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略号一覧

記号	日本語	英語
ALP	アルカリホスファターゼ	Alkaline phosphatase
ALT	アラニンアミノトランスフェラーゼ	Alanine aminotransferase, equivalent to SGPT
AST	アスパラギン酸アミノトランスフェラーゼ	Aspartate aminotransferase, equivalent to SGOT
BMI	体格指数	Body mass index
BUN	血中尿素窒素	Blood urea nitrogen
CRP	C 反応性タンパク	C-reactive protein
CSR	臨床試験総括報告書	Clinical Study Report
CT	コンピューター断層撮影	Computed tomography
GGT	γ-グルタミルトランスフェラーゼ	Gamma-glutamyl transferase
GLP-2	グルカゴン様ペプチド 2	Glucagon-like peptide-2
ICF	同意説明文書	Informed consent form
IDB	統合データベース	Integrated Data Base
IFALD	腸管不全関連肝疾患	Intestinal failure-associated liver disease
ITT	-	Intent-to-Treat
MedDRA	ICH 国際医薬用語集	Medical Dictionary for Regulatory Activities
NTT	テデュグルチド無投与	No-teduglutide treatment
NT, PBO/TED	-	Not treated, placebo/teduglutide group
PBO/TED	-	Placebo/teduglutide group
PK	薬物動態	Pharmacokinetic
PN	経静脈栄養	Parenteral nutrition: includes fluids and electrolytes, and may include energy and micronutrients
PS	経静脈サポート	Parenteral support (also see PN and PN/IV)
QTcF	Fridericia 補正式による補正 QT 間隔	Corrected QT interval using Fridericia’s formula
SAP	統計解析計画書	Statistical analysis plan
SBS	短腸症候群	Short bowel syndrome
SD	標準偏差	Standard deviation
SOC	器官別大分類	System organ class
TED/TED	-	Teduglutide treated group

要旨

本臨床的安全性の概要では、短腸症候群（SBS）患者におけるテデュグルチドの安全性を評価することを目的として、臨床開発プログラムから得られた安全性情報の解析結果を示す。本申請では、成人及び小児 SBS 患者を対象として海外及び国内で実施された第 3 相試験データの解析に焦点を合わせる。また、その他の試験で得られた参考的データも適宜参照する。

重要な安全性所見

- 2020 年 10 月の申請時、テデュグルチドの臨床開発プログラムには臨床試験 27 試験が含まれ、その内訳は第 3 相試験 15 試験、第 2 相試験 3 試験及び第 1 相試験 9 試験であった。このうち、第 3 相試験 5 試験（成人患者を対象とした 3 試験及び小児患者を対象とした 2 試験）は、日本人 SBS 患者のみを対象に実施された。この他にレジストリ試験 1 試験が実施中であるが、日本は未参加である。
- 全体として、この臨床開発プログラムにおいて被験者 718 例がテデュグルチドの投与を受け、うち 613 例が成人、105 例が小児であった。その内訳は以下の通り。
    - 海外試験でテデュグルチドを投与された被験者は 690 例であり、うち 595 例が成人、90 例が小児、5 例が乳児であった。
    - 国内試験でテデュグルチドを投与された被験者は 28 例であり、うち 18 例が成人、8 例が小児、2 例が乳児であった。
- 臨床開発プログラムの対象集団の人口統計学的特性、病歴、及び疾患特性は、本申請で対象予定とする集団（日本人 SBS 患者）を代表するものであった。
- 全体として、発現頻度の最も高かった器官別大分類（SOC）は、「胃腸障害」、「感染症および寄生虫症」、「一般・全身障害および投与部位の状態」であった。これらの SOC に分類される有害事象に新たな傾向や予期しない傾向は認められず、海外試験と国内試験で一貫していた。有害事象の重症度の多くは軽度又は中等度であった。治験薬と関連ありと判断された有害事象のうち、発現頻度が最も高かったのは、腹痛、腹部膨満、悪心、嘔吐等の消化器系の有害事象及び注射部位の紅斑、挫傷、腫脹等の注射部位の有害事象であった。有害事象の多くは非重篤であった。
- 全体として、重篤な有害事象の発現割合が最も高かった SOC は、「感染症および寄生虫症」であった。重篤な有害事象の多くは 1 例に発現した単発の事象であった。治験薬と関連ありとされた重篤な有害事象の SOC には大きなばらつきがあり、経静脈サポート（PS）に使用された中心静脈カテーテルに関連したデバイス関連の感染を除いて、何らかの傾向は認められなかった。PS の投与による感染症は、SBS 患者が一般に経験する重篤な合併症である。
- 医療機器関連の有害事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連した合併症ではなかった。
- 特に注目すべき有害事象の検討において、臨床プログラムの試験全体で、消化管及び肝胆道系の腫瘍の成長、良性腫瘍及び悪性腫瘍の発現は認められず、さらに国内試験で

も、成人及び小児試験のいずれにおいても、腫瘍の成長、良性腫瘍及び悪性腫瘍の発現は認められなかった。

- 臨床プログラムの試験全体で、曝露量が増加しても有害事象の発現頻度は増加しないことから、テデュグルチドの経時的な忍容性が良好であることが示唆された。
- 2020 年 10 月申請時のデータでは、臨床開発プログラム全体の各試験のデータカットオフ時点で死亡例は 6 例であった。
    - CL0600 004 試験では、5[redacted]歳の白人女性が無作為化及び治験薬投与開始前に死亡した。
    - CL0600-021 試験では、6[redacted]歳の白人男性がテデュグルチド投与開始後約 7 ヵ月に非小細胞肺癌により死亡した。
    - 同 CL0600-021 試験において、ホジキン病歴のある 4[redacted]歳男性が治験薬投与開始後約 11 ヵ月に腸癌の全身性増悪（転移性腺癌）により死亡した。
    - 同 CL0600-021 試験において、6[redacted]歳男性が治験薬投与開始後約 28 ヵ月に敗血症により死亡した。
    - TED-C14-004 試験では、3[redacted]歳日本人男性が治験薬投与開始後約 2 ヵ月に急性肝不全及び急性腎不全により死亡した。
    - SHP633-304 試験では、1[redacted]歳白人男性が治験薬投与開始後約 11 ヵ月に SBS の悪化により死亡した。
- 臨床プログラムの試験全体で、臨床検査値、バイタルサイン、体重／体格指数（BMI）、抗テデュグルチド抗体に臨床的に意味のある変化は認められなかった。
- 抗テデュグルチド抗体を検討したところ、抗テデュグルチド抗体の有無と過敏症の有害事象との間に関連は認められず、全ての注射部位反応の重症度は軽度、非重篤であり、投与中止に至ったものはなかった。
- 全ての安全性情報を試験別に評価するとともに、年齢（小児 SBS 患者）及び人種（日本人 SBS 患者）に基づく部分集団別にも評価した。これらの部分集団内で有害事象又は重篤な有害事象の頻度、重症度、又は因果関係に異なる傾向はみられず、その結果は SBS 患者全体でのテデュグルチドの安全性評価と同様であった。
- 全試験における安全性データを総合的に検討した結果、海外試験と国内試験の間に新たな傾向や予測できない懸念は認められなかった。

参考となる市販後安全性情報

- テデュグルチドの市販後の安全性情報は、本文書に示す臨床開発プログラムから得られた海外及び国内のデータと同様であった。
- SBS 患者を対象とした実施中のレジストリ試験で得られた安全性情報は、本文書に記載した海外及び国内試験結果と同様であった。
- クローン病患者におけるテデュグルチドの評価から得られた安全性情報は、本文書に記載した海外及び国内試験結果と同様であった。

- 臨床薬理試験から得られた安全性情報は、本文書に記載した海外及び国内試験結果と同様であった。

1. 医薬品への曝露

1.1　総括的安全性評価計画及び安全性試験の記述

1.1.1　　安全性解析計画

本臨床的安全性の概要では、日本人 SBS 患者におけるテデュグルチドの安全性を評価するうえで重要なテデュグルチドに対する臨床試験の安全性情報を示す。

本概要に記載されている内容は、2020 年 10 月申請時現在のものであり、SHP633-305 試験の中間解析のデータ及び SHP633-301 試験の最終解析のデータのみ更新した。テデュグルチドの安全性は海外 SBS 成人患者及び小児患者、クローン病患者、健康成人及び日本人の SBS 成人患者及び小児患者で検討された。全 27 試験の臨床試験の内訳は、第 3 相試験 15 試験、第 2 相試験 3 試験及び第 1 相試験 9 試験であり、うち第 3 相試験 5 試験（成人試験：3 試験、小児試験：2 試験）は日本人 SBS 患者のみを対象に行われた。この他にレジストリ試験 1 試験が実施中であるが、日本は未参加である。

27 試験のテデュグルチド臨床試験全てのデータを本臨床的安全性の概要に示す。本ガイドラインでは、日本人におけるテデュグルチドの安全性を評価する上で最も適切なデータ、具体的には、本概要 1.1.1.1 及び 1.1.1.2 に記載した成人及び小児の SBS 患者を対象とした海外及び国内第 3 相臨床試験並びにそれらの継続投与試験のデータに焦点を当てる。

Age Group	**Region**	**Completed**		**Ongoing**		
		Phase 3	**Phase 1 or 2**	**Phase 3**	**Phase 1 or 2**	
Adults	Overseas	5	12	0	0	20
	Japan	2	0	1	0	
Pediatrics	Overseas	3	0	2	0	7
	Japan	1	0	1	0	
Total		**11**	**12**	**4**	**0**	**27[1]**

[1] In addition, there is an ongoing, non-interventional global registry study (Study TED-R13-002) that does not currently have sites in Japan.

以下の項では、臨床試験の概要とそのデータ解析法、及び本文書での記載法を示す。特に明記しない限り、全ての試験は完了済みの試験である。各試験の概要については 2.7.6 項を参照のこと。2.7.6 項に、主要な試験デザインの特徴及び試験結果の記述的要約が記載されている。また、本文書に示す安全性情報の収集及び解析に関する情報については、完了した各試験の個々の臨床試験総括報告書（CSR）及び本概要 1.1.1.5 を参照のこと。

テデュグルチド臨床開発プログラムの一部のデータは統合されている。本概要 1.1.1.1、1.1.1.2 及び 1.1.1.3 に特に記載のない限り、本臨床的安全性では全てのデータを試験別に示す。

得られたコア試験のデータは本文及び表で示し、継続投与試験のデータは本文のみで示す。

各試験を通じて、試験デザインの違いにより、異なる方法で解析されている場合がある。例えば、過去の試験でのテデュグルチド無投与（NTT）期間の有無、複数の投与サイクル、又はコア試験で受けた投与（継続投与試験に移行した被験者における先行したコア試験でのプラセボ投与など）に応じて被験者データを解析した場合がある。また、3 ヵ月ごとの有害事象発現時期については一部の試験で解析し、記載した。

最後に、PS という用語は、試験間で異なる意味で使用されたが、本臨床的安全性の概要の目的上、PS は経静脈栄養（PN）及び経静脈栄養／補液（PN/IV）を示し、各試験から引用した表、図及び一覧表ではこれらの略語を使用する。

1.1.1.1　　成人の臨床試験データ

本項では、成人の臨床試験の概要とそのデータ解析法、及び本文書での記載法を示す。

成人を対象とした海外第 3 相コア試験

- 第 3 相プラセボ対照試験 2 試験（CL0600-020 試験［5.3.5.1 項］及び CL0600-004 試験［5.3.5.1 項］）

本概要 1.1.1.3 で述べたとおり、海外成人試験はテデュグルチドの海外での最初の製造販売承認申請（2014 年）のために、統合解析（部分集団解析を含む）を行った。成人を対象とした海外第 3 相コア試験のデータは、利用可能な場合には Overseas Phase 3 Adult Core data（Adult ISS）として統合して又は試験別に示す。

コア試験のデータは、本文及び表（表が利用可能な場合）として示す。Adult ISS の統計解析計画書（SAP）は 5.3.5.3 項に示す。

成人を対象とした海外第 3 相継続投与試験

- 長期継続投与試験 2 試験（CL0600-021 試験［5.3.5.2 項］及び CL0600-005 試験［5.3.5.2 項］）

本概要 1.1.1.3 で述べたとおり、CL0600-021 及び CL0600-005 試験のデータを統合した。統合データが利用可能な場合には統合して本文書に示し、それ以外の場合は試験別に示す。

- 12 ヵ月継続投与試験 1 試験（TED-C11-001 試験［5.3.5.2 項］）

TED-C11-001 試験のデータは統合しなかったため、本文書では独立したデータとして示す。

成人を対象とした国内第 3 相コア試験

- 非盲検第 3 相試験 1 試験（SHP633-306 試験［5.3.5.2 項］）
- 24 週間非盲検第 3 相試験 1 試験（TED-C14-004 試験［5.3.5.2 項］のステージ 2（ステージ 3 及び 4 は継続投与期間であり、別に記載する）

SHP633-306 試験、SHP633-307 試験及び TED-C14-004 試験については曝露状況、有害事象の概要及び有害事象発現時期についてデータを統合し、記載する。

それ以外で SHP633-306 試験及び TED-C14-004 試験のデータは独立したデータとして本文及び表（表が利用可能な場合）を示す。本試験の解析の大部分はステージ 2 のみの解析も行ったため、

これを文章で示した。ステージ 2 のみの解析も行わなかった場合は、継続投与期間の項の試験全体のデータを参照することとした。

成人を対象とした国内第 3 相継続投与試験

- 実施中の非盲検継続投与試験 1 試験（SHP633-307 試験［5.3.5.2 項］）
- 非盲検第 3 相試験 TED-C14-004 試験（5.3.5.2 項）の継続投与期間（ステージ 3 及び 4）

SHP633-306 試験、SHP633-307 試験及び TED-C14-004 試験については曝露状況、有害事象の概要及び有害事象発現時期についてデータを統合し、記載する。
SHP633-307 試験及び TED-C14-004 試験のデータは独立したデータとして示す。TED-C14-004 試験の解析の大部分は、継続投与期間単独での解析は行わなかった。したがって、本文では、コア試験のデータを参照するか、又は試験全体のデータを示す。

1.1.1.2　　小児の臨床試験データ

本項では、小児の臨床試験の概要とそのデータ解析法、及び本文書での記載法を示す。
本概要 1.1.1.3 で述べたとおり、小児 SBS 患者に対するテデュグルチドの海外での製造販売承認申請（2018 年）のために、海外小児試験の統合解析（部分集団解析を含む）を行った。

小児を対象とした海外第 3 相コア試験

- 非盲検第 3 相試験 2 試験（TED-C13-003 試験［5.3.5.2 項］及び TED-C14-006 試験［5.3.5.2 項］）

統合データが利用可能な場合には本文中に示し、これを Overseas Pediatric IDB（Pediatric ISS）とする。コア試験のデータは、本文及び表（表が利用可能な場合）として示す。Pediatric ISS SAP は 5.3.5.3 項に示す。

小児を対象とした海外第 3 相継続投与試験

- 実施中の継続投与試験 2 試験（SHP633-304 試験［5.3.5.2 項］及び SHP633-303 試験［5.3.5.2 項］［前向き期間のみ］）

本概要 1.1.1.3 で述べたとおり、統合データが利用可能な場合には本文中に示す。SHP633-304 試験のカットオフ日は 2018 年 2 月 2 日であり、SHP633-303 試験のカットオフ日は 2018 年 1 月 12 日であった。小児統合データの SAP は 5.3.5.3 項に示す。

乳児を対象とした海外試験

- 無作為化第 3 相試験 1 試験（SHP633-301 試験［5.3.5.2 項、5.3.5.2 項（final）］）

SHP633-301 試験のデータは統合しなかったため、本文書では独立したデータとして示す。

小児を対象とした国内第 3 相コア試験

- 非盲検第 3 相試験 1 試験（SHP633-302 試験［5.3.5.2 項］）

SHP633-302 試験のデータは、以下に記載した場合を除き統合しなかったため本文書では独立したデータとして示す。

小児を対象とした国内第 3 相継続投与試験

- 実施中の継続投与試験 1 試験（SHP633-305 試験［5.3.5.2 項］）

SHP633-305 試験は現在実施中であり、2020 年 4 月 15 日（小児）及び 2020 年 7 月 14 日（乳児）をデータカットオフ日とした、全例（小児コホート 7 例及び乳児コホート 2 例）の 6 ヵ月以上のデータを含む中間解析データを本文書に示す。
SHP633-302 試験及び SHP633-305 試験について、曝露状況、有害事象の概要及び有害事象発現時期についてデータを統合し、記載する。また、これらのデータを試験ごとにも示した。

1.1.1.3　　臨床試験統合データ

本項では、テデュグルチドの臨床開発プログラムから得られた統合データ及び組み入れた集団を示す。これは以前の項と重複している可能性があるが、ここでは明確にするために提示する。

1.1.1.3.1　　成人統合データ

海外第 3 相成人データ

テデュグルチドの最初の海外での製造販売承認申請（2014 年）のため、成人を対象とした臨床試験 17 試験の安全性データを統合した。その後、さらに複数の試験が完了しているため、これらの統合データは本文書に主要なデータソースとして提示せず、本概要 5 の特別な集団及び状況下における安全性の解析に主に用いる。また、部分集団解析を実施し、第 3 相コア試験及びその継続投与試験等の解析結果を示す。部分集団統合データについては本概要 1.1.1.1 に記載する。

Overseas Adult IDB から得られた解析は、本文書では Adult ISS と記載し、参照する。Overseas Adult IDB の SAP は 5.3.5.3 項に記載した。

本文書の部分集団解析に用いた集団を表 2.7.4 - 1 に示す。

表 2.7.4 - 1　海外成人統合データベースに含めた集団

Population	Abbreviation	Studies Included	Total Patients in Population
Overseas Adult Integrated Database Safety Population	Overseas Adult IDB	16 studies total: • Studies CL0600-020 and CL0600-004 (placebo-controlled) • Studies CL0600-005 and CL0600-021 (open-label extension studies)	684 total subjects: • 595 treated with teduglutide • 229 treated with placebo

表 2.7.4 - 1　海外成人統合データベースに含めた集団

Population	Abbreviation	Studies Included	Total Patients in Population
		• Studies CL0600-008 and CL0600-009 (Crohn's disease) • Studies CL0600-006, CL0600-015, 1621/13, C09-001, CL0600-017, CL0600-018, CL0600-022, C10-003, ALX-0600-92001, TED-C10-004 (clinical pharmacology studies)	
SBS Efficacy and Safety Studies	Overseas Adult SESS IDB	• CL0600-020 and CL0600-004 (placebo-controlled) • CL0600-005 and CL0600-021 (open-label extension studies)	232 total subjects: • 173 treated with teduglutide • 59 treated with placebo
SBS Placebo-Controlled Studies	Overseas Adult Core IDB	• CL0600-020 and CL0600-004 (placebo-controlled)	168 total subjects: • 109 treated with teduglutide • 59 treated with placebo

成人を対象とした日本人第 3 相コア試験及び継続投与試験の統合データ

コア試験である TED-C14-004 試験及び SHP633-306 試験並びにこれらの継続投与試験である SHP633-307 試験について曝露状況及び有害事象の概要及び有害事象発現時期のデータを統合した（本概要 1.1.1.1）。

1.1.1.3.2　小児統合データ

海外第 3 相小児データ

TED-C13-003 試験及び TED-C14-006 試験並びに SHP633-304 試験及び SHP633-303 試験（前向き期間）のデータを統合した（本概要 1.1.1.2）。Pediatric IDB SAP は 5.3.5.3 項に示す。

小児を対象とした日本人第 3 相コア試験及び継続投与試験の統合データ

SHP633-302 試験及び SHP633-305 試験について、曝露状況、有害事象の概要及び有害事象発現時期のデータを統合した（本概要 1.1.1.2 項）。

1.1.1.4　参考となる安全性情報

以下の安全性情報を本文中に要約及び／又は相互参照する。

- テデュグルチドの市販後の安全性情報は、本文書に示す海外及び国内のデータと同様であった。これらのデータを要約し、本概要 6.1 に示す。
- 実施中の SBS 患者レジストリ試験（TED-R13-002 試験、5.3.6.2 項）から得られた安全性情報は、本文書に示す海外及び国内のデータと同様であった。これらのデータを要約し、本概要 6.3 に示す。

- クローン病患者を対象とした第 2 相 CL0600-008 試験（5.3.5.4 項）及び非盲検 12 週間継続投与試験 CL0600-009 試験（5.3.5.4 項）で得られたテデュグルチドの安全性情報は、本文書に示す海外及び国内のデータと同様であり、裏付けとなるが、本文書には要約しない。これらの試験の安全性情報は Adult ISS に統合した。個々の試験結果及び IDB の結果については、CSR 及び IDB を参照のこと。
- 臨床薬理試験（CL0600-006 試験［5.3.1.1 項］、CL0600-015 試験［5.3.1.2 項］、1621/13 試験［5.3.3.1 項］、C09-001 試験［5.3.4.1 項］、CL0600-017 試験［5.3.3.3 項］、CL0600-018 試験［5.3.3.3 項］、CL0600-022 試験［5.3.3.1 項］、C10-003 試験［5.3.4.1 項］、ALX-0600-92001 試験［5.3.4.2 項］、TED-C10-004 試験［5.3.4.1 項］）から得られた安全性情報は、本文書に示す海外及び国内のデータと同様であり、裏付けとなるが、本文書には要約しない。これらの試験の安全性情報は Adult ISS に含めた。個々の試験結果及び IDB の結果については、CSR 及び IDB を参照のこと。

1.1.1.5　　安全性情報の収集方法及び解析

本項では、本文中に示すデータについて、各試験で使用した安全性情報の収集及び解析方法の概要及び参照先を示す。収集及び解析方法は試験間で大きく異なる場合があったが、これは臨床開発プログラムが長期間にわたるためである。収集及び解析方法の詳細については CSR を参照のこと。統計手法の詳細については、統合統計解析計画書及び各 CSR に添付されている統計解析計画書を参照のこと。本概要ではこれらについて相互参照を示す。

本臨床的安全性の概要では、有害事象、臨床検査、バイタルサイン、12 誘導心電図、体重／BMI、及び抗テデュグルチド抗体の結果を示す。その他の安全性評価の結果については、各試験の CSR を参照のこと。

本文書に示す結果は、テデュグルチドの安全性の全般的評価に最も重要と考えられる結果である。詳細については、本文中の表の脚注及び各試験の CSR を参照のこと。

1.1.1.5.1　　成人の臨床試験データ

1.1.1.5.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）は治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性をプラセボと比較した二重盲検、無作為化、プラセボ対照、2 群並行群間比較、多施設国際共同、2 ステージ試験であった。被験者をプラセボ群又はテデュグルチド 0.05 mg/kg/日群に 1：1 の割合で無作為に割り付け、連日皮下投与した。Intent-to-Treat（ITT）集団にはテデュグルチド群 43 例及びプラセボ群 43 例が含まれた。本試験では、有害事象、心電図、バイタルサイン、臨床検査値、抗テデュグルチド抗体、並びに尿量及び体重の変化量を評価した。有害事象及び病歴は ICH 国際医薬用語集（MedDRA）ver.12.0 を用いてコード化した。

CL0600-004 試験（5.3.5.1 項）は治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性をプラセボと比較した二重盲検、無作為化、並行群間比較、プラセボ対照、多施設国際共同試験であった。被験者を、プラセボ群、テデュグルチド 0.05 mg/kg/日群又はテデュグルチド 0.10 mg/kg/日群に 1：2：2 の割合で無作為に割り付け、連日皮下投与した。ITT 集団はプラセボ群 16 例、テデュグルチド 0.05 mg/kg/日群 35 例、テデュグルチド 0.10 mg/kg/日群 32 例が含まれた。本試験では、有害事象、心電図、バイタルサイン、臨床検査値、抗テデュグルチド抗体、静脈カテーテル合併症、並びに尿量及び体重の変化量を評価した。有害事象及び病歴は MedDRA ver.7.0 を用いてコード化した。

これらの試験のデータを統合し、病歴及び有害事象を MedDRA ver.12.0 を用いてコード化した。統合解析計画については 5.3.5.3 項 IDB SAP を参照のこと。統合した安全性成績を「Adult ISS」として本文中に示す。

1.1.1.5.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）（CL0600-020 試験の継続投与試験）は治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した非盲検、多施設国際共同、長期継続投与試験であった。コア試験である CL0600-020 試験での投与群を問わず、全ての被験者に対してテデュグルチド 0.05 mg/kg/日を連日皮下投与した。ITT 集団には 88 例が含まれ、全例が 1 回以上の治験薬を投与された。本試験では、有害事象、心電図、バイタルサイン、体重及び BMI、臨床検査値、身体所見、48 時間尿量及び 48 時間経口水分摂取量、抗テデュグルチド抗体、並びに試験終了時の大腸内視鏡検査所見を評価した。有害事象及び病歴は MedDRA ver.12.0 を用いてコード化した。CL0600-021 試験（5.3.5.2 項）の被験者はコア試験での投与群により、以下の 2 群に分類して解析した。

- TED/TED 群：CL0600-020 試験でテデュグルチドを 24 週間投与された
- NT, PBO/TED 群：CL0600-020 試験でプラセボを投与された又は CL0600-020 試験で組入れに適格であったが目標被験者数を上回った後であったため CL0600-021 試験に直接組み入れられた

CL0600-005 試験（5.3.5.2 項）（CL0600-004 試験の継続投与試験）は治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した無作為化、二重盲検、非対照、並行群間比較、多施設国際共同、継続投与試験であった。被験者をテデュグルチド 0.05 mg/kg/日群又はテデュグルチド 0.10 mg/kg/日群に割り付け連日皮下投与した。ITT 集団（65 例）にはテデュグルチド 0.05 mg/kg/日群 31 例、テデュグルチド 0.10 mg/kg/日群 34 例が含まれた。本試験では、有害事象、心電図、バイタルサイン、体重、臨床検査値、48 時間尿量、48 時間経口水分摂取量、静脈カテーテル合併症がみられた被験者の例数及び割合、静脈カテーテル合併症の件数を評価した。有害事象及び病歴は MedDRA ver.7.0 を用いてコード化した。

これらの試験のデータを統合し、病歴及び有害事象を MedDRA ver.12.0 を用いてコード化した。統合解析計画については 5.3.5.3 項 IDB SAP を参照のこと。統合した安全性データは、Adult ISS として本文中に示す。

TED-C11-001 試験（5.3.5.2 項）は、CL0600-020 試験及び CL0600-021 試験を完了した被験者を対象に、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した非盲検、多施設共同、継続投与試験であった。全ての被験者にテデュグルチド 0.05 mg/kg/日を連日皮下投与した。ITT 集団には被験者 14 例が含まれた。有害事象、心電図、バイタルサイン、体重、臨床検査値、48 時間尿量、48 時間経口水分摂取量、抗テデュグルチド抗体、大腸内視鏡検査所見、併用薬、病歴及び人口統計学的特性、静脈カテーテル合併症がみられた被験者の例数及び割合、並びに静脈カテーテル合併症の件数を評価した。有害事象は MedDRA ver.12.0 を用いてコード化した。本試験のデータは統合しなかったため、本文書では独立したデータとして示す。安全性解析計画については 5.3.5.2 項 TED-C11-001 CSR を参照のこと。被験者はコア試験での投与群により、以下の 3 群に分類して解析した。

- NT/TED 群：CL0600-020 試験で治験薬を投与されなかった
- PBO/TED 群：CL0600-020 試験でプラセボを投与された
- TED/TED 群：CL0600-020 試験でテデュグルチドを投与された

1.1.1.5.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）は治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した非盲検、多施設共同試験であった。ITT 集団にはテデュグルチド 0.05 mg/kg/日を連日皮下投与した 7 例が含まれた。有害事象、心電図、バイタルサイン、体重及び BMI、臨床検査値、48 時間尿量の変化、抗テデュグルチド抗体、大腸内視鏡検査所見、併用薬、病歴及び人口統計学的特性、腹部超音波検査所見、食道胃十二指腸内視鏡検査所見、並びに残存結腸の大腸内視鏡検査／S 状結腸内視鏡検査所見を評価した。有害事象は MedDRA ver.21.0 を用いてコード化した。SHP633-306 試験のデータは統合しなかったため、本文書では独立したデータとして示す。安全性解析計画については 5.3.5.2 項 SHP633-306 CSR を参照のこと。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）は、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した多施設共同、非盲検、4 ステージ継続投与試験であった。全ての被験者がテデュグルチド 0.05 mg/kg/日を連日皮下投与された。ITT 集団は、ステージ 2 への参加に適格である被験者全例を含むこととした。組み入れられた 13 例のうち 11 例（84.6%）がステージ 2 に適格であり ITT 集団に含まれた。有害事象、心電図、バイタルサイン、体重及び BMI、臨床検査値、48 時間尿量の変化、抗テデュグルチド抗体、大腸内視鏡検査所見、併用薬、病歴及び人口統計学的特性、腹部超音波検査所見、食道胃十二指腸内視鏡検査所見、並びに残存結腸の大腸内視鏡検査／S 状結腸内視鏡検査所見を評価した。有害事象は

MedDRA ver.17.1 を用いてコード化した。TED-C14-004 試験のデータの多くは統合しなかったため、本文書では独立したデータとして示す。安全性解析計画については 5.3.5.2 項 TED-C14-004 CSR を参照のこと。

1.1.1.5.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした実施中の SHP633-307 試験（5.3.5.2 項）（SHP633-306 試験及び TED-C14-004 試験の継続投与試験）では、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した非盲検、多施設共同、長期継続投与試験であった。本申請のためのデータカットオフ日（2020 年 2 月 4 日）時点で 11 例を組み入れテデュグルチド 0.05 mg/kg/日を連日皮下投与した。SHP633-306 試験から移行した被験者の曝露期間の平均値は 7.25±1.017 ヵ月であり、TED-C14-004 試験から移行した被験者の曝露期間の平均値は 15.40±1.128 ヵ月であった。有害事象、心電図、バイタルサイン、体重及び BMI、臨床検査値、48 時間尿量の変化、抗テデュグルチド抗体、大腸内視鏡検査所見、併用薬、病歴及び人口統計学的特性、腹部超音波検査所見、食道胃十二指腸内視鏡検査所見、並びに残存結腸の大腸内視鏡検査／S 状結腸内視鏡検査所見を評価した。有害事象は MedDRA ver.17.1 を用いてコード化した。SHP633-307 試験のデータは、本概要 1.1.1.3.1 に示した他は統合しなかったため、本文書では独立したデータとして示す。安全性解析計画については 5.3.5.2 項 SHP633-307 CSR を参照のこと。

TED-C14-004 試験（5.3.5.2 項）では、長期継続投与期間（ステージ 3 及びステージ 4）を設けた。安全性評価及び解析方法は、本試験の全てのステージで同一である。本概要 1.1.1.5.1.3 を参照のこと。

1.1.1.5.2　　小児の臨床試験データ

1.1.1.5.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）は、治験スケジュールに従って、テデュグルチド投与の安全性及び忍容性を標準治療と比較した非盲検、4 コホート試験であった。被験者はテデュグルチド群又は標準治療群に組み入れられた。ITT 集団は試験に組み入れられた 42 例が含まれ、うち 37 例がテデュグルチドを連日皮下投与され（うち 0.0125 mg/kg/日群に 8 例、0.025 mg/kg/日群に 14 例、0.05 mg/kg/日群に 15 例）、5 例が標準治療を受けた。有害事象、心電図、バイタルサイン、臨床検査値、抗テデュグルチド抗体、並びに尿量及び体重の変化量を評価した。有害事象は MedDRA ver.12.0 を用いてコード化した。

TED-C14-006 試験（5.3.5.2 項）は、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を標準治療と比較した二重盲検、2 群比較試験であった。被験者はテデュグルチド群又は標準治療群に組み入れられた。ITT 集団には 59 例が含まれ、うち 50 例がテデュグルチドを連日皮下投与され（0.05 mg/kg/日群 26 例、0.025 mg/kg/日群 24 例）、9 例が標準治療を受けた。有害事象、身体所見、心電図、バイタルサイン、臨床検査値、尿量、排便量、抗テデュグルチド抗

体、及び消化管検査所見を評価した。病歴及び手術歴、並びに有害事象は MedDRA ver.19.1 を用いてコード化した。

これら 2 試験の統合解析計画については 5.3.5.3 項 IDB SAP を参照のこと。統合した安全性成績を Pediatric ISS として本文中に示す。統合データについて、病歴及び手術歴、並びに有害事象は MedDRA ver.19.1 を用いてコード化した。

1.1.1.5.2.2　　小児を対象とした海外第 3 相継続投与試験

実施中の SHP633-304 試験（5.3.5.2 項）は、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した前向き期間、非盲検、長期継続投与試験であった。本申請のためのデータカットオフ日（2018 年 2 月 2 日）時点で、55 例が組み入れられた。被験者は、疾患の経過に応じて複数の NTT 期間及び／又は複数の 28 週間テデュグルチド投与サイクルに参加することとした。28 週間の各投与サイクルは、24 週間のテデュグルチド 0.05 mg/kg、1 日 1 回皮下投与と、テデュグルチドを投与しない 4 週間の追跡調査によって構成した。データカットオフ時点で、被験者 21 例における 6 ヵ月（24 週間）以上の前向き期間及び被験者 3 例における 22 週間以上の観察期間が含まれた。有害事象、心電図、バイタルサイン、臨床検査値、抗テデュグルチド抗体、尿量、排便量、消化管特異的検査所見、並びに体重、身長、頭囲（月齢 36 ヵ月まで）、及び BMI の Z スコアを評価した。

実施中の SHP633-303 試験（5.3.5.2 項）（TED-C13-003 試験の継続投与試験）は、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した後向き及び前向き試験であった。本概要では前向き期間のみについて記載する。本申請のためのデータカットオフ日（2018 年 1 月 12 日）時点で、29 例を組み入れ、24 例より前向き期間の同意を取得し、16 例がテデュグルチド 0.05 mg/kg/日の連日皮下投与を受けた。被験者は、疾患の経過に応じて複数の NTT 期間及び／又は複数の 28 週間テデュグルチド投与サイクルに参加することとした。28 週間の各投与サイクルは、24 週間のテデュグルチド 0.05 mg/kg、1 日 1 回皮下投与と、テデュグルチドを投与しない 4 週間の追跡調査によって構成した。本データには被験者 42 例における 6 ヵ月（24 週間）以上の観察期間及び被験者 13 例における 4～5 ヵ月の観察期間が含まれる。有害事象、心電図、バイタルサイン、臨床検査値、抗テデュグルチド抗体、尿量、排便量、消化管特異的検査所見、並びに体重、身長、頭囲（月齢 36 ヵ月まで）、及び BMI の Z スコアを評価した。

中間データカットを設け、これら 2 試験の継続投与試験の安全性情報を統合した。これらを「Pediatric ISS」として本文中に示す。5.3.5.3 項 Pediatric ISS SAP を参照のこと。この統合解析では、病歴、手術歴、及び有害事象を MedDRA ver.19.1 でコード化した。統合解析では安全性解析対象集団を用いて 4 群（0.0125、0.025、0.05 mg/kg/日及び標準治療群）により要約した。テデュグルチド投与を受けた被験者は「全テデュグルチド群」として統合した。

SHP633-304 及び SHP633-303 試験（前向き期間のみ）は、被験者のデータはコア試験及び継続投与試験での投与群により解析した。これら試験での被験者は以下に示した 4 群に分類した。

- NTT/NTT 群：コア試験で標準治療を受け、継続投与試験の前向き期間にもテデュグルチドを投与されていない
- NTT/TED 群：コア試験で標準治療を受け、継続投与試験の前向き期間にテデュグルチドを投与された
- TED/NTT 群：コア試験でテデュグルチドを投与され、継続投与試験の前向き期間にはテデュグルチドを投与されていない
- TED/TED 群：コア試験でテデュグルチドを投与され、継続投与試験の前向き期間にもテデュグルチドを投与された

詳細は 5.3.5.2 項 SHP633-304 CSR Section 9.1 及び 5.3.5.2 項 SHP633-303 CSR Section 9.1 を参照のこと。

1.1.1.5.2.3　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）は、治験スケジュールに従って、テデュグルチド投与の安全性及び忍容性を標準治療と比較した無作為化、多施設共同、2 群比較、非盲検試験であった。被験者はテデュグルチド 0.05 mg/kg/日連日皮下投与（標準治療に加える）群又は標準治療のみを受ける群に無作為化された。中間解析データは、ITT 集団として 6 例（テデュグルチド 0.05 mg/kg/日群 3 例、標準治療群 3 例）を含む（5.3.5.2 項 SHP633-301 Interim CSR, Section 10.3）。データカットオフ日時点で、テデュグルチドへの曝露期間の平均値は 138.3±51.38 日（範囲：79～168 日）であり、うち 2 例の曝露期間は 24 週間（168 日）以上、1 例は 4～12 週間（28～84 日）であった（5.3.5.2 項 SHP633-301 Interim CSR, Section 12.1。有害事象、身体所見、バイタルサイン、体重、身長、頭囲、及び身長／体重比 Z スコア、臨床検査値、尿量、排便量（混合便含む）、並びに抗テデュグルチド抗体を評価した。病歴、手術歴、及び有害事象は MedDRA を用いてコード化する。

最終解析は、ITT 集団として 10 例（テデュグルチド 0.05 mg/kg/日群 5 例、標準治療群 5 例）を含む（5.3.5.2 項 SHP633-301 Final CSR, Section 10.3）。テデュグルチドへの曝露期間の平均値±SD は 149.4±42.15 日（範囲：74～169 日）であり、うち 4 例の曝露期間は 24 週間（168 日）以上、1 例は 4～12 週間未満（28～84 日）であった（5.3.5.2 項 SHP633-301 Final CSR, Section 12.1）。

1.1.1.5.2.4　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）は、治験スケジュールに従ってテデュグルチド投与の安全性、忍容性、有効性、薬力学及び薬物動態を評価した非盲検試験であった。有害事象、身体所見（体重、身長、頭囲［月齢 36 ヵ月まで］、成長曲線の傾向など）、バイタルサイン、（体温、心拍数、血圧）、心電図、臨床検査値（すなわち、生化学的検査、血液学的検査、凝固検査、尿検査）、尿量、排便量（体積又は 1 日あたりの排便回数）、抗テデュグルチド抗体、及び消化管特異的検査所見（大腸内視鏡検査又は S 状結腸内視鏡検査）を評価した。病

歴、手術歴、及び有害事象は MedDRA を用いてコード化した。本試験には被験者 10 例が組み入れられテデュグルチド 0.05 mg/kg/日の連日皮下投与を受けた（ITT 集団）。うち 8 例が小児（小児コホート、1～15 歳）、2 例が乳児（乳児コホート、修正月齢 4 ヵ月～12 ヵ月未満）であった。小児 8 例のうち 6 例が治験実施計画書 Amendment 3 以降の組み入れ例であった。

治験実施計画書 Amendment 3 では、バイアルアダプターの導入を含む、治験薬の調製と投与に用いる補助キットを変更した。また、Amendment 3 では、保護者に対するトレーニング及び治験薬の管理についても変更された。したがって、表のデータは小児コホート全体、Amendment 3 以降に組み入れた小児及び乳児コホートに分けて示した。また、文章中では小児コホート全体と乳児被験者について記載した。

1.1.1.5.2.5　　小児を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-305 試験（SHP633-302 試験の継続投与試験）では、治験スケジュールに従ってテデュグルチド投与の安全性及び忍容性を評価した非盲検、長期継続投与試験である。全ての被験者はテデュグルチド 0.05 mg/kg/日の連日皮下投与を受ける。有害事象、バイタルサイン、臨床検査値、尿量、排便量、抗テデュグルチド抗体、消化管検査所見、並びに体重、身長、頭囲（月齢 36 ヵ月まで）、及び BMI の Z スコアを評価する予定である。病歴、手術歴、及び有害事象は MedDRA ver.20.0 を用いてコード化した。

1.1.2　安全性の試験の記述と叙述

テデュグルチドの安全性を評価した実施中及び完了した臨床試験の概要を表 2.7.4 - 2 に示す。本臨床的安全性の概要には、臨床試験 27 試験の解析結果を含めた。

表 2.7.4 - 2　テデュグルチドの臨床試験一覧 [a]

試験の種類	試験 ID	実施国	試験の状況	試験の目的	試験デザイン	投与群及び被験者数（安全性解析対象集団）	健康被験者又は患者の診断名	投与期間	総括報告書添付場所評価／参考
成人第 3 相試験（8 試験）									
海外第 3 相試験（5 試験）									
海外第 3 相試験－プラセボ対照試験（2 試験）									
有効性、安全性	CL0600-020	海外	完了	有効性、安全性及び忍容性をプラセボと比較検討	第 3 相、多施設共同、無作為化、二重盲検、並行群間比較、プラセボ対照試験	テデュグルチド： 42 例（0.05 mg/kg/日　SC） プラセボ：43 例	SBS 患者	24 週間	Module 5.3.5.1 評価資料
有効性、安全性	CL0600-004	海外	完了	有効性、安全性、忍容性、及び薬物動態をプラセボと比較検討	第 3 相、多施設共同、無作為化、二重盲検、並行群間比較、プラセボ対照試験	プラセボ：16 例 テデュグルチド： 35 例（0.05 mg/kg/日　SC） 32 例（0.10 mg/kg/日　SC）	SBS 患者	24 週間	Module 5.3.5.1 評価資料
海外第 3 相試験－継続投与試験（3 試験）									
継続投与試験	CL0600-021	海外	完了	長期の安全性及び有効性の検討	第 3 相、多施設共同、非盲検、CL0600-020 試験からの継続投与試験	テデュグルチド： 88 例（0.05 mg/kg/日　SC）	SBS 患者	最長 2 年間	Module 5.3.5.2 評価資料
継続投与試験	CL0600-005	海外	完了	長期の安全性及び有効性の検討	第 3 相、多施設共同、無作為化、二重盲検、CL0600-004 試験からの継続投与試験	テデュグルチド： 31 例（0.05 mg/kg/日　SC） 34 例（0.10 mg/kg/日　SC）	SBS 患者	28 週間	Module 5.3.5.2 評価資料
継続投与試験	TED-C11-001	海外	完了	長期の安全性及び有効性の検討	第 3 相、多施設共同、非盲検、CL0600-021 試験からの継続投与試験	テデュグルチド：14 例（0.05 mg/kg/日　SC）	SBS 患者	最長 1 年間	Module 5.3.5.2 参考資料
国内第 3 相試験（3 試験）									
安全性、有効性	SHP633-306	日本	完了	日本人における安全性、有効性、及び薬物動態の検討	第 3 相、多施設共同、非盲検試験	テデュグルチド：7 例（0.05 mg/kg/日　SC）	SBS 患者	24 週間	Module 5.3.5.2 評価資料

表 2.7.4 - 2　テデュグルチドの臨床試験一覧 [a]

試験の種類	試験 ID	実施国	試験の状況	試験の目的	試験デザイン	投与群及び被験者数（安全性解析対象集団）	健康被験者又は患者の診断名	投与期間	総括報告書添付場所評価／参考
安全性、有効性	TED-C14-004	日本	完了	日本人における安全性、有効性、及び薬物動態の検討	長期継続投与期間を含む、第 3 相、非盲検、多施設共同、4 ステージ試験	テデュグルチド：11 例（0.05 mg/kg/日　SC）	SBS 患者	24 週間+長期継続投与期間	Module 5.3.5.2 参考資料
継続投与試験	SHP633-307	日本	実施中 中間解析完了	日本人における長期の安全性、有効性の検討	第 3 相、多施設共同、非盲検、SHP633-306 試験及び TED-C14-004 試験からの継続投与試験	テデュグルチド：11 例（0.05 mg/kg/日　SC）	SBS 患者	長期継続投与 [c]	Module 5.3.5.2 評価資料
小児試験（7 試験）									
海外小児第 3 相試験（5 試験）									
海外小児第 3 相試験－コア試験（2 試験）									
安全性、薬物動態、PD	TED-C13-003	海外	完了	小児における薬物動態プロファイル、安全性、及び忍容性、薬力学的効果を標準治療と比較検討	第 3 相、多施設共同、非盲検試験	テデュグルチド： 8 例（0.0125 mg/kg/日　SC）、 14 例（0.025 mg/kg/日　SC） 15 例（0.05 mg/kg/日　SC） 標準治療：5 例	SBS 患者	12 週間	Module 5.3.5.2 評価資料
安全性、有効性、PD	TED-C14-006	海外	完了	小児における安全性、忍容性、薬物動態、及び有効性／PD の検討	第 3 相、多施設共同、二重盲検試験 非盲検下でテデュグルチド群又は標準治療群を選択 テデュグルチド用量群は二重盲検下で割付	テデュグルチド： 24 例（0.025 mg/kg/日　SC） 26 例（0.05 mg/kg/日　SC） 標準治療：9 例	SBS 患者	24 週間	Module 5.3.5.2 評価資料

表 2.7.4 - 2　テデュグルチドの臨床試験一覧 [a]

