1 (4.0)	0	0	0	0	1 (1.3)
Metastases to liver	肝転移	1 (4.0)	0	0	0	0	0	1 (1.3)
Prostate cancer	前立腺癌	1 (4.0)	0	0	0	0	0	1 (1.3)
Rectal adenocarcinoma	直腸腺癌	0	0	1 (33.3)	0	0	0	1 (1.3)

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Nervous system disorders	**神経系障害**	**9 (36.0)**	**13 (52.0)**	**2 (66.7)**	**2 (100.0)**	**5 (27.8)**	**1 (33.3)**	**32 (42.1)**
Ageusia	味覚消失	0	1 (4.0)	0	0	0	0	1 (1.3)
Areflexia	反射消失	0	1 (4.0)	0	0	0	0	1 (1.3)
Cerebral ischaemia	脳虚血	0	1 (4.0)	0	0	0	0	1 (1.3)
Dizziness	浮動性めまい	1 (4.0)	3 (12.0)	1 (33.3)	0	0	1 (33.3)	6 (7.9)
Headache	頭痛	2 (8.0)	3 (12.0)	0	0	1 (5.6)	1 (33.3)	7 (9.2)
Hypoaesthesia	感覚鈍麻	0	1 (4.0)	0	0	0	0	1 (1.3)
Hyporeflexia	反射減弱	0	0	0	1 (50.0)	0	0	1 (1.3)
Lethargy	嗜眠	2 (8.0)	0	0	0	1 (5.6)	0	3 (3.9)
Monoparesis	不全単麻痺	1 (4.0)	0	0	0	0	0	1 (1.3)
Neuropathy peripheral	末梢性ニューロパチー	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Paraesthesia	錯感覚	0	0	1 (33.3)	0	1 (5.6)	0	2 (2.6)
Paraplegia	対麻痺	0	1 (4.0)	0	0	0	0	1 (1.3)
Petit mal epilepsy	小発作てんかん	0	1 (4.0)	0	0	0	0	1 (1.3)
Presyncope	失神寸前の状態	0	0	1 (33.3)	0	0	0	1 (1.3)
Sciatica	坐骨神経痛	0	2 (8.0)	0	1 (50.0)	0	0	3 (3.9)
Somnolence	傾眠	1 (4.0)	1 (4.0)	0	0	1 (5.6)	0	3 (3.9)
Syncope	失神	1 (4.0)	0	0	0	0	0	1 (1.3)
Tremor	振戦	1 (4.0)	0	0	0	0	0	1 (1.3)
Psychiatric disorders	**精神障害**	**5 (20.0)**	**4 (16.0)**	**0**	**0**	**2 (11.1)**	**1 (33.3)**	**12 (15.8)**
Affective disorder	感情障害	0	0	0	0	1 (5.6)	0	1 (1.3)
Alcohol abuse	アルコール乱用	1 (4.0)	0	0	0	0	0	1 (1.3)
Confusional state	錯乱状態	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Depression	うつ病	2 (8.0)	0	0	0	0	0	2 (2.6)
Insomnia	不眠症	3 (12.0)	4 (16.0)	0	0	1 (5.6)	0	8 (10.5)
Sleep disorder	睡眠障害	0	0	0	0	0	1 (33.3)	1 (1.3)
Renal and urinary disorders	**腎および尿路障害**	**7 (28.0)**	**10 (40.0)**	**1 (33.3)**	**1 (50.0)**	**8 (44.4)**	**0**	**27 (35.5)**
Acute kidney injury	急性腎不全	2 (8.0)	0	0	0	0	0	2 (2.6)
Bladder dilatation	膀胱拡大	0	0	0	0	1 (5.6)	0	1 (1.3)
Calculus urinary	尿路結石	0	1 (4.0)	0	0	0	0	1 (1.3)