試験の種類	試験 ID	実施国	試験の状況	試験の目的	試験デザイン	投与群及び被験者数（安全性解析対象集団）	健康被験者又は患者の診断名	投与期間	総括報告書添付場所評価／参考
海外小児第 3 相試験－継続投与試験（2 試験）									
継続投与試験	SHP633-303	海外	実施中 [1]	小児における長期の安全性及び有効性の検討	第 3 相、後向き及び前向き、非盲検、TED-C13-003 試験からの継続投与試験	テデュグルチド：16 例 [b] （0.05 mg/kg/日　SC） TED/NTT：8 例	SBS 患者	長期継続投与 [c]	Module 5.3.5.2 Module 5.3.5.2 (final) 評価資料
継続投与試験	SHP633-304	海外	実施中 [2]	小児における長期の安全性及び有効性の検討	第 3 相、非盲検、TED-C14-006 試験及び SHP633-301 試験からの継続投与試験	テデュグルチド：49 例 [d] （0.05 mg/kg/日　SC） NTT/NTT：6 例 （中間解析時に SHP633-301 試験からの移行例は含まれない）	SBS 患者	長期継続投与 [c]	Module 5.3.5.2 Module 5.3.5.2 (final) 評価資料
海外乳児第 3 相試験（1 試験）									
安全性、有効性及び薬物動態	SHP633-301	海外	完了 [3] 中間解析完了 最終解析完了	乳児における安全性、有効性／PD 及び薬物動態の検討	第 3 相、無作為化、非盲検試験	中間解析時： テデュグルチド：3 例 （0.05 mg/kg/日　SC） 標準治療：3 例 最終解析時： テデュグルチド：5 例 （0.05 mg/kg/日　SC） 標準治療：5 例	SBS 患者	24 週間	Module 5.3.5.2 Module 5.3.5.2 (final) 参考資料
国内小児・乳児第 3 相試験（2 試験）									
安全性、有効性	SHP633-302	日本	完了	日本人小児における安全性、有効性、及び薬物動態の検討	第 3 相、多施設共同、非盲検試験	テデュグルチド：10 例 （0.05 mg/kg/日　SC）	SBS 患者	24 週間	Module 5.3.5.2 評価資料

表 2.7.4 - 2　テデュグルチドの臨床試験一覧 [a]

試験の種類	試験 ID	実施国	試験の状況	試験の目的	試験デザイン	投与群及び被験者数（安全性解析対象集団）	健康被験者又は患者の診断名	投与期間	総括報告書添付場所評価／参考
継続投与試験	SHP633-305	日本	実施中 中間解析完了	日本人小児における長期の安全性及び有効性の検討	第 3 相、非盲検、SHP633-302 試験からの継続投与試験	テデュグルチド：9 例（小児 7 例、乳児 2 例） （0.05 mg/kg/日　SC）	SBS 患者	長期継続投与 [c]	Module 5.3.5.2 評価資料
臨床薬理試験（10 試験）									
バイオアベイラビリティ（BA）	CL0600-006	海外	完了	BA 皮下注対 1 時間点滴静注	第 1 相、単施設、無作為化、非盲検、2-way クロスオーバー試験	テデュグルチド：14 例 （0.12 mg/kg/dose IV 及び 0.12 mg/kg/dose SC）	健康被験者	2 回の単回投与	Module 5.3.1.1 参考資料
BA	CL0600-015	海外	完了	BA 投与部位	第 1 相、単施設、無作為化、非盲検、3-way クロスオーバー試験	テデュグルチド：18 例 （0.1 mg/kg/dose SC）	健康被験者	3 回の単回投与	Module 5.3.1.2 参考資料
安全性、忍容性、薬物動態	1621/13	海外	完了	単回投与時の安全性、忍容性、薬物動態	第 1 相、単施設、単盲検、プラセボ対照、用量漸増単回投与試験	テデュグルチド：24 例 （4 用量のうちのいずれか：2.5 mg、5.0 mg、7.0 mg 又は 10 mg SC） プラセボ：8 例	健康被験者	単回投与	Module 5.3.3.1 評価資料
安全性、忍容性、薬物動態	CL0600-022	海外	完了	反復投与時の安全性、忍容性、薬物動態	第 1 相、単施設、無作為化、二重盲検、プラセボ対照、用量漸増反復投与試験	テデュグルチド：71 例 （7 用量のうちいずれか：10、15、20、25、30、50 又は 80 mg/日　SC） プラセボ：24 例	健康被験者	8 日間	Module 5.3.3.1 評価資料
内因性要因、薬物動態	CL0600-017	海外	完了	肝機能障害患者における薬物動態	第 1 相、単施設、非盲検、並行群間、前向き、健康人対照試験	テデュグルチド：24 例 （20 mg SC）	健康被験者 肝機能障害患者	単回投与	Module 5.3.3.3 参考資料
内因性要因、薬物動態	CL0600-018	海外	完了	腎機能障害患者における薬物動態	第 1 相、単施設、非盲検、並行群間、前向き、健康人対照試験	テデュグルチド：36 例 （10 mg SC）	健康被験者 腎機能障害患者	単回投与	Module 5.3.3.3 参考資料

表 2.7.4 - 2　テデュグルチドの臨床試験一覧 [a]

試験の種類	試験 ID	実施国	試験の状況	試験の目的	試験デザイン	投与群及び被験者数（安全性解析対象集団）	健康被験者又は患者の診断名	投与期間	総括報告書添付場所評価／参考
QT/QTc	C09-001	海外	完了	QT/QTc	第 1 相、単施設、無作為化、二重盲検（テデュグルチド投与につき）、単回投与、プラセボ及び陽性対照、4 期、チェンジオーバー試験	72 例 （全例：テデュグルチド 5 mg SC、20 mg SC、プラセボ SC、モキシフロキサシン 400 mg oral）	健康被験者	4 回の単回投与	Module 5.3.4.1 評価資料
薬物動態、PD	C10-003	海外	完了	胃内容排出に対する影響の検討	第 1 相、無作為化、二重盲検、プラセボ対照、反復投与試験	テデュグルチド：23 例 （4 mg SC） プラセボ：13 例	健康被験者	10 日間	Module 5.3.4.1 参考資料
薬物動態、PD	TED-C10-004	海外	完了	胆嚢運動及び胆道内腔径に対する影響	第 1 相、無作為化、二重盲検、プラセボ対照、反復投与試験	テデュグルチド：29 例 （4 mg SC） プラセボ：31 例	健康被験者	5 日間	Module 5.3.4.1 参考資料
安全性、忍容性、薬物動態、PD	ALX-0600-92001	海外	完了	安全性及び忍容性、残存腸の水及び主要栄養素の吸収能に対する影響を測定、薬物動態	第 2 相、多施設共同、非盲検、用量漸増パイロット試験	テデュグルチド： 3 例（0.03 mg/kg/日 QD SC） 10 例（0.10 mg/kg/日 QD SC） 4 例（0.15 mg/kg/日 QD SC） 5 例（0.10 又は 0.15 mg/kg/日 BID SC）	SBS 患者	21 日間	Module 5.3.4.2 参考資料
その他の試験ークローン病（2 試験）									
その他の臨床試験	CL0600-008	海外	完了	クローン病患者を対象とする安全性及び有効性試験	第 2 相、多施設共同、無作為化、二重盲検、プラセボ対照、パイロット試験	テデュグルチド： 24 例（0.05 mg/kg/日　SC） 26 例（0.10 mg/kg/日　SC） 25 例（0.20 mg/kg/日　SC） プラセボ：25 例	クローン病患者	8 週間	Module 5.3.5.4 参考資料
その他の臨床試験	CL0600-009	海外	完了	クローン病患者を対象とする継続投与試験	第 2 相、多施設共同、非盲検、CL0600-008 試験からの継続投与試験	テデュグルチド：67 例 （0.10 mg/kg/日　SC）	クローン病患者	12 週間	Module 5.3.5.4 参考資料

2.7.4　臨床的安全性
テデュグルチド

IV=静脈内投与；SC=皮下投与；PD=薬力学；QD=1 日 1 回；BID=1 日 2 回；TED/NTT=先行試験でテデュグルチドを投与され、本試験でテデュグルチドを投与されていない被験者；NTT/NTT=先行試験及び／又は本試験でテデュグルチドを投与されていない被験者

1. 本試験は 2020 年 10 月申請時には実施中であった。本概括評価には 2018 年 1 月のデータカットオフ時点のデータを示す。最終の総括報告書は照会事項回答別添（[redacted]_別添資料）として 20[redacted]年 [redacted]月 [redacted]日に機構へ提出し、5.3.5.2.6 項（final）に格納。最終の総括報告書において結論の変更はなかった。
2. 本試験は 2020 年 10 月申請時には実施中であった。本概括評価には 2018 年 2 月のデータカットオフ時点のデータを示す。その後、2020 年 11 月に最終被験者の最終来院を実施し、試験は完了した。最終の総括報告書は 5.3.5.2.7 項（final）に格納。
3. 本試験は 2020 年 10 月申請時には実施中であった。本概括評価には 2019 年 10 月 9 日のデータカットオフ時点のデータ及び最終の総括報告書のデータを示す。最終の総括報告書は照会事項回答別添（[redacted]_別添資料）として 20[redacted]年 [redacted]月 [redacted]日に機構へ提出した。最終の総括報告書において結論の変更はなかった。最終の総括報告書は 5.3.5.2.12 項（final）に格納。

a　TED-R13-002 試験は実施中のレジストリ試験であり、この表に示さない。テデュグルチド投与の有無に関わらず SBS を有する患者を組み入れた。
b　前向き期間で、治験薬を 1 回以上投与され（安全性解析対象集団）、中間解析に含めた被験者数。
c　本試験では、疾患の経過に応じて無投与期間及び 24 週間投与を繰り返す。
d　先行試験及び／又は本試験でテデュグルチドを投与された被験者数。

1.1.3　考慮すべき非臨床安全性所見

成熟動物を用いた亜慢性及び慢性毒性試験において、腸管、肝胆道（胆嚢を含む）、及び膵管の過形成が認められた。これらの所見はテデュグルチドの薬理作用と一致しており、長期投与後8～13 週間の回復期間内に、程度は様々であるが回復がみられた。

テデュグルチドにおける、細菌を用いた復帰突然変異試験、チャイニーズハムスター卵巣細胞を用いた *in vitro* 染色体異常試験及び *in vivo* マウス小核試験の結果は陰性であった（2.6.6.4.1.1 項、2.6.6.4.1.2 項、2.6.6.4.2.1 項）。

マウス及びラットを用いた 2 年間の皮下がん原性試験において、テデュグルチドのがん原性を評価した。Crl:CD1（ICR）マウスを用いた 2 年間がん原性試験で 1、3.5、及び 12.5 mg/kg/日の用量を評価したところ、テデュグルチド投与に関連した所見として、≥1 mg/kg/日で雄マウスの胆嚢における乳頭状腺腫及び高用量（12.5 mg/kg/日）で空腸における腺癌の増加が認められた（2.6.6.5.1.1 項）。雄マウスの全身曝露量と比較した曝露マージンは、0.05 mg/kg における臨床曝露量のそれぞれ約 12 倍、45 倍及び 186 倍であった。

Wistar Han IGS ラットに 3、10、及び 35 mg/kg/日を皮下投与した 2 年間のがん原性試験では、テデュグルチド投与に関連した悪性新生物は認められなかった。雄では、35 mg/kg/日群で胆管上皮由来の良性腫瘍及び空腸における粘膜の腺腫の統計学的に有意な増加が認められ、これはテデュグルチドの消化吸収活動への影響に関連している可能性がある（2.6.6.5.1.2 項）。雄ラットの全身曝露量と比較した曝露マージンは、0.05 mg/kg における臨床曝露量のそれぞれ約 10 倍、32 倍、及び 155 倍であった。

グルカゴン様ペプチド 2（GLP-2）及びその受容体の発現は、新生児、幼若動物、及び成熟動物で異なることが知られている。ラット及びブタを用いた試験から、腸における GLP-2 受容体発現は新生児で特に高く、出生後は成熟動物レベルまで大きく低下することが明らかになっている（Lovshin et al, 2004；Burrin et al, 2000；Petersen et al, 2001；Burrin et al, 2005；Burrin et al, 2007）。GLP-2 は、成熟ブタと同様にブタ新生児においても、12.5 nmol/kg を 2 時間の点滴静注として 1 日 2 回、5～6 日間投与後に小腸重量及び絨毛高を有意に増加させた（Petersen et al, 2001）。幼若動物を用いた毒性試験は反復投与毒性試験とは異なる動物種で実施されたが、幼若ミニブタにおける所見は成熟マウス、ラット及びサルで認められた所見と類似していた。幼若ミニブタにおいて、新たな毒性又は固有の毒性は認められなかった。

1.2　全般的な曝露状況

1.2.1　被験者数

表 2.7.4 - 3 に示すように、データカットオフ時点において、テデュグルチド臨床開発プログラム全体で 718 例がテデュグルチドの投与を受け、248 例がプラセボ又は標準治療を受けた。テデュグルチドを投与された被験者 718 例の内訳は以下の通り。

- 海外臨床試験で投与を受けた被験者は 690 例であり、うち 595 例が成人、90 例が小児であり、5 例は乳児であった。
- 国内臨床試験で投与を受けた被験者は 28 例であり、うち 18 例が成人、8 例が小児、2 例が乳児であった。

表 2.7.4 - 3　テデュグルチド臨床開発プログラムにおける被験者数 [a]

Study Group	Placebo/SOC N	Teduglutide N	Total N
ADULT CLINICAL STUDIES			
Overseas Phase 3 Adult Studies			
Core Studies			
CL0600-020	43	42	85
CL0600-004	16	67	83
Extension Studies			
CL0600-021	0	88	88
CL0600-005	0	65	65
TED-C11-001	9	5	14
SUPPORTIVE CLINICAL STUDIES			
Clinical Pharmacology Studies			
CL0600-006	0	14	14
CL0600-015	0	18	18
1621/13	8	24	32
CL0600-017	0	24	24
CL0600-018	0	36	36
C09-001	69	72	72
CL0600-022	24	71	95
C10-003	13	23	36
ALX-0600-92001	0	17	17
TED-C10-004	31	29	60
Other Studies—Crohn's Disease			
Placebo-controlled			
CL0600-008	25	75	100
Uncontrolled			
CL0600-009	0	67	67
Pediatric – SBS			
Core Studies			
TED-C13-003	5	37	37
TED-C14-006	9	50	59
SHP633-301	5	5	10
Extension Studies			
SHP633-303	0	19	19
SHP633-304	0	53	53

表 2.7.4 - 3　テデュグルチド臨床開発プログラムにおける被験者数 [a]

Study Group	Placebo/SOC N	Teduglutide N	Total N
Japanese Adult – SBS			
Core Studies			
TED-C14-004	0	11	11
SHP633-306	0	7	7
Extension Studies			
SHP633-307	0	11	11
Japanese Pediatrics – SBS			
Core Studies			
SHP633-302	0	10	10
Extension Studies			
SHP633-305	0	8	8
Grand Total Subjects	248	718	823

SBS=short bowel syndrome; SOC=standard of care.

[a] Note that the date of the original enumeration was 11 May 2020 and the numbers remain current as of 15 Feb 2021.

Note: Studies included CL0600-006, CL0600-015, 1621/13, CL0600-017, CL0600-018, C09-001, CL0600-022, C10-003, TED-C10-004, ALX-0600-92001, CL0600-020 (core study), CL0600-004 (core study), CL0600-021 (extension study), CL0600-005 (extension study), CL0600-008 (core study), CL0600-009 (extension study).

Note: Subjects who received both teduglutide and placebo in a crossover study are counted once in the Placebo column, once in the Teduglutide column, and once in the Total column. In C09-001, 70 of the 72 subjects received a single oral dose of 400 moxifloxacin, a positive control in this crossover study.

Source: Refer to CSRs for the individual studies.

1.2.2　治験薬への曝露

1.2.2.1　成人の臨床試験データ

1.2.2.1.1　成人を対象とした海外第 3 相コア試験

CL0600-020 試験及び CL0600-004 試験におけるテデュグルチド及びプラセボの曝露状況を表 2.7.4 - 4 に示す。テデュグルチド群は 109 例（0.05 mg/kg/日 77 例、0.10 mg/kg/日 32 例）であり、テデュグルチドの総曝露は 46.5 人年であった。プラセボ群は 59 例であり、曝露は 26.2 人年であった。投与期間の平均値及び中央値から、大半の被験者がこれらの試験の 24 週間投与期間を完了したことが示されている。曝露期間が 24 週以上であった被験者はテデュグルチド群で 81 例（74.3% ; 0.05 mg/kg/日 : 53 例、0.10 mg/kg/日 : 28 例）、プラセボ群で 40 例（67.8%）であった。最長曝露期間はテデュグルチド 0.05 mg/kg/日群で 28.9 週、テデュグルチド 0.10 mg/kg/日群で 29.7 週、プラセボ群で 28.0 週であった。

表 2.7.4 - 4　CL0600-020 試験及び CL0600-004 試験：曝露状況（安全性解析対象集団）

Parameter	Placebo (N=59) n (%)	Teduglutide 0.05 mg/kg/day (N=77) n (%)	Teduglutide 0.10 mg/kg/day (N=32) n (%)	Teduglutide All (N=109) n (%)
Duration of Exposure (weeks)				
Mean (SD)	23.07 (4.46)	21.79 (6.98)	23.20 (5.63)	22.20 (6.62)
Median	24.00	24.14	24.43	24.14
Min/Max	2.9/28.0	0.6/28.9	0.9/29.7	0.6/29.7
<1 week, n (%)	0	3 (3.9)	1 (3.1)	4 (3.7)
1 to <4 weeks, n (%)	1 (1.7)	3 (3.9)	0	3 (2.8)
4 to <8 weeks, n (%)	2 (3.4)	2 (2.6)	1 (3.1)	3 (2.8)
8 to <12 weeks, n (%)	0	0	0	0
12 to <16 weeks, n (%)	0	2 (2.6)	1 (3.1)	3 (2.8)
16 to <20 weeks, n (%)	1 (1.7)	0	0	0
20 to <24 weeks, n (%)	15 (25.4)	14 (18.2)	1 (3.1)	15 (13.8)
≥24 weeks, n (%)	40 (67.8)	53 (68.8)	28 (87.5)	81 (74.3)
Number of Person Years of Exposure, n	26.2	32.3	14.3	46.5

Studies included: CL0600-020, CL0600-004.
Note:　Percentages are based upon the number of subjects in the Safety Population.
Note:　Duration of exposure is defined as: (last dose date - first dose date + 1) / 7.
Note:　Person years of exposure is defined as the total weeks of exposure for all subjects divided by 52 weeks.
Source: Module 5.3.5.3 Adult ISS Table 8.1.2

1.2.2.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）では、同意説明文書（ICF）に署名した全 88 例が治験薬の投与を 1 回以上受けた。したがって、安全性解析対象集団と ITT 集団は同一であった。CL0600-021 試験期間中のテデュグルチドの曝露期間（平均値±SD）は 84.97±34.75 週間であり、これに加えて CL0600-020 試験のテデュグルチド群の被験者は、同試験期間中にもテデュグルチド投与を受けていた。治験薬の休薬を調整したところ、曝露期間（平均値±SD）は 84.82±34.67 週間（5.3.5.2 項 CL0600-021 CSR Table 14.3.1.2）であった。

CL0600-005 試験（5.3.5.2 項）では、テデュグルチドの投与を受けた 65 例を ITT 集団とした。テデュグルチドの曝露期間（平均値±SD）は 178.7±47.0 日であり、多くの被験者（49.2%）の曝露期間は 7 又は 8 ヵ月間であった。治験薬の曝露量（平均値±SD）は全体で 815.34±366.83 mg であった（5.3.5.2 項 CL0600-005 CSR Table 14.3.1 及び Listing 16.2.15）。

TED-C11-001 試験（5.3.5.2 項）では、ICF に署名した全 14 例が治験薬の投与を 1 回以上受けた。したがって、安全性解析対象集団と ITT 集団は同一であった。TED-C11-001 試験期間中におけるテデュグルチドの曝露期間（平均値±SD）は 38.92±9.78 週間であり、これに加えて先行し

た CL0600-020 試験及び／又は CL0600-021 試験期間中にもテデュグルチドが投与されていた（5.3.5.2 項 TED-C11-001 CSR Table 14.3.1.1、Appendix 16.2.5、及び Listing 16.2.4.1）。

1.2.2.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）における ITT 集団、PP 集団及び安全性解析対象集団におけるテデュグルチドの曝露状況は表 2.7.4 - 5 のとおりであった。被験者 1 例は 32 日後に治験薬の投与を中止したため PP 集団から除外され、他の 6 例は Week 24 まで治験薬が投与され、治験薬の投与が終了した。安全性解析対象集団におけるテデュグルチドの曝露期間（中央値）は 162 日（範囲：32～171 日）であった。ITT 集団及び安全性解析対象集団は同一であった。PP 集団におけるテデュグルチドの曝露期間は、治験薬の投与を早期に中止した被験者が除外されたため、ITT 集団及び安全性解析対象集団と比較してわずかに長かった。

表 2.7.4 - 5　SHP633-306 試験：曝露状況（ITT、PP 及び安全性解析対象集団）

		Total Teduglutide		
	Statistic	**ITT (N=7)**	**PP (N=6)**	**Safety (N=7)**
Extent of Exposure (days)	n	7	6	7
	Mean (SD)	145.4 (50.16)	164.3 (4.18)	145.4 (50.16)
	Median	162.0	162.5	162.0
	Min, Max	32, 171	161, 171	32, 171
Extent of Exposure Category				
>=4 weeks and <12 weeks	n (%)	1 (14.3)	0 (0.0)	1 (14.3)
>=12 weeks and <24 weeks	n (%)	4 (57.1)	4 (66.7)	4 (57.1)
>=24 weeks	n (%)	2 (28.6)	2 (33.3)	2 (28.6)

Note: Percentages are based on the number of subjects in the respective populations.
Note: Extent of exposure was defined as the number of days on treatment including any period of temporary dose interruption. The calculation is based on first dose date and last dose date.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.3.1

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の安全性解析対象集団（ITT 集団と同一）におけるテデュグルチドの曝露量は表 2.7.4 - 6 のとおりであった。ステージ 2（投与期間 24 週間）終了時のテデュグルチドの曝露期間（平均値±SD）は 147.5±48.73 日（範囲：15～171 日）であった。試験期間全体のテデュグルチドの曝露期間（平均値±SD）は 26.8±17.04 ヵ月（範囲：0.5～41.1 ヵ月）であった。

表 2.7.4 - 6　TED-C14-004 試験：曝露状況（安全性解析対象集団）

Extent of Exposure	**Total Teduglutide (N=11)**
Stage 2 Only (days)	
Mean (SD)	147.5±48.73
Median	168.0
Min/Max	15, 171
Stage 2 Only (months)	
Mean (SD)	4.8 ±1.60
Median	5.5
Min/Max	0.5, 5.6
Any Exposure (months)	
Mean (SD)	26.8±17.04
Median	38.0
Min/Max	0.5, 41.1
Any Exposure	
<6 months, n (%)	3 (27.3)
6 to <12 months, n (%)	0 (0.0)
12 to <24 months, n (%)	1 (9.1)
24 to <30 months, n (%)	0 (0.0)
≥30 months, n (%)	7 (63.6)

Note:　Percentages are based on the safety population.
Note:　Extent of exposure is defined as (last dose date - first dose date +1).
Note:　One month is calculated as 30.4375 days.
Source: Module 5.3.5.2 TED-C14-004 CSR Table 14.3.1.2

1.2.2.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、データカットオフ日（2020 年 2 月 4 日）時点での曝露期間（平均値±SD）は、7.25±1.017 ヵ月（SHP633-306 試験からの継続被験者）及び 15.40±1.128 ヵ月（TED-C14-004 試験からの継続被験者）であった。コア試験からの累積曝露期間（平均値±SD）は、12.65±0.995 ヵ月（SHP633-306 試験からの継続被験者）及び 54.29±1.659 ヵ月（TED-C14-004 試験からの継続被験者）であった（5.3.5.2 項 SHP633-307 CSR Section12.1）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）における継続投与期間及び試験全体の曝露状況（安全性解析対象集団及び同一である ITT 集団）を本概要 1.2.2.1.3 に示す。被験者 11 例中 7 例が本試験の継続投与期間に進み、曝露期間は 30 ヵ月以上であった。

1.2.2.1.5　　成人を対象とした国内第 3 相コア試験及び継続投与試験の統合データ

日本人被験者を対象とした第 3 相試験 3 試験（SHP633-306 試験［5.3.5.2 項］、SHP633-307 試験［5.3.5.2 項］、TED-C14-004 試験［5.3.5.2 項］）におけるテデュグルチドの曝露期間を表 2.7.4 - 7 に示す。これらのデータでは、コア試験の開始日から継続投与試験の追跡期間の終了日までの期間で被験者は 1 回のみ計上された。安全性解析対象集団は ITT 集団と同一である。これらの試験全体で 18 例の被験者がテデュグルチドに曝露された。テデュグルチドの曝露期間（平均値±SD）は 787.1±721.11 日（範囲：15～1709 日）であった。最長投与期間は 51 ヵ月以上 54 ヵ月未満が 4 例、54 ヵ月以上 57 ヵ月未満が 3 例であった。SHP633-306 試験（5.3.5.2 項）と SHP633-307 試験（5.3.5.2 項）のみの統合データについては、2.7.4 項付録 4 Table 1.2 を参照のこと。

表 2.7.4 - 7　SHP633-306、SHP633-307 及び TED-C14-004 試験：曝露状況（ITT 集団、PP 集団、安全性解析対象集団）

		Total Teduglutide		
	Statistic	**ITT (N=18)**	**PP (N=14)**	**Safety (N=18)**
Extent of Exposure (Days)	n	18	14	18
	Mean (SD)	787.1 (721.11)	989.4 (693.17)	787.1 (721.11)
	Median	407.5	1013.0	407.5
	Min, Max	15, 1709	161, 1709	15, 1709
Extent of Exposure (Weeks)	n	18	14	18
	Mean (SD)	112.4 (103.02)	141.3 (99.02)	112.4 (103.02)
	Median	58.2	144.7	58.2
	Min, Max	2, 244	23, 244	2, 244
Extent of Exposure (Months)	n	18	14	18
	Mean (SD)	25.86 (23.692)	32.51 (22.773)	25.86 (23.692)
	Median	13.39	33.28	13.39
	Min, Max	0.5, 56.1	5.3, 56.1	0.5, 56.1

ITT=Intent to Treat, PP=Per Protocol.
Note: All subjects that participated in either SHP633-306, SHP633-307, or TED-c14-004 are accounted for in this table. SHP633-306 and TED-c14-004 are completed core studies. Subjects from both core studies had the option to participate in the SHP633-307 extension study. The population definition is from core study.
Note: Exposure of duration is sum of treatment duration in core study + extension study.
Note: Extent of Observation is defined as [(last follow-up date) - (first dose in core study)+1] /365.25, last may follow-up date may be in core or extension study. Last follow-up date is defined as EOS date if subjects only participated in core studies. If subjects continued to SHP633-307 extension study, the last follow-up date is Feb 04, 2020, inclusive.
Note: Refer to Appendix 4, Table 1.2 for the same table without data from Study TED-C14-004.
Source: 2.7.4 項 付録 4, Table 1.1

1.2.2.2　　小児の臨床試験データ

1.2.2.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データの曝露状況を表 2.7.4 - 8 に示す。テデュグルチド 0.0125 mg/kg/日群の曝露期間は短かったが、これはこの用量が TED-C13-003 試験のみで投与されたためであった。0.025 mg/kg/日群と 0.05 mg/kg/日群の曝露期間は同程度であった。テデュグルチドの曝露期間（平均値±SD）は 0.0125 mg/kg/日群 11.2±2.51 週間（範囲：5～13 週間）、0.025 mg/kg/日群 19.7±5.88 週間（範囲：12～25 週間）、0.05 mg/kg/日群 19.5±5.95 週間（範囲：8～24 週間）であった。これら 2 試験の被験者の大半における曝露期間は 12～24 週間以下であった。

表 2.7.4 - 8　TED-C13-003 試験及び TED-C14-006 試験：曝露状況（安全性解析対象集団）

Parameter	0.0125 mg/kg/day Teduglutide (N=8)	0.025 mg/kg/day Teduglutide (N=38)	0.05 mg/kg/day Teduglutide (N=41)	Total Teduglutide (N=87)
Extent of Exposure (weeks)				
Mean (SD)	11.2 (2.51)	19.7 (5.88)	19.5 (5.95)	18.9 (6.15)
Median	12.0	23.9	23.9	23.7
Min, Max	5, 13	12, 25	8, 24	5, 25
≤12 weeks, n (%)	6 (75.0)	7 (18.4)	5 (12.2)	18 (20.7)
12 - ≤24 weeks, n (%)	2 (25.0)	17 (44.7)	31 (75.6)	50 (57.5)
>24 weeks, n (%)	0	14 (36.8)	5 (12.2)	19 (21.8)

Note:　Extent of exposure is calculated as (date of last teduglutide administration – date of first teduglutide administration + 1)/7.
Note: Percentages are based on the number of subjects in the safety population for each treatment groups.
Source: Module 5.3.5.3 Pediatric ISS Table 5.1

1.2.2.2.2　　小児を対象とした海外第 3 相継続投与試験

実施中の SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データでは（それぞれデータカットオフ日は 2018 年 2 月 2 日及び 2018 年 1 月 12 日）、試験中のテデュグルチドの曝露期間（平均値±SD）は NTT/TED 群 22.3±2.42 週間（範囲：21～24 週間）、TED/TED 群 24.6±8.25 週間（範囲：0.4～47 週間）であった。NTT/TED 群の 2 例の曝露期間はいずれも 12～24 週間以下であった。TED/TED 群では、曝露期間が 12 週間以下の被験者が 3 例（5.0%）、12～24 週間以下の被験者が 28 例（46.7%）、24～48 週間以下の被験者が 29 例（48.3%）であった（5.3.5.3 項 Pediatric ISS Table 5.2）。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

1.2.2.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、テデュグルチドの曝露期間（平均値±SD）は 138.3±51.38 日（範囲：79～168 日）であった。テデュグルチド群の被験者 3 例中 2 例の曝露期間は 24 週間（168 日）以上、残る 1 例は 4～12 週間未満（28 日～84 日未満）であった（5.3.5.2 項 SHP633-301 Interim CSR Section12.1）。

最終解析では、テデュグルチドの曝露期間（平均値±SD）は 149.4±42.15 日（範囲：74～169 日）であった。4 例の曝露期間は 24 週間（168 日）以上、残る 1 例は 4～12 週間未満（28 日～84 日未満）であった（5.3.5.2 項 SHP633-301 Final CSR, Section 12.1）。

1.2.2.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

SHP633-302 試験（5.3.5.2 項）における安全性解析対象集団（ITT 集団と同一）におけるテデュグルチドの曝露状況を表 2.7.4 - 9 に示す。

小児コホート（8 例）では、試験期間中のテデュグルチドの曝露期間（平均値±SD）は 164.4±11.07 日（範囲：137～169 日）であった。

小児コホートの被験者の大半（7 例）は 24 週間のテデュグルチド投与を完了した。乳児コホートの 2 例では試験期間中のテデュグルチドの曝露期間（平均値±SD）は 167.5±0.71 日（各 167、168 日）であり、いずれも 24 週間の投与を終了した。

表 2.7.4 - 9　SHP633-302 試験：曝露状況（安全性解析対象集団）

Parameter	Children[a] After Amendment 3[c] (N=6)	Total Children[a] (N=8)	Infants[b] (N=2)
Extent of Exposure (days)			
Mean (SD)	168.2 (0.41)	164.4 (11.07)	167.5 (0.71)
Median	168.0	168.0	167.5
Min, Max	168, 169	137, 169	167, 168
Any Exposure, n (%)	6 (100.0)	8 (100.0)	2 (100.0)
<4 weeks, n (%)	0	0	0
4-<12 weeks, n (%)	0	0	0
12-<24 weeks, n (%)	0	1 (12.5)	1 (50.0)[d]
≥ 24 weeks, n (%)	6 (100.0)	7 (87.5)	1 (50.0)

SD=standard deviation
a:　Children aged 1 through 15 years.
b:　Infants of 4 through <12 months corrected gestational age.
c:　The number of children enrolled based upon the protocol amendment 3 and 4.
d:　One infant who received the 167 days teduglutide treatment was regarded as the 24-week treatment.
Note:　Extent of Exposure was defined as (last dose date - first dose date +1).
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.3.1.2

1.2.2.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の国内小児第 3 相継続投与試験 SHP633-305 試験（5.3.5.2 項）において、データカットオフ時点で、テデュグルチドの曝露期間（平均値±SD、SHP633-302 試験の曝露期間を含む）は小児コホート（7 例）で 68.33±38.922 週（範囲：24.0～147.9 週間）であった。小児コホート 7 例のうち 6 例はデータカットオフまでに本試験でテデュグルチド投与を 24 週間以上受け（コア試験も含めた総投与期間は 1 年）、残る 1 例はコア試験で経腸の自律性を獲得し、それを維持していたため本試験ではテデュグルチドを投与せず、NTT 期間を継続している。乳児コホート（2 例、2 例ともに SHP633-305 試験の投与例）におけるテデュグルチドの曝露期間（平均値±SD）は 42.93±7.374 週（各乳児ではそれぞれ 37.7 週及び 48.1 週）であった（5.3.5.2 項 SHP633-305 CSR Section 12.1）。

1.2.2.2.6　　小児及び乳児を対象とした国内第 3 相コア試験及び継続試験の統合データ

SHP633-302 試験（5.3.5.2 項）及び SHP633-305 試験（データカットオフ日まで）（5.3.5.2 項）について、曝露状況のデータを統合した。SHP633-302 試験及び SHP633-305 試験に参加した被験者は、SHP633-302 試験の開始から SHP633-305 試験の最終追跡調査日又は SHP633-302 試験のみに参加した場合には SHP633-302 試験の試験終了日までの期間全体で 1 例として計上した。本統合データは安全性解析対象集団について示した（ITT 集団と同一）。これら 2 試験でテデュグルチドを投与された被験者は 10 例（小児 8 例、乳児 2 例）であり、曝露期間（平均値±SD）は 440.2±287.45 日（範囲：137～1136 日）であった。最長の投与期間は、小児 1 例での 36 ヵ月以上 39 ヵ月未満であった（2.7.4 項 付録 4 Table 10.1 参照）。

1.2.3　　被験者の内訳

1.2.3.1　　成人の臨床試験データ

1.2.3.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データの内訳を表 2.7.4 - 10 に要約する。これらの試験を完了した被験者の割合はテデュグルチド群で 87.2%、プラセボ群で 91.5%と高かった。プラセボ群及びテデュグルチド群ともに、最も多かった中止理由は有害事象であった。

表 2.7.4 - 10　CL0600-020 試験及び CL0600-004 試験：被験者の内訳（安全性解析対象集団）

Parameter	Placebo (N=59) n (%)	Teduglutide 0.05 mg/kg/day (N=77) n (%)	Teduglutide 0.10 mg/kg/day (N=32) n (%)	Teduglutide All (N=109) n (%)
Completed Study	54 (91.5)	66 (85.7)	29 (90.6)	95 (87.2)
Discontinued Study	5 (8.5)	11 (14.3)	3 (9.4)	14 (12.8)
Adverse Event	4 (6.8)	8 (10.4)	2 (6.3)	10 (9.2)
Subject Decision/ Withdrawal of Consent	1 (1.7)	2 (2.6)	1 (3.1)	3 (2.8)
Other	0	1 (1.3)	0	1 (0.9)

Studies included: CL0600-020, CL0600-004.
Note:　Percentages are based upon the number of subjects in the Safety Population.
Source: Module 5.3.5.3 Adult ISS Table 2.1.2

1.2.3.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）の被験者の内訳を以下に示す。コア試験である CL0600-020 試験で無作為割付けされた 86 例のうち 78 例が試験を完了し、CL0600-021 試験への組入れ基準を満たしたが、78 例中 2 例が CL0600-021 試験での継続投与を拒否した。残る 76 例に加え、CL0600-020 試験でスクリーニング、最適化、及び安定化を受けたが無作為割付けされず投与を受けていない 12 例が CL0600-021 試験に直接組み入れられ、CL0600-021 試験の総例数は 88 例となった。したがって、CL0600-021 試験の被験者集団は、CL0600-020 試験でスクリーニングを受けたが無作為化されなかった被験者 12 例（NT/TED 群）、CL0600-020 試験でプラセボの投与を受けた被験者 39 例（PBO/TED 群）、CL0600-020 試験でテデュグルチドの投与を受けた被験者 37 例（TED/TED 群）で構成された。登録された 88 例のうち 23 例が中止に至り、その理由は有害事象（16 例）、被験者の判断（4 例）、治験責任医師（又はその指名を受けた者。以降同様とする）の判断（2 例）、死亡（1 例）であった。登録された 88 例を ITT 集団とした。88 例全例が本試験で治験薬の投与を 1 回以上受けており、これらを安全性解析対象集団とした。したがって、ITT 集団と安全性解析対象集団は同一である。試験を完了した被験者は 65 例であった。NT/TED、PBO/TED 及び TED/TED 群の定義については本概要 1.1.1.5.1.2 項を参照のこと。

CL0600-005 試験（5.3.5.2 項）では、コア試験である CL0600-004 試験を完了した 71 例のうち 65 例（91.5%）が CL0600-005 試験への継続を選択した。CL0600-004 試験から継続した 65 例のうち、CL0600-004 試験でテデュグルチド 0.05 mg/kg/日群であった被験者 25 例は、CL0600-005 試験においてもテデュグルチド 0.05 mg/kg/日を継続し、CL0600-004 試験でテデュグルチド 0.10 mg/kg/日群であった被験者 27 例は、CL0600-005 試験においてもテデュグルチド 0.10 mg/kg/日を継続した。また、CL0600-004 試験のプラセボ群 13 例のうち、6 例はテデュグルチド 0.05 mg/kg/日群、7 例はテデュグルチド 0.10 mg/kg/日群に無作為に割り付けられた。CL0600-005 試験へ移行しなかった被験者は 6 例（CL0600-004 試験の各群 2 例）であった。CL0600-005 試験

に登録された 65 例のうち、54 例が試験を完了し、11 例が治験中止に至った。最も多かった中止理由は有害事象（8 例、12.3%）であった。

TED-C11-001 試験（5.3.5.2 項）では、CL0600-021 試験を完了した 14 例が TED-C11-001 試験に登録された。登録された 14 例がテデュグルチドの投与を受け、そのうち 13 例が試験を完了した。完了しなかった 1 例は 243 日間テデュグルチド投与を受けた後に追跡不能となった。14 例全例が本試験で治験薬の投与を 1 回以上受け、これらを安全性解析対象集団とした（したがって、ITT 集団と安全性解析対象集団は同一である）。本試験を完了した 13 例全例が、試験終了時点でテデュグルチドの投与を継続しており、これらの被験者には市販薬に切り替える選択肢を提供した。試験期間が 1 年未満の被験者もいた。

NT/TED、PBO/TED 及び TED/TED 群の定義については本概要 1.1.1.5.1.2 を参照のこと。

1.2.3.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）における被験者の内訳を表 2.7.4 - 11 に示す。ITT 集団の被験者は安全性解析対象集団と同一であった。日本の 5 施設で被験者のスクリーニングを実施した。被験者 7 例が登録された。登録された被験者 7 例全例にテデュグルチドを投与し、全例を安全性解析対象集団とした。6 例（85.7%）が Week 24 を完了し、4 例（57.1%）を継続投与試験に組み入れ、テデュグルチドの投与を継続した。1 例（14.3%）が治験責任医師の判断により投与を中止した。

表 2.7.4 - 11　SHP633-306 試験：被験者の内訳（安全性解析対象集団）

Parameter	**Total Teduglutide n (%) Safety (N=7)**
Enrolled	7
Treated	7 (100.0)
Completed Treatment (Week 24)	6 (85.7)
Did the subject enroll in the extension study?	
No	2 (28.6)
Yes	4 (57.1)
Early Treatment Discontinuation	1 (14.3)
Physician Decision	1 (14.3)

Note:　Percentages are based on the number of subjects in the respective populations.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.1.2

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）における被験者の内訳を表 2.7.4 - 12 に示す。ステージ 2 は 24 週間の投与期間であり、ステージ 3 及び 4 は継続投与期間であった。日本の 5 施設で被験者をスクリーニングし、同意書に署名した 13 例を登録した。13 例のうち 2 例はステージ 2 の選択／除外基準を満たさなかったため、ステージ 2 に不適格であった。ス

テージ 2 の参加基準を満たした全 11 例がテデュグルチドの投与を受け、これらの被験者を安全性解析対象集団とした。ステージ 2 の早期中止例は 2 例であり、その理由は、有害事象（急性肝不全）1 例（9.1%）及び同意撤回 1 例（9.1%）であった。ステージ 2 を完了したが、下痢の有害事象によりステージ 3 への移行に同意しなかった被験者が 1 例（9.1%）認められた。ステージ 3 において同意を撤回した被験者は 1 例（9.1%）であった。ステージ 3 を完了した被験者は 7 例（63.6%）であり、テデュグルチド投与を 30 ヵ月以上受けた。ステージ 4 で中止に至った被験者はおらず、7 例が試験を完了し、テデュグルチドの総投与期間は 38～41 ヵ月であった。ITT 集団の被験者は安全性解析対象集団と同一であった。

表 2.7.4 - 12　TED-C14-004 試験：被験者の内訳（安全性解析対象集団）

Population	**Total Teduglutide (N=11) n (%)**
Enrolled[a]	13
Treated	11 (100.0)
Eligible for Stage 2[b]	11 (100.0)
Completed Stage 2	9 (81.8)
Discontinued Stage 2 Early	2 (18.2)
Adverse Event	1 (9.1)
Withdrawal by Subject	1 (9.1)
Completed Stage 2 but did not consent to Stage 3[c,d]	1 (9.1)
Completed Stage 3 - Visit 7 (12 Months Total Treatment)	8 (72.7)
Completed Stage 3 - (30 Months Total Treatment)	7 (63.6)
Discontinued Stage 3/Study Early	1 (9.1)
Withdrawal by Subject	1 (9.1)
Completed Stage 4[e]	7 (63.6)
Discontinued Stage 4 /Study Early	0 (0.0)

[a] All-enrolled subjects include all subjects who provided signed informed consent form.
[b] Stage 2 is a 24-week dosing period.
[c] Stage 3 is the long-term extension portion of the study for up to 24 months after Stage 2.
[d] Subject [redacted] completed Stage 2; however, did not continue onto Stage 3 due to an adverse event of diarrhea (see TED-C14-004 CSR Table 14.3.2.13). The reason for not continuing to Stage 3 is not a variable captured in the database for subjects that did not early terminate in Stage 2.
[e] Stage 4 is the long-term extension portion of the study after Stage 3 until end of study.
Note: Percentages are based on the safety population.
Source: Module 5.3.5.2 TED-C14-004 CSR Table 14.1.2.2

1.2.3.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、中間データカットオフ時点（2020 年 2 月 4 日）で 11 例（SHP633-306 試験から移行：4 例、TED-C14-004 試験から移行：7 例）を組み入れた。登録した 11 例全例に 0.05mg/kg/日のテデュグルチドが投与され、これら 11 例を安全性解析対象集団及び薬物動態（PK）解析対象集団とした。データカットオフ時点で 11

例全例がテデュグルチドの投与を継続しており、中止例はなかった（5.3.5.2 項 SHP633-307 CSR Section10.1）。

日本人被験者を対象とした TED-C14-004 試験では、継続投与期間（ステージ 3 及び 4）を設けた。試験全体の被験者の内訳を本概要 1.2.3.1.3 に示す。

1.2.3.2　小児の臨床試験データ

1.2.3.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データにおける被験者の内訳を表 2.7.4 - 13 に示す。安全性解析対象集団のうち、87 例がテデュグルチド群、14 例が標準治療群であった。これら 2 試験におけるテデュグルチド群 87 例の内訳は、8 例が 0.0125 mg/kg/日、38 例が 0.025 mg/kg/日、41 例が 0.05 mg/kg/日であった。2 例が投与を完了せず、治験中止に至った。中止理由は、治験実施計画書の不遵守（0.0125 mg/kg/日：1 例）、同意撤回（0.05 mg/kg/日：1 例）であった。

表 2.7.4 - 13　TED-C13-003 試験及び TED-C14-006 試験：被験者の内訳（安全性解析対象集団）

	0.0125 mg/kg/day Teduglutide (N=8) n(%)	0.025 mg/kg/day Teduglutide (N=38) n(%)	0.05 mg/kg/day Teduglutide (N=41) n(%)	Total Teduglutide (N=87) n(%)	Standard of Care (N=14) n(%)	Total (N=101) n(%)
TED-C13-003 and TED-C14-006 Safety Population	8	38	41	87	14	101
Completed Treatment	7 (87.5)	38 (100.0)	40 (97.6)	85 (97.7)	-	-
Did not Complete Treatment	1 (12.5)	0	1 (2.4)	2 (2.3)	-	-
Primary Reason for Treatment Withdrawal						
Withdrawal of Consent and/or Assent	0	0	1 (2.4)	1 (1.1)	-	-
Protocol Non-Compliance	1 (12.5)	0	0	1 (1.1)	-	-
Completed Study	7 (87.5)	38 (100.0)	40 (97.6)	85 (97.7)	14 (100.0)	99 (98.0)
Did Not Complete Study	1 (12.5)	0	1 (2.4)	2 (2.3)	0	2 (2.0)
Primary Reason for Study Withdrawal						
Withdrawal of Consent and/or Assent	0	0	1 (2.4)	1 (1.1)	0	1 (1.0)

表 2.7.4 - 13　TED-C13-003 試験及び TED-C14-006 試験：被験者の内訳（安全性解析対象集団）

	0.0125 mg/kg/day Teduglutide (N=8) n(%)	0.025 mg/kg/day Teduglutide (N=38) n(%)	0.05 mg/kg/day Teduglutide (N=41) n(%)	Total Teduglutide (N=87) n(%)	Standard of Care (N=14) n(%)	Total (N=101) n(%)
Protocol Non-Compliance	1 (12.5)	0	0	1 (1.1)	0	1 (1.0)

Note: Percentages are based on the number of subjects in the safety population for each treatment group.
Note: Subjects who participated in the standard of care cohort in TED-C13-003 and later also participated in TED-C14-006 are counted separately for each study.
Source: Module 5.3.5.3 Pediatric ISS Table 2.1

1.2.3.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データにおける被験者の内訳を表 2.7.4 - 14 に示す。コア試験及び継続投与試験の両試験で安全性解析対象集団の被験者は 79 例であった。データカットオフ時点の内訳は、NTT/NTT 群 6 例、NTT/TED 群 2 例、TED/NTT 群 11 例、TED/TED 群 60 例であった。TED/TED 群の 1 例が医師の判断により投与中止に至った。データカットオフ時点で、77 例（97.5%）が継続投与試験を継続中であり、その内訳は NTT/NTT 群 5 例（83.3%）、NTT/TED 群 2 例（100.0%）、TED/NTT 群 11 例（100.0%）、TED/TED 群 59 例（98.3%）であった。2 例（2.5%）が継続投与試験を中止した。その理由は、NTT/NTT 群の 1 例（16.7%）が追跡不能、TED/TED 群の 1 例（1.7%）が死亡であった。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

表 2.7.4 - 14　SHP633-303 試験及び SHP633-304 試験：被験者の内訳（安全性解析対象集団）

	NTT/NTT (N=6) n(%)	NTT/TED (N=2) n(%)	TED/NTT (N=11) n(%)	TED/TED (N=60) n(%)	Total (N=79) n(%)
SHP633-303 & SHP633-304 Safety Population	6	2	11	60	79
Primary Reason for Treatment Withdrawal					
Physician Decision	-	0	-	1 (1.7)	-
Completed Study	0	0	0	0	0
Ongoing	5 (83.3)	2 (100.0)	11 (100.0)	59 (98.3)	77 (97.5)
Withdrawal from Study	1 (16.7)	0	0	1 (1.7)	2 (2.5)

表 2.7.4 - 14　SHP633-303 試験及び SHP633-304 試験：被験者の内訳（安全性解析対象集団）

	NTT/NTT (N=6) n(%)	NTT/TED (N=2) n(%)	TED/NTT (N=11) n(%)	TED/TED (N=60) n(%)	Total (N=79) n(%)
Primary Reason for Study Withdrawal					
Lost to Follow-up	1 (16.7)	0	0	0	1 (1.3)
Death	0	0	0	1 (1.7)	1 (1.3)

Note: Percentages are based on the number of subjects in the safety population for each treatment group.
Note: NTT/NTT - Subjects in the standard of care arms of the core studies who had not received teduglutide treatment in the prospective portions of the extension studies
NTT/TED - Subjects in the standard of care arms of the core studies who then received teduglutide treatment in the prospective portions of the extension studies
TED/NTT - Subjects who received teduglutide treatment in the core studies but had not received teduglutide in the prospective portions of the extension studies
TED/TED - Subjects who received teduglutide treatment in both the core and prospective portions of the extension studies
Source: Module 5.3.5.3 Pediatric ISS Table 2.2

1.2.3.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、9 例をスクリーニングし、6 例を無作為化した。テデュグルチド群に 3 例、標準治療群に 3 例の被験者を組み入れた。テデュグルチド群の 3 例全例が治験薬を投与され、2 例が Week 24 の投与期間を完了し、このうち 1 例は Week 28 に試験を完了し、他の被験者 1 例は複数の中断基準（escape criteria）を満たしたため追跡期間を中止し継続投与試験に登録された。残る 1 例はデータカットオフ時点で継続中であり、Week 11 に到達していた。標準治療群 3 例のうち、1 例は Week 24 の投与期間を完了し、1 例は親／保護者の意思により投与期間中（Week 6）に中止し、1 例はデータカットオフ時点で継続中であり、Week 1 に到達していた。データカットオフ時点（2019 年 10 月 9 日）で、被験者 1 例がスクリーニング中であった（5.3.5.2 項 SHP633-301 Interim CSR Section 10.1）。

最終解析時点で、13 例をスクリーニングし、10 例を無作為化し、テデュグルチド群に 5 例、標準治療群に 5 例の被験者を組み入れた。テデュグルチド群の 5 例全例が治験薬を投与され、4 例が Week 24 の投与期間を完了した。1 例は Day 75 にテデュグルチド投与を中断した（両親が複数の有害事象が治験薬によるものであると考えたため、両親の判断でテュグルチドを中止したことによる。これは安全性のための治験責任医師の判断ではなく、治験責任医師が両親から報告を受けた）。4 例が試験を完了し、1 例は複数の中断基準（escape criteria）を満たしたため追跡期間を中止し継続投与試験に登録された。標準治療群 5 例のうち、4 例は Week 24 の投与期間を完了し、1 例は親／保護者による同意撤回により Week 6 の来院時に中止した（5.3.5.2 項 SHP633-301 Final CSR Section 10.1）。

1.2.3.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）の ITT 集団における被験者の内訳を表 2.7.4 - 15 に示す。被験者 10 例（1～15 歳の小児 8 例及び修正月齢 4～12 ヵ月未満の乳児 2 例）を組み入れ、治験薬を投与した。小児被験者 8 例中 7 例は 24 週の投与期間を終了した。1 例は有害事象により治験薬投与を中止した。全例を 4 週間追跡し、試験を完了した。

乳児被験者はともに 28 週間の試験期間を完了した。

表 2.7.4 - 15　SHP633-302 試験：被験者の内訳（ITT 集団）

Parameter	Children[a] After Amendment 3[c] (N=6) n (%)	Total Children[a] (N=8) n (%)	Infants[b] (N=2) n (%)
Screened	6	8	2
Enrolled	6	8	2
Treated	6 (100.0)	8 (100.0)	2 (100.0)
Completed Treatment (Week 24)	6 (100.0)	7 (87.5)	2 (100.0)
Early Treatment Discontinuation	0	1 (12.5)	0
Adverse Event	0	1 (12.5)	0
Completed Study (Week 28)	6 (100.0)	8 (100.0)	2 (100.0)

a: Children aged 1 through 15 years.
b: Infants of 4 through <12 months corrected gestational age.
c: The number of children enrolled based upon the protocol amendment 3 and 4.
Note: Screened subjects are defined as those who provided signed Informed Consent Form.
Note: Subjects were enrolled in the study when they met all eligibility criteria at screening and at Visit 2/baseline.
Note: Percentages were based on the Intention-to-Treat (ITT) population.
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.1.2.1

1.2.3.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、9 例（小児 7 例、乳児 2 例）を組み入れた。コア試験である SHP633-302 試験でテデュグルチドを投与され、経腸の自律性が維持されているため SHP633-305 試験ではテデュグルチドの投与を受けていない小児被験者 1 例も、安全性解析対象集団に含めた（5.3.5.2 項 SHP633-305 CSR Table 16）。本被験者は SHP633-305 試験で NTT 期間を継続中である。小児コホートにおいて、データカットオフ日までにテデュグルチドを投与された小児被験者 6 例は、全例がデータカットオフ時点で投与を継続中であった。治験薬投与中止例又は試験中止例はいなかった。乳児コホートでは、データカットオフ時点で両乳児被験者ともテデュグルチドの投与を受けており、試験を継続中であった（5.3.5.2 項 SHP633-305 CSR Section 10.1）。

1.3　治験対象集団の人口統計学的特性及びその他の特性

1.3.1　　人口統計学的特性

1.3.1.1　　成人の臨床試験データ

1.3.1.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の人口統計学的特性を表 2.7.4 - 16 に示す。テデュグルチド群とプラセボ群の人口統計学的特性は同様であった。CL0600-020 試験及び CL0600-004 試験では女性（54.1%）が男性（45.9%）よりもやや多かった。年齢（平均値）はテデュグルチド群では 49.7 歳（範囲：19～79 歳）で、プラセボ群では 49.6 歳（範囲：18～82 歳）であった。全ての投与群において多くの被験者が 65 歳未満であった。被験者の 90%以上がヒスパニック及びラテン系以外の白人であった。被験者の多くは米国以外の実施医療機関で登録された。体重（平均値）はいずれの投与群も約 60 kg であり、類似していた。

表 2.7.4 - 16　CL0600-020 試験及び CL0600-004 試験：人口統計学的特性（安全性解析対象集団）

Parameter	Placebo (N=59) n (%)	Teduglutide 0.05 mg/kg/day (N=77) n (%)	Teduglutide 0.10 mg/kg/day (N=32) n (%)	Teduglutide All (N=109) n (%)
Gender, n (%)				
Male	26 (44.1)	37 (48.1)	13 (40.6)	50 (45.9)
Female	33 (55.9)	40 (51.9)	19 (59.4)	59 (54.1)
Age (years), Mean (SD)	49.6 (15.4)	49.4 (13.3)	50.3 (14.0)	49.7 (13.5)
Age Category (years), n (%)				
<65 years	51 (86.4)	66 (85.7)	29 (90.6)	95 (87.2)
≥65 years	8 (13.6)	11 (14.3)	3 (9.4)	14 (12.8)
Race, n (%)				
White	56 (94.9)	73 (94.8)	30 (93.8)	103 (94.5)
Black	2 (3.4)	3 (3.9)	2 (6.3)	5 (4.6)
Other	1 (1.7)	1 (1.3)	0	1 (0.9)
Geographic Region, n (%)				
US	15 (25.4)	18 (23.4)	10 (31.3)	28 (25.7)
Ex-US	44 (74.6)	59 (76.6)	22 (68.8)	81 (74.3)
Weight at Baseline (kg), Mean (SD)	61.6 (11.8)	61.0 (10.3)	60.1 (10.1)	60.8 (10.2)
BMI at Baseline (kg/m^2), Mean (SD)	22.1 (3.1)	21.8 (3.1)	21.9 (2.7)	21.9 (3.0)

BMI=body mass index; US=United States
Studies included: CL0600-020, CL0600-004.
Note: Age is calculated as the age at informed consent.
Note: Race and ethnicity are presented for subjects for which a value was provided. For Race, White corresponds to categories of 'White' and 'Caucasian', Black corresponds to categories of 'Black' and 'African American or Black', and Other corresponds to all other categories that contain a value for race. Note: Ethnicity was collected in study CL0600-020 only.
Source: Module 5.3.5.3 Adult ISS Table 3.1.2

1.3.1.1.2　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）では、登録された被験者の多くが白人（84/88 例、95.5%）であり、45～65 歳（年齢［平均値］50.9 歳、範囲：18～82 歳）であった。88 例中 15 例（17.0%）が 65 歳以上であった。性別の分布は男性 41/88 例（46.6%）、女性 47/88 例（53.4%）であった。ベースラインの人口統計学的特性は NT, PBO/TED 群（NT/TED 群及び PBO/TED 群の統合）及び

TED/TED 群の間で同様であった。安全性解析対象集団と ITT 集団は同一であるため、人口統計学的特性も同一であった（5.3.5.2 項 CL0600-021 CSR Table 14.1.3.1、Listing 16.2.4.1）。

CL0600-005 試験（5.3.5.2 項）では、ベースラインの人口統計学的特性は投与群間で概ね同様であった。本試験に登録された被験者の多くは白人（90.8%）であり、20～80 歳（平均値：48.5 歳）であり、被験者の 36.9%が 55 歳以上であった。参加した男性と女性の比率は同程度であった（男性 50.8%、女性 49.2%）。PS 量カテゴリーがレベル 1 であった被験者は少なく（15.4%）、大半（56.9%）が PS 量カテゴリーレベル 2 であった。（レベル 1：静脈内投与のみ、レベル 2：PS を週に 3～5 日、レベル 3：PS を週に 6～7 日）いずれの PS 量カテゴリーについても、投与群間で統計学的有意差は認められなかった。また、人口統計学的特性及びベースライン特性のいずれについても、投与群間で統計学的有意差は認められなかった（$p > 0.05$）（5.3.5.2 項 CL0600-005 CSR Table 14.1.1.2.1 及び 14.1.1.3.1）。

TED-C11-001 試験（5.3.5.2 項）では、組み入れられた被験者の多くは白人（12/14 例、85.7%）であり、コア試験である CL0600-020 試験登録時の年齢は 45～65 歳（年齢［平均値］55.9 歳、範囲 40～80 歳）であった。2/14 例（14.3%）が 65 歳以上であった。性別の分布は女性 10/14 例（71.4%）、男性 4/14 例（28.6%）であった。安全性解析対象集団及び ITT 集団の人口統計学的特性は同一であった（5.3.5.2 項 TED-C11-001 CSR Table 14.1.2.1、Listing 16.2.3.1）。

1.3.1.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）の人口統計学的特性及びベースライン特性の要約を表 2.7.4 - 17 に示す。同意取得時における安全性解析対象集団の年齢（平均値±SD）は 40.4±8.92 歳であり、5 例（71.4%）が 45 歳未満であった。また 7 例全例が日本人、4 例（57.1%）が女性、3 例（42.9%）が男性であった。身長は 160.5±5.83 cm、体重 48.9±7.12 kg、BMI は 19.0±2.57 kg/m^2 であった（いずれも平均値±SD）。ITT 集団及び安全性解析対象集団が同一であったことから、人口統計学的特性及びベースラインの特性は ITT 集団及び安全性解析対象集団で同一であった。PP 集団から除外された被験者は 1 例のみであったため、人口統計学的特性及びベースライン特性は、PP 集団の被験者並びに ITT 集団及び安全性解析対象集団で類似していた。

表 2.7.4 - 17　SHP633-306 試験：人口統計学的特性（安全性解析対象集団）

Parameter	Statistic	Total Teduglutide Safety (N=7)
Age at Informed Consent (years)	Mean (SD)	40.4 (8.92)
Age Category at Informed Consent (years)		
<45	n (%)	5 (71.4)
>=45 and <65	n (%)	2 (28.6)
Sex		
Male	n (%)	3 (42.9)
Female	n (%)	4 (57.1)
Race		
Asian	n (%)	7 (100.0)
Ethnicity		
Not Hispanic or Latino	n (%)	7 (100.0)
Height (cm) at Screening	Mean (SD)	160.5 (5.83)
Weight (kg) at Baseline	Mean (SD)	48.9 (7.12)
BMI (kg/m^2) at Baseline	Mean (SD)	19.0 (2.57)

Note:　Percentages are based on the number of subjects in the respective populations.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.1.3

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の安全性解析対象集団における人口統計学的特性及びベースライン特性を表 2.7.4 - 18 に示す。同意取得時の年齢（平均値±SD）は 40.9±12.4 歳であり、大半（7 例、63.6%）が 45 歳未満であった。被験者の多くは男性であった（8 例、72.7%）。全ての被験者が日本人であった。身長は 167.1±7.6 cm、体重は 55.9±8.7 kg、BMI は 20.0±2.7 kg/m^2 であった（いずれも平均値±SD）。ITT 集団と安全性解析対象集団は同一であった（5.3.5.2 項 TED-C14-004 CSR Table 14.1.3.2）。

表 2.7.4 - 18　TED-C14-004 試験：人口統計学的特性（安全性解析対象集団）

Parameter	Total Teduglutide (N=11)
Age at Informed Consent (years), Mean (SD)	40.9 (12.41)
Age Category at Informed Consent (years), n (%)	
<45 years	7 (63.6)
45-<65 years	4 (36.4)
≥65 years	0
Sex, n (%)	
Male	8 (72.7)
Female	3 (27.3)
Race, n (%)	
Japanese	11 (100.0)
Ethnicity	
Not Hispanic or Latino	11 (100.0)
Height at Baseline (cm), Mean (SD)	167.06 (7.59)
Weight at Baseline (kg), Mean (SD)	55.85 (8.66)
BMI at Baseline (kg/m^2), Mean (SD)	19.98 (2.73)

Note:　Percentages are based on the safety population.
Source: Module 5.3.5.2 TED-C14-004 CSR Table 14.1.3.2

1.3.1.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、同意取得時の年齢（平均値±SD）は 41.8±8.78 歳であり、6 例（54.5%）が 45 歳未満であった。65 歳以上の被験者はいなかった。被験者全 11 例が日本人、7 例（63.6%）が男性、4 例（36.4%）が女性であった。身長は 165.35±7.068 cm、体重は 53.57±10.660 kg、BMI は 19.49±3.114 kg/m^2 であった（いずれも平均値±SD、5.3.5.2 項 SHP633-307 CSR Section10.4.1）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間における人口統計学的特性及びベースライン特性については、本概要 1.3.1.1.3 を参照のこと。

1.3.1.2　小児の臨床試験データ

1.3.1.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データにおける人口統計学的特性及びベースライン特性を表 2.7.4 - 19 に示す。被験者の年齢（平均値±SD）は 5.5±3.7 歳であり、大半の被験者が 1～12 歳未満であった（92.1%）。被験者の大半は男性（68.3%）、白人（71.3%）、ヒスパニック系及びラテン系以外（66.3%）であった。被験者の成長パラメータは、体重及び身長で年齢層の平均値を下回っていた。BMI の Z スコアは、

0.0125 mg/kg/日群を除く全ての投与群で 0 付近であったことから、一部の被験者は慢性栄養障害のために発育不良であったことが示唆された。

表 2.7.4 - 19　TED-C13-003 試験及び TED-C14-006 試験：人口統計学的特性（安全性解析対象集団）

	0.0125 mg/kg/day Teduglutide (N=8)	0.025 mg/kg/day Teduglutide (N=38)	0.05 mg/kg/day Teduglutide (N=41)	Total Teduglutide (N=87)	Standard of Care (N=14)	Total (N=101)
Age at Baseline (years), Mean (SD)	5.1 (4.6)	5.9 (3.6)	5.6 (3.6)	5.7 (3.6)	4.4 (4.1)	5.5 (3.7)
Age Group at Baseline of TED-C13-003/ TED-C14-006, n (%)						
1 - <12 years	7 (87.5)	35 (92.1)	38 (92.7)	80 (92.0)	13 (92.9)	93 (92.1)
12 - <18 years	1 (12.5)	3 (7.9)	3 (7.3)	7 (8.0)	1 (7.1)	8 (7.9)
Sex, n (%)						
Male	6 (75.0)	27 (71.1)	27 (65.9)	60 (69.0)	9 (64.3)	69 (68.3)
Female	2 (25.0)	11 (28.9)	14 (34.1)	27 (31.0)	5 (35.7)	32 (31.7)
Race, n (%)						
White	6 (75.0)	27 (71.1)	34 (82.9)	67 (77.0)	5 (35.7)	72 (71.3)
Black or African American	2 (25.0)	4 (10.5)	4 (9.8)	10 (11.5)	2 (14.3)	12 (11.9)
Asian	0	1 (2.6)	2 (4.9)	3 (3.4)	2 (14.3)	5 (5.0)
Other	0	2 (5.3)	0	2 (2.3)	2 (14.3)	4 (4.0)
Not allowed based on local regulations	0	3 (7.9)	1 (2.4)	4 (4.6)	3 (21.4)	7 (6.9)
Not applicable	0	1 (2.6)	0	1 (1.1)	0	1 (1.0)
Ethnicity, n (%)						
Hispanic or Latino	1 (12.5)	11 (28.9)	8 (19.5)	20 (23.0)	4 (28.6)	24 (23.8)
Not Hispanic or Latino	7 (87.5)	23 (60.5)	31 (75.6)	61 (70.1)	6 (42.9)	67 (66.3)
Not reported	0	3 (7.9)	1 (2.4)	4 (4.6)	3 (21.4)	7 (6.9)
Not applicable	0	1 (2.6)	1 (2.4)	2 (2.3)	1 (7.1)	3 (3.0)
Weight Z-Score at Baseline, Mean (SD)	-1.29 (0.95)	-0.72 (1.05)	-0.83 (1.02)	-0.82 (1.03)	-0.29 (0.98)	-0.75 (1.04)
Height Z-Score at Baseline, Mean (SD)	-1.07 (0.83)	-1.18 (1.17)	-1.24 (1.27)	-1.20 (1.18)	-0.44 (1.55)	-1.09 (1.26)
BMI Z-Score at Baseline, Mean (SD)	-0.56 (0.64)	0.07 (1.03)	-0.02 (1.08)	-0.03 (1.03)	0.05 (0.77)	-0.02 (1.00)

BMI=body mass index
Note: Percentages are based on the number of subjects in the safety population for each treatment groups.
Note: Body mass index (BMI) is calculated as body weight in kg divided by height in meters squared, when both body weight and height are collected.
Note: Z-score is calculated as (observed value - median value of the reference population) / standard deviation value of reference population. Centers for Disease Control and Prevention (age ≥2 years old) and World Health Organization (age <2 years old) Z-score calculation charts are used for calculation.
Source: Module 5.3.5.3 Pediatric ISS Table 3.1

1.3.1.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データにおける被験者の年齢（平均値±SD）は 5.8±3.8 歳であり、大半の被験者が 1 歳～12 歳未満であった（91.1%）。被験者の大半は男性（68.4%）、白人（72.2%）、ヒスパニック系及びラテン系以外（62.0%）であった。体重及び身長は年齢層の平均値を下回っていた。TED/NTT 群及び TED/TED 群の BMI の Z スコアは 0 に近かったことから、一部の被験者は慢性栄養障害のために発育不良であったことが示唆された。各試験の人口統計学的データは各試験の CSR を、また統合データについては 5.3.5.3 項 Pediatric ISS Table 3.2 を参照のこと。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

1.3.1.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、修正月齢（平均値±SD）は 8.2±2.33 ヵ月であり、被験者の修正月齢は 2 群間で同程度であった。被験者の大部分は 6～12 ヵ月（83.3%）であり、テデュグルチド群の 1 例は 4～6 ヵ月未満であった。テデュグルチド群の 1 例を除く全例が男性であった。標準治療群のアジア人 1 例を除き、全例が白人であり、ヒスパニック又はラテン系の被験者はいなかった。標準治療群の 1 例では、ベースラインの体重 Z スコアが−2.62、体重/身長比 Z スコアが−2.15 であった（5.3.5.2 項 SHP633-301 Interim CSR Appendix 16.2.4、Listing 16.2.4.1）。ベースライン時における体重及び体重/身長比 Z スコア（平均値）の 2 群間の不均衡はこの被験者によるものであった。残りの被験者の成長パラメータは、妊娠期間で補正した平均値の SD±1 以内であった（5.3.5.2 項 SHP633-301 Interim CSR Section 10.4.1、Table 14.1.4.1.3、Table 14.1.4.2.3）。

最終解析では、被験者の修正月齢（平均値±SD）は 2 群間で同程度であった。全体で修正月齢（平均値±SD）は 8.4±2.71 ヵ月であった。被験者の大部分（70.0%）は修正月齢 6～12 ヵ月であり、テデュグルチド群の 2 例（40.0%）及び標準治療群の 1 例（20.0%）は修正月齢 4～6 ヵ月未満であった。テデュグルチド群の 1 例及び標準治療群の 2 例を除く全例が男性であった。各投与群で 1 例のアジア人を除き全例が白人であり、ヒスパニック又はラテン系の被験者はいなかった。安全性解析対象集団では、ベースラインの Z スコア（平均値）は、体重が−0.7±1.43、身長が−0.2±1.64、体重/身長比が−0.7±1.12 であり、2 投与群間で同様であった。テデュグルチド群の 1 例では、ベースラインの体重 Z スコアが−3.7、及び体重/身長比 Z スコアが−2.4 であり、標準治療群の 1 例では、ベースラインの体重 Z スコアが−2.8、及び体重/身長比 Z スコアが−2.2 であった（5.3.5.2 項 SHP633-301 Final CSR Section 10.4.1、Table 14.1.4.1.3、Table 14.1.4.2.3、及び Appendix 16.2.4、Listing 16.2.4.1）。

1.3.1.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）の ITT 集団における人口統計学的特性及びベースライン特性を表 2.7.4 - 20 に示す。小児コホートにおける被験者の年齢（平均値±SD）は 7.0±3.57 歳であり、男性は 7 例（87.5%）であった。

乳児コホートの被験者 2 例の修正月齢（平均値±SD）は 10.0±1.20 ヵ月で、男女各 1 例であった。

小児及び乳児ともに、身長／年齢比 Z スコア及び BMI／年齢比 Z スコアは低値であった。これらの値は 0 未満であり、これらの被験者は慢性的な栄養欠乏のための発育不全であったことが示唆された。ベースライン時の体重／年齢比 Z スコア（平均値±SD）は、小児コホートで−1.92±1.379、乳児コホートで−2.92±2.671 であった。

表 2.7.4 - 20　SHP633-302 試験：人口統計学的特性（ITT 集団）

Parameters	Children[a] After Amendment 3 (N=6)	Total Children[a] (N=8)	Infants[b] (N=2)
Age of Children (years), Mean (SD)	7.1 (3.92)	7.0 (3.57)	-
Age of Infants (months), Mean (SD)			
Chronological Age	-	-	10.8 (1.84)
Corrected gestational age	-	-	10.0 (1.20)
Sex, n (%)			
Male	5 (83.3)	7 (87.5)	1 (50.0)
Female	1 (16.7)	1 (12.5)	1 (50.0)
Race, n (%)			
Japanese	6 (100.0)	8 (100.0)	2 (100.0)
Height or Length for Age Z-Score at Baseline, Mean (SD)	-1.78 (1.42)	-2.15 (1.39)	-3.65 (1.14)
Weight for Age Z-Score at Baseline, Mean (SD)	-1.61 (1.41)	-1.92 (1.38)	-2.92 (2.67)
BMI for Age Z-Score at Baseline (For only children), Mean (SD)	-0.86 (1.73)	-0.86 (1.51)	-
Weight for Length Z-Score at Baseline (For only infants), Mean (SD)	-	-	-1.35 (4.91)
Head Circumference for Age Z-Score at Baseline, Mean (SD)	2.63 (-)[d]	2.63 (-)[d]	0.04 (2.81)

SD=standard deviation
a: Children aged 1 through 15 years.
b: Infants of 4 through <12 months corrected gestational age.
c: The number of children enrolled based upon the protocol amendment 3 and 4.
d: n=1.
Note: Head circumference was scheduled to be collected only for subjects ≤36 months of age.
Note: BMI and BMI for age Z-score were only calculated for children ≥2 years of age.
Note: A z-score was the deviation of the value for an individual from the mean value of the reference population divided by the standard deviation for the reference population. Z-scores for infants were based on the corrected gestational age.
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.1.3.1

1.3.1.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、ベースライン（SHP633-302 試験開始時）における小児コホート全体の年齢（平均値±SD）は、6.70±3.754 歳、男性の割合は 85.7%（6/7 例）であり、乳児コホートの修正月齢（平均値±SD）は 9.95±1.202 ヵ月、男女 1 例ずつであった。小児及び乳児のベースライン（SHP633-302 試験開始時）の成長パラメータは体重、身長及び BMI の年齢比 Z スコアが低く、これらの被験者は慢性疾患又は栄養不足のために発育不全であったことが示唆された（5.3.5.2 項 SHP633-305 CSR Section 10.4）。

1.3.2　　短腸症候群病歴

試験ごとに、個々の治験デザインに応じて異なる情報を収集している場合がある。本項では、入手可能な場合は、SBS の病歴、手術歴及びベースライン時の PS 使用期間を示す。

1.3.2.1　　成人の臨床試験データ

1.3.2.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データにおける病歴及び手術歴は、プラセボ群とテデュグルチド群とで類似していた。プラセボ群及びテデュグルチド群の約 1/3 の被験者は腸切除の主な理由としてクローン病を、別の約 1/3 の被験者は腸閉塞の主な理由として血管疾患を有していた。テデュグルチド群（58.7%）及びプラセボ群（62.7%）の被験者の多くは消化管ストーマを有していなかった。消化管ストーマを有する被験者のうち、多くは空腸ストーマ又は回腸ストーマであり、結腸ストーマは少数であった。被験者の多くは結腸の連続性を有しており（テデュグルチド群 64.2%、プラセボ群 57.6%）、ベースライン前の大腸内視鏡検査では多くの被験者が正常であり（テデュグルチド群 82.4%、プラセボ群 75.0%）、腸異形成又は悪性腫瘍の症例は認められなかった。残存結腸の割合はテデュグルチド群 64.9%、プラセボ群 69.3%であった。残存小腸の長さ（平均値）はテデュグルチド群 72.2 cm、プラセボ群 71.0 cm であった。テデュグルチド群の 24 例（22.4%）及びプラセボ群の 17 例（28.8%）は回腸末端部を有していた。回腸末端部が残存する被験者のうち回盲弁を有したのは、テデュグルチド群 11 例（45.8%）及びプラセボ群 11 例（64.7%）であった（5.3.5.3 項 Adult ISS Table 6.1.1）。プラセボ群、テデュグルチド 0.05 mg/kg/日群、及び 0.10 mg/kg/日群において、ベースライン時の週間 PS 量の平均値（被験者日誌データによる）はそれぞれ 12.7 L、11.4 L、及び 12.9 L であった。静脈アクセスのタイプは、全ての投与群で主に中心静脈カテーテル（86.4%～87.5%）であった（5.3.5.3 項 Adult ISS 5.3.5.3.2 項 ISS Table 5.1.1）。

1.3.2.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）では、腸切除の主な原因は血管疾患（29/88 例、33.0%）に次いで「その他」の理由（22/88 例、25.0%）、及びクローン病（16/88 例、18.2%）であった。ストーマを有する被験者は 36/88 例（40.9%）であり、空腸ストーマ／回腸ストーマが最も多かった（27/36 例、75.0%）。残存小腸の長さ（平均値±SD）は 67.3±52.60 cm（範囲：5～250 cm）であった。TED/TED 群の被験者では、残存小腸の長さ（77.4 cm）が NT, PBO/TED 群（59.8 cm）に比べて長かった。結腸の連続性が認められなかった被験者は 34/88 例（38.6%）であった。残存結腸の割合（平均値）は 62.5%であった。NT, PBO/TED 群における残存結腸の割合（67.5%）は、TED/TED 群（55.0%）に比べて高かった。26/88 例（29.5%）で回腸末端部が残存していた。14/88 例（15.9%）で回盲弁が温存されていた（5.3.5.2 項 CL0600-021 CSR Section 11.2.1、Table 14.1.3.3）。PS 開始からの使用年数（平均値±SD）は 6.41±6.27 年であった。アクセスは大半の被験者（89.8%）で中心静脈であった。スクリーニング時の PS 使用歴は NT, PBO/TED 群と TED/TED 群で同様であった。被験者全体の、医師処方データに基づくベースライン時の週間 PS 量（以降 PS 処方量とする。平均値±SD）は 12.07±7.56 L であり、週間 PS 施行日数（平均値±SD）は 5.6±1.68 日であった。各投与群において、ベースライン時の週間 PS 処方量（平均値±SD）は、NT, PBO/TED 群で 11.58±7.44 L、TED/TED 群で 12.75±7.77 L であった。ベースライン時の PS 使用歴は、NT, PBO/TED 群と TED/TED 群で同様であった（5.3.5.2 項 CL0600-021 CSR Section 11.2.1、Appendix 16.2 Listing 16.2.4.2）。

CL0600-005 試験（5.3.5.2 項）では、腸切除の主な原因はクローン病（24/65 例、36.9%）次いで血管疾患（21/65 例、32.3%）であった。ストーマを有する被験者は 21/65 例（32.3%）であり、回腸ストーマ（9/65 例、42.9%）又は空腸ストーマ（9/65 例、42.9%）が最も多かった。残存小腸の長さ（平均値±SD）は 61.5±39.17 cm（範囲：10～200 cm）であった。結腸が切除された被験者は 19 例（29.2%）であった。結腸が存在する残りの 46 例（70.8%）における残存結腸の割合は、12 例では 90%以上～100%未満、18 例では 50%超～90%以下、16 例では 50%以下であった。回腸末端部が残存していた 12 例のうち、7 例で回盲弁が温存されていた。大半の被験者（69.2%）では、残存回腸の長さが手術により測定された（5.3.5.2 項 CL0600-005 CSR Section 11.2）。登録時の週間 PS 処方量（平均値±SD）は、プラセボ/0.05 mg/kg/日群及び 0.05/0.05 mg/kg/日群でそれぞれ 9.0±4.38 L 及び 9.8±4.37 L、プラセボ/0.10 mg/kg/日群及び 0.10/0.10 mg/kg/日群でそれぞれ 11.1±4.89 L 及び 13.1±6.28 L であった。静脈アクセスは大半の被験者（89.2%）で中心静脈であり、頸静脈アクセスは 24.6%であった。残りの被験者では、肘前又はその他の静脈アクセスラインが使用された。過去 6 ヵ月間に、被験者の 26.2%が静脈ライン感染の治療を受けていた（5.3.5.2 項 CL0600-005 CSR Section 11.2、Table 14.1.1.6.1、Listing 16.2.7.3、Listing 16.2.7.4）。

TED-C11-001 試験（5.3.5.2 項）では、腸切除の主な原因は「その他」の理由（5/14 例、35.7%）次いで血管疾患（4/14 例、28.6%）であった。ストーマを有する被験者は 5/14 例（35.7%）であり、回腸ストーマが最も多かった（ストーマを有する被験者 5 例中 3 例、60.0%）。残存小腸の長さ（平均値±SD）は 73.1±47.28 cm（範囲：17～190 cm）であった。結腸

の連続性が認められなかった被験者は 6/14 例（42.9%）であった（5.3.5.2 項 TED-C11-001 CSR Section 11.2.1、Table 14.1.2.3）。PS 開始からの使用年数（平均値±SD）は 5.99±7.42 年であった。被験者全体で、ベースライン時の週間 PS 処方量（平均値±SD）は 11.29±8.55 L であった。週間 PS 施行日数（平均値±SD）は 5.8±1.37 日であった。予想されたとおり、この集団におけるスクリーニング時の PS 使用歴はこれまでの試験で認められた使用歴と同様であった（5.3.5.2 項 TED-C11-001 CSR 11.2.1、Table 14.1.2.4、Table 14.1.2.5）。

1.3.2.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）で、SBS と診断された主な理由はクローン病であった（6/7 例、85.7%）。ストーマは 7 例中 5 例（71.4%）に存在し、全例が回腸ストーマを有していた。7 例中 4 例（57.1%）で結腸が残存しており、残存結腸の割合（平均値±SD）は 31.3±14.4%であった。残存小腸の長さが既知であった 5/7 例（71.4%）のうち、全例が 60cm 以上残存していた（233.4±133.48cm）。本試験の 7 例はいずれも回腸末端部を有していなかった。SBS の罹病期間（平均値±SD）は 19.3±6.76 年であった（5.3.5.2 項 SHP633-306 CSR Table 14.1.4）。PS 開始からの使用年数（平均値±SD）は 11.1±3.86 年であった。スクリーニング時及びベースライン時の週間 PS 処方量（平均値±SD）は、それぞれ 13.7±6.82L/週及び 14.9±6.66L/週であった。スクリーニング時及びベースライン時の週間 PS 施行日数の平均値は 7.0 日であった（5.3.5.2 項 SHP633-306 CSR Table 14.1.5）。安全性解析対象集団のうち、クローン病の既往歴のある 6/7 例（85.7%）では、6 例全例がベースライン時に臨床寛解（非活動性クローン病）であった（5.3.5.2 項 SHP633-306 CSR Table 14.1.6）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む）における SBS の罹病期間（平均値±SD）は 6.6±3.6 年であった。腸切除の主な原因はクローン病（8/11 例、72.7%）であった。残存小腸の長さ及び残存結腸の長さの測定法は、手術 9/11 例（81.8%）、X 線検査 1/11 例（9.1%）、内視鏡検査 1/11 例（9.1%）であった。ストーマを有する被験者は 6/11 例（54.5%）であった。うち回腸ストーマが 5/6 例（83.3%）、空腸ストーマが 1/6 例（16.7%）であった。6/11 例（54.5%）で結腸が残存していた。これらの被験者の残存結腸の割合（平均値±SD）は 61.7±31.3%であった。結腸の連続性が認められなかった被験者は 1/6 例（16.7%）であった。残存小腸の長さ（平均値±SD）は 102.7±80.4 cm であった。被験者の多く（8/11 例、72.7%）において、残存小腸の長さは 60 cm 以上であった。回腸末端部及び回盲弁が温存されていたのは 1/11 例（9.1%）であった（5.3.5.2 項 TED-C14-004 CSR Section 10.4.2.1、Table 14.1.4.2）。PS 開始からの使用年数（平均値±SD）は 5.2±3.6 年であった。週間 PS 処方量（平均値±SD）は 17.8±8.7 L/週、被験者日誌に基づく PS 量（平均値±SD）は 17.3±8.8 L/週であった。PS 処方カロリー量（平均値±SD）は 9708±3001 kcal/週、被験者日誌による PS カロリー量（平均値±SD）は 9533±3003 kcal/週であった。処方データに基づく週間 PS 施行日数及び被験者日誌に基づく週間 PS 施行日数（平均値±SD）はいずれも 7±0 日であった（5.3.5.2 項 TED-C14-004 CSR 10.4.2.2、Table 14.1.5.2）。

1.3.2.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、SBS の平均罹病期間は 12.65±8.457 年であった。SBS と診断された主な理由は、クローン病が 9/11 例（81.8%）であった。ストーマを有する被験者は 7/11 例（63.6%）、うち回腸ストーマは 6 例（85.7%）、空腸ストーマは 1 例（14.3%）であった。被験者 6 例（54.5%）に残存結腸が認められ、残存結腸の割合（平均値±SD）は 48.7±27.76%であった。被験者 10 例に残存小腸の長さが判明しているが、9/11 例（81.8%）では、全例が 60 cm 以上残存していた（残存小腸の長さ［平均値±SD］は被験者全体で 174.5±127.42 cm、SHP633-306 試験から移行した被験者：320.0±81.85 cm、TED-C14-004 試験から移行した被験者：112.1±83.66 cm）。本試験に組み入れた 11 例のうち、回腸末端部を有する被験者はいなかった（5.3.5.2 項 SHP633-307 CSR Section 10.4.2）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）における SBS の病歴については、本概要 1.3.2.1.3 を参照のこと。

1.3.2.2　　小児の臨床試験データ

1.3.2.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データによると、これら 2 試験の被験者における SBS の主な原因は腹壁破裂（31.7%、32/101 例）、中腸軸捻転（29.7%、30/101 例）、及び壊死性腸炎（17.8%、18/101 例）であった。残存小腸の長さ（平均値±SD）は推定 44.7±33.00 cm であった。ストーマを有する被験者は 17.8%（18/101 例）であった。ストーマを有する被験者のうち、61.1%（11/18 例）が空腸ストーマ、27.8%（5/18 例）が回腸ストーマ、11.1%（2/18 例）が結腸ストーマであった。被験者の多く（92.1%、93/101 例）で結腸が残存していた。残存結腸の割合（平均値±SD）は 66.4±32.57%であった。結腸が残存していた被験者のうち、6 例（6.5%）では結腸の連続性が認められなかった。回腸末端部が残存していた被験者の割合は 30.7%（31/101 例）であった。回腸末端部が残存していた被験者のうち、26 例（83.9%）で回盲弁が温存されていた（全体の 25.7%）。PS 開始からの使用期間（平均値±SD）は 5.0±3.35 年であった。被験者の大半（61.4%）では、ベースライン時に 50 mL/kg/日以上の PS を使用していた。各試験の結果は CSR 又は 5.3.5.3 項 Pediatric ISS Table 3.1、ISS Table 4.1 を参照のこと。

1.3.2.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）において、SBS の主な原因は腹壁破裂（32.9%、26/79 例）、中腸軸捻転（31.6%、25/79 例）、及び壊死性腸炎（16.5%、13/79 例）であった。残存小腸の長さ（平均値±SD）は推定 43.9±34.48 cm であった。ストーマを有する被験者は 19.0%（15/79 例）であった。そのうち、73.3%（11/15 例）が空腸ストーマ、13.3%（2/15 例）が回腸ストーマ、13.3%（2/15 例）が結腸ストーマであった。

被験者の 93.7%（74/79 例）で結腸が残存していた。残存結腸の割合（平均値±SD）は 65.8±32.72%であった。結腸が残存していた被験者のうち、93.2%（69/79 例）では残存結腸の連続性が認められなかった。回腸末端部が残存していた被験者の割合は 34.2%（27/79 例）であった。回腸末端部が残存していた被験者のうち、81.5%（22/27 例）で回盲弁が温存されていた（全体の 27.8%）。PS 開始からの使用期間（平均値±SD）は 5.3±3.37 年であった。被験者の大半（58.2%）は、ベースライン時に 50 mL/kg/日以上の PS を使用していた。各試験の人口統計学的データは各試験の CSR を、また統合データについては 5.3.5.3 項 Pediatric ISS Table 3.2 及び Table 4.2 を参照のこと。

1.3.2.2.3　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、SBS の主な原因は腹壁破裂（各群 2 例）及び壊死性腸炎（各群 1 例）であった。残存小腸の長さの平均値（6 例中 5 例で手術により測定）は、テデュグルチド群で 27.7±12.50 cm、標準治療群で 19.0±13.53 cm、全体で 23.3±12.58 cm であった。ストーマを有する患者はいなかった。全ての被験者は結腸が残存しており、残存結腸の割合（平均値±SD）は全体で 71.0±6.52%であった。全ての被験者で残存結腸の連続性が認められた。回腸末端部を有する被験者はなかった（5.3.5.2 項 SHP633-301 Interim CSR Section10.4.3.1、Table14.1.4.4.2）。

最終解析では、SBS の主な原因は腹壁破裂（テデュグルチド群 3 例、及び標準治療群 2 例）、壊死性腸炎（テデュグルチド群 1 例、及び標準治療群 2 例）、腸管閉鎖（テデュグルチド群 1 例）、及びその他（標準治療群 1 例）であった。残存小腸の長さの平均値（10 例中 9 例で手術により測定、5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.4、Listing 16.2.4.3）は、テデュグルチド群で 23.4±10.69 cm、標準治療群で 35.0±34.92 cm、全体で 29.2±25.10 cm であった。標準治療群の 1 例がストーマ（結腸瘻造設）を有していた。全ての被験者は結腸が残存しており、残存結腸の割合（平均値±SD）は全体で 65.6±23.37%であった。9 例（90.0%）で残存結腸の連続性が認められ、テデュグルチド群の 1 例は回盲弁を有していた（5.3.5.2 項 SHP633-301 Final CSR Section 10.4.3.1、Table 14.1.4.4.2）。

1.3.2.2.4　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）で、小児コホートにおける SBS の罹患期間（平均値±SD）は 7.0±3.56 年であった。SBS の主な原因は中腸軸捻転（6 例、75%）であった。残存小腸の長さ（平均値±SD）は 23.1±15.86cm で、全例に結腸が残存し、残存結腸の割合（平均値±SD）は 82.5±32.40%であった。8 例中 5 例（62.5%）は回腸末端部を有し、4 例（50.0%）は回盲弁を有していた。

乳児コホートの 2 例では、SBS 病歴（平均値±SD）は 10.7±1.93 ヵ月であった。乳児被験者 1 例の SBS の原因は中腸軸捻転であり、他の 1 例は先天性中腸欠損であった。残存小腸の長さ（平均値±SD）は 6.0±5.66cm であった。2 例とも結腸が残存し、残存結腸の長さ（平均値±

SD）は 75.0±35.36%であった。2 例中 1 例は回腸末端部と回盲弁を有していた。詳細は 5.3.5.2 項 SHP633-302 CSR Table 14.1.4.1 を参照のこと。

1.3.2.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、小児コホートの SBS の罹患期間（平均値±SD）は 6.66±3.737 年（SHP633-302 試験開始時）であった。SBS の主な原因は、中腸軸捻転（6 例、85.7%）であった。残存小腸の長さ（平均値±SD）は 22.00±17.056 cm であった。小児コホートの各被験者では結腸は少なくとも 30%以上残存しており、結腸残存率（平均値±SD）は 90.00±26.458%であった。ストーマを有する小児被験者はいなかった。小児コホート 7 例中 5 例（71.4%）が回腸末端部を有し、そのうち 4 例（80.0%）が回盲弁を有していた。Amendment 前に登録されたのは小児コホートの 1 例のみであったため、Amendment 以降に登録した 6 例の小児のデータは小児コホート全体と同様であった（Amendment 以降の解析については本概要 1.1.1.5.2.4 を参照）。乳児コホートの SBS の罹患歴（平均値±SD）は 10.66±1.928 ヵ月（SHP633-302 試験開始時）であり、ほぼ生後すぐの発症であった。SBS の主な原因は、中腸軸捻転及び中腸の先天的欠損が各 1 例であった。乳児被験者 2 例はいずれもストーマを有していなかった。残存小腸の長さ（平均値±SD）は 6.00±5.657 cm であった。結腸は、乳児被験者 1 例では 50%、他の 1 例は 100%残存していた。乳児被験者 1 例は回腸末端部及び回盲弁を有していた（5.3.5.2 項 SHP633-305 CSR Section 10.5.1 参照）。

2. 有害事象

本項では特に断りのない限り、有害事象とは TEAE であり、重篤な有害事象とは試験治療下の重篤な有害事象を示す。

2.1 有害事象の解析

2.1.1 比較的よく見られる有害事象

2.1.1.1 有害事象の概要

2.1.1.1.1 成人の臨床試験データ

2.1.1.1.1.1 成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データにおける有害事象の概要を表 2.7.4 - 21 に示す。