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Dysuria	排尿困難	0	1 (4.0)	1 (33.3)	0	1 (5.6)	0	3 (3.9)
Haematuria	血尿	4 (16.0)	1 (4.0)	0	0	2 (11.1)	0	7 (9.2)
Haemorrhage urinary tract	尿路出血	0	1 (4.0)	0	0	0	0	1 (1.3)
Hydronephrosis	水腎症	1 (4.0)	2 (8.0)	0	0	1 (5.6)	0	4 (5.3)
Lower urinary tract symptoms	下部尿路症状	1 (4.0)	0	0	0	0	0	1 (1.3)
Micturition frequency decreased	排尿回数減少	0	1 (4.0)	0	0	0	0	1 (1.3)
Micturition urgency	尿意切迫	0	0	0	0	1 (5.6)	0	1 (1.3)
Nocturia	夜間頻尿	2 (8.0)	0	0	0	0	0	2 (2.6)
Pollakiuria	頻尿	0	2 (8.0)	0	0	1 (5.6)	0	3 (3.9)
Urethral stenosis	尿道狭窄	0	0	0	0	1 (5.6)	0	1 (1.3)
Urinary incontinence	尿失禁	0	1 (4.0)	0	1 (50.0)	3 (16.7)	0	5 (6.6)
Urinary retention	尿閉	0	1 (4.0)	0	0	2 (11.1)	0	3 (3.9)
Urinary tract inflammation	尿路の炎症	0	0	1 (33.3)	0	0	0	1 (1.3)
Reproductive system and breast disorders	**生殖系および乳房障害**	**5 (20.0)**	**3 (12.0)**	**0**	**1 (50.0)**	**3 (16.7)**	**1 (33.3)**	**13 (17.1)**
Breast tenderness	乳房圧痛	0	1 (4.0)	0	0	0	0	1 (1.3)
Erectile dysfunction	勃起不全	1 (4.0)	0	0	0	0	0	1 (1.3)
Gynaecomastia	女性化乳房	1 (4.0)	2 (8.0)	0	1 (50.0)	2 (11.1)	1 (33.3)	7 (9.2)
Pelvic pain	骨盤痛	2 (8.0)	1 (4.0)	0	0	1 (5.6)	0	4 (5.3)
Penile oedema	陰茎浮腫	1 (4.0)	0	0	0	0	0	1 (1.3)
Respiratory, thoracic and mediastinal disorders	**呼吸器、胸郭および縦隔障害**	**7 (28.0)**	**7 (28.0)**	**0**	**1 (50.0)**	**5 (27.8)**	**1 (33.3)**	**21 (27.6)**
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	0	1 (4.0)	0	0	0	0	1 (1.3)
Cough	咳嗽	1 (4.0)	1 (4.0)	0	1 (50.0)	1 (5.6)	0	4 (5.3)
Dyspnoea	呼吸困難	4 (16.0)	1 (4.0)	0	1 (50.0)	0	0	6 (7.9)
Dyspnoea exertional	労作性呼吸困難	0	1 (4.0)	0	0	0	0	1 (1.3)
Epistaxis	鼻出血	1 (4.0)	1 (4.0)	0	0	1 (5.6)	1 (33.3)	4 (5.3)
Oropharyngeal pain	口腔咽頭痛	0	0	0	0	1 (5.6)	0	1 (1.3)