テデュグルチド群では 99 例（90.8%）に 778 件の有害事象が発現した。多くの被験者の有害事象は軽度又は中等度であった。重度の有害事象は 31 例（28.4%）に 69 件認められた。治験薬と関連ありと判断された有害事象は、57 例（52.3%）に 202 件認められた。重篤な有害事象は、39 例（35.8%）に 80 件認められ、そのうち 10 例（9.2%）に認められた 14 件が治験薬と関連ありと判断された。中止に至った有害事象は 10 例（9.2%）に 17 件認められた。

プラセボ群では 49 例（83.1%）に 372 件の有害事象が発現した。多くは軽度又は中等度であった。重度の有害事象は 16 例（27.1%）に 43 件認められた。治験薬と関連ありと判断された有害事象は、21 例（35.6%）に 62 件認められた。重篤な有害事象は 17 例（28.8%）に 34 件認められたが、いずれの事象も治験薬と関連なしと判断された。中止に至った有害事象は 4 例（6.8%）に 5 件認められた。

これらの試験期間中、いずれの投与群においても死亡に至った有害事象は認められなかった。

表 2.7.4 - 21　CL0600-020 試験及び CL0600-004 試験：有害事象の概要（安全性解析対象集団）

			Teduglutide					
	Placebo (N=59)		0.05 mg/kg/day (N=77)		0.10 mg/kg/day (N=32)		All (N=109)	
Parameter	n (%)	E	n (%)	E	n (%)	E	n (%)	E
Any TEAE								
No	10 (16.9)	0	9 (11.7)	0	1 (3.1)	0	10 (9.2)	0
Yes	49 (83.1)	372	68 (88.3)	530	31 (96.9)	248	99 (90.8)	778
TEAE Severity (per subject)								
Mild	45 (76.3)	184	58 (75.3)	286	26 (81.3)	155	84 (77.1)	441
Moderate	34 (57.6)	145	50 (64.9)	182	24 (75.0)	86	74 (67.9)	268
Severe	16 (27.1)	43	25 (32.5)	62	6 (18.8)	7	31 (28.4)	69

表 2.7.4 - 21　CL0600-020 試験及び CL0600-004 試験：有害事象の概要（安全性解析対象集団）

			Teduglutide					
	Placebo (N=59)		0.05 mg/kg/day (N=77)		0.10 mg/kg/day (N=32)		All (N=109)	
Parameter	n (%)	E	n (%)	E	n (%)	E	n (%)	E
TEAE Relationship								
Not Related	47 (79.7)	310	62 (80.5)	392	31 (96.9)	184	93 (85.3)	576
Related	21 (35.6)	62	38 (49.4)	138	19 (59.4)	64	57 (52.3)	202
Any TESAE	17 (28.8)	34	28 (36.4)	64	11 (34.4)	16	39 (35.8)	80
TESAE Severity								
Mild	5 (8.5)	6	6 (7.8)	8	7 (21.9)	9	13 (11.9)	17
Moderate	7 (11.9)	9	16 (20.8)	25	2 (6.3)	3	18 (16.5)	28
Severe	8 (13.6)	19	12 (15.6)	31	4 (12.5)	4	16 (14.7)	35
TESAE Relationship								
Not Related	17 (28.8)	34	23 (29.9)	52	9 (28.1)	14	32 (29.4)	66
Related	0	0	8 (10.4)	12	2 (6.3)	2	10 (9.2)	17
TEAEs Leading to Premature Discontinuation	4 (6.8)	5	8 (10.4)	14	2 (6.3)	3	10 (9.2)	17
AEs Leading to Death	0	0	0	0	0	0	0	0

E = Total number of events; TEAE = Treatment emergent adverse event; TESAE = Treatment emergent serious adverse event.
Studies included: CL0600-020, CL0600-004.
Note: Percentages are based upon the number of subjects in the Safety Population.
Note: Treatment emergent adverse events are defined as any adverse event with a start date on or after the date of first dose and within thirty days after discontinuation of study drug.
Note: Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note: All adverse events were coded using MedDRA version 12.0.
Source: Module 5.3.5.3 Adult ISS Table 9.1.2

2.1.1.1.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）の統合データにおいて、145 例（94.8%）に 1457 件の有害事象が発現した。それぞれ試験別の有害事象の概要は 5.3.5.2 項 CL0600-021 CSR Table 12-2、5.3.5.2 項 CL0600-005 CSR Table 12-2、2.7.6.項を参照のこと。有害事象の大部分は軽度又は中等度であった。重度の有害事象は 58 例（37.9%）に 138 件発現した。治験責任医師により治験薬と関連ありと判断された有害事象は 70 例（45.8%）に 197 件認められた。中止に至った有害事象は 24 例（15.7%）に 35 件発現した。試験期間中に重篤な有害事象が 83 例（54.2%）に 179 件発現した。このうち 14 件は治験責任医師により治験薬と関連ありと判断された。試験期間中に、死亡に至った有害事象が 3 例に発現した（5.3.5.3 項 Adult ISS Table 9.1.3）。

TED-C11-001 試験（5.3.5.2 項）（統合されていない）の有害事象の概要は 5.3.5.2 項 TED-C11-001 CSR Table 14.3.1.2 及び 2.7.6 項を参照のこと。試験期間中に 14 例全例に有害事象が発現した。有害事象の大部分は、軽度又は中等度であった。治験責任医師により治験薬と関連ありと判断された有害事象は 3 例（21.4%）に 6 件発現した。中止に至った有害事象は発現しなかった。

重篤な有害事象が 5 例（35.7%）に発現し、いずれも治験責任医師により治験薬と関連なしと判断された。試験期間中に死亡例は認められなかった。

2.1.1.1.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）における有害事象の概要を表 2.7.4 - 22 に示す。試験期間中に 7 例全例に 34 件の有害事象が発現した。有害事象の大部分は軽度又は中等度であった。治験薬と関連ありと判断された有害事象は、被験者 4 例（57.1%）に 6 件発現した。重篤な有害事象が被験者 3 例（42.9%）で 5 件発現したが、いずれも治験薬と関連なしと判断された。被験者 1 例（14.3%）に発現した 2 件の重篤な有害事象は重度であった。被験者 1 例（14.3%）に治験薬の投与中止に至った有害事象が発現した。試験期間中に死亡例は認められなかった。

表 2.7.4 - 22　SHP633-306 試験：有害事象の概要（安全性解析対象集団）

	Total Teduglutide (N=7)	
Parameter	**Subjects n (%)**	**Events**
Any TEAE	7 (100.0)	34
TEAE Severity		
Mild	7 (100.0)	30
Moderate	2 (28.6)	2
Severe	1 (14.3)	2
TEAE Highest Severity		
Mild	4 (57.1)	
Moderate	2 (28.6)	
Severe	1 (14.3)	
TEAE Relationship		
Not Related	7 (100.0)	28
Related	4 (57.1)	6
TEAE Highest Relationship		
Not Related	3 (42.9)	
Related	4 (57.1)	
Any TESAE	3 (42.9)	5
TESAE Severity		
Mild	2 (28.6)	2
Moderate	1 (14.3)	1
Severe	1 (14.3)	2
TESAE Relationship		
Not Related	3 (42.9)	5
Related	0 (0.0)	0
TEAE Leading to Study Treatment Discontinuation	1 (14.3)	2
TEAE Leading to Death	0 (0.0)	0

Note: Percentages are based on the Safety population.
Note: Treatment-emergent AEs (TEAEs) were defined as AEs whose onset occurred, severity worsened, or intensity increased after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA 21.0.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.3.2.1

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）について、ステージ 2 における有害事象の概要を表 2.7.4 - 23 に示す。ステージ 2 では、10 例（90.9%）に 87 件の有害事象が発現した。有害事象の多くは軽度又は中等度であった。治験薬と関連ありと判断された有害事象は 7 例（63.6%）に 18 件認められた。重篤な有害事象は 6 例（54.5%）に 15 件認められた。このうち、3 例（27.3%）に認められた 8 件の重篤な有害事象は重度と判断され、また 1 例（9.1%）に認められた 3 件の重篤な有害事象は治験薬と関連ありと判断された。被験者 2 例（18.2%）が有害事象により中止に至った。別の 1 例はステージ 2 を完了したが、有害事象のためにステージ 3 へは移行しなかった。死亡に至った有害事象が 1 例（9.1%）に 2 件認められた。これらの事象の簡潔な叙述及び詳細な叙述については、それぞれ 5.3.5.2 項 TED-C14-004 CSR 14.3.3 項及び 2.7.6 項を参照のこと。また、死亡に至った有害事象については本概要 2.1.2 及び 2.7.4 項 付録 1 を参照のこと。

表 2.7.4 - 23　TED-C14-004 試験：ステージ 2 における有害事象の概要（安全性解析対象集団）

	Teduglutide (N=11)	
Parameter	**Subjects n (%)**	**Events**
Any TEAE		
No	1 (9.1)	
Yes	10 (90.9)	87
TEAE Severity		
Mild	10 (90.9)	66
Moderate	2 (18.2)	7
Severe	3 (27.3)	14
TEAE Highest Severity		
Mild	7 (63.6)	
Moderate	0	
Severe	3 (27.3)	
TEAE Relationship		
Not Related	10 (90.9)	69
Related	7 (63.6)	18
TEAE Highest Relationship		
Not Related	3 (27.3)	
Related	7 (63.6)	

表 2.7.4 - 23　TED-C14-004 試験：ステージ 2 における有害事象の概要（安全性解析対象集団）

Parameter	Teduglutide (N=11) Subjects n (%)	Events
Any TESAE	6 (54.5)	15
TESAE Severity		
Mild	4 (36.4)	7
Moderate	0	0
Severe	3 (27.3)	8
TESAE Relationship		
Not Related	6 (54.5)	12
Related	1 (9.1)	3
TEAEs Leading to Premature Discontinuation[a]	2 (18.2)	2
TEAEs Leading to Death	1 (9.1)	2

n=number of subjects experiencing the event; TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event

[a] Subject [redacted] completed Stage 2; however, did not continue onto Stage 3 due to an adverse event of diarrhea (see TED-C14-004 CSR Table 14.3.2.13). The reason for not continuing to Stage 3 is not a variable captured in the database for subjects that did not early terminate in Stage 2.

Note: Percentages are based on the safety population.
Note: Treatment-emergent adverse events are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study drug.
Note: Relationship to study treatment is based upon investigator assessment.
Note: Subjects are counted no more than once for incidence, but can be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA J 17.1.
Source: Module 5.3.5.2 TED-C14-004 CSR Table 14.3.2.1.1

2.1.1.1.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）について、有害事象の概要を 5.3.5.2 項 SHP633-307 CSR Table 14 及び 2.7.6 項に示す。試験期間中、被験者 11 例中 9 例（81.8%）に 64 件の有害事象が発現した。有害事象の大部分は軽度又は中等度であった。治験責任医師により治験薬と関連ありと判断された有害事象は、TED-C14-004 試験から移行した被験者 1 例（9.1%）に 1 件みられた。重篤な有害事象が 7 例（63.6%）に 15 件発現し、いずれも治験薬との関連なしと判断された。重度の有害事象は 2 例（18.2%）に 5 件発現し、2 例とも TED-C14-004 試験から移行した被験者であった。治験薬の投与中止に至った有害事象、特に注目すべき有害事象及び死亡例は認められなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）のステージ 3 及び 4（継続投与期間）では、8 例全例に 135 件の有害事象が認められた（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.1.2、2.7.6 項）。継続投与期間中に報告された有害事象の多くは軽度又は中等度であった。治験薬と関連ありと判断された有害事象は 1 例（12.5%）に 1 件認められた。重篤な有害事象は 5 例（62.5%）に 18 件認められた。このうち、3 例（37.5%）に発現した 9 件は重度であ

り、1 例（12.5%）に発現した 1 件は治験薬と関連ありと判断された。継続投与期間中に有害事象により中止に至った被験者はいなかった。本試験の継続投与期間中に死亡例は認められなかった。

2.1.1.1.1.5　　成人を対象とした国内第 3 相コア試験及び継続投与試験の統合データ

日本人被験者を対象とした SHP633-306 試験、SHP633-307 試験及び TED-C14-004 試験の統合データについて、有害事象の概要を表 2.7.4 - 24 に示した。なお、試験ごとの有害事象の概要は前述した。全体では、18 例全例に有害事象、1 例に死亡（2.1.2.1.3 項）、11 例に重篤な有害事象（2.1.3.1.3 項）、3 例に中止に至った有害事象（2.1.4.1.1.3 項）がみられた。統合データの安全性の結果は個々の試験結果と同様であり、新たな安全性の問題は特定されなかった。SHP633-306 試験（5.3.5.2 項）と SHP633-307 試験（5.3.5.2 項）の 2 試験のみの統合データについては、2.7.4 項　付録 4 Table 3.2 を参照のこと。

表 2.7.4 - 24　SHP633-306、SHP633-307、TED-C14-004 試験：有害事象の概要（安全性解析対象集団）

	Teduglutide Subjects (N=18)
Parameter	**n (%)**
Number of subjects evaluated	18
All AEs	18 (100.0)
Number of deaths	1 (5.6)
Number of subjects with SAEs other than deaths	11 (61.1)
Number of subjects who discontinued	3 (16.7)

n=number of subjects experiencing the event; TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event
Note:　Number of deaths is based on AEs with a Fatal outcome or have an SAE reason of Death. Number of subjects with SAEs other than deaths is based on Serious AEs that wasn't Fatal. Number of Subjects who discontinued based on AEs with "Drug Withdrawn".
Source: 2.7.4 項　付録 4, Table 3.1

2.1.1.1.2　　小児の臨床試験データ

2.1.1.1.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、有害事象全体、12 週以内に発現した有害事象、12～24 週以内に発現した有害事象、及び治験薬投与中止後に発現した有害事象の概要を 5.3.5.3 項 Pediatric ISS Table 6.1 に示す。期間別（12 週以内、12～24 週以内）の有害事象の発現頻度において、期間による特定の傾向は認められなかった。有害事象の発現頻度は治験薬投与中止後の方が低かったが、これはおそらく追跡調査期間が短かったためである。

また、これら 2 試験の統合データにおける有害事象の概要を表 2.7.4 - 25 に示す。有害事象は 0.0125 mg/kg 群で 8 例全例に 57 件、0.025 mg/kg 群で 38 例全例に 384 件、0.05 mg/kg 群で 40 例（97.6%）に 459 件、標準治療群で 14 例全例に 104 件発現した。有害事象の多くは軽度又は中等度であった。テデュグルチド用量群間の比較では有害事象の重症度に特定の傾向はみられなかったが、標準治療群よりもテデュグルチド群において重度の有害事象の発現頻度が高かった。治験薬と関連ありと判断された有害事象は、0.0125 mg/kg 群の 2 例（25.0%）に 7 件、0.025 mg/kg 群の 13 例（34.2%）に 25 件、0.05 mg/kg 群の 12 例（29.3%）に 56 件発現し、全ての用量群で同程度であった。重篤な有害事象は 0.0125 mg/kg 群の 4 例（50.0%）に 4 件、0.025 mg/kg 群の 22 例（57.9%）に 50 件、0.05 mg/kg 群の 28 例（68.3%）に 61 件、標準治療群の 7 例（50.0%）に 16 件発現した。このうち、治験薬と関連ありと判断された重篤な有害事象は 2 件であり、いずれも 0.025 mg/kg 群での発現であった。重篤な有害事象の発現頻度は、全ての用量群及び標準治療群で同程度であった。中止に至った有害事象及び死亡例は認められなかった。

小児の初回製造販売承認申請時、海外小児データを様々な部分集団で統合解析した。有害事象の要約を、年齢（5.3.5.3 項 Pediatric ISS Table 28.1）、性別（5.3.5.3 項 Pediatric ISS Table 34.1）、人種（5.3.5.3 項 Pediatric ISS Table 40.1）、地域（5.3.5.3 項 Pediatric ISS Table 46.1）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 52.1）に基づく部分集団について解析したところ、一部の部分集団では症例数が極めて少なかったものの、有害事象の発現頻度に部分集団による特定の傾向は認められなかった。

表 2.7.4 - 25　TED-C13-003 試験及び TED-C14-006 試験：有害事象の概要（安全性解析対象集団）

	0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)		Standard of Care (N=14)	
Category	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**
Any TEAE	8 (100.0)	57	38 (100.0)	384	40 (97.6)	459	86 (98.9)	900	14 (100.0)	104
TEAE Highest Severity[a]										
Mild	1 (12.5)		10 (26.3)		12 (29.3)		23 (26.4)		6 (42.9)	
Moderate	5 (62.5)		19 (50.0)		13 (31.7)		37 (42.5)		7 (50.0)	
Severe	2 (25.0)		9 (23.7)		15 (36.6)		26 (29.9)		1 (7.1)	
TEAE Relationship										
Not Related	8 (100.0)	50	38 (100.0)	359	40 (97.6)	403	86 (98.9)	812	-	
Related	2 (25.0)	7	13 (34.2)	25	12 (29.3)	56	27 (31.0)	88	-	
Any TESAE	4 (50.0)	4	22 (57.9)	50	28 (68.3)	61	54 (62.1)	115	7 (50.0)	16
TESAE Relationship										
Not Related	4 (50.0)	4	21 (55.3)	48	28 (68.3)	61	53 (60.9)	113	-	

表 2.7.4 - 25　TED-C13-003 試験及び TED-C14-006 試験：有害事象の概要（安全性解析対象集団）

	0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)		Standard of Care (N=14)	
Category	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**
Related	0	0	2 (5.3)	2	0	0	2 (2.3)	2	-	
TEAE Leading to Treatment Discontinuation	0	0	0	0	0	0	0	0	-	
TEAE Leading to Death	0	0	0	0	0	0	0	0	0	0

E=number of events; n=number of subjects; TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event
Note: Percentages are based on the number of subjects in the safety population for each treatment group.
Note: Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
[a] Only highest severity per subject is counted for incidence and percentage.
Source: Module 5.3.5.3 Pediatric ISS Table 6.1

2.1.1.1.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）の試験ごとでみられた有害事象の概要を、5.3.5.2 項 SHP633-304 CSR Table 15、5.3.5.2 項 SHP633-303 CSR Table 21（前向き期間のみ）及び 2.7.6 項に示す。SHP633-304 試験及び SHP633-303 試験（前向き期間のみ）の統合データにおける有害事象は、NTT/TED 群の 1 例（50.0%）に 5 件、TED/NTT 群の 8 例（72.7%）に 21 件、TED/TED 群の 56 例（93.3%）に 433 件発現した。有害事象の大部分は軽度又は中等度であった。治験薬と関連ありと判断された有害事象は、TED/TED 群の 12 例（20.0%）に 17 件認められ、NTT/TED 群及び TED/NTT 群では認められなかった。重篤な有害事象は、NTT/TED 群では認められず、TED/NTT 群の 5 例（45.5%）に 5 件、TED/TED 群の 30 例（50.0%）に 62 件発現した。このうち、治験薬と関連ありと判断されたのは TED/TED 群の 2 例（3.3%）にみられた 2 件であった。治験薬の投与中止に至った有害事象は TED/TED 群の 1 例（1.7%）に 1 件認められた。死亡に至った有害事象は TED/TED 群の 1 例（1.7%）に 1 件認められ、治験薬と関連なしとされた（5.3.5.3 項 Pediatric ISS Table 6.2.2）。死亡に至った有害事象の叙述については、5.3.5.2 項 SHP633-304 CSR Section 14.3.3 又は 2.7.6 項及び本概要 2.1.2.2.2 を参照のこと。

小児の初回製造販売承認申請時、海外小児データを様々な部分集団で統合解析した。有害事象の要約を、年齢（5.3.5.3 項 Pediatric ISS Table 28.2.2）、性別（5.3.5.3 項 Pediatric ISS Table 34.2.2）、人種（5.3.5.3 項 Pediatric ISS Table 40.2.2）、地域（5.3.5.3 項 Pediatric ISS Table 46.2.2）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 52.2.2）に基づく部分集団について解析したところ、一部の部分集団では症例数が極めて少なかったものの、有害事象の発現頻度に部分集団による傾向は認められなかった。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

2.1.1.1.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、テデュグルチド群の 3 例全例に 29 件、標準治療群の 2 例（66.7%）に 12 件の有害事象が発現した。有害事象の大部分は軽度又は重度であった。治験薬と関連ありとされた有害事象はテデュグルチド群の 1 例に 1 件認められた。重篤な有害事象はテデュグルチド群の 2 例（66.7%）に 2 件、標準治療群の 1 例（33.3%）に 1 件認められた。いずれの重篤な有害事象も治験薬との関連なしと判断された。投与中止に至った有害事象及び死亡例は認められなかった（5.3.5.2 項 SHP633-301 Interim CSR Section 12.2.1、Table 14.3.1.1）。

最終解析では、全体で 10 例（100%）に 87 件の有害事象が発現した。有害事象の大部分は軽度であった。テデュグルチド群の 2 例（40.0%）に、治験責任医師によって治験薬と関連があると判断された 9 件の有害事象が発現した。重篤な有害事象はテデュグルチド群の 4 例（80.0%）に 5 件、標準治療群の 3 例（60.0%）に 6 件認められた。いずれの重篤な有害事象も治験薬との関連なしと判断された。投与中止に至った有害事象は、テデュグルチド群の 1 例に 5 件発現した。特に注目すべき有害事象及び有害事象による死亡例はなかった（5.3.5.2 項 SHP633-301 Final CSR、Section 12.2.1、Table 14.3.1.1）。

2.1.1.1.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）の有害事象の概要は表 2.7.4 - 26 のとおりであった。

小児コホートでは、被験者 8 例全例に有害事象が 93 件発現し、このうち 6 例（75.0%）で発現した 20 件は、治験薬と関連ありと判断された。有害事象の大部分は軽度又は中等度であった。重症とされた有害事象は 2 例（25.0%）に 2 件認められた。小児コホートでは重篤な有害事象が 6 例（75.0%）に 15 件認められ、うち 1 件は治験薬と関連ありと判断された。被験者 1 例が有害事象により試験を中止した。

小児及び乳児いずれのコホートでも、死亡例及び特に注目すべき有害事象は認められなかった。

表 2.7.4 - 26　SHP633-302 試験：有害事象の概要（安全性解析対象集団）

Description	Children[a] After Amendment 3[c] (N=6), n (%)	Total Children[a] (N=8), n (%)	Infants[b] (N=2), n (%)
Number of subjects with			
At least one TEAE	6 (100.0), [67]	8 (100.0), [93]	2 (100.0), [19]
At least one TEAE related to the IP	4 (66.7), [17]	6 (75.0), [20]	0
At least one TESAE	4 (66.7), [9]	6 (75.0), [15]	2 (100.0), [9]
At least one TESAE related to the IP	1 (16.7), [1]	1 (12.5), [1]	0
TEAE Severity			
Mild	6 (100.0), [54]	8 (100.0), [76]	1 (50.0), [12]
Moderate	3 (50.0), [12]	4 (50.0), [15]	2 (100.0), [7]
Severe	1 (16.7), [1]	2 (25.0), [2]	0
Number of subjects with TEAE Highest Severity			
Mild	3 (50.0)	3 (37.5)	0
Moderate	2 (33.3)	3 (37.5)	2 (100.0)
Severe	1 (16.7)	2 (25.0)	0
TESAE Severity			
Mild	1 (16.7), [1]	2 (25.0), [3]	1 (50.0), [3]
Moderate	3 (50.0), [7]	4 (50.0), [10]	2 (100.0), [6]
Severe	1 (16.7), [1]	2 (25.0), [2]	0
TEAE leading to discontinuation	0	1 (12.5), [1]	0
TEAE leading to death	0	0	0
TEAE with special interest	0	0	0

TEAE=treatment-emergent adverse event; TESAE=treatment-emergent serious adverse event
n (%): the number of subjects with any TEAE and its percentage, [　] : total number of events
a:　Children aged 1 through 15 years.
b:　Infants of 4 through <12 months corrected gestational age.
c:　The number of children enrolled based upon the protocol amendment 3 and 4.
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.3.2.1

2.1.1.1.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ日までに小児コホートでは 7 例（100%）に 101 件の有害事象が発現した。うち 2 例（28.6%）に発現した 2 件が治験薬と関連ありとされた。全ての有害事象は軽度又は中等度であった。重篤な有害事象は 6 例（85.7%）に 18 件発現したが、いずれも治験薬と関連なしとされた。死亡、中止に至った有害事象及び特に注目すべき有害事象はみられなかった。乳児コホートでは 2 例（100%）に 12 件の有害事象が発現した。うち 4 件が重篤な有害事象であった。有害事象の大部分は軽度又は中等度であり、重度の有害事象は 1 例に発現した急性膵炎（重篤な有害事象）であった。治験薬と関連ありとされた有害事象、死亡、中止に至った有害事象及び特に注目すべき有害事象はみられなかった（5.3.5.2 項 SHP633-305 CSR Section 12.2.1）。

2.1.1.1.2.6　小児及び乳児を対象とした国内第 3 相コア試験及び継続投与試験の統合データ

SHP633-302 試験（5.3.5.2 項）及び SHP633-305 試験（データカットオフ日まで）（5.3.5.2 項）について、有害事象発現データを統合解析した。各試験別の結果は前項に示した。被験者 10 例（100%）に有害事象が発現したが、死亡例は認められなかった。重篤な有害事象は 9 例（90%）に発現し（本概要 2.1.3.2）、中止例は 1 例（10%）であった（本概要 2.1.4.1.2）。統合された安全性データは試験別の結果と同様であり、新たな安全上の問題は認められなかった（2.7.4 項付録 4 Table 13.1 を参照）。

2.1.1.2　有害事象

2.1.1.2.1　成人の臨床試験データ

2.1.1.2.1.1　成人を対象とした海外第 3 相コア試験

CL0600-020 試験及び CL0600-004 試験の試験ごとの有害事象一覧をそれぞれ 5.3.5.1 項 CL0600-020 CSR Table 12-3、5.3.5.1 項 CL0600-004 CSR Table 12-3、2.7.6 項に示す。

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データのテデュグルチド群で 2%以上に報告された有害事象を表 2.7.4 - 27 に示す。

テデュグルチド群で頻度の高い SOC は「胃腸障害」（60.6%）、「感染症および寄生虫症」（57.8%）、「全身障害および投与局所様態」（45.0%）であった。テデュグルチド群 109 例で頻度の高い（10%以上）有害事象は、腹痛（28.4%）、悪心（25.7%）、腹部膨満（16.5%）、消化管ストーマ合併症（15.6%）、頭痛（15.6%）、嘔吐（13.8%）、鼻咽頭炎（12.8%）、尿路感染（12.8%）、注射部位血腫（11.0%）であった（表 2.7.4 - 27）。

プラセボ群で頻度の高い SOC は「感染症および寄生虫症」（52.5%）、「胃腸障害」（44.1%）、「全身障害および投与局所様態」（33.9%）であった。プラセボ群 59 例で頻度の高い有害事象は腹痛（20.3%）、悪心（20.3%）、頭痛（13.6%）、尿路感染（11.9%）、嘔吐（10.2%）、下痢（10.2%）、体重減少（10.2%）であった（表 2.7.4 - 27）。

表 2.7.4 - 27　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群全体で 2%以上に認められた有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Placebo (N=59)		Teduglutide 0.05 mg/kg/day (N=77)		Teduglutide 0.10 mg/kg/day (N=32)		Teduglutide All (N=109)	
		n (%)	E	n (%)	E	n (%)	E	n (%)	E
Gastrointestinal Disorders	胃腸障害	26 (44.1)	81	47 (61.0)	154	19 (59.4)	70	66 (60.6)	224
Abdominal pain	腹痛	12 (20.3)	16	20 (26.0)	26	11 (34.4)	12	31 (28.4)	38
Nausea	悪心	12 (20.3)	16	18 (23.4)	27	10 (31.3)	13	28 (25.7)	40
Abdominal distension	腹部膨満	1 (1.7)	2	15 (19.5)	21	3 (9.4)	4	18 (16.5)	25
Vomiting	嘔吐	6 (10.2)	12	9 (11.7)	14	6 (18.8)	8	15 (13.8)	22
Flatulence	鼓腸	4 (6.8)	4	7 (9.1)	14	2 (6.3)	2	9 (8.3)	16
Diarrhoea	下痢	6 (10.2)	9	4 (5.2)	5	3(9.4)	3	7 (6.4)	8
Abdominal pain upper	上腹部痛	1 (1.7)	1	4 (5.2)	5	2 (6.3)	4	6 (5.5)	9
Abdominal discomfort	腹部不快感	1 (1.7)	1	3 (3.9)	4	2 (6.3)	3	5 (4.6)	7
Dyspepsia	消化不良	2 (3.4)	2	1 (1.3)	1	3 (9.4)	4	4 (3.7)	5
Abdominal pain lower	下腹部痛	0	0	2 (2.6)	4	1 (3.1)	1	3 (2.8)	5
Abdominal tenderness	腹部圧痛	2 (3.4)	2	1 (1.3)	1	2 (6.3)	2	3 (2.8)	3
Constipation	便秘	2 (3.4)	3	3 (3.9)	3	0	0	3 (2.8)	3
General Disorders and Administration Site Conditions	全身障害および投与局所様態	20 (33.9)	47	30 (39.0)	56	19 (59.4)	44	49 (45.0)	100
Injection site haematoma	注射部位血腫	3 (5.1)	4	4 (5.2)	4	8 (25.0)	9	12 (11.0)	13
Fatigue	疲労	5 (8.5)	5	5 (6.5)	6	5 (15.6)	7	10 (9.2)	13
Pyrexia	発熱	5 (8.5)	6	7 (9.1)	8	3 (9.4)	3	10 (9.2)	11
Oedema peripheral	末梢性浮腫	2 (3.4)	3	8 (10.4)	9	1 (3.1)	1	9 (8.3)	10
Injection site erythema	注射部位紅斑	0	0	3 (3.9)	3	5 (15.6)	5	8 (7.3)	8
Injection site pain	注射部位疼痛	0	0	1 (1.3)	4	4 (12.5)	5	5 (4.6)	9
Asthenia	無力症	1 (1.7)	1	3 (3.9)	3	1 (3.1)	1	4 (3.7)	4
Chest pain	胸痛	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Pain	疼痛	2 (3.4)	3	0	0	3 (9.4)	3	3 (2.8)	3

表 2.7.4 - 27　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群全体で 2%以上に認められた有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Placebo (N=59)		Teduglutide 0.05 mg/kg/day (N=77)		Teduglutide 0.10 mg/kg/day (N=32)		Teduglutide All (N=109)	
		n (%)	E	n (%)	E	n (%)	E	n (%)	E
Infections and Infestations	感染症および寄生虫症	31 (52.5)	58	43 (55.8)	98	20 (62.5)	40	63 (57.8)	138
Nasopharyngitis	鼻咽頭炎	2 (3.4)	3	9 (11.7)	12	5 (15.6)	7	14 (12.8)	19
Urinary tract infection	尿路感染	7 (11.9)	8	10 (13.0)	14	4 (12.5)	5	14 (12.8)	19
Catheter sepsis	カテーテル敗血症	2 (3.4)	3	5 (6.5)	11	4 (12.5)	5	9 (8.3)	16
Influenza	インフルエンザ	1 (1.7)	1	4 (5.2)	4	4 (12.5)	4	8 (7.3)	8
Catheter related infection	カテーテル関連感染	1 (1.7)	1	6 (7.8)	7	0	0	6 (5.5)	7
Catheter site infection	カテーテル留置部位感染	2 (3.4)	2	3 (3.9)	3	0	0	3 (2.8)	3
Pharyngitis	咽頭炎	1 (1.7)	2	3 (3.9)	3	0	0	3 (2.8)	3
Pneumonia	肺炎	1 (1.7)	1	3 (3.9)	6	0	0	3 (2.8)	6
Upper respiratory tract infection	上気道感染	3 (5.1)	5	3 (3.9)	3	0	0	3 (2.8)	3
Injury, Poisoning and Procedural Complications	傷害、中毒および処置合併症	13 (22.0)	26	21 (27.3)	28	11 (34.4)	18	32 (29.4)	46
Gastrointestinal stoma complication	消化管ストーマ合併症	3 (5.1)	3	13 (16.9)	14	4 (12.5)	5	17 (15.6)	19
Device breakage	医療機器破損	2 (3.4)	2	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Procedural pain	処置による疼痛	1 (1.7)	1	1 (1.3)	1	2 (6.3)	2	3 (2.8)	3
Procedural site reaction	処置後局所反応	1 (1.7)	1	1 (1.3)	3	2 (6.3)	2	3 (2.8)	5
Investigations	臨床検査	12 (20.3)	35	18 (23.4)	25	4 (12.5)	5	22 (20.2)	30
Weight increased	体重増加	3 (5.1)	3	4 (5.2)	4	0	0	4 (3.7)	4
Metabolism and Nutrition Disorders	代謝および栄養障害	15 (25.4)	18	12 (15.6)	15	5 (15.6)	6	17 (15.6)	21
Decreased appetite	食欲減退	2 (3.4)	2	5 (6.5)	6	3 (9.4)	3	8 (7.3)	9
Dehydration	脱水	5 (8.5)	5	3 (3.9)	3	1 (3.1)	1	4 (3.7)	4
Musculoskeletal and Connective Tissue Disorders	筋骨格系および結合組織障害	14 (23.7)	21	12 (15.6)	22	11 (34.4)	15	23 (21.1)	37
Arthralgia	関節痛	3 (5.1)	4	4 (5.2)	7	3 (9.4)	3	7 (6.4)	10
Back pain	背部痛	3 (5.1)	4	1 (1.3)	1	3 (9.4)	3	4 (3.7)	4

表 2.7.4 - 27　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群全体で 2%以上に認められた有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Placebo (N=59)		Teduglutide 0.05 mg/kg/day (N=77)		Teduglutide 0.10 mg/kg/day (N=32)		Teduglutide All (N=109)	
		n (%)	E	n (%)	E	n (%)	E	n (%)	E
Muscle spasms	筋痙縮	4 (6.8)	4	2 (2.6)	3	2 (6.3)	2	4 (3.7)	5
Musculoskeletal chest pain	筋骨格系胸痛	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Nervous System Disorders	神経系障害	9 (15.3)	24	16 (20.8)	40	10 (31.3)	21	26 (23.9)	61
Headache	頭痛	8 (13.6)	12	10 (13.0)	31	7 (21.9)	13	17 (15.6)	44
Dizziness	浮動性めまい	2 (3.4)	3	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Paraesthesia	錯感覚	0	0	1 (1.3)	1	2 (6.3)	2	3 (2.8)	3
Psychiatric Disorders	精神障害	1 (1.7)	3	7 (9.1)	12	3 (9.4)	4	10 (9.2)	16
Insomnia	不眠症	0	0	3 (3.9)	7	1 (3.1)	1	4 (3.7)	8
Anxiety	不安	0	0	3 (3.9)	3	0	0	3 (2.8)	3
Respiratory, Thoracic and Mediastinal Disorders	呼吸器、胸郭および縦隔障害	10 (16.9)	15	13 (16.9)	17	2 (6.3)	3	15 (13.8)	20
Cough	咳嗽	0	0	4 (5.2)	4	1 (3.1)	1	5 (4.6)	5
Dyspnoea	呼吸困難	0	0	3 (3.9)	3	0	0	3 (2.8)	3
Oropharyngeal pain	口腔咽頭痛	2 (3.4)	2	2 (2.6)	3	1 (3.1)	1	3 (2.8)	4
Skin and Subcutaneous Tissue Disorders	皮膚および皮下組織障害	7 (11.9)	7	10 (13.0)	14	5 (15.6)	5	15 (13.8)	19
Erythema	紅斑	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Night sweats	寝汗	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Rash	発疹	0	0	3 (3.9)	3	0	0	3 (2.8)	3
Vascular Disorders	血管障害	5 (8.5)	6	10 (13.0)	15	1 (3.1)	1	11 (10.1)	16
Hypertension	高血圧	1 (1.7)	1	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3

E = Total number of events; TEAE = Treatment emergent adverse event; TESAE = Treatment emergent serious adverse event.
Studies included: CL0600-020, CL0600-004.
Note:　Percentages are based upon the number of subjects in the Safety Population.
Note:　Treatment emergent adverse events are defined as any adverse event with a start date on or after the date of first dose and within thirty days after discontinuation of study drug.
Note:　Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note:　All adverse events were coded using MedDRA Version 12.0.
Source: Module 5.3.5.3 Adult　ISS Table 9.3.2

2.1.1.2.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験及び CL0600-005 試験の試験ごとの有害事象一覧をそれぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.2.9、5.3.5.2 項 CL0600-005 CSR Table 12-3、2.7.6 項に示す。

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）の統合データについて、テデュグルチド群（153 例）で認められた有害事象を 5.3.5.3 項 Adult ISS Table 9.3.3 に要約する。頻度の高い SOC は、「胃腸障害」（60.6%）、「感染症および寄生虫症」（57.8%）、並びに「全身障害および投与局所様態」（45.0%）であった。テデュグルチド群で頻度の高い（10%以上）有害事象は、腹痛（20.9%）、悪心（16.3%）、体重減少（16.3%）、尿路感染（14.4%）、頭痛（12.4%）、下痢（11.8%）、発熱（11.8%）、腹部膨満（11.1%）、無力症（11.8%）、鼻咽頭炎（11.8%）、嘔吐（10.5%）であった（5.3.5.3 項 Adult ISS Table 9.6.3）。

TED-C11-001 試験（5.3.5.2 項）（統合されていない）で発現した有害事象を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.2.10、Appendix 16.2.7 Listing 16.2.6.1 及び 2.7.6 項に示す。テデュグルチド群で最も頻度の高い有害事象は、グループ化 PT の発現頻度で分類した場合、無力状態及び下痢であり、いずれも 14 例中 3 例（21.4%）で報告された。その他の有害事象は全て 2 例以下で報告された。

2.1.1.2.1.3　　成人を対象とした海外第 3 相試験統合データ（有害事象発現時期）

2014 年のテデュグルチドの初回の製造販売承認申請時に、海外成人コア試験 CL0600-020 試験（5.3.5.2 項）及び CL0600-004 試験（5.3.5.2 項）並びに海外成人継続試験 CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）の全テデュグルチド群を対象に、有害事象発現までの期間を解析した（5.3.5.3 項 Adult ISS Table 66）。

テデュグルチド投与開始後、報告された有害事象のうち最も多く発現した期間の区分は 4 期間（Week 1～3、Week 4～11、Week 12～23 及び Week 24～36）であり、うち 4 週未満に最も多く発現した有害事象（5%以上に発現）は腹痛、悪心、注射部位反応、消化管ストーマ合併症、腹部膨満、頭痛、上気道感染及び水分過負荷であった。これらの有害事象の発現頻度は経時的に減少した。テデュグルチド投与 48 週から 72 週までの期間に 5%以上の被験者で発現した有害事象は、カテーテル敗血症（8/117 例）6.8%、上気道感染（7/117 例）6.0%、カテーテル留置部位関連反応（6/117 例）5.1%であった。テデュグルチドの作用機序に基づくと、消化管及び水分過負荷の有害事象は予期できるものであった。有害事象発現時期にその他の傾向は認められなかった。

2.1.1.2.1.4　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）の安全性解析対象集団における有害事象を表 2.7.4 - 28 に示す。有害事象は 7 例全例に 34 件認められた。頻度の高い SOC は、「胃腸障害」4 例（57.1%）、「一般・全身障害および投与部位の状態」、「感染症および寄生虫症」及び「傷害、中毒および処置合併症」各 3 例（42.9%）であった。有害事象の大部分は単一の被験者

における単一の事象であった。2 例以上に認められた有害事象は、腹部膨満、注射部位反応、発熱及び上咽頭炎各 2 例（28.6%）であった。

表 2.7.4 - 28　SHP633-306 試験：有害事象一覧（安全性解析対象集団）

		Total Teduglutide (N=7)	
		All-causality TEAEs	
System Organ Class Preferred Term		Subjects n (%)	Events
Any TEAE		7 (100.0)	34
Blood and lymphatic system disorders	血液およびリンパ系障害	2 (28.6)	2
Anaemia	貧血	1 (14.3)	1
Polycythaemia	赤血球増加症	1 (14.3)	1
Gastrointestinal disorders	胃腸障害	4 (57.1)	6
Abdominal distension	腹部膨満	2 (28.6)	2
Abdominal pain	腹痛	1 (14.3)	1
Abdominal pain lower	下腹部痛	1 (14.3)	1
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (14.3)	1
Nausea	悪心	1 (14.3)	1
General disorders and administration site conditions	一般・全身障害および投与部位の状態	3 (42.9)	4
Injection site reaction	注射部位反応	2 (28.6)	2
Pyrexia	発熱	2 (28.6)	2
Hepatobiliary disorders	肝胆道系障害	1 (14.3)	1
Cholelithiasis	胆石症	1 (14.3)	1
Infections and infestations	感染症および寄生虫症	3 (42.9)	4
Nasopharyngitis	上咽頭炎	2 (28.6)	2
Device related infection	医療機器関連感染	1 (14.3)	1
Medical device site infection	医療機器使用部位感染	1 (14.3)	1
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	3 (42.9)	4
Gastrointestinal stoma complication	消化管ストーマ合併症	1 (14.3)	1
Muscle contusion	筋挫傷	1 (14.3)	1
Rib fracture	肋骨骨折	1 (14.3)	1
Spinal compression fracture	脊椎圧迫骨折	1 (14.3)	1
Metabolism and nutrition disorders	代謝および栄養障害	1 (14.3)	1
Hypozincaemia	低亜鉛血症	1 (14.3)	1
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	1 (14.3)	1
Back pain	背部痛	1 (14.3)	1
Nervous system disorders	神経系障害	1 (14.3)	4

表 2.7.4 - 28　SHP633-306 試験：有害事象一覧（安全性解析対象集団）

System Organ Class Preferred Term		Total Teduglutide (N=7) All-causality TEAEs Subjects n (%)	Events
Epilepsy	てんかん	1 (14.3)	3
Headache	頭痛	1 (14.3)	1
Reproductive system and breast disorders	生殖系および乳房障害	1 (14.3)	1
Menorrhagia	月経過多	1 (14.3)	1
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (28.6)	2
Epistaxis	鼻出血	1 (14.3)	1
Oropharyngeal pain	口腔咽頭痛	1 (14.3)	1
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	2 (28.6)	3
Dry skin	皮膚乾燥	1 (14.3)	1
Haemorrhage subcutaneous	皮下出血	1 (14.3)	1
Urticaria	蕁麻疹	1 (14.3)	1
Vascular disorders	血管障害	1 (14.3)	1
Phlebitis	静脈炎	1 (14.3)	1

Note: Percentages are based on the Safety Population.
Note: Treatment-emergent AEs (TEAEs) were defined as AEs whose onset occurred, severity worsened, or intensity increased after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: Subjects were counted no more than once for incidence but could be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA 21.0
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.3.2.2

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）について、ステージ 2 で 2 例以上に認められた有害事象を表 2.7.4 - 29 に要約する。ステージ 2 では、10 例（90.9%）に 87 件の有害事象が発現した。ステージ 2 において頻度の高い SOC は、「胃腸障害」（72.7%）、「一般・全身障害および投与部位の状態」（54.5%）、「臨床検査」（54.5%）、並びに「感染症および寄生虫症」（45.5%）であった。頻度の高い（20%以上）有害事象は、医療機器関連感染（45.5%）、腹痛（36.4%）、及び発熱（36.4%）であった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.2.1）。医療機器関連の感染事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。

表 2.7.4 - 29　TED-C14-004 試験：ステージ 2 で 2 例以上に認められた有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Teduglutide (N=11) Subjects n (%)	Events
Any TEAE		10 (90.9)	87
Eye Disorders	眼障害	2 (18.2)	2
Gastrointestinal Disorders	胃腸障害	8 (72.7)	21
Abdominal pain	腹痛	4 (36.4)	4
Abdominal distension	腹部膨満	2 (18.2)	2
Vomiting	嘔吐	2 (18.2)	2
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	6 (54.5)	17
Pyrexia	発熱	4 (36.4)	4
Device occlusion	医療機器閉塞	2 (18.2)	3
Injection site reaction	注射部位反応	2 (18.2)	2
Infections and Infestations	感染症および寄生虫症	5 (45.5)	15
Device related infection	医療機器関連感染	5 (45.5)	8
Investigations	臨床検査	6 (54.5)	9
Metabolism and Nutrition Disorders	代謝および栄養障害	3 (27.3)	5
Dehydration	脱水	2 (18.2)	2
Nervous System Disorders	神経系障害	3 (27.3)	3
Headache	頭痛	2 (18.2)	2
Renal and Urinary Disorders	腎および尿路障害	2 (18.2)	2
Respiratory, Thoracic and Mediastinal Disorders	呼吸器、胸郭および縦隔障害	3 (27.3)	3
Upper respiratory tract inflammation	上気道の炎症	2 (18.2)	2
Skin and Subcutaneous Tissue Disorders	皮膚および皮下組織障害	2 (18.2)	2

n=number of subjects experiencing the event; TEAE=treatment-emergent adverse event
Note: Percentages are based on the safety population.
Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study drug.
Note: Subjects are counted no more than once for incidence, but can be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA J 17.1.
Source: Module 5.3.5.2 TED-C14-004 CSR, Table 14.3.2.2.1

2.1.1.2.1.5　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）で発現した有害事象を 5.3.5.2 項 SHP633-307 CSR Table 15、2.7.6 項に示す。被験者 9 例（81.8%）に 64 件の有害事象が発現した。頻度の高い SOC は、「感染症および寄生虫症」（81.8%）、次いで「皮膚および皮下組織障

害」（45.5%）及び「胃腸障害」（36.4%）であった。頻度の高い有害事象（25%以上）は、医療機器関連感染（45.5%）、インフルエンザ（36.4%）及び鼻咽頭炎（27.3%）であった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）のステージ 3 及び 4 で発現した有害事象を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.2.2 及び 2.7.6 項に示す。被験者 8 例全例に 135 件の有害事象が認められた。頻度の高い SOC は、「胃腸障害」（75.0%）、「感染症および寄生虫症」（87.5%）、「筋骨格系および結合組織障害」（62.5%）、「神経系障害」（75.0%）、「代謝および栄養障害」（50.0%）、並びに「一般・全身障害および投与部位の状態」（50.0%）であった。頻度の高い（20%以上）有害事象は、医療機器関連感染（62.5%）、頭痛（62.5%）、鼻咽頭炎（62.5%）、関節痛（50.0%）、悪心（37.5%）、発熱（37.5%）、カテーテル留置部位疼痛（25.0%）、医療機器閉塞（25.0%）、脱水（25.0%）、接触性皮膚炎（25.0%）、下痢（25.0%）、インフルエンザ（25.0%）、不眠症（25.0%）、口腔咽頭痛（25.0%）、口内炎（25.0%）、血管痛（25.0%）であった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.2.2）。医療機器関連感染及び医療機器閉塞の事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。

2.1.1.2.1.6　成人を対象とした国内第 3 相コア試験及び継続投与試験の統合データ（有害事象発現時期）

国内第 3 相成人コア試験 SHP633-306 試験（5.3.5.2 項）、SHP633-307 試験（5.3.5.2 項）及び TED-C14-004 試験（5.3.5.2 項）の統合データにおける発現時期別の有害事象の発現状況を 2.7.4 項 付録 4 Table 3.1 に示す。全体で頻度の高い SOC（30%以上）は、「胃腸障害」（83.3%）、「感染症および寄生虫症」（66.7%）、「一般・全身障害および投与部位の状態」（55.6%）であった。頻度の高い（30%以上）有害事象は、医療機器関連感染（55.6%）、発熱（44.4%）、鼻咽頭炎及び頭痛（各 38.9%）、腹部膨満（33.3%、2.7.4 項 付録 4 Table 3.1）であった。

全ての有害事象を発現時期別に検討したところ、大半の事象は投与開始後数ヵ月間に発現し（2.7.4 項 付録 4 Table 3.1）、海外で実施された成人を対象とした第 3 相試験（本概要 2.1.1.2.1.3）で報告された有害事象の発現時期と同様であった。全体として、統合データの安全性の結果は個々の試験結果と一致しており、新たな安全性の問題は特定されなかった。SHP633-306 試験及び SHP633-307 試験のみの統合データについては、2.7.4 項 付録 4 Table 3.2 を参照のこと。

2.1.1.2.2　小児の臨床試験データ

2.1.1.2.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験及び TED-C14-006 試験の統合データのテデュグルチド群全体で 5 例以上に認められた有害事象を表 2.7.4 - 30 に要約する。試験ごとの結果は 5.3.5.2 項 TED-C13-003 CSR Section 12.2.2、5.3.5.2 項 TED-C14-006 CSR Section 12.2.2、2.7.6 項に示す。

有害事象は 0.0125 mg/kg 群で 8 例全例に 57 件、0.025 mg/kg 群で 38 例全例に 384 件、0.05 mg/kg 群で 40 例（97.6%）に 459 件、標準治療群で 14 例全例に 104 件発現した。

テデュグルチド群全体で頻度の高い SOC は、「感染症および寄生虫症」（85.1%）、「胃腸障害」（72.4%）、並びに「一般・全身障害および投与部位の状態」（59.8%）であった。標準治療群で頻度の高い SOC はテデュグルチド群と概ね同様であったが、「代謝および栄養障害」はテデュグルチド群で高かった。

テデュグルチド群で頻度の高い（15%以上）有害事象は、嘔吐（35.6%）、発熱（33.3%）、上気道感染（29.9%）、咳嗽（21.8%）、腹痛（18.4%）、下痢（17.2%）、鼻咽頭炎（16.1%）、及び医療機器関連感染（16.1%）であった（5.3.5.3 項 Pediatric ISS Table 8.1）。標準治療群で 15%以上の被験者に認められた有害事象は、嘔吐（42.9%）、発熱（42.9%）、上気道感染（42.9%）、咳嗽（28.6%）、及び鼻咽頭炎（21.4%）であった（5.3.5.3 項 Pediatric ISS Table 8.1）。

腹痛、腹部膨満、悪心、注射部位内出血、鼻炎、及びインフルエンザは、標準治療群よりもテデュグルチド群において多かった。これらの事象は、成人 SBS 患者を対象としたプラセボ対照試験のテデュグルチド群でも多く認められた。

成人を対象としたプラセボ対照試験において、テデュグルチド群でみられた有害事象の一部（嘔吐、上気道感染、鼻咽頭炎、咳嗽など）の発現は、小児では標準治療群よりもテデュグルチド群において少なかった。

これまでに成人テデュグルチド群では発現頻度が高くなかった有害事象が、小児テデュグルチド群では標準治療例よりも多く認められた場合があった。それらは、便量増加、疲労、医療機器関連感染、医療機器破損、医療機器位置異常、アラニンアミノトランスフェラーゼ増加、及びアスパラギン酸アミノトランスフェラーゼ増加であった。これらの事象を新たな副作用として分類するにはエビデンスが不十分であった。これら 2 試験における有害事象データは、症例数が非常に少ない標準治療例では選択バイアスや報告バイアスがかかりやすく、また感度が低かった。TED-C14-006 試験ではテデュグルチドの用量は盲検化されていたが、両試験ともにテデュグルチド群への割付けは非盲検であった。さらに、これら 2 試験では、小児にテデュグルチドを投与するか否かを保護者が選択した。中心静脈ライン合併症の頻度が高い小児や、腸管不全関連肝疾患（IFALD）の重症度が高い小児の保護者ほど、実験的治療を試みる意欲が高かった可能性がある。IFALD の小児のアミノトランスフェラーゼ値は、感染の際に一過性の上昇を示すことが多い。認められたアミノトランスフェラーゼ増加のうち、治験責任医師により治験薬と関連ありと判断されたものはなかった。

年齢（5.3.5.3 項 Pediatric ISS Table 29.1）、性別（5.3.5.3 項 Pediatric ISS Table 35.1）、人種（5.3.5.3 項 Pediatric ISS Table 41.1）、地域（5.3.5.3 項 Pediatric ISS Table 47.1）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 53.1）に基づく部分集団について有害事象を確認したところ、一部の部分集団では症例数が極めて少なかったものの、有害事象の発現頻度に部分集団による特定の傾向は認められなかった。

表 2.7.4 - 30　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群全体で 5 例以上の被験者に認められた有害事象一覧（安全性解析対象集団）

		0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)		Standard of Care (N=14)	
Category		**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**	**n(%)**	**E**
Any TEAE		8 (100.0)	57	38 (100.0)	384	40 (97.6)	459	86 (98.9)	900	14 (100.0)	104
Gastrointestinal Disorders	胃腸障害	4 (50.0)	14	29 (76.3)	87	30 (73.2)	119	63 (72.4)	220	6 (42.9)	20
Vomiting	嘔吐	0	0	16 (42.1)	33	15 (36.6)	46	31 (35.6)	79	6 (42.9)	8
Abdominal Pain	腹痛	1 (12.5)	1	5 (13.2)	10	10 (24.4)	22	16 (18.4)	33	1 (7.1)	1
Diarrhoea	下痢	0	0	9 (23.7)	10	6 (14.6)	10	15 (17.2)	20	2 (14.3)	3
Nausea	悪心	1 (12.5)	3	5 (13.2)	5	5 (12.2)	11	11 (12.6)	19	1 (7.1)	1
Abdominal Pain Upper	上腹部痛	0	0	3 (7.9)	8	3 (7.3)	3	6 (6.9)	11	1 (7.1)	1
Abdominal Distension	腹部膨満	1 (12.5)	2	1 (2.6)	1	3 (7.3)	4	5 (5.7)	7	0	0
Faecal Volume Increased	便量増加	1 (12.5)	1	2 (5.3)	2	2 (4.9)	2	5 (5.7)	5	0	0
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	4 (50.0)	6	21 (55.3)	35	27 (65.9)	62	52 (59.8)	103	8 (57.1)	14
Pyrexia	発熱	1 (12.5)	1	10 (26.3)	14	18 (43.9)	25	29 (33.3)	40	6 (42.9)	10
Fatigue	疲労	0	0	1 (2.6)	1	5 (12.2)	12	6 (6.9)	13	0	0
Injection Site Bruising	注射部位内出血	0	0	3 (7.9)	4	2 (4.9)	4	5 (5.7)	8	0	0
Infections and Infestations	感染症および寄生虫症	7 (87.5)	13	32 (84.2)	76	35 (85.4)	86	74 (85.1)	175	11 (78.6)	29
Upper Respiratory Tract Infection	上気道感染	2 (25.0)	3	12 (31.6)	17	12 (29.3)	14	26 (29.9)	34	6 (42.9)	7
Device Related Infection	医療機器関連感染	1 (12.5)	1	5 (13.2)	9	8 (19.5)	10	14 (16.1)	20	0	0
Nasopharyngitis	鼻咽頭炎	2 (25.0)	2	5 (13.2)	5	7 (17.1)	10	14 (16.1)	17	3 (21.4)	3
Viral Infection	ウイルス感染	0	0	3 (7.9)	4	4 (9.8)	5	7 (8.0)	9	2 (14.3)	3
Gastroenteritis Viral	ウイルス性胃腸炎	1 (12.5)	1	3 (7.9)	3	2 (4.9)	2	6 (6.9)	6	1 (7.1)	1
Influenza	インフルエンザ	0	0	3 (7.9)	3	3 (7.3)	3	6 (6.9)	6	0	0

表 2.7.4 - 30　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群全体で 5 例以上の被験者に認められた有害事象一覧（安全性解析対象集団）

Category		0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)		Standard of Care (N=14)	
		n(%)	E	n(%)	E	n(%)	E	n(%)	E	n(%)	E
Rhinitis	鼻炎	0	0	1 (2.6)	1	5 (12.2)	6	6 (6.9)	7	0	0
Ear Infection	耳感染	1 (12.5)	1	1 (2.6)	1	3 (7.3)	3	5 (5.7)	5	1 (7.1)	1
Investigations	臨床検査	4 (50.0)	4	19 (50.0)	50	13 (31.7)	53	36 (41.4)	107	4 (28.6)	8
Alanine Aminotransferase Increased	アラニンアミノトランスフェラーゼ増加	0	0	8 (21.1)	8	4 (9.8)	4	12 (13.8)	12	0	0
Blood Bicarbonate Decreased	血中重炭酸塩減少	1 (12.5)	1	5 (13.2)	6	4 (9.8)	5	10 (11.5)	12	2 (14.3)	2
Aspartate Aminotransferase Increased	アスパラギン酸アミノトランスフェラーゼ増加	0	0	6 (15.8)	6	1(2.4)	1	7 (8.0)	7	0	0
Metabolism and Nutrition Disorders	代謝および栄養障害	3 (37.5)	4	12 (31.6)	27	11 (26.8)	12	26 (29.9)	43	1 (7.1)	1
Dehydration	脱水	1 (12.5)	1	8 (21.1)	13	2 (4.9)	2	11 (12.6)	16	1 (7.1)	1
Nervous System Disorders	神経系障害	1 (12.5)	6	8 (21.1)	11	10 (24.4)	24	19 (21.8)	41	1 (7.1)	5
Headache	頭痛	1 (12.5)	5	5 (13.2)	6	7 (17.1)	17	13 (14.9)	28	1 (7.1)	3
Product Issues	製品の問題	2 (25.0)	3	12 (31.6)	16	8 (19.5)	10	22 (25.3)	29	1 (7.1)	1
Device Breakage	医療機器破損	1 (12.5)	1	6 (15.8)	8	3 (7.3)	4	10 (11.5)	13	0	0
Device Dislocation	医療機器位置異常	0	0	4 (10.5)	4	1 (2.4)	1	5 (5.7)	5	0	0
Respiratory, Thoracic and Mediastinal Disorders	呼吸器、胸郭および縦隔障害	2 (25.0)	5	10 (26.3)	13	20 (48.8)	29	32 (36.8)	47	4 (28.6)	10
Cough	咳嗽	1 (12.5)	3	4 (10.5)	5	14 (34.1)	16	19 (21.8)	24	4 (28.6)	5
Skin and Subcutaneous Tissue Disorders	皮膚および皮下組織障害	0	0	9 (23.7)	30	9 (22.0)	16	18 (20.7)	46	5 (35.7)	6
Rash	発疹	0	0	2 (5.3)	4	3 (7.3)	7	5 (5.7)	11	1 (7.1)	1

E=number of events; MedDRA=Medical Dictionary for Regulatory Activities; n=number of subjects; TEAE=treatment-emergent adverse event
Note:　Percentages are based on the number of subjects in the safety population in each treatment group.
Note:　Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.

Note:　Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Source: Module 5.3.5.3 Pediatric ISS Table 7.1

2.1.1.2.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）でみられた有害事象は 5.3.5.2 項 SHP633-304 CSR Table 16、5.3.5.2 項 SHP633-303 CSR Table 22 及び 2.7.6 項に示す。

SHP633-304 試験及び SHP633-303 試験（前向き期間）の統合データにおいて、有害事象は NTT/TED 群で 1 例（50.0%）に 5 件、TED/NTT 群で 8 例（72.7%）に 21 件、TED/TED 群で 56 例（93.3%）に 433 件発現した。TED/TED 群で有害事象の発現頻度が高かったのは、この群でテデュグルチドの曝露量が大きかったためと考えられる。TED/NTT 群における有害事象は、テデュグルチド投与の数ヵ月後に発現したことから、基礎疾患によるものと考えられる。

全 TED 群（SHP633-304 試験又は SHP633-303 試験のいずれかにおいてテデュグルチド投与を受けた被験者）73 例で頻度の高い SOC は、「感染症および寄生虫症」（64.4%）、「胃腸障害」（54.8%）、並びに「臨床検査」（32.9%）であった。全 TED 群で 10%以上の被験者に認められた有害事象は、嘔吐（28.8%）、上気道感染（19.2%）、発熱（16.4%）、腹痛（15.1%）、下痢（11.0%）、ウイルス感染（11.0%）、アラニン・アミノトランスフェラーゼ増加（11.0%）であった（5.3.5.3 項 Pediatric ISS Table 8.2）。

年齢（5.3.5.3 項 Pediatric ISS Table 29.2.2）、性別（5.3.5.3 項 Pediatric ISS Table 35.2.2）、人種（5.3.5.3 項 Pediatric ISS Table 41.2.2）、地域（5.3.5.3 項 Pediatric ISS Table 47.2.2）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 53.2.2）に基づく部分集団について、継続投与試験で発現した有害事象を確認したところ、一部の部分集団では症例数が極めて少なかったものの、有害事象の発現頻度に部分集団による特定の傾向は認められなかった。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

2.1.1.2.2.3　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析では、テデュグルチド群の 3 例全例に 29 件、標準治療群の 2 例（66.7%）に 12 件の有害事象が発現した。テデュグルチド群において、頻度の高い SOC は、「感染症および寄生虫症」3 例（100.0%）、「胃腸障害」2 例（66.7%）、「血液およびリンパ系障害」2 例（66.7%）であった。頻度の高い有害事象は、2 例（66.7%）に認められた嘔吐であった。「製品の問題」では、テデュグルチド群の 2 例（66.7%）に 3 件の有害事象が認められたが、いずれも PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった（5.3.5.2 項 SHP633-301 Interim CSR Section 12.2.2、Table 14.3.1.2）。

5.3.5.2 項 SHP633-301 Interim CSR Section 12.2.2 で考察したように、29 件の有害事象のうち 20 件がテデュグルチド群の 1 例によるものであったが、これらは肝生検、回腸ストーマの修復、粘液瘻及びストーマの反転を含む広範な医学的及び手術歴と一致していた。この被験者に認められた複数の有害事象は、被験者の基礎疾患である肝疾患（肝酵素の上昇）及びこの患者集団で予想

される有害事象（消化管合併症、感染症、貧血、フェリチン低値、中心カテーテルの損傷及び機能障害、おむつ皮膚炎）と一致しており、治験薬と関連なしとされた。

最終解析では、10 例（100%）に 87 件の有害事象が発現した。テデュグルチド群において、頻度の高い SOC は、「感染症および寄生虫症」4 例（80.0%）並びに「胃腸障害」及び「製品の問題」各 3 例（60.0%）であった。頻度の高い有害事象は、3 例（60.0%）に認められた嘔吐、各 2 例（40.0%）に認められた下痢、排便回数増加、発熱、上咽頭炎及び医療機器破損であった。「製品の問題」では、テデュグルチド群の 3 例（60.0%）に 4 件の有害事象が認められた。いずれも PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。標準治療群において、頻度の高い SOC は、「胃腸障害」、「感染症および寄生虫症」、及び「臨床検査」各 3 例（60.0%）であった。頻度の高い有害事象は、各 2 例（40.0%）に認められた生歯及び上気道感染であった（5.3.5.2 項 SHP633-301 Final CSR Section 12.2.2、Table 14.3.1.2）。

5.3.5.2 項 SHP633-301 Final CSR Section 12.2.2 で考察したように、87 件の有害事象のうち 20 件がテデュグルチド群の 1 例によるものであったが（5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.7、Listing 16.2.7.1）、これらは肝生検、回腸ストーマの修復、粘液瘻及びストーマの反転を含む広範な病歴及び手術歴と一致しており（5.3.5.2 項 SHP633-301 Final CSR Section 10.4.2）、この患者集団で予期される有害事象であり、治験薬と関連なしとされた。この被験者の血液学的検査値は基準範囲外であり、ベースライン時に AST、ALT、γ－グルタミルトランスフェラーゼ（GGT）、及びアルカリホスファターゼ値上昇が認められ、これらは基礎疾患である肝疾患と一致していた（5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.8、Listing 16.2.8.1 及び Listing 16.2.8.2）。

2.1.1.2.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）の有害事象の発現状況は表 2.7.4 - 31 のとおりであった。小児コホートの 8 例全例に 93 件、乳児コホートの 2 例全例に 19 件の有害事象が認められた。

小児コホートで頻度の高い SOC は、「感染症および寄生虫症」（87.5%）、「皮膚および皮下組織障害」（87.5%）、「胃腸障害」（75.0%）、「一般・全身障害および投与部位の状態」（62.5%）、「代謝および栄養障害」（50.0%）であった。小児コホートで頻度の高い有害事象は、ウイルス性上気道感染が 6 例（75.0%）に 6 件、発疹が 4 例（50.0%）6 件、医療機器関連感染が 4 例（50.0%）5 件、注射部位紅斑が 3 例（37.5%）12 件、医療機器損傷が 3 例（37.5%）3 件であった。被験者全体で、医療機器関連の感染事象は全て PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。

表 2.7.4 - 31　SHP633-302 試験：有害事象一覧（安全性解析対象集団）

		Children[a] After Amendment 3[c] (N=6)		Total Children[a] (N=8)		Infants[b] (N=2)	
SOC PT		**n (%)**	**No of Events**	**n (%)**	**No of Events**	**n (%)**	**No of Events**
Any TEAEs		6 (100.0)	67	8 (100.0)	93	2 (100.0)	19
Gastrointestinal disorders	胃腸障害	4 (66.7)	7	6 (75.0)	11	1 (50.0)	1
Abdominal distension	腹部膨満	1 (16.7)	1	1 (12.5)	1	0	0
Abdominal pain	腹痛	1 (16.7)	1	2 (25.0)	2	0	0
Constipation	便秘	1 (16.7)	1	2 (25.0)	2	0	0
Dental caries	齲歯	1 (16.7)	1	1 (12.5)	1	0	0
Enterocolitis	腸炎	1 (16.7)	1	2 (25.0)	2	1 (50.0)	1
Gastritis	胃炎	1 (16.7)	1	1 (12.5)	1	0	0
Proctalgia	肛門周囲痛	1 (16.7)	1	1 (12.5)	1	0	0
Enteritis	小腸炎	0	0	1 (12.5)	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	3 (50.0)	23	5 (62.5)	33	2 (100.0)	4
Injection site erythema	注射部位紅斑	2 (33.3)	9	3 (37.5)	12	0	0
Catheter site granuloma	カテーテル留置部位肉芽腫	1 (16.7)	1	1 (12.5)	1	0	0
Injection site bruising	注射部位内出血	1 (16.7)	5	2 (25.0)	9	0	0
Injection site pain	注射部位疼痛	1 (16.7)	1	1 (12.5)	1	0	0
Injection site rash	注射部位発疹	1 (16.7)	4	1 (12.5)	4	0	0
Injection site reaction	注射部位反応	1 (16.7)	1	1 (12.5)	1	0	0
Pyrexia	発熱	1 (16.7)	2	2 (25.0)	3	2 (100.0)	4
Injection site haematoma	注射部位血腫	0	0	1 (12.5)	1	0	0
Injection site induration	注射部位硬結	0	0	1 (12.5)	1	0	0
Immune system disorders	免疫系障害	0	0	2 (25.0)	2	0	0
Anaphylactic reaction	アナフィラキシー反応	0	0	1 (12.5)	1	0	0
Food allergy	食物アレルギー	0	0	1 (12.5)	1	0	0
Infections and infestations	感染症および寄生虫症	5 (83.3)	17	7 (87.5)	24	2 (100.0)	6
Viral upper respiratory tract infection	ウイルス性上気道感染	4 (66.7)	4	6 (75.0)	6	1 (50.0)	1
Device related infection	医療機器関連感染	3 (50.0)	3	4 (50.0)	5	1 (50.0)	2
Adenovirus infection	アデノウイルス感染	1 (16.7)	1	1 (12.5)	1	0	0
Gastroenteritis	胃腸炎	1 (16.7)	1	1 (12.5)	1	0	0
Gingivitis	歯肉炎	1 (16.7)	1	1 (12.5)	1	0	0
Hand-foot-and-mouth disease	手足口病	1 (16.7)	1	2 (25.0)	2	0	0
Influenza	インフルエンザ	1 (16.7)	1	1 (12.5)	1	0	0

表 2.7.4 - 31　SHP633-302 試験：有害事象一覧（安全性解析対象集団）

		Children[a] After Amendment 3[c] (N=6)		Total Children[a] (N=8)		Infants[b] (N=2)	
SOC PT		**n (%)**	**No of Events**	**n (%)**	**No of Events**	**n (%)**	**No of Events**
Medical device site infection	医療機器使用部位感染	1 (16.7)	3	2 (25.0)	5	0	0
Pharyngitis streptococcal	レンサ球菌性咽頭炎	1 (16.7)	1	1 (12.5)	1	0	0
Rhinitis	鼻炎	1 (16.7)	1	1 (12.5)	1	0	0
Otitis media	中耳炎	0	0	0	0	1 (50.0)	1
Upper respiratory tract infection	上気道感染	0	0	0	0	1 (50.0)	2
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (33.3)	3	2 (25.0)	3	1 (50.0)	1
Frostbite	凍傷	1 (16.7)	1	1 (12.5)	1	0	0
Gastrostomy tube site complication	胃瘻管部合併症	1 (16.7)	2	1 (12.5)	2	0	0
Vaccination complication	ワクチン接種合併症	0	0	0	0	1 (50.0)	1
Investigations	臨床検査	1 (16.7)	1	1 (12.5)	1	0	0
Amylase increased	アミラーゼ増加	1 (16.7)	1	1 (12.5)	1	0	0
Metabolism and nutrition disorders	代謝および栄養障害	3 (50.0)	3	4 (50.0)	4	0	0
Dehydration	脱水	1 (16.7)	1	1 (12.5)	1	0	0
Hypertriglyceridaemia	高トリグリセリド血症	1 (16.7)	1	1 (12.5)	1	0	0
Hyperzincaemia	高亜鉛血症	1 (16.7)	1	1 (12.5)	1	0	0
Hyperlipasaemia	高リパーゼ血症	0	0	1 (12.5)	1	0	0
Nervous system disorders	神経系障害	1 (16.7)	1	1 (12.5)	1	0	0
Headache	頭痛	1 (16.7)	1	1 (12.5)	1	0	0
Product issues	製品の問題	3 (50.0)	3	3 (37.5)	3	0	0
Device damage	医療機器損傷	3 (50.0)	3	3 (37.5)	3	0	0
Reproductive system and breast disorders	生殖系および乳房障害	1 (16.7)	1	1 (12.5)	1	0	0
Balanoposthitis	亀頭包皮炎	1 (16.7)	1	1 (12.5)	1	0	0
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	0	0	0	0	1 (50.0)	3
Upper respiratory tract inflammation	上気道の炎症	0	0	0	0	1 (50.0)	3
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	5 (83.3)	8	7 (87.5)	10	1 (50.0)	4
Rash	発疹	4 (66.7)	6	4 (50.0)	6	0	0
Dry skin	皮膚乾燥	1 (16.7)	1	2 (25.0)	2	1 (50.0)	1
Eczema	湿疹	1 (16.7)	1	1 (12.5)	1	0	0
Dermatitis contact	接触皮膚炎	0	0	0	0	1 (50.0)	1

表 2.7.4 - 31　SHP633-302 試験：有害事象一覧（安全性解析対象集団）

		Children[a] After Amendment 3[c] (N=6)		Total Children[a] (N=8)		Infants[b] (N=2)	
SOC PT		n (%)	No of Events	n (%)	No of Events	n (%)	No of Events
Dermatitis diaper	おむつ皮膚炎	0	0	1 (12.5)	1	1 (50.0)	2

PT=preferred term; SOC=System Organ Class; TEAE=treatment-emergent adverse event
a: Children aged 1 through 15 years.
b: Infants of 4 through <12 months corrected gestational age.
c: The number of children enrolled based upon the protocol amendment 3 and 4.
Note: TEAEs were defined as any adverse events whose onset occurred, severity worsens or intensity increases during or after receiving the study medication.
Note: Subjects were counted no more than once for incidence but counted multiple times for the number of events.
Note: SOCs and PTs were coded using MedDRA 20.0.
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.3.2.2

2.1.1.2.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、小児コホートでは 7 例（100.0%）に 101 件、乳児コホートでは 2 例（100.0%）に 12 件の有害事象が発現した。小児コホートで頻度の高い有害事象の SOC は「胃腸障害」（100.0%）、「感染症および寄生虫症」（85.7%）、「製品の問題」（71.4%）、「皮膚および皮下組織障害」（71.4%）並びに「傷害、中毒および処置合併症」（57.1%）であった。頻度の高い有害事象は、ウイルス性上気道感染（4 例［57.1%］21 件）、医療機器破損（3 例［42.9%］5 件）、発熱（3 例［42.9%］3 件）であった。医療機器関連の有害事象は全て、PS に使用した中心静脈カテーテルの合併症であり、テデュグルチドの調製及び投与に使用した医療機器に関連したものではなかった。乳児コホートでは、両乳児に発現した有害事象の SOC は「感染症および寄生虫症」のみであった。PT 別の有害事象はいずれも乳児各 1 例に発現した事象であった。医療機器関連の有害事象は全て、PS に使用した中心静脈カテーテルの合併症であり、テデュグルチドの調製及び投与に使用した医療機器に関連したものではなかった（5.3.5.2 項 SHP633-305 CSR Section 12.2.2 参照）。

2.1.1.2.2.6　小児及び乳児を対象とした国内第 3 相コア試験及び継続投与試験の統合データ（有害事象発現頻度及び時期）

SHP633-302 試験（5.3.5.2 項）及び SHP633-305 試験（データカットオフ日まで）（5.3.5.2 項）について、有害事象発現データを統合解析した。各試験別の結果は前項に示した。小児及び乳児全体の統合解析において、頻度の高い有害事象の SOC は「胃腸障害（100%）」、「感染症および寄生虫症（100%）」及び「皮膚および皮下組織障害（90.0%）」であり、頻度の高い有害事象（40%以上）は、ウイルス性上気道感染（80.0%）、発熱（60.0%）、医療機器関連感染（50.0%）、皮膚乾燥（50.0%）及び発疹（40.0%）であった（2.7.4 項 付録 4 Table 13.1）。全ての有害事象を発現時期別に検討したところ、大半の事象は投与開始後数ヵ月間に発現し（2.7.4 項 付録 4 Table

13.1)、これは海外成人第 3 相試験（本概要 2.1.1.2.1.3）及び国内成人第 3 相試験（本概要 2.1.1.2.1.6）による結果と同様であった。全体として、統合データの安全性の結果は個々の試験結果と一致しており、新たな安全性の問題は特定されなかった（2.7.4 項 付録 4 Table 13.1）。

2.1.1.3　重症度別有害事象

2.1.1.3.1　成人の臨床試験データ

2.1.1.3.1.1　成人を対象とした海外第 3 相コア試験

CL0600-020 試験及び CL0600-004 試験の重症度別有害事象の発現状況を 5.3.5.1 項 CL0600-020 CSR Table 14.3.2.4、Table 14.3.2.5、5.3.5.1 項 CL0600-004 CSR Table 14.3.1.6、2.7.6 項に示す。

CL0600-020 及び CL0600-004 試験の統合データにおいて、有害事象の多くは軽度又は中等度であった（5.3.5.3 項 Adult ISS Table 9.1.2）。有害事象の最大重症度が軽度であった被験者は、テデュグルチド群 109 例のうち 22 例（20.2%）及びプラセボ群 59 例のうち 13 例（22.0%）であり、最大重症度が中等度であった被験者は、テデュグルチド群で 46 例（42.2%）及びプラセボ群で 20 例（33.9%）であった。最大重症度が重度であった被験者は、テデュグルチド群で 31 例（28.4%）及びプラセボ群で 16 例（27.1%）であった（5.3.5.3 項 Adult ISS Table 9.1.2）。

重度の有害事象のうち、テデュグルチド群で 2 例以上に認められた事象を表 2.7.4 - 32 に示す。重度の報告が最も多かった SOC は「胃腸障害」（14.7%）であった。

テデュグルチド群で頻度の高い（3 例以上）重度の有害事象は腹痛（4.6%）、腹部膨満（4.6%）、カテーテル敗血症（3.7%）及び悪心（2.8%）であった。

プラセボ群で重度の報告が最も多かった SOC は「感染症および寄生虫症」（13.6%）であった。2 例以上に認められた重度の有害事象は中心静脈カテーテル感染 2 例（3.4%）であった（5.3.5.3 項 Adult ISS Table 9.8.2）。

表 2.7.4 - 32　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群で 2 例以上に認められた重度の有害事象一覧（安全性解析対象集団）

			Teduglutide		
Parameter		**Placebo (N=59) n (%)**	**0.05 mg/kg/day (N=77) n (%)**	**0.10 mg/kg/day (N=32) n (%)**	**All (N=109) n (%)**
Gastrointestinal Disorders	胃腸障害	3 (5.1)	12 (15.6)	4 (12.5)	16 (14.7)
Abdominal pain	腹痛	0	5 (6.5)	0	5 (4.6)
Nausea	悪心	0	3 (3.9)	0	3 (2.8)
Abdominal distension	腹部膨満	1 (1.7)	5 (6.5)	0	5 (4.6)
Vomiting	嘔吐	0	2 (2.6)	0	2 (1.8)
Small intestinal obstruction	小腸閉塞	0	1 (1.3)	1 (3.1)	2 (1.8)

General Disorders and Administration Site Conditions	全身障害および投与局所様態	3 (5.1)	3 (3.9)	0	3 (2.8)
Pyrexia	発熱	1 (1.7)	2 (2.6)	0	2 (1.8)
Hepatobiliary Disorders	肝胆道系障害	1 (1.7)	3 (3.9)	0	3 (2.8)
Cholecystitis acute	急性胆嚢炎	0	2 (2.6)	0	2 (1.8)
Infections and Infestations	感染症および寄生虫症	8 (13.6)	6 (7.8)	1 (3.1)	7 (6.4)
Catheter sepsis	カテーテル敗血症	1 (1.7)	3 (3.9)	1 (3.1)	4 (3.7)
Nervous System Disorders	神経系障害	1 (1.7)	3 (3.9)	1 (3.1)	4 (3.7)
Headache	頭痛	0	1 (1.3)	1 (3.1)	2 (1.8)

Studies included: CL0600-020, CL0600-004.
Note: Percentages are based upon the number of subjects in the Safety Population.
Note: Treatment emergent adverse events are defined as any adverse event with a start date on or after the date of first dose and within thirty days after discontinuation of study drug.
Note: Subjects are counted no more than once for the maximum severity per System Organ Class and Preferred Term.
Note: All adverse events were coded using MedDRA version 12.0.
Source: Module 5.3.5.3 Adult ISS Table 9.8.2

2.1.1.3.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）については、重症度別の有害事象データは統合せず、試験別に示す。

CL0600-021 試験（5.3.5.2 項）の重症度別有害事象及び最大重症度別有害事象をそれぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.1.7、Table 14.3.1.8、2.7.6 項に示す。本試験では、大半の被験者に認められた有害事象は軽度（75/88 例、85.2%）又は中等度（69/88 例、78.4%）であった。重度の有害事象は 42/88 例に 110 件認められた（5.3.5.2 項 CL0600-021 CSR Table 12-2）。3 例以上でみられた重度の有害事象は腹痛（5.7%）、悪心（3.4%）、尿路感染（3.4%）及び消化管ストーマ合併症（ストーマを有する 36 例中 8.3%）であった。

CL0600-005 試験（5.3.5.2 項）の重度の有害事象（全体で 3 例以上）を 5.3.5.2 項 CL0600-005 CSR Table 12-5 に要約し、重症度別有害事象を 5.3.5.2 項 CL0600-005 CSR Table 14.3.2.4、2.7.6 項に示す。大半の被験者に認められた有害事象は中等度又は重度であった。試験期間中に 18 例（27.7%）に重度の有害事象が認められた。1 年実薬群では、重度の有害事象の発現頻度はテデュグルチド 0.05 mg/kg/日群（20.0%、5/25 例）に比べてテデュグルチド 0.10 mg/kg/日群（37.0%、10/27 例）において高かった。6 ヵ月実薬群では、テデュグルチド 0.05 mg/kg/日群の 1 例（16.7%）及び 0.10 mg/kg/日群の 2 例（28.6%）に重度の有害事象が認められた。1 年実薬群では、重度の頭痛がテデュグルチド 0.10 mg/kg/日群の 3 例（11.1%、3/27 例）に認められたが、テデュグルチド 0.05 mg/kg/日群では認められなかった。6 ヵ月実薬群では重度の頭痛は認められなかった。

TED-C11-001 試験（5.3.5.2 項）の全重症度別の有害事象及び最大重症度別の有害事象をそれぞれ 5.3.5.2 項 TED-C11-001 CSR Table 14.3.1.5、Table 14.3.1.6 及び 2.7.6 項に示す。本試験では、大

半の被験者に認められた有害事象は軽度（11/14 例、78.6%）又は中等度（11/14 例、78.6%）であった（5.3.5.2 項 TED-C11-001 CSR Table 12-2、2.7.6 項）。重度の有害事象は 4 例に発現した。

2.1.1.3.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）の重症度別有害事象の発現状況を 5.3.5.2 項 SHP633-306 CSR Table 14.3.2.8a 及び 2.7.6 項に示す。有害事象の大半は軽度または中等度であった。軽度の有害事象は 7 例全例に 30 件、中等度の有害事象は 2 例（28.6%）に 2 件、重度の有害事象は 1 例（14.3%）に 2 件発現した。重度の有害事象はてんかん 2 件であり、いずれも重篤であり、治験責任医師により治験薬との関連なしとされた。詳細については、5.3.5.2 項 SHP633-306 CSR Section 12.3.1.2 及び 5.3.5.2 項 SHP633-306 CSR Listing16.2.7 を参照のこと。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の重症度別の有害事象の発現状況を 5.3.5.2 項 TED-C14-004 CSR, Table 14.3.2.4.1 に示す。本試験のステージ 2 で認められた有害事象の多くは軽度又は中等度であった。ステージ 2 の期間中に、軽度の有害事象が 10 例（90.9%）に 66 件、中等度の有害事象が 2 例（18.2%）に 7 件、重度の有害事象が 3 例（27.3%）に 14 件認められた。重度の有害事象の多くは被験者番号：[redacted] にみられ、この被験者はその後死亡した（5.3.5.2 項 TED-C14-004 CSR Table 12.3.1.1)。

2.1.1.3.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）の安全性解析対象集団における重症度別有害事象を 5.3.5.2 項 SHP633-307 CSR Table 14.3.2.8a に、安全性解析対象集団における治験薬との因果関係が否定できない最大重症度別有害事象を 5.3.5.2 項 SHP633-307 CSR Table 14.3.2.8 又は 2.7.6 項に示す。有害事象の大部分は軽度又は中等度であった。重度の有害事象は 2 例（18.2%）に 5 件発現した。重度の有害事象は、器具関連感染 3 件、腸炎 1 件及び鎖骨下静脈閉塞 1 件であった。これらの事象はいずれも治験責任医師により治験薬との関連なしと判断された。詳細については 5.3.5.2 項 SHP633-307 CSR Section12.2.3.2 を参照のこと。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）のステージ 3 及び 4（継続投与期間のみ）の最大重症度別の有害事象を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.4.2 及び 2.7.6 項に示す。本期間中に認められた有害事象の多くは軽度又は中等度であり、軽度の有害事象が 8 例全例に 92 件、中等度の有害事象が 8 例全例に 34 件認められた（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.4.2)。重度の有害事象は 3 例（37.5%）に 9 件認められた（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.4.2)。

2.1.1.3.2　　小児の臨床試験データ

2.1.1.3.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験及び TED-C14-006 試験の統合データでの最大重症度別有害事象を 5.3.5.3 項 Pediatric ISS Table 10.1 に示す。試験ごとの重症度別の表を 5.3.5.2 項 TED-C13-003 CSR Table 14.3.2.4、5.3.5.2 項 TED-C14-006 CSR Table 14.3.1.5、2.7.6 項に示す。

統合データでの有害事象の大部分は軽度又は中等度であった。重度の有害事象の多くはテデュグルチド群の 1 例で認められたものであった。テデュグルチド群の 2 例以上に認められた重度の有害事象は、発熱（7 例、8.0%）、医療機器関連感染（5 例、5.7%）、医療機器破損（4 例、4.6%）、上気道感染（2 例、2.3%）、インフルエンザ（2 例、2.3%）、医療機器関連敗血症（2 例、2.3%）、及び脱水（2 例、2.3%）であった。標準治療群における重度の有害事象は全て 1 例（7.1%）に認められたものであった（表 2.7.4 - 33）。

表 2.7.4 - 33　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群における重度の有害事象一覧（安全性解析対象集団）

Category		0.0125 mg/kg/day Teduglutide (N=8) n(%)	0.025 mg/kg/day Teduglutide (N=38) n(%)	0.05 mg/kg/day Teduglutide (N=41) n(%)	Total Teduglutide (N=87) n(%)	Standard of Care (N=14) n(%)
Any Severe TEAE		2 (25.0)	9 (23.7)	15 (36.6)	26 (29.9)	1 (7.1)
Gastrointestinal Disorders	胃腸障害	0	2 (5.3)	2 (4.9)	4 (4.6)	0
Vomiting	嘔吐	0	1 (2.6)	0	1 (1.1)	0
Diarrhoea	下痢	0	0	1 (2.4)	1 (1.1)	0
Abdominal Distension	腹部膨満	0	1 (2.6)	0	1 (1.1)	0
Haematochezia	血便排泄	0	1 (2.6)	0	1 (1.1)	0
Haematemesis	吐血	0	0	1 (2.4)	1 (1.1)	0
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	0	3 (7.9)	4 (9.8)	7 (8.0)	1 (7.1)
Pyrexia	発熱	0	3 (7.9)	4 (9.8)	7 (8.0)	1 (7.1)
Immune System Disorders	免疫系障害	0	0	1 (2.4)	1 (1.1)	0
Anaphylactic Reaction	アナフィラキシー反応	0	0	1 (2.4)	1 (1.1)	0
Infections and Infestations	感染症および寄生虫症	1 (12.5)	5 (13.2)	8 (19.5)	14 (16.1)	1 (7.1)
Upper Respiratory Tract Infection	上気道感染	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Device Related Infection	医療機器関連感染	1 (12.5)	2 (5.3)	2 (4.9)	5 (5.7)	0
Viral Infection	ウイルス感染	0	0	1 (2.4)	1 (1.1)	0
Gastroenteritis Viral	ウイルス性胃腸炎	0	1 (2.6)	0	1 (1.1)	1 (7.1)

表 2.7.4 - 33　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群における重度の有害事象一覧（安全性解析対象集団）

Category		0.0125 mg/kg/day Teduglutide (N=8)	0.025 mg/kg/day Teduglutide (N=38)	0.05 mg/kg/day Teduglutide (N=41)	Total Teduglutide (N=87)	Standard of Care (N=14)
		n(%)	n(%)	n(%)	n(%)	n(%)
Influenza	インフルエンザ	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Catheter Site Infection	カテーテル留置部位感染	0	0	1 (2.4)	1 (1.1)	0
Device Related Sepsis	医療機器関連敗血症	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Parainfluenzae Virus Infection	パラインフルエンザウイルス感染	0	0	1 (2.4)	1 (1.1)	0
Respiratory Tract Infection	気道感染	0	0	1 (2.4)	1 (1.1)	0
Pneumonia	肺炎	0	0	1 (2.4)	1 (1.1)	0
Investigations	臨床検査	1 (12.5)	0	1 (2.4)	2 (2.3)	0
Blood Albumin Decreased	血中アルブミン減少	0	0	1 (2.4)	1 (1.1)	0
Influenza A Virus Test Positive	A 型インフルエンザウイルス検査陽性	1 (12.5)	0	0	1 (1.1)	0
Metabolism and Nutrition Disorders	代謝および栄養障害	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Dehydration	脱水	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Nervous System Disorders	神経系障害	0	1 (2.6)	1 (2.4)	2 (2.3)	0
Depressed Level of Consciousness	意識レベルの低下	0	0	1 (2.4)	1 (1.1)	0
Generalised Tonic-Clonic Seizure	全身性強直性間代性発作	0	1 (2.6)	0	1 (1.1)	0
Product Issues	製品の問題	0	3 (7.9)	3 (7.3)	6 (6.9)	0
Device Breakage	医療機器破損	0	3 (7.9)	1 (2.4)	4 (4.6)	0
Device Occlusion	医療機器閉塞	0	0	1 (2.4)	1 (1.1)	0
Device Malfunction	医療機器機能不良	0	0	1 (2.4)	1 (1.1)	0
Psychiatric Disorders	精神障害	0	0	1 (2.4)	1 (1.1)	0
Irritability	易刺激性	0	0	1 (2.4)	1 (1.1)	0
Skin and Subcutaneous Tissue Disorders	皮膚および皮下組織障害	0	1 (2.6)	0	1 (1.1)	0
Rash	発疹	0	1 (2.6)	0	1 (1.1)	0

MedDRA=Medical Dictionary for Regulatory Activities; n=number of subjects; TEAE=treatment-emergent adverse event
Note: Percentages are based on the number of subjects in the safety population in each treatment group.
Note: Subjects are counted no more than once for incidence. Only maximum severity per subject per system organ class (per preferred term) is counted for incidence and percentage.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Source: Module 5.3.5.3 Pediatric ISS Table 10.1

2.1.1.3.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）の重症度別有害事象の発現状況を 5.3.5.2 項 SHP633-304 Table 14.3.2.3、5.3.5.2 項 SHP633-303 Table 14.3.2.3、2.7.6 項に示す。

SHP633-304 試験及び SHP633-303 試験（前向き期間）の統合データによる有害事象の大部分は軽度又は中等度であった。TED/TED 群の 2 例（3.3%）に認められた医療機器関連感染を除き、継続投与試験における重度の有害事象は全て 1 例のみに認められたものであった。（5.3.5.3 項 Pediatric ISS Table 10.2.2、Table 13.2.2）。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

2.1.1.3.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析での最大重症度別有害事象の発現状況を 5.3.5.2 項 SHP633-301 CSR Table 14.3.1.7 及び 2.7.6.項に示す。有害事象の大部分は軽度又は中等度であった。試験期間中に重度の有害事象が 2 件（各投与群で 1 件）発現した。その内訳は、テデュグルチド群の 1 例及び標準治療群の 1 例（いずれもテデュグルチド投与用機器ではなく、PS の投与に使用された中心静脈カテーテルに関連する）であった。重度の有害事象はいずれも治験責任医師により関連なしと判断された（5.3.5.2 項 SHP633-301 Interim CSR Appendix 16.2.7 Listing 16.2.7.1）。

最終解析での最大重症度別有害事象の発現状況を 5.3.5.2 項 SHP633-301 Final Table 14.3.1.7 及び 2.7.6 項に示す。有害事象の大部分は軽度又は中等度であった。試験期間中に重度の有害事象が 3 件発現した（テデュグルチド群 1 件、及び標準治療群 2 件）。その内訳は、テデュグルチド群の 1 例に医療機器リークが発現し（テデュグルチド投与用機器ではなく、PS の投与に使用された中心静脈カテーテルに関連する）、標準治療群 2 例にそれぞれ医療機器関連感染の事象が発現した。重度の有害事象はいずれも被験者の入院のため重篤であり、治験責任医師により治験薬と関連なしとされた（5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.7 Listing 16.2.7.1）。