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）（続き）

MedDRA SOC PT (Ver.18.0)	器官別大分類 基本語	100mg b.i.d. (N=25) n (%)	200mg b.i.d. (N=25) n (%)	300mg b.i.d. (N=3) n (%)	500mg b.i.d. (N=2) n (%)	700mg b.i.d.[a] (N=18) n (%)	900mg b.i.d. (N=3) n (%)	Total (N=76) n (%)
Pharyngeal erythema	咽頭紅斑	0	1 (4.0)	0	0	0	0	1 (1.3)
Pleural effusion	胸水	0	0	0	0	1 (5.6)	0	1 (1.3)
Pulmonary embolism	肺塞栓症	1 (4.0)	0	0	0	0	0	1 (1.3)
Rales	ラ音	0	1 (4.0)	0	0	1 (5.6)	0	2 (2.6)
Rhinorrhoea	鼻漏	0	0	0	0	1 (5.6)	0	1 (1.3)
Sleep apnoea syndrome	睡眠時無呼吸症候群	0	1 (4.0)	0	0	0	0	1 (1.3)
Wheezing	喘鳴	1 (4.0)	0	0	0	0	0	1 (1.3)
Skin and subcutaneous tissue disorders	**皮膚および皮下組織障害**	**5 (20.0)**	**5 (20.0)**	**2 (66.7)**	**1 (50.0)**	**5 (27.8)**	**1 (33.3)**	**19 (25.0)**
Actinic keratosis	日光角化症	0	1 (4.0)	0	0	0	0	1 (1.3)
Angioedema	血管浮腫	0	0	0	0	1 (5.6)	0	1 (1.3)
Dry skin	皮膚乾燥	2 (8.0)	1 (4.0)	0	0	0	0	3 (3.9)
Erythema	紅斑	1 (4.0)	0	1 (33.3)	1 (50.0)	0	0	3 (3.9)
Hyperhidrosis	多汗症	0	0	0	0	1 (5.6)	0	1 (1.3)
Nail discolouration	爪変色	0	0	1 (33.3)	0	0	0	1 (1.3)
Night sweats	寝汗	1 (4.0)	1 (4.0)	0	0	0	0	2 (2.6)
Onychoclasis	爪破損	0	1 (4.0)	0	0	0	0	1 (1.3)
Pruritus	そう痒症	1 (4.0)	0	0	0	0	0	1 (1.3)
Rash	発疹	1 (4.0)	0	1 (33.3)	0	2 (11.1)	1 (33.3)	5 (6.6)
Skin atrophy	皮膚萎縮	0	0	0	0	1 (5.6)	0	1 (1.3)
Skin lesion	皮膚病変	0	1 (4.0)	0	0	0	0	1 (1.3)
Urticaria	蕁麻疹	0	0	0	0	1 (5.6)	0	1 (1.3)
Vascular disorders	**血管障害**	**9 (36.0)**	**7 (28.0)**	**1 (33.3)**	**1 (50.0)**	**4 (22.2)**	**2 (66.7)**	**24 (31.6)**
Aortic arteriosclerosis	大動脈硬化症	0	0	0	1 (50.0)	0	0	1 (1.3)
Circulatory collapse	循環虚脱	1 (4.0)	0	0	0	0	0	1 (1.3)
Deep vein thrombosis	深部静脈血栓症	1 (4.0)	0	1 (33.3)	0	0	0	2 (2.6)
Flushing	潮紅	1 (4.0)	0	0	0	1 (5.6)	0	2 (2.6)
Hot flush	ほてり	1 (4.0)	3 (12.0)	0	0	2 (11.1)	1 (33.3)	7 (9.2)
Hypertension	高血圧	3 (12.0)	2 (8.0)	1 (33.3)	0	3 (16.7)	0	9 (11.8)
Intermittent claudication	間欠性跛行	1 (4.0)	0	0	0	0	0	1 (1.3)

付表 2.7.6.10.a.1-1 治験薬投与開始から本試験の終了来院時までに発現した有害事象（SAF）（続き）

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Lymphoedema	リンパ浮腫	0	1 (4.0)	1 (33.3)	0	0	1 (33.3)	3 (3.9)
Lymphostasis	リンパうっ滞	0	1 (4.0)	0	0	0	0	1 (1.3)
Orthostatic hypotension	起立性低血圧	1 (4.0)	0	0	0	0	0	1 (1.3)
Pelvic venous thrombosis	骨盤静脈血栓症	0	1 (4.0)	0	0	0	0	1 (1.3)
Poor peripheral circulation	末梢循環不良	0	0	0	0	1 (5.6)	0	1 (1.3)
Superficial vein prominence	表在静脈隆起	0	1 (4.0)	0	0	0	0	1 (1.3)

a: Dose changed for 1 patient at month 28 from 700mg to 600mg b.i.d. due to change from the capsule to tablet formulation.

Source : 5.3.5.2.1 R-11102/Table 14.3.1.1.3, 14.3.1.2.1.3