2.1.1.3.2.4　　小児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）の重症度別有害事象の発現状況を 5.3.5.2 項 SHP633-302 CSR Table 14.3.2.4a に示す。有害事象の大部分は軽度又は中等度であった。小児コホートでは、重度の医療機器使用部位感染の有害事象が 2 例（25.0%）に 2 件報告され、いずれも重篤であった。これらの事象は治験薬と関連なしとされた。乳児コホートでは、有害事象は全て軽度又は中等度であった。

2.1.1.3.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、乳児被験者 1 例に重度かつ重篤な急性膵炎が認められたが、治験薬との因果関係は否定された。その他の全ての有害事象は軽度又は中等度であった（本概要 2.1.3.2.5、5.3.5.2 項 SHP633-305 CSR Section 12.2.3.2 参照）。

2.1.1.4　　治験薬と関連ありと判断された有害事象

2.1.1.4.1　　成人の臨床試験データ

2.1.1.4.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）の治験薬と関連ありとされた有害事象を、5.3.5.1 項 CL0600-020 CSR Table 14.3.2.6、Table 14.3.2.7 に、CL0600-004 試験（5.3.5.1 項）の因果関係別有害事象を 5.3.5.1 項 CL0600-004 CSR Table 14.3.1.7 に、又は 2.7.6 項に示す。CL0600-020 試験及び CL0600-004 試験の統合データにおいてテデュグルチド群全体で 2%以上に認められた治験薬と関連ありと判断された有害事象を表 2.7.4 - 34 に示す。

テデュグルチド群で報告された治験薬と関連ありと判断された有害事象のうち、頻度の高い SOC は、「胃腸障害」（33.0%）、「全身障害および投与局所様態」（26.6%）並びに「傷害、中毒および処置合併症」（17.4%）であった。テデュグルチド群で報告された治験薬と関連ありと判断された有害事象のうち、頻度の高い（10%以上）事象は、消化管ストーマ合併症（13.8%）、悪心（12.8%）、腹部膨満（10.1%）及び腹痛（10.1%）であった。

プラセボ群で報告された治験薬と関連ありと判断された有害事象のうち、頻度の高い SOC は、「胃腸障害」（23.7%）並びに「全身障害および投与局所様態」（13.6%）であった。プラセボ群で報告された治験薬と関連ありと判断された有害事象のうち、比較的発現頻度の高い（10%以上）有害事象は、悪心（11.9%）及び腹痛（11.9%）であった（表 2.7.4 - 34）。

表 2.7.4 - 34　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群全体で 2%以上に認められた治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

				Teduglutide					
		Placebo (N=59)		0.05 mg/kg/day (N=77)		0.10 mg/kg/day (N=32)		All (N=109)	
Parameter		**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**
Gastrointestinal Disorders	胃腸障害	14 (23.7)	35	27 (35.1)	69	9 (28.1)	23	36 (33.0)	92
Nausea	悪心	7 (11.9)	9	11 (14.3)	15	3 (9.4)	5	14 (12.8)	20
Abdominal distension	腹部膨満	0	0	10 (13.0)	14	1 (3.1)	2	11 (10.1)	16
Abdominal pain	腹痛	7 (11.9)	8	9 (11.7)	12	2 (6.3)	2	11 (10.1)	14
Vomiting	嘔吐	1 (1.7)	1	5 (6.5)	6	2 (6.3)	4	7 (6.4)	10

表 2.7.4 - 34　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群全体で 2%以上に認められた治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

				Teduglutide					
		Placebo (N=59)		0.05 mg/kg/day (N=77)		0.10 mg/kg/day (N=32)		All (N=109)	
Parameter		**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**
Flatulence	鼓腸	4 (6.8)	4	5 (6.5)	5	0	0	5 (4.6)	5
Abdominal tenderness	腹部圧痛	1 (1.7)	1	1 (1.3)	1	2 (6.3)	2	3 (2.8)	3
Constipation	便秘	2 (3.4)	3	3 (3.9)	3	0	0	3(2.8)	3
General Disorders and Administration Site Conditions	全身障害および投与局所様態	8 (13.6)	12	14 (18.2)	26	15(46.9)	23	29(26.6)	49
Injection site haematoma	注射部位血腫	3 (5.1)	4	4 (5.2)	4	6 (18.8)	7	10 (9.2)	11
Injection site erythema	注射部位紅斑	0	0	3 (3.9)	3	5 (15.6)	5	8 (7.3)	8
Injection site pain	注射部位疼痛	0	0	1 (1.3)	4	4 (12.5)	4	5 (4.6)	8
Oedema peripheral	末梢性浮腫	0	0	4 (5.2)	5	1 (3.1)	1	5 (4.6)	6
Injury, Poisoning and Procedural Complications	傷害、中毒および処置合併症	3 (5.1)	4	13 (16.9)	15	6 (18.8)	8	19 (17.4)	23
Gastrointestinal stoma complication	消化管ストーマ合併症	3 (5.1)	3	12 (15.6)	13	3 (9.4)	4	15 (13.8)	17
Investigations	臨床検査	3 (5.1)	3	6 (7.8)	6	2 (6.3)	3	8 (7.3)	9
Weight increased	体重増加	2 (3.4)	2	3 (3.9)	3	0	0	3 (2.8)	3
Metabolism and Nutrition Disorders	代謝および栄養障害	1 (1.7)	1	4 (5.2)	5	3 (9.4)	3	7 (6.4)	8
Decreased appetite	食欲減退	1 (1.7)	1	3 (3.9)	4	2 (6.3)	2	5 (4.6)	6
Nervous System Disorders	神経系障害	3 (5.1)	4	3 (3.9)	4	1 (3.1)	1	4 (3.7)	5
Skin and Subcutaneous Tissue Disorders	皮膚および皮下組織障害	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Erythema	紅斑	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3
Vascular Disorders	血管障害	0	0	2 (2.6)	2	1 (3.1)	1	3 (2.8)	3

E = Total number of events; TEAE = Treatment emergent adverse event; TESAE = Treatment emergent serious adverse event.
Studies included: CL0600-020, CL0600-004.
Note: Percentages are based upon the number of subjects in the Safety Population.
Note: Treatment emergent adverse events are defined as any adverse event with a start date on or after the date of first dose and within thirty days after discontinuation of study drug.
Note: Related AEs include AEs that were 'possibly related', 'probably related', 'related' or with relationship missing.
Note: Subjects are counted no more than once for incidence of System Organ Class and Preferred Term but can be counted multiple times for the number of events.
Note: All adverse events were coded using MedDRA version 12.0.
Source: Module 5.3.5.3 Adult ISS, Table 9.16.1

2.1.1.4.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）については、因果関係別の有害事象は統合せず、試験別に本項に示す。

CL0600-021 試験（5.3.5.2 項）で治験薬と関連ありとされた有害事象を 5.3.5.2 項 CL0600-021 CSR Table 14.3.1.9、Table 14.3.1.10 及び 2.7.6 項に要約する。治験薬と関連ありと判断された有害事象は、46/88 例（52.3%）に認められた（5.3.5.2 項 CL0600-021 CSR Table 12-2）。関連ありと判断された有害事象のうち、発現頻度の高い有害事象は、胃腸の有害事象（腹痛、悪心、腹部膨満、鼓腸、嘔吐など）、並びに体液貯留及び注射部位紅斑であった（5.3.5.2 項 CL0600-021 CSR Table 14.3.1.9）。

CL0600-005 試験（5.3.5.2 項）における治験薬と関連ありとされた有害事象を 5.3.5.2 項 CL0600-005 CSR Table 14.3.2.1、Table 14.3.2.5 及び 2.7.6 項に要約する。被験者 25 例（38.5%）に治験薬と関連ありと判断された有害事象が認められた。1 年実薬群では、治験薬と関連ありと判断された有害事象の発現頻度はテデュグルチド 0.05 mg/kg/日群（24%、6/25 例）と比べてテデュグルチド 0.10 mg/kg/日群（40.7%、11/27 例）で高かった。6 ヵ月実薬群では、テデュグルチド 0.05 mg/kg/日群の 4 例（66.7%）及び 0.10 mg/kg/日群の 4 例（57.1%）に治験薬と関連ありと判断された有害事象がみられた。6 ヵ月実薬群及び 1 年実薬群では、治験薬と関連ありと判断された有害事象の多くが腹痛、注射部位紅斑及び腸管ストーマ合併症であった（5.3.5.2 項 CL0600-005 CSR Table 12-6）。

TED-C11-001 試験（5.3.5.2 項）における治験薬と関連ありとされた有害事象を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.1.7、Table 14.3.1.8 及び 2.7.6 項に要約する。有害事象 120 件中 6 件が治験薬と関連ありと判断された（5.3.5.2 項 TED-C11-001 CSR Table 12-2）。治験薬と関連ありと判断された有害事象は、消化器関連有害事象（腹痛、下痢、結腸ポリープ等）並びに早期満腹及び注射部位血腫であった（5.3.5.2 項 TED-C11-001 CSR Table 14.3.1.8）。

2.1.1.4.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）において、治験薬と関連ありとされた有害事象を表 2.7.4 - 35 に示す。被験者 4 例（57.1%）に 6 件の治験薬と関連ありとされた有害事象が認められた。2 例以上に認められた治験薬と関連ありとされた有害事象の SOC は、「胃腸障害」2 例（28.6%）であった。治験薬と関連ありとされた有害事象の大部分は、1 例にみられた単発の事象であった。2 例以上にみられた治験薬と関連ありとされた有害事象は、2 例（28.6%）にみられた腹部膨満であった。

表 2.7.4 - 35　SHP633-306 試験：治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

		Total Teduglutide (N=7)	
		Related	
System Organ Class Preferred Term		**Subjects n (%)**	**Events**
Any TEAE		4 (57.1)	6
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (14.3)	1

表 2.7.4 - 35　SHP633-306 試験：治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

System Organ Class Preferred Term		Total Teduglutide (N=7) Related Subjects n (%)	Events
Polycythaemia	赤血球増加症	1 (14.3)	1
Gastrointestinal disorders	胃腸障害	2 (28.6)	2
Abdominal distension	腹部膨満	2 (28.6)	2
General disorders and administration site conditions	一般・全身障害および投与部位の状態	1 (14.3)	1
Injection site reaction	注射部位反応	1 (14.3)	1
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (14.3)	1
Gastrointestinal stoma complication	消化管ストーマ合併症	1 (14.3)	1
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	1 (14.3)	1
Oropharyngeal pain	口腔咽頭痛	1 (14.3)	1

Note: Percentages are based on the Safety Population.
Note: Treatment-emergent AEs (TEAEs) were defined as AEs whose onset occurred, severity worsened, or intensity increased after receiving the study medication.
Note: Subjects were counted no more than once for incidence (highest category), but could be counted multiple times for the number of events. All events with a given relationship were counted.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms were coded using MedDRA 21.0.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.3.2.9a

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）について、ステージ 2 で認められた治験薬と関連ありと判断された有害事象のうち 2 例以上に発現した事象を表 2.7.4 - 36 に示す。ステージ 2 では治験薬と関連ありと判断された有害事象は 7 例（63.6%）に 18 件認められた。治験薬と関連ありと判断された有害事象で発現頻度の高い SOC は、「胃腸障害」（36.4%）及び「一般・全身障害および投与部位の状態」（18.2%）であった。ステージ 2 で認められた治験薬と関連ありと判断された有害事象の多くは 1 例に発現した単発の事象であった。複数例に認められた治験薬と関連ありとされた有害事象は、腹痛 2 例（18.2%、2 件）、注射部位反応 2 例（18.2%、2 件）及び嘔吐 2 例（18.2%、2 件）であった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.6.1）。

表 2.7.4 - 36　TED-C14-004 試験：ステージ 2 で 2 例以上に認められた治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Teduglutide (N=11) Subjects n (%)	Events
Any Treatment-related TEAE		7 (63.6)	18
Gastrointestinal Disorders	胃腸障害	4 (36.4)	11
Abdominal pain	腹痛	2 (18.2)	2
Vomiting	嘔吐	2 (18.2)	2
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	2 (18.2)	3
Injection site reaction	注射部位反応	2 (18.2)	2

n=number of subjects experiencing the event; TEAE=treatment-emergent adverse event
Note: Percentages are based on the safety population.
Note: Relationship to study treatment is based upon investigator assessment.
Note: Treatment-emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study drug.
Note: Subjects are counted no more than once for incidence, but can be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA J 17.1.
Source: Module 5.3.5.2 TED-C14-004 CSR, Table 14.3.2.5.1

2.1.1.4.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）について、因果関係別有害事象を 5.3.5.2 項 SHP633-307 CSR Section 12.2.3.1、5.3.5.2 項 SHP633-307 CSR Table 14.3.2.9、Table 14.3.2.9a、2.7.6 項に示す。治験責任医師により治験薬との関連ありと判断された有害事象は、1/11 例（9.1%）に 1 件認められた（TED-C14-004 試験から移行した被験者）。本事象の SOC は「皮膚および皮下組織障害」、PT は皮下出血であり、軽度、非重篤とされた（Day 1494 での発現）。有害事象のために治験薬及びその他の処置は取られず、Day 1497 に回復した（SHP633-307 CSR Listing 16.2.7）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）のステージ 3 及び 4 で、因果関係別有害事象を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.5.2 及び 2.7.6 項に示す。本期間中に治験薬と関連ありと判断された有害事象が 1 例（12.5%）に 1 件発現した（発熱）。（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.5.2）。

2.1.1.4.2　　小児の臨床試験データ

2.1.1.4.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の試験ごとの因果関係別有害事象を 5.3.5.2 項 TED C13 003 CSR Table 14.3.2.5、Table 14.3.2.6、5.3.5.2 項 TED C14 006 CSR Table 14.3.1.3、2.7.6 項に示す。

TED-C13-003 試験及び TED-C14-006 試験の統合データにおいて、テデュグルチド群で 2 例以上に認められた治験薬と関連ありと判断された有害事象を表 2.7.4 - 37 に要約する。テデュグルチド用量群間で、治験薬と関連ありと判断された有害事象の発現頻度に特定の傾向は認められなかった。治験薬と関連ありと判断された有害事象は、0.0125 mg/kg 群の 2 例（25.0%）に 7 件、0.025 mg/kg 群の 13 例（34.2%）に 25 件、0.05 mg/kg 群の 12 例（29.3%）に 56 件発現した。テデュグルチド群で認められた治験薬と関連ありと判断された有害事象の発現頻度が高い SOC は、「胃腸障害」（16.1%）並びに「一般・全身障害および投与部位の状態」（12.6%）であった。テデュグルチド群の被験者の 3%以上に認められた治験薬と関連ありと判断された有害事象は、腹痛（5.7%）、嘔吐（4.6%）、及び注射部位内出血（3.4%）であった（5.3.5.3 項 Pediatric ISS Table 9.1）。

表 2.7.4 - 37　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群で 2 例以上の被験者にみられた治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

		0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)	
		n(%)	E	n(%)	E	n(%)	E	n(%)	E
Any Related TEAE		2 (25.0)	7	13 (34.2)	25	12 (29.3)	56	27 (31.0)	88
Eye Disorders	眼障害	0	0	0	0	3 (7.3)	3	3 (3.4)	3
Lid Sulcus Deepened	眼瞼溝深化	0	0	0	0	2 (4.9)	2	2 (2.3)	2
Gastrointestinal Disorders	胃腸障害	2 (25.0)	4	6 (15.8)	12	6 (14.6)	31	14 (16.1)	47
Abdominal Pain	腹痛	0	0	2 (5.3)	6	3 (7.3)	11	5 (5.7)	17
Vomiting	嘔吐	0	0	1 (2.6)	1	3 (7.3)	10	4 (4.6)	11
Abdominal Distension	腹部膨満	1 (12.5)	1	0	0	1 (2.4)	1	2 (2.3)	2
Dyschezia	排便障害	0	0	0	0	2 (4.9)	2	2 (2.3)	2
Flatulence	鼓腸	0	0	2 (5.3)	2	0	0	2 (2.3)	2
Nausea	悪心	1 (12.5)	2	0	0	1 (2.4)	3	2 (2.3)	5
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	1 (12.5)	2	5 (13.2)	6	5 (12.2)	9	11 (12.6)	17
Injection Site Bruising	注射部位内出血	0	0	2 (5.3)	3	1 (2.4)	3	3 (3.4)	6
Injection Site Haemorrhage	注射部位出血	0	0	0	0	2 (4.9)	3	2 (2.3)	3
Injury, Poisoning and Procedural Complications	傷害、中毒および処置合併症	0	0	1 (2.6)	1	1 (2.4)	4	2 (2.3)	5
Stoma Complication	ストーマ合併症	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2
Nervous System Disorders	神経系障害	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2
Headache	頭痛	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2

E=number of events; MedDRA=Medical Dictionary for Regulatory Activities; n=number of subjects; TEAE=treatment-emergent adverse event
Note:　Percentages are based on the number of subjects in the safety population in each treatment group.
Note:　Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note:　Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Source: Module 5.3.5.3 Pediatric ISS Table 9.1

2.1.1.4.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）の試験ごとで認められたその他の治験薬と関連ありと判断された有害事象を 5.3.5.2 項 SHP633-304 CSR Table 14.3.2.4、5.3.5.2 項 SHP633-303 CSR Table 14.3.2.4、2.7.6 項に示す。

SHP633-304 試験及び SHP633-303 試験（前向き期間）の統合データにおいて、TED/TED 群の 12 例（20.0%）に 17 件の治験薬と関連ありと判断された有害事象が認められた。NTT/TED 群及び TED/NTT 群では、いずれも治験薬と関連ありと判断された有害事象は認められなかった。TED/TED 群では注射部位腫脹が 2 例（3.3%）に 2 件認められた。TED/TED 群の 1 例（1.7%）に注射部位疼痛及び注射部位紅斑がそれぞれ 2 件認められた。その他の事象は、いずれも 1 例にみられた単発の事象であった（5.3.5.3 項 Pediatric ISS Table 9.2）。テデュグルチド群の 3%以上に認められた治験薬と関連ありとされた有害事象は、腹痛（5.6%）、嘔吐（5.6%）、悪心（3.4%）、注射部位内出血（3.4%）、注射部腫脹（3.4%）及びストーマ合併症（3.4%）であった（5.3.5.3 項 Pediatric ISS Table 9.3）。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 項を参照のこと。

2.1.1.4.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析で認められた治験薬と関連ありと判断された有害事象を 5.3.5.2 項 SHP633-301 CSR Table 14.3.1.3、2.7.6 項に示す。治験薬と関連ありとされた有害事象はテデュグルチド群の 1 例（33.3%）にみられた 1 件（アラニンアミノトランスフェラーゼ増加）であった。本被験者は後に継続投与試験に登録された。詳細については 5.3.5.2 項 SHP633-301 Interim CSR Section 12.2.3.1 を参照のこと。

最終解析で認められた治験薬と関連ありと判断された有害事象を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.1.3、2.7.6 項に示す。治験責任医師により治験薬と関連ありとされた有害事象は 2 例（20.0%）にみられた 9 件であった。2 例はどちらもテデュグルチド群での発現であった。うち 8 件は被験者 1 例に発現し（腹部膨満、胃腸音異常、嘔吐［5 件］、及び便量増加）、また本被験者では治験薬と関連なしとされた胃腸関連の有害事象が複数発現し、治験薬の投与は中断され、再開されなかった。本被験者の最終評価は Day207 であった（叙述は 5.3.5.2 項 SHP633-301 Final CSR Section 14.3.3 参照）。残る 1 例にはアラニンアミノトランスフェラーゼ増加の有害事象が 2 件発現し、2 回目の事象が治験責任医師により治験薬と関連ありとされた。治験責任医師によりこの事象は中等度とされ、被験者のビリルビン値は正常範囲内であり、治験薬に関する措置は取られなかった。本被験者は後に継続投与試験に登録された。詳細については 5.3.5.2 項 SHP633-301 Final CSR Section 12.2.3.1 を参照のこと。

2.1.1.4.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験における因果関係別の有害事象の発現状況は、表 2.7.4 - 38 のとおりであった。治験薬と関連ありとされた有害事象は、小児コホートで 6 例（75.0%）に 20 件であった。被験者 2 例以上に発現した治験薬と関連ありとされた有害事象は、注射部位紅斑 9 件（3 例、37.5%）、腹痛 2 件（2 例、25.0%）であった。うち 1 例に認められた腹痛は重篤かつ中等度であった。

乳児コホートでは、治験薬と関連ありとされた有害事象は認められなかった。

表 2.7.4 - 38　SHP633-302 試験：治験薬と関連ありと判断された有害事象一覧（安全性解析対象集団）

SOC PT		Children[a] After Amendment 3[c] (N=6)		Total Children[a] (N=8)		Infants[b] (N=2)	
		n (%)	Events	n (%)	Events	n (%)	Events
Any TEAEs Related to Treatment		4 (66.7)	17	6 (75.0)	20	0	0
Gastrointestinal disorders	胃腸障害	1 (16.7)	2	3 (37.5)	4	0	0
Abdominal pain	腹痛	1 (16.7)	1	2 (25.0)	2	0	0
Constipation	便秘	0	0	1 (12.5)	1	0	0
Gastritis	胃炎	1 (16.7)	1	1 (12.5)	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	3 (50.0)	14	4 (50.0)	15	0	0
Injection site erythema	注射部位紅斑	2 (33.3)	8	3 (37.5)	9	0	0
Injection site pain	注射部位疼痛	1 (16.7)	1	1 (12.5)	1	0	0
Injection site rash	注射部位発疹	1 (16.7)	4	1 (12.5)	4	0	0
Injection site reaction	注射部位反応	1 (16.7)	1	1 (12.5)	1	0	0
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	1 (16.7)	1	1 (12.5)	1	0	0
rash	発疹	1 (16.7)	1	1 (12.5)	1	0	0

SOC=System Organ Class; PT=preferred term
a: Children aged 1 through 15 years.
b: Infants of 4 through <12 months corrected gestational age.
c: The number of children enrolled based upon the protocol amendment 3 and 4.
Note: Relationship to study treatment was based upon investigator assessment.
Note: Subjects were counted multiple times if they had multiple AEs with different relationship.
Note: SOCs and PTs were coded using MedDRA 20.0.
Source: Module 5.3.5.2 SHP633-302 CSR, Table 14.3.2.5a

2.1.1.4.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、小児コホートでは治験薬と関連ありとされた有害事象が 2 例（28.6%）に 2 件認められた（胃障害及び注射部位疼痛）。乳児コホートでは、治験薬と関連ありとされた有害事象はみられなかった（5.3.5.2 項 SHP633-305 CSR Section 12.2.3.1 参照）。

2.1.2　　死亡

2020 年 10 月申請時のデータでは、テデュグルチドの臨床開発プログラム全体の各試験のデータカットオフ時点で死亡例は 6 例であった。死亡した被験者で認められた有害事象の一覧を 2.7.4 項付録 1 に示す。

2.1.2.1　　成人の臨床試験データ

2.1.2.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）における安全性の叙述を 5.3.5.1 項 CL0600-020 CSR Section 14.3.3、5.3.5.1 項 CL0600-004 CSR Section 14.3.3、2.7.6 項に示す。CL0600-020 試験では死亡例の報告はなく、CL0600-004 試験において、試験治療下ではなくスクリーニング期間中（無作為化及び治験薬投与開始前）に、1 例が死亡した。叙述の要約を以下に示す。

> 被験者は 5[redacted]歳の白人女性被験者（被験者番号：[redacted]）で、クローン病及び肺炎の既往歴があり、2005 年 1 月 20 日に本試験に登録された。本事象発現時に被験者は無作為化され、治験薬の投与を受けていなかった。被験者は、結腸の連続性あり、ストーマなし、残存小腸の長さ 70 cm であり、抗リン脂質抗体症候群に関連した血栓症による大規模な腸切除を受けていた。同年 3 月 10 日（Day 50）、被験者は死亡しているのを発見された。治験責任医師の判断では、被験者の死亡は大量の上部消化管出血によるものであった。詳細は 5.3.5.1 項 CL0600 004 CSR Section 12.3.1.1 又は 2.7.6 項を参照のこと。

テデュグルチドの開発プログラム全体でみられた死亡について、2.7.4 項 付録 1 に一覧を示す。

2.1.2.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）では、3 例の死亡が報告された（いずれも CL0600-021 試験）。以下に簡潔な叙述を示す。

CL0600-021 試験において、被験者は 6[redacted]歳の白人男性（被験者番号：[redacted]）であり、喫煙歴（約 30 年間、1 日約 30 本）及びアスベスト曝露歴（期間不明）があった。CL0600-020 試験ではプラセボを投与され、その後本試験に組み入れられた。治験薬の投与開始から約 3 ヵ月後に非小細胞肺癌と診断された。腰仙椎のコンピューター断層撮影（CT）により変性増殖性変化と腫瘍転移が示され、骨シンチグラフィーは多病巣性転移を示した。ビノレルビン及びカルボプラチンによる化学療法が行われた。被験者は試験治療の開始から約 7 ヵ月後に死亡し、死因は非小細胞肺癌と報告された。剖検は行われなかった。CL0600-021 CSR Table 14.3.2.6、CL0600-021 CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

CL0600-021 試験において、被験者は 4[redacted]歳男性（被験者番号：[redacted]）であり、ホジキン病、放射線によるコーカル壊死及び原発性肝疾患の既往歴があった。投与開始 11 ヵ月後に生検により転移性腺癌と診断され、約 10 日後に死亡した。剖検では原発部位は確定できず、死因は腸癌の全身悪性腫瘍とされた。患者病歴をさらに精査したところ、テデュグルチドによる治療を開始する 6 ヵ月前に腹部 CT 検査が実施され、肝腫大が認められた。その後、この CT は再検討され、転移性腺癌の診断時に 2 回目の CT スキャンを実施したところ、最初の CT では報告されていなかった肝臓の限局性病変が明らかになった。原発腫瘍はおそらく消化管にあると考えられたが、正確な位置は不明であった。治験責任医師により、当該重篤な有害事象は重度であり、治験薬と関連ありと判断された。CL0600-021 CSR Table 14.3.2.6 及び CL0600-021 CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

CL0600-021 試験において、被験者は 6[redacted]歳男性（被験者番号：[redacted]）であり、腸間膜動脈塞栓症に続発した大腸切除、心房細動、左下肢の血栓後症候群、慢性心不全及び高血圧の既往があった。被験者は CL0600-020 試験でテデュグルチド投与を開始し、CL0600-021 試験で継続投与を受けた。CL0600-020 試験において、テデュグルチド投与開始 28 ヵ月後にブロビアックカテーテルと尿路感染による敗血症により入院した。尿培養で大腸菌、血液培養で表皮ブドウ球菌、メチシリン耐性黄色ブドウ球菌が確認された。経験的抗生物質療法（レンダチン、チプリノル、バンコマイシン）と後にクリンダマイシンが投与されたが、患者の全身状態は改善せず、椎間板炎を併発した。患者の状態が突然悪化した後、被験者は CL0600-020 試験でテデュグルチドによる治療を開始した約 28 ヵ月後に死亡した。敗血症は治験責任医師により重度、治験薬と関連なしとされた。CL0600-021 CSR Table 14.3.2.6、CL0600-021 CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

TED-C11-001 試験（5.3.5.2 項）では、試験実施中に死亡例は認められなかった。

2.1.2.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）では死亡例はみられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）における安全性の叙述を 5.3.5.2 項 TED-C14-004 CSR Section 14.3.3 及び 2.7.6 項に示す。本試験では、1 例の死亡が報告された（ステージ 2）。以下に簡潔に叙述する。

TED-C14-004 試験において、被験者は 3[redacted]歳の日本人男性（被験者番号：[redacted]）で先天性微絨毛封入症、小腸移植及びその後の拒絶反応、PS を必要とする SBS、高血圧症、腎疾患に伴う貧血、難治性下痢、慢性、ステロイド誘発性骨粗鬆症、糖尿病及び副腎機能不全の既往歴があった。試験 Day 13 に腸閉塞、腸炎、グラム陰性菌性敗血症及び急性肝不全が発現したが、関連する脳症は認められなかった。肝生検では、胆汁うっ滞及び門脈圧亢進症を伴うステージ 3 線維症の慢性肝疾患を示した。その時点で治験薬の投与が中止され、追跡調査の結果、持続性敗血症、*C.parapsilosis* 真菌血症、低血圧、急性腎不全、心停止、呼吸不全が認められた。68 日目に急性肝不全及び急性腎不全により死亡した。治験責任医師は、急性肝不全は治験薬と関連あり、急性腎不全は関連なしと判断した。治験依頼者による症例の追跡調査（肝臓専門医及び薬物性肝障害の独立した専門医による検討を含む）では、被験者の急性肝不全は、肝毒性障害（敗血症、完全静脈栄養、肝毒性薬）による可能性が最も高く、治験薬とおそらく関連なし（unlikely）と結論づけられた。注目すべきは、被験者のベースラインの慢性肝疾患の病歴である。治験依頼者は、被験者の急性肝不全の発現は治験薬と関連なしと結論づけた。詳細な叙述については、TED-C14-004 CSR Table 14.3.2.14 及び SHP633-304 CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

テデュグルチドの開発プログラム全体でみられた死亡について、2.7.4 項付録 1 に一覧を示す。

2.1.2.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では死亡例はみられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）では、上述のとおり（本概要 2.1.2.1.3）、ステージ 2 で 1 例が死亡したが、継続期間（ステージ 3 及び 4）における死亡例は報告されていない。

テデュグルチドの開発プログラム全体でみられた死亡について、2.7.4 項 付録 1 に一覧を示す。

2.1.2.2　小児の臨床試験データ

2.1.2.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）では死亡例はみられなかった。

2.1.2.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）における安全性の叙述を 5.3.5.2 項 SHP633-304 CSR Section 14.3 及び 2.7.6 項並びに 5.3.5.2 項 SHP633-303 Section 14.3 及び 2.7.6 項に示す。これらの試験期間中、1 例が死亡した（SHP633-304 試験）。以下に簡潔な叙述を示す。

> 被験者は 1[redacted]歳の白人男性（被験者番号：[redacted]）であり、SBS、中腸軸捻転に加えて、脳性麻痺、水頭症、及び発作障害の病歴があった。TED-C14-006 試験においてテデュグルチド 0.05 mg/kg/日の投与が開始され、約 11 ヵ月後に SHP633-304 試験においてテデュグルチドの最終投与を受けた。被験者はホスピスケアに移行した。治験責任医師によると、被験者の家族は、被験者は PS を外すことができず、SBS 及び併存疾患の両者に関連して生活の質が低下したため、終末期ケア及び在宅ホスピスを継続することを選択した。その直後に被験者は SBS の悪化により死亡した。この事象は、治験責任医師により、重度であり、テデュグルチドとの関連なしと判断された。詳細は SHP633-304 CSR Table 14.3.4.6、SHP633-304 CSR Section 14.3.3 及び 2.7.6 項を参照のこと。

テデュグルチドの開発プログラム全体でみられた死亡について、2.7.4 項 付録 1 に一覧を示す。

2.1.2.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）では死亡例はみられなかった。

中間解析のための安全性に関する叙述を 5.3.5.2 項 SHP633-301 Interim CSR Section 14.3.3 及び 2.7.6 項に示す。

最終解析のための安全性に関する叙述を 5.3.5.2 項 SHP633-301 Final CSR Section 14.3.3 及び 2.7.6 項に示す。

テデュグルチドの開発プログラム全体でみられた死亡例について、2.7.4 項付録 1 に一覧を示す。

2.1.2.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験では死亡例はみられなかった。

2.1.2.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の国内第 3 相小児継続投与試験 SHP633-305 試験（5.3.5.2 項）では、安全性に関する叙述を 5.3.5.2 項 SHP633-305 CSR, Section 14.3.3 及び 2.7.6 項に記載した。本試験のデータカットオフ日までに死亡は報告されなかった。

テデュグルチドの開発プログラム全体でみられた死亡例について、2.7.4 項 付録 1 に一覧を示す。

2.1.3　　その他の重篤な有害事象

テデュグルチドの臨床開発プログラム全体で重篤な有害事象を発現した被験者における有害事象の一覧を 2.7.4 項 付録 2 に示す。

2.1.3.1　　成人の臨床試験データ

2.1.3.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験及び CL0600-004 試験の統合データに基づき、重篤な有害事象を全体として、また因果関係別に示す。

重篤な有害事象

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）のテデュグルチド群で 2 例以上に発現した重篤な有害事象を表 2.7.4 - 39 に示す。重篤な有害事象の大半は 1 例に発現した単発の事象であった。

テデュグルチド群で頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（22.9%）であった。テデュグルチド群 109 例中 5 例以上に認められた重篤な有害事象は、カテーテル敗血症（7.3%）及びカテーテル関連感染（5.5%）であった。

プラセボ群で頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（16.9%）並びに「傷害、中毒および処置合併症」（13.6%）であった。プラセボ群 59 例中 3 例以上に認められた重篤な有害事象は、中心静脈カテーテル感染（5.1%）及び菌血症（5.1%）であった（5.3.5.3 項 Adult ISS Table 9.11.2）。

治験薬と関連ありと判断された重篤な有害事象

治験薬と関連ありと判断された重篤な有害事象は 10 例に 14 件認められた（5.3.5.3 項 Adult ISS Table 9.1.2）。10 例の内訳は、CL0600-020 試験の 2 例（いずれもテデュグルチド 0.05 mg/kg/日群）、CL0600-004 試験の 8 例（テデュグルチド 0.05 mg/kg/日群 6 例、テデュグルチド 0.10 mg/kg/日群 2 例）であった。治験薬と関連ありと判断された重篤な有害事象は、小腸閉塞（2 例 2 件）、胆嚢炎（1 例 2 件）並びに急性胆嚢炎、小腸狭窄、腸閉塞、短腸症候群（医師記載

用語：SBS の悪化）、腹痛、痔出血、昏睡、薬物濃度増加、過眠症及びうっ血性心不全が各 1 例に 1 件発現した（5.3.5.3 項 Adult ISS Table 9.12.1）。

表 2.7.4 - 39　CL0600-020 試験及び CL0600-004 試験：テデュグルチド群で 2 例以上に認められた重篤な有害事象一覧（安全性解析対象集団）

				Teduglutide					
		Placebo (N=59)		0.05 mg/kg/day (N=77)		0.10 mg/kg/day (N=32)		All (N=109)	
Parameter		**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**	**n (%)**	**E**
Gastrointestinal Disorders	胃腸障害	0	0	5 (6.5)	8	2 (6.3)	2	7 (6.4)	10
Small intestinal obstruction	小腸閉塞	0	0	1 (1.3)	1	1 (3.1)	1	2 (1.8)	2
General Disorders and Administration Site Conditions	全身障害および投与局所様態	2 (3.4)	2	4 (5.2)	4	0	0	4 (3.7)	4
Pyrexia	発熱	0	0	2 (2.6)	2	0	0	2 (1.8)	2
Hepatobiliary Disorders	肝胆道系障害	1 (1.7)	1	4 (5.2)	6	0	0	4 (3.7)	6
Cholecystitis acute	急性胆嚢炎	0	0	2 (2.6)	2	0	0	2 (1.8)	2
Infections and Infestations	感染症および寄生虫症	10 (16.9)	17	20 (26.0)	37	5 (15.6)	7	25 (22.9)	44
Catheter sepsis	カテーテル敗血症	1 (1.7)	2	4 (5.2)	8	4 (12.5)	5	8 (7.3)	13
Catheter related infection	カテーテル関連感染	1 (1.7)	1	6 (7.8)	6	0	0	6 (5.5)	6
Urinary tract infection	尿路感染	1 (1.7)	1	3 (3.9)	6	0	0	3 (2.8)	6
Central line infection	中心静脈カテーテル感染	3 (5.1)	3	2 (2.6)	2	0	0	2 (1.8)	2
Pneumonia	肺炎	0	0	2 (2.6)	2	0	0	2 (1.8)	2
Injury, Poisoning and Procedural Complications	傷害、中毒および処置合併症	8 (13.6)	9	1 (1.3)	1	4 (12.5)	4	5 (4.6)	5
Device dislocation	医療機器位置異常	2 (3.4)	2	0	0	2 (6.3)	2	2 (1.8)	2
Investigations	臨床検査	0	0	2 (2.6)	2	0	0	2 (1.8)	2
Nervous System Disorders	神経系障害	0	0	2 (2.6)	3	0	0	2 (1.8)	3
Surgical and Medical Procedures	外科および内科処置	1 (1.7)	1	0	0	2 (6.3)	2	2 (1.8)	2

E = Total number of events; TEAE = Treatment emergent adverse event; TESAE = Treatment emergent serious adverse event.
Studies included: CL0600-020, CL0600-004.
Note: Percentages are based upon the number of subjects in the Safety Population.
Note: Treatment emergent adverse events are defined as any adverse event with a start date on or after the date of first dose and within thirty days after discontinuation of study drug.
Note: Subjects are counted no more than once for incidence of System Organ Class and Preferred Term but can be counted multiple times for the number of events.
Note: All adverse events were coded using MedDRA version 12.0.
Source: Module 5.3.5.3 Adult ISS Table 9.11.2

2.1.3.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）でみられた重篤な有害事象をそれぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.2.1 並びに 5.3.5.2 項 CL0600-005 CSR Table 12−7、Table 14.3.2.6 及び 2.7.6 項に示す。CL0600-021 試験及び CL0600-005 試験の統合データにおいて発現した重篤な有害事象を 5.3.5.3 項 Adult ISS Table 9.11.3 に示す。

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）の試験期間中に重篤な有害事象が 83 例（54.2%）に 179 件発現した。これら試験で認められた重篤な有害事象の多くは、各 1 例で報告された単発の事象であった。最も頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（31.4%）であった。テデュグルチド群 153 例で頻度の高い（5 例以上）重篤な有害事象は、カテーテル敗血症（7.2%）、カテーテル菌血症（5.2%）、及び中心静脈カテーテル感染（5.2%）であった（5.3.5.3 項 Adult ISS Table 9.11.3）。治験責任医師により治験薬と関連ありと判断された重篤な有害事象は、10 例（6.5%）に 14 件認められた（5.3.5.3 項 Adult ISS Table 9.1.3）。

TED-C11-001 試験（5.3.5.2 項）では、14 例中 5 例（35.7%）に重篤な有害事象が 14 件発現した（5.3.5.2 項 TED-C11-001 CSR Table 12-2）。うち複数回発現した事象は 1 件（肺炎）のみであった（1 例で 2 回）。治験薬と関連ありと判断された重篤な有害事象は認められなかった。特に注目すべき有害事象に関連した重篤な有害事象が 1 例に 2 件認められた（5.3.5.2 項 TED-C11-001 CSR Table 12-5、TED-C11-001 CSR 12.2.3.1 項に定義）。本事象の詳細な叙述を 5.3.5.2 項 TED-C11-001 CSR 14.3.3 項及び 2.7.6 項に示す。

2.1.3.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）で発現した重篤な有害事象の一覧を表 2.7.4 - 40 に示す。重篤な有害事象の詳細は 5.3.5.2 項 SHP633-306 CSR Table 23 に示す。被験者 3 例（42.9%）に 5 件の重篤な有害事象が発現した。試験期間中に報告された重篤な有害事象は、1 例にみられた 2 件（てんかん）を除き、いずれも各 1 例による単発の事象であった。重篤な有害事象による中止例はなく、いずれも転帰は回復であった。治験責任医師により治験薬と関連ありとされた重篤な有害事象はなかった。1 例（14.3%）に認められた 2 件のてんかんは治験責任医師により重度と判断された。詳細は 5.3.5.2 項 SHP633-306 CSR 12.2.3.2、12.3.1.2 項及び 2.7.6 項に記載する。

表 2.7.4 - 40　SHP633-306 試験：重篤な有害事象一覧（安全性解析対象集団）

System Organ Class Preferred Term		Total Teduglutide (N=7) All-causality TEAEs Subjects n (%)	Events
Any TESAE		3 (42.9)	5
Infections and infestations	感染症および寄生虫症	2 (28.6)	2
Device related infection	医療機器関連感染	1 (14.3)	1
Medical device site infection	医療機器使用部位感染	1 (14.3)	1
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (14.3)	1
Spinal compression fracture	脊椎圧迫骨折	1 (14.3)	1
Nervous system disorders	神経系障害	1 (14.3)	2
Epilepsy	てんかん	1 (14.3)	2

Note: Percentages are based on the Safety population.
Note: Treatment-emergent AEs (TEAEs) were defined as AEs whose onset occurred, severity worsened, or intensity increased after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: Subjects were counted no more than once for incidence but could be counted multiple times for the number of events.
Note: System organ classes and preferred terms were coded using MedDRA 21.0.
Source: Module 5.3.5.2 SHP633-306 CSR Table 14.3.2.3

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）で発現した重篤な有害事象の一覧を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.7.1 及び 2.7.6 項に示す。治験薬投与開始前に重篤な有害事象が 2 例に 6 件認められ、このうち 4 件は医療機器関連感染であった（5.3.5.2 項 TED-C14-004 CSR 12.3.1.2 項）。ステージ 2 では、6 例（54.5%）に 15 件の重篤な有害事象が認められた。ステージ 2 で頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（45.5%）であった。ステージ 2 で報告された重篤な有害事象の多くは、1 例に発現した単発の事象であった。ステージ 2 で頻度の高い重篤な有害事象は、医療機器関連感染（5 例、45.5%、7 件）であった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.8.1）。医療機器関連感染の事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。治験薬と関連ありとされた重篤な有害事象は被験者 1 例（9.1%）に 3 件（急性肝不全、腸炎、腸閉塞）発現した。ステージ 2 で 2 例以上に認められた重篤な有害事象を表 2.7.4 - 41 に示す。

表 2.7.4 - 41　TED-C14-004 試験：ステージ 2 で 2 例以上に認められた重篤な有害事象一覧（安全性解析対象集団）

System Organ Class/ Preferred Term		Teduglutide (N=11) Subjects n (%)	Events
Any TESAE		6 (54.5)	15
Infections and Infestations	感染症および寄生虫症	5 (45.5)	8
Device related infection	医療機器関連感染	5 (45.5)	7

AE=adverse event; E=number of events; n=number of subjects experiencing the event; TEAE=treatment-emergent adverse event
Note: Percentages are based on the safety population.
Note: Treatment-emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens, or intensity increases after receiving the study drug.
Note: Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note: System organ classes and preferred terms are coded using MedDRA/J 17.1.
Source: Module 5.3.5.2 TED-C14-004 CSR, Table 14.3.2.7.1

2.1.3.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）で発現した重篤な有害事象の一覧を 5.3.5.2 項 SHP633-307 CSR Table 14.3.2.3 及び 2.7.6 項に示す。重篤な有害事象は 7 例（63.6%）に 15 件認められた。治験期間中に報告された重篤な有害事象は、4 例に 9 件認められた医療機器関連感染を除き、全て 1 例に 1 件のみ発現した単発の事象であった。器具に関連した重篤な有害事象は全て、テデュグルチド投与用機器ではなく、PS の投与に用いられた中心静脈カテーテルによるものであった。全ての重篤な有害事象は治験薬と関連なしとされた（SHP633-307 CSR Section 12.3.1.2）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）のステージ 3 及び 4 で発現した重篤な有害事象の一覧を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.7.2 及び 2.7.6 項に示す。本期間中、重篤な有害事象が 5 例（62.5%）に 18 件認められた。頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（62.5%）であった。報告された重篤な有害事象の多くは、各 1 例による単発の事象であった。最も頻度の高い重篤な有害事象は、医療機器関連感染（5 例、62.5%、12 件）であった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.7.2）。医療機器関連の感染事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。治験薬と関連ありとされた重篤な有害事象は被験者 1 例（12.5%）に 1 件（発熱）発現した。

2.1.3.2　　小児の臨床試験データ

2.1.3.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の試験ごとの重篤な有害事象の一覧を、5.3.5.2 項 TED-C13-003 CSR Table 14.3.2.7、5.3.5.2 項 TED-C14-006 CSR Table 14.3.2.1、2.7.6 項に示す。統合データについては以下に重篤な有害事象全体及び因果関係別に示す。

重篤な有害事象

テデュグルチド群全体で 2 例以上に認められた重篤な有害事象を表 2.7.4 - 42 に示す。重篤な有害事象は 0.0125 mg/kg 群の 4 例（50.0%）に 4 件、0.025 mg/kg 群の 22 例（57.9%）に 50 件、0.05 mg/kg 群の 28 例（68.3%）に 61 件、標準治療群の 7 例（50.0%）に 16 件認められた。

テデュグルチド群で頻度の高かった重篤な有害事象の SOC は、「感染症および寄生虫症」（37.9%）並びに「一般・全身障害および投与部位の状態」（19.5%）であった。テデュグルチド群の 5%以上に認められた重篤な有害事象は、発熱（18.4%）、医療機器関連感染（13.8%）、医療機器破損（6.9%）、及び脱水（5.7%）であった。

標準治療群で頻度の高かった重篤な有害事象の SOC は、「感染症および寄生虫症」（35.7%）並びに「一般・全身障害および投与部位の状態」（21.4%）であった。標準治療群の 10%以上の被験者に認められた重篤な有害事象は、発熱（21.4%）、真菌血症（14.3%）、及びウイルス感染（14.3%）であった。

重篤な有害事象については、年齢（5.3.5.3 項 Pediatric ISS Table 30.1）、性別（5.3.5.3 項 Pediatric ISS Table 36.1）、人種（5.3.5.3 項 Pediatric ISS Table 42.1）、地域（5.3.5.3 項 Pediatric ISS Table 48.1）及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 54.1）に基づく各部分集団における要約も示した。一部の部分集団では症例数が極めて少なかったものの、重篤な有害事象の発現頻度に部分集団による特定の傾向は認められなかった。

治験薬と関連ありと判断された重篤な有害事象

Pediatric のデータカットオフ時点で、治験薬と関連ありと判断された重篤な有害事象が 0.025 mg/kg/日群の 2 例（5.3%）に 2 件認められた（イレウス及び糞塊）。データカットオフ後、糞塊としてコード化された重篤な有害事象に関する追跡情報を治験責任医師から入手した。治験責任医師は、被験者が介入なしに自然に排便したことを確認した。摘便及び下剤の投与は行われなかった。治験責任医師は糞塊の存在を否定したが、当該被験者に認められた閉塞は硬便によるものと判断した。糞塊は認められなかったため、治験責任医師の報告に基づき、安全性データベースにおける事象名はデータカット後に硬便及び胃腸管閉塞に更新された。したがって、テデュグルチド群の 2 例における治験薬と関連ありと判断された重篤な有害事象の件数を 3 件（硬便、胃腸管閉塞、及びイレウス）に更新する（5.3.5.3 項 Pediatric ISS Table 12.1）。

表 2.7.4 - 42　TED-C13-003 試験及び TED-C14-006 試験：テデュグルチド群全体で 2 例以上に認められた重篤な有害事象一覧（安全性解析対象集団）

Category		0.0125 mg/kg/day Teduglutide (N=8)		0.025 mg/kg/day Teduglutide (N=38)		0.05 mg/kg/day Teduglutide (N=41)		Total Teduglutide (N=87)		Standard of Care (N=14)	
		n(%)	E	n(%)	E	n(%)	E	n(%)	E	n(%)	E
Any TESAE		4 (50.0)	4	22 (57.9)	50	28 (68.3)	61	54 (62.1)	115	7 (50.0)	16
General Disorders and Administration Site Conditions	一般・全身障害および投与部位の状態	1 (12.5)	1	5 (13.2)	7	11 (26.8)	12	17 (19.5)	20	3 (21.4)	5
Pyrexia	発熱	1 (12.5)	1	5 (13.2)	7	10 (24.4)	11	16 (18.4)	19	3 (21.4)	5
Infections and Infestations	感染症および寄生虫症	2 (25.0)	2	13 (34.2)	20	18 (43.9)	29	33 (37.9)	51	5 (35.7)	10
Device Related Infection	医療機器関連感染	1 (12.5)	1	5 (13.2)	9	6 (14.6)	8	12 (13.8)	18	0	0
Influenza	インフルエンザ	0	0	2 (5.3)	2	2 (4.9)	2	4 (4.6)	4	0	0
Upper Respiratory Tract Infection	上気道感染	0	0	2 (5.3)	2	2 (4.9)	2	4 (4.6)	4	0	0
Viral Infection	ウイルス感染	0	0	0	0	2 (4.9)	2	2 (2.3)	2	2 (14.3)	2
Catheter Site Infection	カテーテル留置部位感染	0	0	0	0	3 (7.3)	3	3 (3.4)	3	0	0
Parainfluenzae Virus Infection	パラインフルエンザウイルス感染	0	0	2 (5.3)	2	1 (2.4)	1	3 (3.4)	3	0	0
Device Related Sepsis	医療機器関連敗血症	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2	0	0
Metabolism and Nutrition Disorders	代謝および栄養障害	0	0	4 (10.5)	6	3 (7.3)	4	7 (8.0)	10	0	0
Dehydration	脱水	0	0	4 (10.5)	4	1 (2.4)	1	5 (5.7)	5	0	0
Hypokalaemia	低カリウム血症	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2	0	0
Metabolic Acidosis	代謝性アシドーシス	0	0	1 (2.6)	1	1 (2.4)	1	2 (2.3)	2	0	0
Product Issues	製品の問題	0	0	5 (13.2)	6	5 (12.2)	5	10 (11.5)	11	1 (7.1)	1
Device Breakage	医療機器破損	0	0	4 (10.5)	5	2 (4.9)	2	6 (6.9)	7	0	0

E=number of events; MedDRA=Medical Dictionary for Regulatory Activities; n=number of subjects; TESAE=treatment-emergent serious adverse event
Note:　Percentages are based on the number of subjects in the safety population for each treatment group.
Note:　Subjects are counted no more than once for incidence but can be counted multiple times for the number of events.
Note:　Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Source: Module 5.3.5.3 Pediatric ISS Table 11.1

2.1.3.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間）の試験ごとの重篤な有害事象一覧を 5.3.5.2 項 SHP633-304 CSR Table 19、5.3.5.2 項 SHP633-303 CSR Table 26、2.7.6 項に示す。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 項を参照のこと。

重篤な有害事象

SHP633-304 試験及び SHP633-303 試験（前向き期間）の統合データで、重篤な有害事象は NTT/TED 群では認められず、TED/NTT 群で 5 例（45.5%）に 5 件、TED/TED 群で 30 例（50.0%）に 62 件発現した。最も頻度の高い重篤な有害事象の SOC は、「感染症および寄生虫症」（24.7%）であった。全 TED 群で 3%以上の被験者に認められた重篤な有害事象は、発熱（13.7%）、医療機器関連感染（9.6%）及びインフルエンザ（4.1%）であった（5.3.5.3 項 Pediatric ISS Table 11.2.2）。重篤な有害事象については、年齢（5.3.5.3 項 Pediatric ISS Table 30.2.2）、性別（5.3.5.3 項 Pediatric ISS Table 36.2.2）、人種（5.3.5.3 項 Pediatric ISS Table 42.2.2）、地域（5.3.5.3 項 Pediatric ISS Table 48.2.2）及びベースラインの PS 量（5.3.5.3 項 Pediatric ISS Table 54.2.2）に基づく各部分集団における要約も示した。一部の部分集団では症例数が極めて少なかったものの、重篤な有害事象の発現頻度に部分集団による傾向は認められなかった。

治験薬と関連ありと判断された重篤な有害事象

TED/TED 群において、治験薬と関連ありと判断された重篤な有害事象（代謝性アシドーシス）が 1 件認められた。また、投薬過誤が誤って治験薬と関連ありと判断された重篤な有害事象として臨床データベースに登録されたが、本事象は臨床的に重要な徴候又は症状を伴っていなかったため、重篤とはみなされない。NTT/TED 群及び TED/NTT 群では、全ての重篤な有害事象は治験薬と関連なしとされた。治験薬と関連ありと判断された重篤な有害事象の要約を 5.3.5.3 項 Pediatric ISS Table 12.2 に示す。

2.1.3.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）で発現した重篤な有害事象一覧を 5.3.5.2 項 SHP633-301 Interim CSR Section 12.3.1.2、5.3.5.2 項 SHP633-301 Interim CSR Table14.3.1.4 又は 2.7.6 項に示す。被験者 3 例に 3 件の重篤な有害事象が発現し、内訳はテデュグルチド群 2 例、標準治療群 1 例であった。テデュグルチド群では、重篤な有害事象の SOC は、「一般・全身障害および投与部位の状態」（33.3%）並びに「製品の問題」（33.3%）であった。テデュグルチド群に発現した 2 件の重篤な有害事象の内訳は、1 件は発熱であり（叙述は 5.3.5.2 項 SHP633-301 Interim CSR Section 14.3.3、2.7.6 項を参照）、他の 1 件は医療機器機能不良（テデュグルチド投与用機器ではなく、PS の投与に使用された中心静脈カテーテルに関連する。最終解析時に本事象名は医療機器リー

クに変更）であった。標準治療群では 1 例が医療機器関連感染を発現した。全ての重篤な有害事象は治験責任医師により治験薬と関連なしと判断された（5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.1.5）。医療機器機能不良及び医療機器関連感染は重度であり、いずれも被験者の入院が必要であった（5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.2.1）。

最終解析で発現した重篤な有害事象一覧を 5.3.5.2 項 SHP633-301 Final CSR Section 12.3.1.2、5.3.5.2 項 SHP633-301 Final CSR Table 14.3.1.4 又は 2.7.6 項に示す。全体で 7 例に 11 件の重篤な有害事象が報告された。その内訳はテデュグルチド群 4 例（80.0%）、標準治療群 3 例（60.0%）であった。

テデュグルチド群では、重篤な有害事象の SOC は、「製品の問題」2 例（40.0%）、及び「一般・全身障害および投与部位の状態」、及び「免疫系障害」各 1 例（20.0%）であった。試験期間中に 5 件の重篤な有害事象が報告され、全ての事象について治験責任医師は治験薬と関連なしと判断した。内訳は、発熱が 1 例に 2 件、並びに免疫反応、医療機器破損及び医療機器リーク（テデュグルチド投与用機器ではなく、PS の投与に使用された中心静脈カテーテルに関連する）が各 1 例に 1 件発現した。詳細は 5.3.5.2 項 SHP633-301 Final CSR Section 12.3.1.2、叙述は 5.3.5.2 項 SHP633-301 Final CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

標準治療群では、発現した重篤な有害事象の SOC は、「感染症および寄生虫症」2 例（40.0%）、及び「臨床検査」、「代謝および栄養障害」、「神経系障害」、及び「製品の問題」各 1 例（20.0%）であった。試験期間中に合計で 6 件の重篤な有害事象が報告され、全ての事象について治験責任医師は治験薬と関連なしと判断した。2 例（40.0%）に医療機器関連感染が発現、1 例（20.0%）にトランスアミナーゼ上昇が発現、1 例（20.0%）に代謝性アシドーシス、運動失調、並びに医療機器閉塞がすべて発現した。詳細は 5.3.5.2 項 SHP633-301 Final CSR Section 12.3.1.2、叙述は 5.3.5.2 項 SHP633-301 Final CSR Section 14.3.3 又は 2.7.6 項を参照のこと。

2.1.3.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）における重篤な有害事象を表 2.7.4 - 43 に示した。小児コホートでは、6 例（75.0%）に 15 件の重篤な有害事象が発現した。小児コホートで 2 例以上に認められた重篤な有害事象は、医療機器関連感染 3 例（37.5%）4 件、医療機器使用部位感染 2 例（25.0%）3 件及び腸炎 2 例（25.0%）2 件であり、医療機器関連の感染事象は全て、PS 投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。

小児コホートでは、治験薬と関連ありとされた重篤な有害事象は被験者 1 例に 1 件（腹痛）のみ発現した。この被験者は 24 週間の投与期間を完了した。本事象は追跡期間中の発現であり、治験責任医師はテデュグルチドの中止によるものと判断した。継続投与試験でテデュグルチドが再開されるまでは、症状の改善のために PS と食事の量の減少が必要であった（2.7.6 項、5.3.5.2 項 SHP633-302 CSR Section 14.3.3 を参照）。

小児コホートの被験者 1 例でアナフィラキシー反応の重篤な有害事象が報告され、重症度は軽度と判断され、治験薬の投与が中止された。本被験者は [redacted] 歳の男児で、アレルギー反応（食物、牛乳、医薬品、ゴム）の既往歴があった。本試験の数年前にメロンによる蕁麻疹のエピソードを

経験し、メロンに対する IgE は陽性であった。テデュグルチドの投与開始後 137 日目にアナフィラキシー反応が発現し、当該事象により入院し、治験薬の投与を中止した。入院中、エピネフリン注射、アタラックス P 注射を行い、回復した。アナフィラキシー反応発現日に学校でメロンを摂取したことから、本事象は治験薬によるものではなく、メロン摂取によるものと考えられた。詳細については、5.3.5.2 項 SHP633-302 CSR Section 14.3.3 及び 2.7.6 項を参照のこと。

乳児コホートでは 2 例全例に 9 件の重篤な有害事象が発現した。被験者 2 例ともに発現した重篤な有害事象は、中等度の発熱であった。また、1 例の乳児に発現した医療機器関連感染は中等度であり、上気道感染及び上気道の炎症（各 1 例に発現）はいずれも軽度であった。乳児コホートで発現した重篤な有害事象はいずれも治験薬と関連なしとされた。

表 2.7.4 - 43　SHP633-302 試験：重篤な有害事象一覧（安全性解析対象集団）

SOC PT		Children[a] After Amendment 3[c] (N=6)		Total Children[a] (N=8)		Infants[b] (N=2)	
		n (%)	Events	n (%)	Events	n (%)	Events
Any TESAE		4 (66.7)	9	6 (75.0)	15	2 (100.0)	9
Gastrointestinal disorders	胃腸障害	2 (33.3)	2	3 (37.5)	3	0	0
Abdominal pain	腹痛	1 (16.7)	1	1 (12.5)	1	0	0
Enterocolitis	腸炎	1 (16.7)	1	2 (25.0)	2	0	0
General disorders and administration site conditions	一般・全身障害および投与部位の状態	0	0	0	0	2 (100.0)	4
Pyrexia	発熱	0	0	0	0	2 (100.0)	4
Immune system disorders	免疫系障害	0	0	1 (12.5)	1	0	0
Anaphylactic reaction	アナフィラキシー反応	0	0	1 (12.5)	1	0	0
Infections and infestations	感染症および寄生虫症	3 (50.0)	6	5 (62.5)	10	2 (100.0)	4
Device related infection	医療機器関連感染	2 (33.3)	2	3 (37.5)	4	1 (50.0)	2
Adenovirus infection	アデノウイルス感染	1 (16.7)	1	1 (12.5)	1	0	0
Gastroenteritis	胃腸炎	1 (16.7)	1	1 (12.5)	1	0	0
Medical device site infection	医療機器使用部位感染	1 (16.7)	2	2 (25.0)	3	0	0
Hand-foot-and-mouth disease	手足口病	0	0	1 (12.5)	1	0	0
Upper respiratory tract infection	上気道感染	0	0	0	0	1 (50.0)	2
Product issues	製品の問題	1 (16.7)	1	1 (12.5)	1	0	0
Device damage	医療機器損傷	1 (16.7)	1	1 (12.5)	1	0	0
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	0	0	0	0	1 (50.0)	1
Upper respiratory tract inflammation	上気道の炎症	0	0	0	0	1 (50.0)	1

SOC=system organ class; PT=preferred term
a: Children aged 1 through 15 years.
b: Infants of 4 through <12 months corrected gestational age.
c: The number of children enrolled under the protocol amendment 3 and 4.

Note: Subjects were counted no more than once for incidence, but counted multiple times for the number of events.
Note: SOCs and PTs were coded using MedDRA 20.0.
Source: Module 5.3.5.2 SHP633-302 CSR Table 14.3.2.7

2.1.3.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で小児コホートでは 6 例（85.7%）に 18 件の重篤な有害事象が発現した。小児コホートで 2 例以上に認められた重篤な有害事象は、医療機器破損（3 例［42.9%］5 件）及び医療機器関連感染（2 例［28.6%］3 件）であった。医療機器関連の有害事象は全て、PS に使用した中心静脈カテーテルの合併症であり、テデュグルチドの調製及び投与に使用した医療機器に関連したものではなかった。治験薬と関連ありとされた重篤な有害事象はみられなかった。乳児コホートでは 2 例（100%）に 4 件の重篤な有害事象が発現した。これらのうち 1 例に認められた急性膵炎は重度であった。本事象はテデュグルチドの投与を中断し、治療を行い、回復した。本事象は治験薬と関連なしとされた。（叙述は 5.3.5.2 項 SHP633-305 CSR, Section 14.3.4［被験者番号：[redacted]］を参照）。その他、乳児コホートで認められた重篤な有害事象はアデノウイルス性胃腸炎、痙攣発作及び上気道感染（各 1 例）であり、いずれも治験薬と関連なしとされた（5.3.5.2 項 Section SHP633-305 CSR, Section 12.3.1.2 参照）。

2.1.4　　その他の重要な有害事象

2.1.4.1　　中止に至った有害事象

テデュグルチドの臨床開発プログラム全体で有害事象のために中止に至った被験者の有害事象一覧を 2.7.4 項付録 3 及び各試験の CSR（以下の項にリンクを示す）に示す。

2.1.4.1.1　　成人の臨床試験データ

2.1.4.1.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）において、中止に至った有害事象を発現したのはテデュグルチド群の被験者の 9.2%、プラセボ群の被験者の 6.8%であった。中止に至った有害事象の多くは各 1 例で認められた単発の事象であった。テデュグルチド群の 2 例以上に発現した中止に至った有害事象は、腹部膨満及び便秘であった（5.3.5.3 項 Adult ISS Table 9.9.1 及び 2.7.4 項付録 3）。

2.1.4.1.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）では、中止に至った有害事象のデータは統合せず、試験別に示す。2.7.6 項も参照のこと。

CL0600-021 試験（5.3.5.2 項）について、中止に至った被験者に発現した有害事象一覧を 5.3.5.2 項 CL0600-021 CSR Table 14.3.2.7 及び 2.7.4 項付録 3 に要約する。中止に至った有害事象

（試験治療下及び非試験治療下）を 5.3.5.2 項 CL0600-021 CSR Table 12-7 に示す。中止に至った有害事象は 88 例中 15 例（17.0%）に 23 件認められた。内訳は、TED/TED 群の被験者が 37 例中 3 例（8.1%）、NT, PBO/TED 群の被験者が 51 例中 12 例（23.5%）であった。また、1 例（被験者番号：[redacted]）がコア試験（CL0600-020 試験）で発現した有害事象により中止に至ったが、本試験では非試験治療下での発現とみなされた。これら有害事象のために治験中止に至った被験者 16 例（試験治療下 15 例及び非試験治療下 1 例）の叙述を 5.3.5.2 項 CL0600-021 CSR 14.3.3 項に示す。

CL0600-005 試験（5.3.5.2 項）では、中止に至った有害事象は試験期間中に 8 例（12.3%）に認められた（5.3.5.2 項 CL0600-005 CSR Table 14.3.2.1）。有害事象のために中止に至った被験者の詳細を 5.3.5.2 項 CL0600-005 CSR Table 14.3.2.8 に示す。中止に至った有害事象の内訳は、腹痛が 3 例、嘔吐が 2 例、カテーテル菌血症、咳嗽、悪心、結腸腺腫（2008 年 8 月に過形成性結腸ポリープに再分類）、炎症性腸疾患、及び脳血管発作が各 1 例であった。中止に至った有害事象を 5.3.5.2 項 CL0600-005 CSR Table 12-9 及び 2.7.4 項付録 3 に示す。

治験薬と関連ありと判断された有害事象のために中止に至った 4 例の叙述を 5.3.5.2 項 CL0600-005 CSR 14.3.3 項に示す。治験薬と関連ありと判断された中止に至った有害事象は 4 例に 6 件認められた。中止に至った治験薬と関連ありと判断された有害事象及び関連なしと判断された有害事象の件数は同程度であった（それぞれ 6 件及び 5 件）。治験薬と関連ありと判断された中止に至った有害事象が認められた 4 例の簡潔な叙述を 5.3.5.2 項 CL0600-005 CSR 12.3.3.1 項に示す。

TED-C11-001 試験（5.3.5.2 項）では、有害事象のために中止に至った被験者はみられなかった（5.3.5.2 項 TED-C11-001 CSR Table 14.3.2.7）。

2.1.4.1.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）で中止に至った被験者に発現した有害事象一覧を表 2.7.4 - 44 に示す。被験者 1 例（14.3%）が 2 件の有害事象により治験薬の投与中止に至った。いずれの有害事象も軽度であり、非重篤、治験責任医師により治験薬と関連ありとされ、投与中止後に回復した。

表 2.7.4 - 44　SHP633-306 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Site ID - Subject ID	Race	Sex	Age	Preferred Term		Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome
[redacted]	Asian	Female	3[redacted]	Oropharyngeal pain	口腔咽頭痛	No/ Mild/ Related	Drug withdrawn/ Drug treatment given	Continuous/ Recovering/ Resolving
				Gastrointestinal stoma complication	消化管ストーマ合併症	No/ Mild/ Related	Drug withdrawn/ Drug treatment given	Continuous/ Recovered/ Resolved

Note:　Relationship to study treatment is based upon investigator assessment.
Note:　System organ classes and preferred terms were coded using MedDRA 21.0.
Note:　Reported terms were collected on the eCRFs.
Source: Module 5.3.5.2 Study SHP633-306 CSR Table 24

日本人被験者を対象とした TED-C14-004 試験において中止に至った被験者に発現した有害事象一覧を 5.3.5.2 項 TED-C14-004 CSR Section 12.3.3 項に示す。TED-C14-004 試験において中止に至った有害事象（2 例［18.2%］2 件）はいずれもステージ 2 での発現であった。（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.12.1）。被験者 1 例（被験者番号：[redacted]）は下痢のために中止した。別の 1 例（被験者番号：[redacted]）は急性肝不全のために中止しその後死亡に至った。中止に至った事象はいずれも治験責任医師により治験薬と関連ありと判断された。試験期間中に認められた中止に至った有害事象を発現した被験者にみられた有害事象を表 2.7.4 - 45 に示す。有害事象のために中止に至った被験者の詳細な叙述については、5.3.5.2 項 TED-C14-004 CSR Table 14.3.3 を参照のこと。

表 2.7.4 - 45　TED-C14-004 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Race/ Sex/ Age	Preferred Term		Start Date and Time Day, Relative Day/Stop Date and Time, Relative Day	Duration (Days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken Outcome	Frequency/ Outcome
Subject ID [redacted]							
Japanese/ Male/ 4[redacted]	Intestinal transit time increased	腸通過時間延長	31AUG2015 15/		No/ Mild/ Related	Dose not changed/ Drug treatment	Continuous/ Not recovered/Not resolved
	Lipase increased	リパーゼ増加	31AUG2015 15/ 12OCT2015 57	43	No/ Mild/ Not Related	Dose not changed/ None	Continuous/ Recovered/ Resolved
	Abdominal pain upper	上腹部痛	07DEC2015 113/ 01MAR2016 198	86	No/ Mild/ Related	Dose not changed/ None	Intermittent/ Recovered/ Resolved
	Diarrhoea	下痢	31JAN2016 168/ 01MAR2016 198	31	No/ Mild/ Related	Drug withdrawn/ None/ Recovered/Resolved	Intermittent/ Recovered/ Resolved
	Vomiting	嘔吐	31JAN2016 168/ 08FEB2016 176	9	No/ Mild/ Related	Dose not changed/ None	Intermittent/ Recovered/ Resolved
Subject ID [redacted]							
Japanese/ Male/ 3[redacted]	Headache	頭痛	21AUG2015:21:00:00 1/ 21AUG2015:22:00:00 1	1	No/ Mild/ Not Related	Dose not changed/ Drug treatment	Intermittent/ Recovered/ Resolved
	Device related infection	医療機器関連感染	24AUG2015:21:00:00 4/ 30AUG2015:15:00:00 10	7	Yes/ Mild/ Not Related	Dose not changed/ Drug treatment	Continuous/ Recovered/ Resolved
	Oedema	浮腫	02SEP2015 13/		No/ Moderate/ Not Related	Dose not changed/ Drug treatment	Intermittent/ Not recovered/ Not resolved
	Balanitis candida	カンジダ性亀頭炎	02SEP2015 13/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Intermittent/ Not recovered/ Not resolved

表 2.7.4 - 45　TED-C14-004 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Race/ Sex/ Age	Preferred Term		Start Date and Time Day, Relative Day/Stop Date and Time, Relative Day	Duration (Days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken Outcome	Frequency/ Outcome
	Device related infection	医療機器関連感染	02SEP2015 13/ 19SEP2015 30	18	No/ Severe/ Not Related	Dose not changed/ Drug treatment	Continuous/ Recovered/ Resolved
	Enterocolitis	腸炎	02SEP2015:19:00:00 13/ 18SEP2015 29	17	Yes/ Severe/ Related	Drug interrupted/ Drug treatment	Continuous/ Recovered/ Resolved
	Intestinal obstruction	腸閉塞	02SEP2015:19:00:00 13/ 18SEP2015 29	17	Yes/ Severe/ Related	Drug interrupted/ Drug treatment	Continuous/ Recovered/ Resolved
	Malnutrition	栄養障害	02SEP2015:19:00:00 13/		No/ Severe/ Not Related	Drug interrupted/ Drug treatment	Continuous/ Not recovered/ Not resolved
	Anaemia	貧血	03SEP2015 14/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Continuous/ Not recovered/ Not resolved
	Disseminated intravascular coagulation	播種性血管内凝固	05SEP2015 16/	53	No/ Severe/ Not Related	Dose not changed/ Drug treatment	Continuous/
	Acute hepatic failure	急性肝不全	05SEP2015 16/ 27OCT2015:12:40:00 68	53	Yes/ Severe/ Related	Drug withdrawn/ Multiple	Continuous/ Fatal
	Hyper bilirubinaemia	高ビリルビン血症	06SEP2015 17/		No/ Mild/ Not Related	Dose not changed/ None	Continuous/
	Oral herpes	口腔ヘルペス	07SEP2015 18/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Continuous/ Not recovered/Not resolved
	Pancreatitis	膵炎	07SEP2015 18/ 04OCT2015 45	28	No/ Moderate/ Related	Dose not changed/ Drug treatment	Continuous/ Recovered/Resolved

表 2.7.4 - 45　TED-C14-004 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Race/ Sex/ Age	Preferred Term		Start Date and Time Day, Relative Day/Stop Date and Time, Relative Day	Duration (Days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken Outcome	Frequency/ Outcome
	Pruritus	そう痒症	10SEP2015 21/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Intermittent/
	Hyper glycaemia	高血糖	11SEP2015 22/ 16SEP2015 27	6	No/ Moderate/ Not Related	Dose not changed/ Drug treatment	Continuous/ Recovered/ Resolved
	Mouth haemorrhage	口腔内出血	16SEP2015 27/		No/ Mild/ Not Related	Dose not changed/ None	Intermittent/
	Sepsis	敗血症	20SEP2015 31/ 14OCT2015 55	25	Yes/ Severe/ Not Related	Dose not changed/ Multiple	Continuous/ Recovered/ Resolved
	Device occlusion	医療機器閉塞	21SEP2015 32/ 21SEP2015 32	1	No/ Mild/ Not Related	Dose not changed/ None	Continuous/ Recovered/ Resolved
	Enterocolitis	腸炎	21SEP2015 32/ 13OCT2015 54	23	No/ Severe/ Not Related	Dose not changed/ Drug treatment	Continuous/ Recovered/ Resolved
	Hypo glycaemia	低血糖症	21SEP2015 32/ 21SEP2015 32	1	No/ Mild/ Not Related	Dose not changed/ None	Continuous/ Recovered/ Resolved
	Oxygen saturation decreased	酸素飽和度低下	21SEP2015 32/		No/ Moderate/ Not Related	Dose not changed/ Non-drug treatment	Continuous/
	Urine output decreased	尿量減少	22SEP2015 33/		No/ Moderate/ Not Related	Dose not changed/ None	Intermittent/
	Cardiac failure acute	急性心不全	22SEP2015 33/		No/ Severe/ Not Related	Dose not changed/ Multiple	Continuous/

表 2.7.4 - 45　TED-C14-004 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Race/ Sex/ Age	Preferred Term		Start Date and Time Day, Relative Day/Stop Date and Time, Relative Day	Duration (Days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken Outcome	Frequency/ Outcome
	Myalgia	筋肉痛	22SEP2015 33/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Intermittent/ Not recovered/ Not resolved
	Respiratory failure	呼吸不全	22SEP2015 33/ 13OCT2015 54	2	No/ Severe/ Not Related	Dose not changed/ Non-drug treatment	Continuous/ Recovered /Resolved
	Eye oedema	眼球浮腫	23SEP2015 34/		No/ Mild/ Not Related	Dose not changed/ Drug treatment	Continuous/
	Oral candidiasis	口腔カンジダ症	23SEP2015 34/		No/ Moderate/ Not Related	Dose not changed/ Drug treatment	Continuous/
	Hypothermia	低体温	24SEP2015 35/ 24SEP2015 35	1	No/ Mild/ Not Related	Dose not changed/ None	Intermittent/ Recovered/ Resolved
	Renal failure acute	急性腎不全	22OCT2015 63/ 27OCT2015:12:40:00 68	6	Yes/ Severe/ Not Related	Dose not changed/ None	Intermittent/ Fatal

Note:　Treatment-emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens, or intensity increases after receiving the study drug.
Note:　Relationship to study treatment is based upon investigator assessment.
Note:　Preferred terms are coded using MedDRA J 17.1.
Source: Module 5.3.5.2 TED-C14-004 CSR, Table 14.3.2.13

2.1.4.1.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）の試験期間中、有害事象により中止に至った被験者はいなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間では、ステージ 3 及びステージ 4 において有害事象により中止に至った被験者はいなかった（5.3.5.2 項 TED-C14-004 CSR Table 14.3.2.12.2）。

2.1.4.1.2　　小児の臨床試験データ

2.1.4.1.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データで、有害事象のために中止に至った被験者はいなかった（5.3.5.2 項 TED-C13-003 CSR Table 14.3.2.12、5.3.5.2 項 TED-C14-006 CSR Table 14.3.2.4）。

2.1.4.1.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-303 試験（5.3.5.2 項）では、前向き期間中に治験薬の投与中止（SHP633-303 CSR、Table 14.3.4.4）又は試験中止（5.3.5.2 項 SHP633-303 CSR Table 14.3.4.5）に至った有害事象は認められなかった。

SHP633-304 試験（5.3.5.2 項）では、胆汁うっ滞の既往歴がある被験者 1 例が、重篤な有害事象（血中ビリルビン増加、中等度）のために治験薬の投与中止に至った（5.3.5.2 項 SHP633-304 CSR Table 14.3.4.4 及び 2.7.4 項付録 3）。本事象は治験責任医師により医原性鉄過剰に関連したものと判断され、治験薬と関連なしとされた。本被験者は試験を継続しているにもかかわらず（5.3.5.2 項 SHP633-304 CSR Listing 16.2.1.1）、誤って胆汁うっ滞の悪化（中等度、関連なし）により治験中止に至ったと報告された（5.3.5.2 項 SHP633-304 CSR Table 14.3.4.5）。別の 1 例は SBS の悪化により治験中止に至った。この SBS 悪化は、重度であり、治験薬と関連なしと判断された。本被験者は後に本事象のために死亡した（本概要 2.1.2 参照）。
NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 項を参照のこと。

2.1.4.1.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析ではデータカットオフ日までに、有害事象のために中止に至った被験者はいなかった（5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.2.2）。

最終解析において、中止に至った有害事象を 5.3.5.2 項 SHP633-301 Final CSR Section 12.3.1.3 に示す。全体で、テデュグルチド群の 1 例に、中止に至った有害事象が 5 件報告された（嘔吐［2 件］、胃腸音異常、易刺激性、及び便量増加）（5.3.5.2 項 SHP633-301 Final CSR Table 14.3.2.2）。

本被験者の両親が複数の有害事象が治験薬に起因すると考えたため、Day 75（Week 10 の来院後）にテデュグルチド投与を中断した。これは安全性による治験責任医師の判断ではなく、治験責任医師は両親の判断について報告を受けた（5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.5、Listing 16.2.5.3）。嘔吐（Day 86～Day 96）、胃腸音異常（Day 72～Day 207）、便量増加（Day 96～Day 135）については、治験責任医師により軽度であると判断され、Day 72～Day 96 の嘔吐は中等度とされ、いずれも治験薬と関連ありとされた。Day 72～Day 207 の易刺激性は治験薬と関連なし、軽度とされた。すべての事象は軽快/回復したものの、治験薬の投与は再開されなかった。被験者は試験を完了した。叙述は 5.3.5.2 項 SHP633-301 Final CSR Section 14.3.3 参照。

2.1.4.1.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）で、被験者 1 例（被験者番号：[redacted]、[redacted] 歳、男性）が重篤な有害事象により治験薬の投与中止に至った。本事象はテデュグルチドの投与開始後 137 日に発現したアナフィラキシー反応であった。アナフィラキシー反応については 2.1.3.2.4 項を参照のこと。事象は治験薬と関連なしと判断されたが、治験薬の投与は中止された。治験薬の投与中止に至った有害事象の発現頻度を 5.3.5.2 項 SHP633-302 CSR Table 14.3.2.13 に示す。

試験期間中に本被験者に発現した全ての有害事象の一覧を表 2.7.4 - 46 に示す。5.3.5.2 項 SHP633-302 CSR Section 14.3.3、2.7.6 項に叙述を示す。

表 2.7.4 - 46　SHP633-302 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Subject ID: [redacted]

Race/ Sex/ Age	Preferred Term		Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	AE Duration	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome
Asian/ Male/[redacted]	Injection site induration	注射部位硬結	10FEB2017 (3)/ 15FEB2017 (8)	6	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Injection site haematoma	注射部位血腫	10FEB2017 (3)/ 21FEB2017 (14)	12	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Injection site erythema	注射部位紅斑	13FEB2017 (6)/ 14FEB2017 (7)	2	No/ Mild/ Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Dry skin	皮膚乾燥	15FEB2017 (8)/Ongoing		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Not Recovered/ Not Resolved
	Injection site bruising	注射部位内出血	17FEB2017 (10)/ 24FEB2017 (17)	8	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Injection site bruising	注射部位内出血	20FEB2017 (13)/ 27FEB2017 (20)	8	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Injection site bruising	注射部位内出血	23FEB2017 (16)/ 01MAR2017 (22)	7	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Injection site erythema	注射部位紅斑	25FEB2017 (18)/ 25FEB2017 (18)	1	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Medical device site infection	医療機器使用部位感染	01MAR2017 (22)/ 25JUN2017 (138)	117	No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Recovered/ Resolved

表 2.7.4 - 46　SHP633-302 試験：中止に至った被験者にみられた有害事象一覧（安全性解析対象集団）

Subject ID: [redacted]

Race/ Sex/ Age	Preferred Term		Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	AE Duration	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome
	Enteritis	小腸炎	15MAR2017 (36)/ 29MAR2017 (50)	15	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Enterocolitis	腸炎	29MAR2017 (50)/ 08MAY2017 (90)	41	Yes/ Mild/ Not Related	Dose Not Changed/ Drug Treatment/Non-Drug Treatment	Continuous/ Recovered/ Resolved
	Injection site bruising	注射部位内出血	14MAY2017 (96)/ 23MAY2017 (105)	10	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Viral upper respiratory tract infection	ウイルス性上気道感染	20MAY2017 (102)/ 27MAY2017 (109)	8	No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/ Resolved
	Injection site erythema	注射部位紅斑	23MAY2017 (105)/ 27MAY2017 (109)	5	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved
	Anaphylactic reaction	アナフィラキシー反応	24JUN2017 (137)/ 28JUN2017 (141)	5	Yes/ Mild/ Not Related	Drug Withdrawn/ Drug Treatment	Continuous/ Recovered/ Resolved
	Medical device site infection	医療機器使用部位感染	26JUN2017 (139)/ 09AUG2017 (183)	45	Yes/ Severe/ Not Related	Not Applicable/ Drug Treatment/Non-Drug Treatment	Continuous/ Recovered/ Resolved
	Abdominal pain	腹痛	08JUL2017 (151)/ 09AUG2017 (183)	33	No/ Mild/ Related	Not Applicable/ Drug Treatment/Non-Drug Treatment	Continuous/ Recovered/ Resolved

Note: All the AEs for subjects who had an adverse event leading to study drug discontinuation are listed.
Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases during or after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 20.0.
Note: Reported terms are collected on the eCRF.
Note: Infants are of 4 - <12 months corrected gestational age.
Source: Module 5.3.5.2 Study SHP633-302 CSR Table 14.3.2.14

2.1.4.1.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で中止に至った有害事象は認められなかった。なお、データカットオフ直後に重度の急性膵炎のリスクのため試験参加を中止した被験者がみられた。この中止は本中間解析には反映されていない（叙述は、5.3.5.2 項 SHP633-305 CSR, Section 14.3.4［被験者番号：[redacted]］参照）。

2.1.5　　特に注目すべき有害事象

2.1.5.1　　定義

特に注目すべき有害事象はテデュグルチドの開発プログラム中に改訂されたため、試験間で異なる場合がある。本項では複数の試験で用いられた特に注目すべき有害事象の定義を示す。

成人試験である TED-C14-004 試験、SHP633-306 試験及び SHP633-307 試験並びに小児試験である TED-C13-003 試験、TED-C14-006 試験、SHP633-301 試験、SHP633-302 試験、SHP633-303 試験、SHP633-304 試験及び SHP633-305 試験では特に注目すべき有害事象は以下の事象と定義した。

- 既存の結腸ポリープの成長
- 肝胆道系を含む消化器における良性の上皮腫瘍
- 腫瘍の成長（消化器又は肝胆道系に限定しない良性及び／又は悪性腫瘍）

TED-C14-004 試験、SHP633-302 試験、SHP633-303 試験、SHP633-304 試験、SHP633-306 試験及び SHP633-307 試験では規制要件に基づき特に注目すべき有害事象の迅速な報告が求められた。

また、TED-C13-003 試験及び TED-C14-006 試験では、特に注目すべき有害事象は以下の事象と定義した。

- 結腸ポリープ
- 消化管閉塞
- 以下のカテゴリーを含むその他のイベント
  - 胆嚢及び胆管疾患
  - 膵疾患
  - 循環器疾患

また、CL0600-021 試験及び TED-C11-001 試験では、特に注目すべき有害事象は以下の事象と定義した。

- 悪性腫瘍
- 結腸ポリープ
- 消化管閉塞
- 胆嚢、胆管及び膵疾患
- 水分過負荷

2.1.5.2　　結果

CL0600-021 試験

被験者 50 例が、試験中、終了時、又は追跡期間中に 51 回の大腸内視鏡検査を受けた。うち 9 例に投与期間中 24 ヵ月間又は終了時に、消化管ポリープが認められた。ポリープの所見が 6 件有害事象として報告され、他の 3 件は報告されなかった。ポリープは全て結腸内視鏡で発見された。ポリープが認められた 9 例中 5 例の生検所見には腺腫の報告が含まれた。Month 24 の結腸内視鏡所見のうち 4 件は、治験責任医師により臨床的に重要と判断された。Month 24 にポリープが認められた 4 例では、臨床的に重要ではない異常と報告された。必要な試験手順以外での大腸内視鏡検査において、別の 2 例で試験期間中にポリープが認められた。また、別の 1 例に直腸ポリープの内視鏡所見が認められ、その後の生検で炎症が認められた。詳細は 5.3.5.2 項 CL0600-021 CSR Section 12.2.3.1 を参照のこと。

被験者番号：[redacted] は、テデュグルチドの初回投与を試験 CL0600-021 試験で受けた。ホジキン病（化学療法及び放射線療法を受けた）の既往歴があり、試験中止後 30 日以内に死亡した。死亡は、重篤な有害事象であった転移性腺癌の発現後 10 日、治験薬投与開始後 11 ヵ月であった。本事象は治験責任医師により治験薬と関連ありと判断された。詳細は 2.7.4 項付録 1、本概要 2.1.2.1.2、5.3.5.2 項 CL0600-021 CSR Section 12.3.1.1 参照。

被験者番号：[redacted] は、CL0600-021 試験で最初にテデュグルチドの投与を受け、投与開始後 3 ヵ月に非小細胞肺癌と診断され、診断後 5 ヵ月に死亡した。本事象は治験責任医師により治験薬との関連なしと判断された。詳細は 2.7.4 項付録 1、本概要 2.1.2.1.2、5.3.5.2 項 CL0600-021 CSR Section 12.3.1.1 参照。

被験者番号：[redacted] は CL0600-020 試験でテデュグルチドの投与を受け、投与開始後約 2 年に扁平上皮癌と診断された。治験責任医師は当該事象を治験薬との関連なしと判断した（5.3.5.2 項 CL0600-021 CSR Section 12.6 参照）。

TED-C11-001 試験

被験者 10 例が、初診時、治験期間中の予定外の来院時、及び／又は試験終了時／早期中止時に 14 回の大腸内視鏡検査を受けた。うち 4 例に消化管ポリープが認められ、うち 2 例は有害事象（結腸ポリープ）として報告された（被験者番号：[redacted]［NT/TED 群］及び被験者番号：[redacted]［PBO/TED 群］、5.3.5.2 項 TED-C11-001 CSR Section 16.2, Listing 16.2.6.1）。他の 2 例（被験者番号：[redacted]［PBO/TED 群］及び被験者番号：[redacted]［TED/TED 群］）に認めら

れたポリープは、CL0600-021 試験で既に報告されていたものであり、上記の要約内容に含まれている。

- 被験者番号：[redacted] は、試験開始後 4 ヵ月に初回の大腸内視鏡検査（テデュグルチド投与開始後約 28 ヵ月）を受け、下行結腸に 1 個の小さなポリープを認め、生検で痔核と診断された。
- 被験者番号：[redacted] は Month 12 に大腸内視鏡検査（テデュグルチド投与開始後 36 ヵ月）を受け、管状腺腫が認められた。
- 被験者 [redacted] は、CL0600-021 試験の初回来院時及び試験終了来院時（テデュグルチド投与開始後それぞれ 24 ヵ月及び 36 ヵ月）に結腸ポリープが認められた。
- 被験者番号：[redacted] は、TED-C11-001 試験の初回来院時（テデュグルチド投与開始後 30 ヵ月、CL0600-021 試験の最終来院時）に結腸鏡検査を行い 2 個の有茎性ポリープを切除し、これらは管状腺腫と一致していた。

本試験では、消化管閉塞、胆嚢、胆管、膵臓に関連する事象、悪性腫瘍の有害事象はみられなかった。脱水は 1/14 例（7.1%）に 1 件、水分過負荷は 2/14 例（14.3%）に 4 件認められた。水分過負荷（被験者番号：[redacted]）では、軽度の間欠的事象（医師記載用語：左下肢浮腫）が 1 件、中等度の持続的事象（逐語的に両側下肢浮腫）が 1 件認められた。いずれの事象も約 1 ヵ月半持続した。いずれの事象も処置なく回復した。被験者番号：[redacted] には、それ以上の処置なく回復した軽度の間欠的事象（医師記載用語：左下肢浮腫）と、治験薬以外の薬剤の変更を必要とし、試験終了時に継続中であった軽度の持続的事象（医師記載用語：末梢性浮腫）が認められた（5.3.5.2 項 TED-C11-001 CSR Section 14 Table 14.3.2.10、Section 16.2.7 Listing 16.2.6.1）。詳細は 5.3.5.2 項 TED-C11-001 CSR Section 12.2.3.1 を参照のこと。

SHP633-304 試験

SHP633-304 試験期間中、大腸内視鏡検査で有茎性ポリープが 1 例に認められた。この特に注目すべき有害事象の重症度は中等度であり、治験責任医師により治験薬との関連なしと評価された。ポリープは生検も切除もされなかった。治験薬及びその他の処置は行われず、被験者は試験を継続した。約 2 ヵ月後の追跡大腸内視鏡検査では、結腸にポリープは認められなかった（5.3.5.2 項 SHP633-304 CSR Section 12.3.1.3）。

国内の成人又は小児を対象とした試験において、結腸ポリープ、腫瘍の成長及び良性／悪性腫瘍はみられなかった。

2.1.6　器官別又は症候群別有害事象の解析

本項では SOC 別の有害事象について記載する。本臨床的安全性の概要に示したテデュグルチドの安全性プロファイルは、SBS 患者集団の特徴、テデュグルチド投与の作用部位及び投与経路の既知のプロファイルと同様であった。

臨床開発プログラムの臨床試験において、有害事象を報告した被験者の割合が最も高かったSOCは、「胃腸障害」、「感染症および寄生虫症」、「一般・全身障害および投与部位の状態」であった。テデュグルチドを投与した日本人成人及び小児患者における安全性データは、テデュグルチドを投与した外国人SBS成人及び小児患者における安全性データと同様であった。

「胃腸障害」、「感染症および寄生虫症」、「一般・全身障害および投与部位の状態」に分類される有害事象について、全試験を通して検討した結果、新たな又は予期しない傾向又はシグナルは認められず、海外試験と国内試験間で概ね一貫していた。SOC別の有害事象を以下に示す。

- 海外第3相成人コア試験：本概要 2.1.1.2.1.1
- 海外第3相成人継続投与試験：本概要 2.1.1.2.1.2
- 日本人第3相成人コア試験：本概要 2.1.1.2.1.4
- 日本人第3相成人継続投与試験：本概要 2.1.1.2.1.5
- 海外第3相小児コア試験：本概要 2.1.1.2.2.1
- 海外第3相小児継続投与試験：本概要 2.1.1.2.2.2
- 海外乳児試験：本概要 2.1.1.2.2.3
- 日本人第3相小児コア試験：本概要 2.1.1.2.2.4

2.1.6.1　　胃腸障害

海外試験及び国内試験いずれの試験においても（CL0600-020試験及びCL0600-004試験ではプラセボ投与例を含む。本概要 2.1.1.3.1.1 参照）、テデュグルチドを投与した成人及び小児患者における「胃腸障害」は一貫して最も発現頻度の高いSOCに含まれていた。SBS患者では、「胃腸障害」に分類される有害事象は基礎疾患と同様であるため、予測し得る。試験を通して「胃腸障害」に分類される有害事象を検討した結果海外試験と国内試験間で新たな又は予期しない傾向は認められなかった。

2.1.6.2　　感染症および寄生虫症

海外試験及び国内試験いずれの試験においても（CL0600-020試験及びCL0600-004試験ではプラセボ投与例を含む。本概要 2.1.1.3.1.1 参照）、テデュグルチドを投与した成人及び小児患者における「感染症及び寄生虫症」は一貫して最も発現頻度の高いSOCに含まれていた。SBS患者では、デバイス関連の感染事象は一般にPS投与に使用される中心静脈カテーテルに起因したものであり、予測し得る。テデュグルチドの開発プログラムでは、医療機器関連の感染事象は全て、PS投与に使用した中心静脈カテーテルに関連したものであり、テデュグルチド投与用機器に関連したものではなかった。「感染症および寄生虫症」に分類される有害事象を全試験で検討した結果、海外試験と国内試験間で新たな又は予期しない傾向又はシグナルは認められなかった。

2.1.6.3　　一般・全身障害および投与部位の状態

海外及び国内試験いずれの試験においても（CL0600-020 試験及び CL0600-004 試験ではプラセボ投与例を含む。本概要 2.1.1.3.1.1 参照）、テデュグルチドを投与した成人及び小児患者における「一般・全身障害および投与部位の状態」は一貫して最も発現頻度の高い SOC に含まれていた。「一般・全身障害および投与部位の状態」の SOC に含まれる有害事象を全試験で検討した結果、海外試験と国内試験間で新たな又は予期しない傾向又はシグナルは認められなかった。

2.2　叙述

各試験について、死亡、重篤な有害事象の叙述を 5 項の CSR 及び 2.7.6 項の付録に示す。

3.　臨床検査値の評価

3.1　臨床検査値の経時変化

3.1.1　　成人の臨床試験データ

3.1.1.1　　成人を対象とした海外第 3 相コア試験

3.1.1.1.1　　生化学的検査

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データの生化学的検査値及びベースラインからの変化量において、全体として各測定項目で変化が認められたが、臨床的に意味のある変化ではなかった。5.3.5.3 項 Adult ISS Table 10.1.2（肝機能検査）、5.3.5.3 項 Adult ISS Table 10.2.2（腎機能検査）、及び 5.3.5.3 項 Adult ISS Table 10.3.2（その他の検査項目）を参照のこと。

3.1.1.1.2　　血液学的検査

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データについて、血液学的検査値及びベースラインからの変化量を 5.3.5.3 項 Adult ISS Table 10.7.2 に示す。テデュグルチド群では、血小板数及び白血球数（平均値）が増加した。しかし、これらの変化は臨床的に重要なものではなかった。残りの検査項目については、臨床的に意味のある変化は認められなかった。血液学的検査値のベースラインからエンドポイントまでの高値又は低値への変動を 5.3.5.3 項 Adult ISS Table 10.8.2 に示す。血液学的検査値に臨床的に意味のある変化はみられなかった。

3.1.1.1.3　　尿検査

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）については、尿検査値及びベースラインからの変化量は統合せず、各試験の CSR に示す。

CL0600-020 試験（5.3.5.1 項）については、尿検査値の平均値及び中央値のベースラインからの経時変化を示す（5.3.5.1 項 CL0600-020 CSR Table 14.3.3.1、Table 14.3.3.2、Table 14.3.3.3、Table 14.3.3.4、Table 14.3.3.5、及び Table 14.3.3.6）。全体として、各検査項目に臨床的に意味のある群間差は認められなかった。

CL0600-004 試験（5.3.5.1 項）の尿検査値の経時変化を 5.3.5.1 項 CL0600-004 CSR Section 12.4.1.3 及び 5.3.5.1 項 CL0600-004 CSR Table 14.3.4.2.84、Table 14.3.4.2.85、Table 14.3.4.2.86、Table 14.3.4.2.87、Table 14.3.4.2.88、Table 14.3.4.2.89、Table 14.3.4.2.90 に示す。異常値を 5.3.5.1 項 CL0600-004 CSR Table 14.3.4.1.3（被験者別・投与群別）及び 5.3.5.1 項 CL0600-004 CSR Listing 16.2.8.4.1、Listing 16.2.8.4.2 に示す。基準値を 5.3.5.1 項 CL0600-004 CSR Table 14.3.4.1.3 に示す。ITT 集団において基準値外への変動及び変動の方向を調査したところ、大半の臨床検査項目では、基準値外への変動が認められた被験者数は投与群間で同程度であった。

3.1.1.2　　成人を対象とした海外第 3 相継続投与試験

3.1.1.2.1　　生化学的検査

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）について、生化学的検査値及びベースラインからの変化量は統合せず、本項に試験別に示す。

CL0600-021 試験（5.3.5.2 項）について、肝機能検査値、腎機能検査値、脂質、その他の生化学的検査値の経時変化を、それぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.1.1、Table 14.3.4.2、Table 14.3.4.3、Table 14.3.4.4、Table 14.3.4.5、及び Table 14.3.4.6 に示す。全体として、各検査項目に臨床的に意味のあるベースラインからの変化は認められなかった。肝機能検査値、腎機能検査値、脂質、その他の生化学的検査値のベースライン時からエンドポイント時までの変動の要約を、それぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.7、Table 14.3.4.8、Table 14.3.4.9 及び Table 14.3.4.10 に示す。全体として、各検査項目に臨床的に意味のあるベースラインからの変動は認められなかった。肝機能検査値及び腎機能検査値について、ベースラインからの経時変化率が 10%を超えた被験者について示した（5.3.5.2 項 CL0600-021 CSR Table 14.3.4.13 及び Table 14.3.4.14）。また、PS 量が 50%以上減少した被験者について、ベースラインから試験終了時までの肝機能検査値を 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.1.2 に示した。

CL0600-005 試験（5.3.5.2 項）について、生化学的検査値（平均値）、これらのデータのベースラインからの経時変化、及びシフトテーブルを 5.3.5.2 項 CL0600-005 CSR Section 12.4.1、Table 14.3.4.1.1～Table 14.3.4.23.3 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.2.1 に示す。いずれの来院時にも、いずれの検査項目にも意味のある変化は認められず、ベースライン時から Week 28 まで又はベースラインから最終投与週までの変化量にも意味のある変化は認められなかった。シフトテーブルにおいて、いずれの検査項目についても意味のある変化はみられなかった。CL0600-005 試験のベースライン時の生化学的検査値、ベースラインから Week 28 及び最終投与週までの変化量を 5.3.5.2 項 CL0600-005 CSR Table 12-10 に示す。

TED-C11-001 試験（5.3.5.2 項）について、肝機能検査値、腎機能検査値、脂質、その他の生化学的検査値（平均値）及び中央値の経時変化を、それぞれ 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.1、Table 14.3.4.2、Table 14.3.4.3 及び Table 14.3.4.4 に示す。全体として、各検査項目に臨床的に意味のあるベースラインからの変化は認められなかった。肝機能検査値、腎機能検査値、脂質、その他の生化学的検査値のベースライン時からエンドポイント時までの変動の要約を、それぞれ 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.7、Table 14.3.4.8、Table 14.3.4.9 及び Table 14.3.4.10 に示す。全体として、各検査項目に臨床的に意味のあるベースラインからの変動は認められなかった。肝機能検査値及び腎機能検査値について、ベースラインからの経時変化率が 10%を超えた被験者について示した（5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.13、Table 14.3.4.14）。

3.1.1.2.2　　血液学的検査

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）について、血液学的検査値及びベースラインからの変化量は統合せず、本項に試験別に示す。

CL0600-021 試験（5.3.5.2 項）について、血液学的検査値のベースラインからの経時変化及び最終投与日までの変化、並びにシフトテーブルをそれぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.5 及び Table 14.3.4.11 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 CL0600-021 CSR Appendix 16.2 Listing 16.2.8.3 に示す。変化量（平均値）及びシフトテーブルのいずれも、いずれの検査項目についても臨床的に意味のある変化はみられなかった。

CL0600-005 試験（5.3.5.2 項）について、血液学的検査値（平均値）、これらのデータのベースラインからの経時変化、及びシフトテーブルを 5.3.5.2 項 CL0600-005 CSR Section 12.4.1.2、Table 14.3.4.24.1～14.3.4.37.3 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.3.1 に示す。血液学的検査で基準値外となった個々の異常値も、基準値とともに被験者別・投与群別に 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.3.2 に示す。ベースライン時の血液学的検査値、ベースラインから Week 28 及び最終投与週までの変化量を 5.3.5.2 項 CL0600-005 CSR Table 12-11 に示す。いずれの来院時にも、いずれの検査項目にも意味のある変化は認められず、ベースライン時から Week 28 まで又は最終投与週までの変化量にも意味のある変化は認められなかった。シフトテーブルにおいて、いずれの検査項目についても意味のある変化はみられなかった。

TED-C11-001 試験（5.3.5.2 項）について、血液学的検査値のベースラインからの経時変化及び最終投与日までの変化、並びにシフトテーブルをそれぞれ 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.5 及び Table 14.3.4.11 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 TED-C11-001 CSR Listing 16.2.7.3 に示す。経時的な変化量（平均値）及びシフトテーブルにおいて、いずれの検査項目についても臨床的に意味のある変化はみられなかった。

3.1.1.2.3　　尿検査

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）について、尿検査値及びベースラインからの変化量は統合せず、本項に試験別に示す。

CL0600-021 試験（5.3.5.2 項）について、尿検査値のベースラインからの経時変化及び最終投与日までの変化、並びにシフトテーブルをそれぞれ 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.6 及び Table 14.3.4.12 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 CL0600-021 CSR Listing 16.2.8.4 に示す。経時変化（平均値）及びシフトテーブルにおいて、いずれの検査項目についても臨床的に意味のある変化はみられなかった。

CL0600-005 試験（5.3.5.2 項）について、尿検査値（平均値）、これらのデータのベースラインからの経時変化、及びシフトテーブルを 5.3.5.2 項 CL0600-005 CSR Section 12.4.1.3、Table 14.3.4.38.1～14.3.4.41.3 に示す。このデータの詳細（基準値を含む）を 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.4.1 に示す。ベースライン時及びベースラインから Week 28 及び最終投与

週までの尿検査値の変化量を 5.3.5.2 項 CL0600-005 CSR Table 12-12 に示す。いずれの来院時にも、いずれの検査項目にも意味のある変化は認められず、ベースライン時から Week 28 及び最終投与週までにも意味のある変化は認められなかった。シフトテーブルにおいて、いずれの検査項目についても意味のある変化はみられなかった。

TED-C11-001 試験（5.3.5.2 項）について、尿検査値のベースラインからの経時変化及び最終投与日までの変化、並びにシフトテーブルをそれぞれ 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.6 及び Table 14.3.4.12 に示す。また、これらのデータの詳細（基準値を含む）を 5.3.5.2 項 TED-C11-001 CSR Listing 16.2.7.4 に示す。経時変化（平均値）及びシフトテーブルにおいて、いずれの検査項目についても臨床的に意味のある変化はみられなかった。

3.1.1.3　成人を対象とした国内第 3 相コア試験

3.1.1.3.1　生化学的検査

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）期間中、生化学的検査値に臨床的に意味のある変化は認められなかった。ベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.1 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）期間中の生化学的検査値のベースラインから最終投与日までの変化量を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.3.1 に示す（全ての試験期間［コア期間及び継続投与期間］を含む）。ビリルビン及びリパーゼ（平均値）の上昇が認められたが、これは被験者番号：[redacted] のみの上昇によるものと考えられた。試験期間中、その他の臨床的に意味のある生化学的検査値の変化は認められなかった。

3.1.1.3.2　血液学的検査

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）期間中、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.2 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）期間中、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.3.2 に示す。

3.1.1.3.3　尿検査

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）期間中、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院までの変化量を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.3 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）期間中、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.3.3 に示す。

3.1.1.4　　成人を対象とした国内第 3 相継続投与試験

3.1.1.4.1　　生化学的検査

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）期間中、生化学的検査値に臨床的に意味のある変化は認められなかった。生化学検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.1 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間に、生化学的検査値に臨床的に意味のある変化は認められなかった。試験期間中に得られた生化学的検査値は、試験全体の結果として本概要 3.1.1.3 に示す。

3.1.1.4.2　　血液学的検査

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）期間中、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.2 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間に得られた血液学的検査値は本概要 3.1.1.3 に示す。

3.1.1.4.3　　尿検査

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）期間中、ベースラインから試験終了時にかけて尿中ナトリウム値に変化が認められたが、臨床的に意味があるとは考えられなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.3 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間に得られた尿検査値は本概要 3.1.1.3 に示す。

3.1.2　小児の臨床試験データ

3.1.2.1　小児を対象とした海外第 3 相コア試験

3.1.2.1.1　生化学的検査

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、試験期間中、生化学的検査値に臨床的に意味のある変化は認められなかった。生化学的検査値及びベースラインから各来院日までの変化量を 5.3.5.3 項 Pediatric ISS Table 14.1 に示す。

3.1.2.1.2　血液学的検査

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、試験期間中、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.3 項 Pediatric ISS Table 15.1 に示す。

3.1.2.1.3　尿検査

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、試験期間中、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.3 項 Pediatric ISS Table 16.1 に示す。

3.1.2.2　小児を対象とした海外第 3 相継続投与試験

3.1.2.2.1　生化学的検査

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、生化学的検査値に臨床的に意味のある変化は認められなかった。テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中における生化学的検査値及びベースラインから各来院日までの変化量をそれぞれ 5.3.5.3 項 Pediatric ISS Table 14.2.1、Table 14.2.2.1 及び Table 14.2.2.2 に示す。

3.1.2.2.2　血液学的検査

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、血液学的検査値に臨床的に意味のある変化は認められなかった。テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中における血液学的検査値及びベースラインから各来院日までの変化量をそれぞれ 5.3.5.3 項 Pediatric ISS Table 15.2.1、ISS Table 15.2.2.1 及び ISS Table 15.2.2.2 に示す。

3.1.2.2.3　　尿検査

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、尿検査値に臨床的に意味のある変化は認められなかった。テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中における尿検査値及びベースラインからの変化量をそれぞれ 5.3.5.3 項 Pediatric ISS Table 16.2.1、ISS Table 16.2.2.1 及び ISS Table 16.2.2.2 に示す。

3.1.2.3　　乳児を対象とした海外試験

3.1.2.3.1　　生化学的検査

SHP633-301 試験（5.3.5.2 項）の中間解析では、データカットオフ日までに、生化学的検査値に臨床的に意味のある変化は認められなかった。生化学検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.4.1 に示す。

最終解析では、標準治療群の ALT 増加及びトランスアミナーゼ値上昇（各 1 例）及びテデュグルチド群の ALT 増加（1 例）を除いて、生化学的検査値に臨床的に意味のある変化は認められなかった。生化学検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.1 に示す。

3.1.2.3.2　　血液学的検査

SHP633-301 試験（5.3.5.2 項）の中間解析では、データカットオフ日までに、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.4.2 に示す。

最終解析では、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.2 に示す。

3.1.2.3.3　　尿検査

実施中の SHP633-301 試験（5.3.5.2 項）の中間解析では、データカットオフ日までに、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.4.3 に示す。

最終解析では、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.3 に示す。

3.1.2.4　小児及び乳児を対象とした国内第 3 相コア試験

3.1.2.4.1　生化学的検査

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）のベースラインから Week 28 までに、生化学的検査値に臨床的に意味のある変化は認められなかった。生化学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.1 に示す。

3.1.2.4.2　血液学的検査

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）のベースラインから Week 28 までに、血液学的検査値に臨床的に意味のある変化は認められなかった。血液学的検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.2 に示す。

3.1.2.4.3　尿検査

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）のベースラインから Week 28 までに、尿検査値に臨床的に意味のある変化は認められなかった。尿検査値及びベースラインから各来院日までの変化量を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.3 に示す。

3.1.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

3.1.2.5.1　生化学的検査

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、被験者の大部分で生化学検査に基準範囲外の異常値が認められたが、以下に述べたものを除き顕著なものはなかった。リパーゼ増加が小児被験者 1 例及び乳児被験者 1 例に認められた。小児被験者 1 例（被験者番号：[redacted]）では軽度の血中リパーゼ増加（CTCAE グレード 3）が有害事象として報告され、データカットオフ時点で未回復であった。本有害事象は治験薬との関連なしとされた（5.3.5.2 項 SHP633-305 CSR Table 14.3.2.19）。乳児被験者 1 例では基準値上限（ULN）の 3 倍を超えるリパーゼ増加が認められたが、有害事象として報告されなかった（叙述は 5.3.5.2 項 SHP633-305 CSR, Section 14.3.4［被験者番号：[redacted]］）。アラニンアミノトランスフェラーゼ（ALT）上昇が小児被験者 1 例及び乳児被験者 1 例に認められた。いずれも中等度の上昇であり、小児被験者では非特異的な基礎疾患による一過性の上昇、乳児被験者では高用量の抗痙攣薬による上昇であった。また、小児被験者では ULN の 3 倍を超えるアミラーゼ増加、マグネシウム低値（0.4114 mmol/L 未満）、トリグリセリド高値（5.65 mmol/L 超）及びカリウム高値（6.5 mmol/L 超）が各 1 例にみられ、乳児被験者ではグルコース増加（13.875 mmol/L 超）が 1 例にみられた（5.3.5.2 項 SHP633-305 CSR Table 14.3.3.8）。これらの顕

著な異常値はいずれも有害事象として報告されなかった（5.3.5.2 項 SHP633-305 CSR, Section 12.4.2.1）。

3.1.2.5.2　　血液学的検査

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、被験者の大部分で血液学的検査値の基準範囲外の異常値が認められたが、顕著な異常はいずれのサイクルのいずれの期間においても認められなかった（5.3.5.2 項 SHP633-305 CSR, Section 12.4.2.1）。

3.1.2.5.3　　尿検査

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、被験者 3 例に基準範囲外の値がみられたが、いずれも顕著な異常ではなかった（被験者番号：[redacted]［白血球数高値：Cycle 1 の投与終了時］、被験者番号：[redacted]［赤血球数高値：ベースライン］及び被験者番号：[redacted]［白血球数高値：ベースライン、Cycle 1 Week 12、Cycle 1 Week 20 及び Cycle 2 Week 1］）（5.3.5.2 項 SHP633-305 CSR, Section 12.4.2.1）。

3.2　個々の臨床的に重要な異常

3.2.1　　成人の臨床試験データ

3.2.1.1　　成人を対象とした海外第 3 相コア試験

3.2.1.1.1　　生化学的検査

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）において、ベースライン後にみられた血液生化学検査の顕著な異常値の要約を 5.3.5.3 項 Adult ISS Table 10.5.2 に示す。被験者の大部分は基礎疾患のため長期間にわたり PS を必要としていたため（平均値：6 年）、ベースライン時に生化学検査値異常が多くの被験者で認められた。

テデュグルチド群で最も多くみられたベースライン後の異常は C 反応性タンパク（CRP）21 mg/L 以上であった（テデュグルチド群 24%、プラセボ群 8.6%）。肝臓の生化学マーカーについて、異常が認められた被験者の割合は、テデュグルチド群とプラセボ群とで同程度であった。テデュグルチド群及びプラセボ群でそれぞれ、アルカリホスファターゼ（ALP）が基準値上限（ULN）の 2 倍超（14.3% vs 16.9%）、アラニンアミノトランスフェラーゼ（ALT）が ULN の 3 倍超（5.7% vs 5.1%）、アスパラギン酸アミノトランスフェラーゼ（AST）が ULN の 3 倍超（1.9% vs 1.7%）及び総ビリルビンが ULN の 2 倍超（3.8% vs 3.4%）であった。γ-グルタミルトランスフェラーゼ（GGT）100 U/L 超を示した被験者の割合はテデュグルチド群に比べて、プラ

セボ群が高かった（36.2% vs 44.1%）。血中尿素窒素（BUN）、クレアチニンといった腎機能の検査項目は、ベースライン後に異常値を示す被験者の割合はテデュグルチド群に比べてプラセボ群が高い傾向がみられた。膵酵素はテデュグルチド群とプラセボ群とで異常値を示す被験者の割合が同程度であり、それぞれアミラーゼ 350 IU/L 超（1% vs 0%）、リパーゼが ULN の 3 倍超（2.9% vs 1.7%）であった。その他の重要な検査項目は、重炭酸塩減少（34.7% vs 50%）、マグネシウム減少（14.3% vs 23.7%）であった。

3.2.1.1.2　　血液学的検査

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）について、ベースライン後にみられた血液学的検査値の顕著な異常の要約を 5.3.5.3 項 Adult ISS Table 10.9.2 に示す。最も多くみられた顕著な異常はヘマトクリット低値であり、プラセボ群の 25/59 例（42%）、テデュグルチド 0.05 mg/kg/日群の 24/74 例（32%）、テデュグルチド 0.10 mg/kg/日群の 8/31 例（26%）に認められた。

3.2.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）については、臨床的に重要な個々の異常値データは統合しなかったため、本項に試験別に示す。全体として、これらの成人を対象とした試験の臨床検査値データに何らかの傾向や安全性上の懸念はみられなかった。

3.2.1.2.1　　生化学的検査

CL0600-021 試験（5.3.5.2 項）において、ベースライン後にみられた顕著な生化学的検査値異常の要約を 5.3.5.2 項 CL0600-021 CSR Table 12-8 に示す。本試験期間中に顕著な生化学的検査値異常が認められた被験者一覧を 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.17 に示す。最も多くみられた（被験者の 20%超）顕著な生化学的検査値異常は、重炭酸塩減少（79.5%）、GGT 増加（47.7%）、カルシウム減少（37.5%）、マグネシウム減少（29.5%）、CRP 増加（21.6%）、及び BUN 増加（20.5%）であった（5.3.5.2 項 CL0600-021 CSR Table 12-8）。

CL0600-005 試験（5.3.5.2 項）において、生化学的検査値異常の要約を 5.3.5.2 項 CL0600-005 CSR Section 12.4.3 に、生化学検査異常値を示した被験者一覧を 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.2.2 に示す。治験責任医師により報告された臨床的に重要な所見のみられた被験者は、1 年実薬群で、テデュグルチド 0.05mg/kg/日で 12 例（48.0%）、0.10 mg/kg/日で 10 例（37.0%）であり、6 ヵ月実薬群で、0.05 mg/kg/日群で 2 例（33.3%）、0.10 mg/kg/日群で 3 例（42.9%）であった。主な臨床検査値異常は、アルカリホスファターゼ上昇、ALT 上昇、AST 上昇、GGT 上昇、尿酸上昇、アルブミン減少、アミラーゼ上昇、プレアルブミン低値、ヘマトクリット低値、ヘモグロビン低値及び CRP 異常であった。生化学的検査値に何らかの傾向や安全性上の懸念はみられなかった。

TED-C11-001 試験（5.3.5.2 項）について、ベースライン後にみられた顕著な生化学的検査値異常の要約を 5.3.5.2 項 TED-C11-001 CSR Table 12-6 に示す。本試験期間中に生化学的検査値の顕著な異常が認められた被験者の一覧を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.15 に示す。生化学的検査値の顕著な異常が認められた被験者の一覧を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.17 に示す。両投与群を併せて 3 例以上に発現した顕著な生化学的検査値異常は、GGT 増加（5 例）、カルシウム減少及び BUN 減少（各 4 例）、重炭酸塩増加、マグネシウム増加、CRP 増加、及びリパーゼ増加（各 3 例）であった（5.3.5.2 項 TED-C11-001 CSR Table 12-6）。

3.2.1.2.2　血液学的検査

CL0600-021 試験（5.3.5.2 項）において、ベースライン後にみられた顕著な血液学的検査値異常の要約を 5.3.5.2 項 CL0600-021 CSR Table 12-9 に示す。本試験期間中に血液学的検査値の顕著な異常が認められた個々の被験者を 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.18 に示す。最も多くみられた（20%超）顕著な血液学的検査値異常はヘマトクリット低値（35.2%）及びヘモグロビン低値（20.5%）であった（5.3.5.2 項 CL0600-021 CSR Table 12-9）。

CL0600-005 試験（5.3.5.2 項）では、臨床的に重要な生化学的検査及び血液学的検査値異常が、1 年実薬群（テデュグルチド 0.05 mg/kg/日群の 12/25 例［48.0%］、テデュグルチド 0.10 mg/kg/日群の 10/27 例［37.0%］）及び 6 ヵ月実薬群（テデュグルチド 0.05 mg/kg/日群の 2/6 例［33.3%］、テデュグルチド 0.10 mg/kg/日群の 3/7 例［42.9%］）において認められた（5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.3.2）。血液学的検査値異常が認められた被験者の一覧を 5.3.5.2 項 CL0600-005 CSR Listing 16.2.17.3.2 に示す。

TED-C11-001 試験（5.3.5.2 項）について、ベースライン後にみられた顕著な血液学的検査値異常の要約を 5.3.5.2 項 TED-C11-001 CSR Table 12-7 に示す。顕著な生化学的検査値異常及び血液学的検査値異常が認められた被験者の一覧を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.18 に示す。顕著な血液学的検査異常は、ヘマトクリット低値（3 例）及びヘモグロビン低値（2 例）のみであった（5.3.5.2 項 TED-C11-001 CSR Table 12-7）。

3.2.1.3　成人を対象とした国内第 3 相コア試験

3.2.1.3.1　生化学的検査

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）におけるベースライン後の顕著な生化学検査異常の概要を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.4 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8,Listing 16.2.8.4 に示す。肝機能について、アルブミン 20 g/L 以下、ALP が ULN の 2 倍超、GGT が 100 U/L 以上が各 1 例（14.3%）であった。ALT、AST、ビリルビンの顕著な上昇はなかった。腎機能では、BUN 又はクレアチニンの顕著な上昇はみられなかった。その他の顕著な臨床検査値異常は、CRP が 21 mg/L 以上、カルシウムが 2.1 mmol/L 以下及びマグネシウムが基準値下限（LLN）未満が各 2 例（28.6%）並びにトリグリセリド

5.6 mmol/L 以上が 1 例（14.3%）であった。これらの所見は臨床的に意味があるとは考えられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む）について、ベースライン後にみられた顕著な生化学的検査値異常の要約を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.3.8 に示す。肝機能については、ALP が ULN の 2 倍超、GGT が 100 U/L 以上が各 4 例（36.4%）、ALT が ULN の 3 倍超が 2 例（18.2%）並びにビリルビンが ULN の 2 倍超が 1 例（9.1%）であった。腎機能については、BUN が 10.7 mmol/L 以上が 1 例（9.1%）であった。クレアチニンの顕著な上昇は認められなかった。膵酵素については、リパーゼが ULN の 3 倍超が 1 例（9.1%）であった。アミラーゼ値が顕著に上昇した被験者はいなかった。その他の顕著な臨床検査値異常として、CRP が 21 mg/L 以上、マグネシウム LLN 未満が各 4 例（36.4%）、カルシウム 2.1 mmol/L 以下が 3 例（27.3%）並びにグルコース 13.9 mmol/L 以上及びトリグリセリド 5.6 mmol/L 以上が各 1 例（9.1%）であった。これらの所見は臨床的に意味があるとは考えられなかった。

3.2.1.3.2　血液学的検査

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）におけるベースライン後の顕著な血液学的検査値異常の要約を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.5 に示す。顕著な血液学的検査値異常の被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8, Listing 16.2.8.5 に示す。顕著な異常は、ヘマトクリット低値（男性 0.37 v/v 以下、女性 0.32 v/v 以下）及びヘモグロビン低値（男性 115 g/L 以下、女性 95 g/L 以下）が各 3 例（42.9%）にみられた。これらの所見は臨床的に意味があるとは考えられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む）について、ベースライン後にみられた顕著な血液学的検査値異常の要約を 5.3.5.2 項 TED-C14-004 CSR Table 14.3.3.9 に示す。血液学的検査で最も多く認められた顕著な異常はヘマトクリット低値であり、3 例（27.3%）にみられた。顕著なヘマトクリット上昇が 1 例（12.5%）、顕著なヘモグロビン低値が 1 例（9.1%）、顕著な血小板数低値が 1 例（9.1%）であった。これらの所見は臨床的に意味があるとは考えられなかった。

3.2.1.4　成人を対象とした国内第 3 相継続投与試験

3.2.1.4.1　生化学的検査

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、ベースライン後の顕著な生化学検査値異常の要約を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.4 に示す。肝機能について、アルブミン 20 g/L 以下、ALP が ULN の 2 倍超、GGT が 100 U/L 以上が各 1 例（9.1%）でみられた。ALT、AST、ビリルビンの著しい上昇はなかった。腎機能では、BUN 又はクレアチニンの顕著な上昇はみられなかった。その他の顕著な臨床検査値異常は、CRP 21 mg/L 以上が 1 例（9.1%）、

カルシウム 2.1 mmol/L 以下が 2 例（18.2%）、マグネシウムの LLN 未満が 4 例（36.4%）にみられた。これらの所見は臨床的に意味があるとは考えられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間については、本概要 3.2.1.3.1 を参照のこと。

3.2.1.4.2　　血液学的検査

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、ベースライン後の顕著な血液学的検査値異常の要約を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.5 に示す。顕著な異常は、ヘマトクリット低値（男性 0.37 v/v 以下、女性 0.32 v/v 以下）4 例（36.4%）、ヘモグロビン低値（男性 115 g/L 以下、女性 95 g/L 以下）3 例（27.3%）、白血球数低値（2.8×10^9/L 以下）2 例（18.2%）であった。これらの所見は臨床的に意味があるとは考えられなかった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間については、本概要 3.2.1.3.2 を参照のこと。

3.2.2　　小児の臨床試験データ

小児を対象とした試験の臨床検査値データに何らかの傾向や安全性上の懸念はみられなかった。

3.2.2.1　　小児を対象とした海外第 3 相コア試験

3.2.2.1.1　　生化学的検査

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、ベースライン後にみられた顕著な生化学的検査値異常の要約を 5.3.5.3 項 Pediatric ISS Table 17.1 に示す。肝機能について、テデュグルチド群の 3 例（3.4%）で ALT が ULN の 8 倍超、1 例（1.1%）で ALP が ULN の 5 倍超、1 例（1.1%）でビリルビン値が ULN の 3 倍超、1 例（1.1%）で直接ビリルビン値が 34.208 µmol/L 超となった。腎機能検査値については、テデュグルチド群の 2 例（2.3%）で BUN が 12.495 mmol/L を超えた。膵酵素については、テデュグルチド群の 2 例（2.3%）でリパーゼが ULN の 3 倍を超えた。テデュグルチド群の 4 例（4.6%）にリン酸塩の顕著な異常（2.254 mmol/L 超）が認められた。テデュグルチド群の 2 例（2.3%）に CRP の顕著な異常（100 mg/L 以上）及びリン酸塩の顕著な異常（0.644 mmol/L 未満）が認められた。テデュグルチド群の各 1 例（1.1%）に以下の顕著な臨床検査値異常が認められた：グルコース 13.875 mmol/L 超、カリウム 2.5 mmol/L 未満、カリウム 6.5 mmol/L 超、マグネシウム 0.4114 mmol/L 未満、トリグリセリド 5.65 mmol/L 超。これらの所見は臨床的に意味があるとは考えられなかった。標準治療群の被験者では、ベースライン後の顕著な臨床検査値異常は認められなかった。

これら 2 試験の統合データでベースライン後にみられた顕著な生化学的検査値異常について、年齢（5.3.5.3 項 Pediatric ISS Table 31.1）、性別（5.3.5.3 項 Pediatric ISS Table 37.1）、人種（5.3.5.3 項 Pediatric ISS Table 43.1）、地域（5.3.5.3 項 Pediatric ISS Table 49.1）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 55.1）に基づく部分集団別の要約も示す。一部の部分集団では症例数が極めて少なかったものの、ベースライン後の顕著な臨床検査値異常の発現頻度に部分集団による傾向は認められなかった。

3.2.2.1.2　　血液学的検査

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、ベースライン後にみられた顕著な血液学的検査値異常の要約を 5.3.5.3 項 Pediatric ISS Table 18.1 に示す。テデュグルチド群の 4 例（4.6%）に顕著な白血球低値（2×10^9/L 未満）が認められた。テデュグルチド群の 3 例（3.4%）に顕著な血小板数低値（75×10^9/L 未満）が認められた。テデュグルチド群の 2 例（2.3%）に顕著な好中球低値（0.5×10^9/L 未満）が認められた。これらの所見は臨床的に意味があるとは考えられなかった。標準治療群の 1 例（7.1%）に顕著な好中球低値（0.5×10^9/L 未満）が認められた。

これら 2 試験の統合データでベースライン後にみられた顕著な血液学的検査値異常について、年齢（5.3.5.3 項 Pediatric ISS Table 32.1）、性別（5.3.5.3 項 Pediatric ISS Table 38.1）、人種（5.3.5.3 項 Pediatric ISS Table 44.1）、地域（5.3.5.3 項 Pediatric ISS Table 50.1）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 56.1）に基づく部分集団別の要約も示す。一部の部分集団では症例数が極めて少なかったものの、ベースライン後の顕著な臨床検査値異常の発現頻度に部分集団による傾向は認められなかった。

3.2.2.2　　小児を対象とした海外第 3 相継続投与試験

3.2.2.2.1　　生化学的検査

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中におけるベースライン後にみられた顕著な生化学的検査値異常の要約を 5.3.5.3 項 Pediatric ISS Table 17.2.1、ISS Table 17.2.2.1、及び ISS Table 17.2.2.2 に示す。テデュグルチド投与開始前に、1 例（20.0%）にマグネシウムの顕著な異常（1.2342 mmol/L 超）、1 例（20.0%）にリン酸塩の顕著な異常（2.254 mmol/L 超）が認められた。テデュグルチド投与中／投与後に、以下の肝機能検査値の顕著な異常が認められた：8 例（12.9%）で ALT が ULN の 8 倍超、1 例（1.6%）で AST が ULN の 8 倍超、1 例（1.6%）で直接ビリルビンが 34.208 µmol/L 超、1 例（1.6%）でビリルビンが ULN の 3 倍超。腎機能検査値については、投与を受けた被験者 3 例（4.8%）で BUN が 12.495 mmol/L を超えた。膵酵素については、テデュグルチド群の 9 例（14.5%）でリパーゼが ULN の 3 倍超であった。CRP の顕著な異常（100 mg/L 以上）及びリン酸塩の顕著な異常

（2.254 mmol/L 超）が 2 例（3.2%）に認められた。カルシウムの顕著な異常（3 mmol/L 超）及びグルコースの顕著な異常（13.875 mmol/L 超）が 1 例（1.6%）に認められた。テデュグルチド休薬期間中に、ALT の顕著な異常（ULN の 8 倍超）、アミラーゼの顕著な異常（ULN の 3 倍超）、及びマグネシウムの顕著な異常（0.4114 mmol/L 未満）が各 1 例（6.7%）に認められた。

3.2.2.2.2　血液学的検査

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中におけるベースライン後にみられた顕著な血液学的検査値異常の要約を 5.3.5.3 項 Pediatric ISS Table 18.2.1、ISS Table 18.2.2.1、ISS Table 18.2.2.2 に示す。

これら試験のテデュグルチド投与開始前には、顕著な血液学的検査値異常は認められなかった。テデュグルチド投与中／投与後に、以下の顕著な血液学的検査値異常が各 1 例（1.1%）に認められた：好中球数 0.5×10^9/L 未満、白血球数 2×10^9/L 未満、及び白血球数 30×10^9/L 超。テデュグルチド休薬期間中に、ヘモグロビンの顕著な異常（70 g/L 未満）が 1 例（6.7%）に認められた。これらの所見は臨床的に意味があるとは考えられなかった。

これら試験のテデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中それぞれにおけるベースライン後にみられた顕著な血液学的検査値異常について、年齢（5.3.5.3 項 Pediatric ISS Table 32.2.1、ISS Table 32.2.2.1、ISS Table 32.2.2.2）、性別（5.3.5.3 項 Pediatric ISS Table 38.2.1、ISS Table 38.2.2.1、ISS Table 38.2.2.2）、人種（5.3.5.3 項 Pediatric ISS Table 44.2.1、ISS Table 44.2.2.1、ISS Table 44.2.2.2）、地域（5.3.5.3 項 Pediatric ISS Table 50.2.1、ISS Table 50.2.2.1、ISS Table 50.2.2.2）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 56.2.1、ISS Table 56.2.2.1、ISS Table 56.2.2.2）に基づく部分集団別の要約も示す。一部の部分集団では症例数が極めて少なかったものの、ベースライン後の顕著な臨床検査値異常の発現頻度に部分集団による傾向は認められなかった。

3.2.2.3　乳児を対象とした海外試験

3.2.2.3.1　生化学的検査

SHP633-301 試験（5.3.5.2 項）の中間解析において、顕著な生化学的検査値異常は認められなかった。ベースライン以降の生化学検査異常値を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.4.4 に示す。

最終解析におけるベースライン以降の生化学検査異常値を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.4 に示す。顕著な生化学的検査値異常の基準を満たした被験者一覧を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.7 に示す。

3.2.2.3.2　血液学的検査

SHP633-301 試験（5.3.5.2 項）の中間解析において、顕著な血液学的検査値異常は認められなかった。ベースライン以降の顕著な血液学的検査異常値を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.4.5 に示す。

最終解析におけるベースライン以降の顕著な血液学的検査異常値を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.5 に示す。顕著な血液学的検査値異常の基準を満たした被験者一覧を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.4.8 に示す。

3.2.2.4　小児及び乳児を対象とした国内第 3 相コア試験

3.2.2.4.1　生化学的検査

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）について、顕著な生化学検査値異常の要約を 5.3.5.2 項 SHP633-302 CSR Section 12.4.2.2 に被験者ごとの一覧を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.7 に示す。小児被験者 1 例、乳児被験者 1 例の計 2 例に顕著な異常がみられた。小児被験者 1 例で血清トリグリセリドの上昇が認められた。ベースライン値は 1.38 mmol/L であったが、経時的に上昇し、6 週目には 13.35 mmol/L（基準値:> 5.65mmol/L）に達した。高トリグリセリド血症は有害事象として報告され、その程度は軽度であり、治験薬との関連なしとされた。本被験者はこの期間中、カテーテル関連血流感染のため入院し、抗真菌薬による治療を受けた。また、本被験者は腸炎のためにも入院した。その後、トリグリセリド値は減少し、投与終了時で 3.97 mmol/L、試験終了時で 3.01 mmol/L であった。乳児被験者 1 例で顕著なリパーゼ上昇（ULN の 3 倍超）が認められ、本乳児被験者のリパーゼのベースライン値は 46 U/L であったが、テデュグルチド投与後に経時的に上昇し、Week 2 には臨床的に異常とされる（ULN の 3 倍超）106 U/L に達した。リパーゼ値はさらに上昇し、投与 6 週後には 507 U/L まで上昇した。その後、この値は徐々に減少した。リパーゼ値は投与終了時で 34 U/L、試験終了時で 36 U/L であった。アミラーゼは試験期間を通じて正常範囲内（28~100 U/L）であったが、低値であった（Week 10 に 22 U/L、Week 12 に 23 U/L）。リパーゼ上昇は有害事象として報告されなかった。

3.2.2.4.2　血液学的検査

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）期間中、血液学的検査値に臨床的に意味のある異常値は認められなかった。ベースライン後の顕著な血液学的検査値異常の要約を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.6 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-302 CSR Table 14.3.3.8 に示す。

3.2.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

3.2.2.5.1　　生化学的検査

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）における、データカットオフ日までの被験者ごとの生化学検査値を、5.3.5.2 項 SHP633-305 CSR Listing 16.2.8.1 に記載した。本試験のベースラインとして、コア試験（SHP633-302 試験）のベースライン値を用いた（SHP633-305 CSR Section 12.4.1）。

3.2.2.5.2　　血液学的検査

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）における、データカットオフ日までの被験者ごとの血液学的検査値を、5.3.5.2 項 SHP633-305 CSR Listing 16.2.8.2 に記載した。本試験のベースラインとして、コア試験（SHP633-302 試験）のベースライン値を用いた（SHP633-305 CSR Section 12.4.1）。

4. バイタルサイン、身体的所見及び安全性に関連する他の観察項目

4.1　バイタルサイン

4.1.1　　成人の臨床試験データ

4.1.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）の統合データによると、ベースライン後にみられた収縮期血圧、拡張期血圧、心拍数、及び体温の顕著な異常の発現頻度はいずれの試験でも低かった。また、ベースライン後にみられた収縮期血圧、拡張期血圧、及び心拍数のベースラインからの顕著な異常変動の発現頻度は、成人を対象とした海外第 3 相コア試験 2 試験のプラセボ群とテデュグルチド群で同程度であった。

ベースライン後にみられたバイタルサインの顕著な異常の要約を 5.3.5.3 項 Adult ISS Table 11.3.2 に、被験者ごとの一覧を 5.3.5.3 項 Adult ISS Table 11.4.1 に示す。

4.1.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）のデータは統合せず、試験別に示す。

CL0600-021 試験（5.3.5.2 項）について、脈拍数、収縮期血圧、拡張期血圧、及び口腔体温のベースラインから各来院日又は最終投与日までの変化は、臨床的に意味のあるものではなかった。バイタルサインのベースラインからの経時変化及び最終投与日までの変化量を 5.3.5.2 項 CL0600-021 CSR Table 14.3.6.1 に示す。ベースライン後にみられたバイタルサインの顕著な異常の要約を 5.3.5.2 項 CL0600-021 CSR Table 14.3.6.2 に、被験者ごとの一覧を Table 14.3.6.3 に示す。

CL0600-005 試験（5.3.5.2 項）の 6 ヵ月実薬群及び 1 年実薬群のいずれにおいても、脈拍数、収縮期血圧、拡張期血圧、及び口腔体温のベースラインから Week 28 又は最終投与週までの変化量は、臨床的に意味のあるものではなかった。バイタルサイン測定値の経時変化を 5.3.5.2 項 CL0600-005 CSR Table 14.3.5.1 及び Table 14.3.5.2 に示す。

TED-C11-001 試験（5.3.5.2 項）について、脈拍数、収縮期血圧、拡張期血圧、及び口腔体温のベースラインから各来院日又は最終投与日までの変化は、臨床的に意味のあるものではなかった。バイタルサインのベースラインからの経時変化及び最終投与日までの変化量を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.6.1 に示す。ベースライン後にみられたバイタルサインの顕著な異常の要約を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.6.2 に、被験者ごとの一覧を Table 14.3.6.3 に示す。

4.1.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）において、バイタルサインに臨床的に意味のある変化は認められなかった。バイタルサイン、体重及び BMI 及びベースラインからの変化の要約を 5.3.5.2 項 SHP633-306 CSR Table 14.3.4 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8 Listing 16.2.8.11 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む）について、バイタルサインのベースラインから最終投与日までの変化量を 5.3.5.2 項 TED-C14-004 CSR Table 40 に示す。全体として、試験期間中に、臨床的に意味のあるバイタルサイン（脈拍数、収縮期血圧、拡張期血圧、及び口腔体温）の変化は認められなかった。バイタルサイン測定値及びベースラインからの変化量を来院日別に 5.3.5.2 項 TED-C14-004 CSR Table 14.3.5.1 に要約し、被験者ごとの一覧を 5.3.5.2 項 TED-C14-004 CSR Appendix 16.2.8、Listing 16.2.8.11 に示す。

4.1.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）において、バイタルサイン、体重及び BMI に臨床的に意味のある変化は認められなかった。バイタルサイン、体重及び BMI 及びベースラインからの変化量を 5.3.5.2 項 SHP633-307 CSR Table 14.3.4 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-307 CSR Appendix 16.2.8 Listing 16.2.8.11 に示す。

TED-C14-004 試験（5.3.5.2 項）の継続投与期間については、本概要 4.1.1.3 を参照のこと。

4.1.2　　小児の臨床試験データ

4.1.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、バイタルサイン測定値に臨床的に意味のある変化は認められなかった。バイタルサイン値及びベースラインからの変化量を 5.3.5.3 項 Pediatric ISS Table 20.1 に示す。

4.1.2.2　　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データについて、バイタルサイン測定値に臨床的に意味のある変化は認められなかった。テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中におけるバイタルサイン値及びベースラインからの変化量をそれぞれ 5.3.5.3 項 Pediatric ISS Table 20.2、ISS Table 20.3.2.1、及び ISS Table 20.3.2.2 に示す。

4.1.2.3　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析において、脈拍数、収縮期血圧、拡張期血圧及び体温に臨床的に意味のある変化は認められなかった。バイタルサイン値及びベースラインからの変化量を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.5.1 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-301 Interim CSR Appendix 16.2.8 Listing 16.2.8.7 に示す。

最終解析において、脈拍数、収縮期血圧、拡張期血圧及び体温に臨床的に意味のある変化は認められなかった。バイタルサイン値及びベースラインからの変化量を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.5.1 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.8 Listing 16.2.8.7 に示す。

4.1.2.4　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）において、1～15 歳の小児及び修正月齢 4～12 ヵ月の乳児の脈拍、血圧及び体温に臨床的に意味のある変化は認められなかった。バイタルサイン値及びベースラインからの変化量を 5.3.5.2 項 SHP633-302 CSR Table 14.3.4.2 に示す。被験者ごとの一覧を 5.3.5.2 項 SHP633-302 CSR Appendix 16.2.9, Listing 16.2.8.10 に示す。

4.1.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、データカットオフ時点で、脈拍数、血圧及び体温に臨床的に意味のある変化は認められなかった。

投与期間及び NTT 期間におけるバイタルサインのベースライン（コア試験である SHP633-302 試験のベースライン）からの変化量をそれぞれ 5.3.5.2 項 SHP633-305 CSR Table 14.3.4.3 及び Table 14.3.4.4 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-305 CSR Listing 16.2.8.9 に示す。

4.2　心電図

独立した QT 評価試験である C09-001 試験、反復投与臨床薬理試験である CL0600-022 試験（探索的に実施した後向き解析）、反復投与臨床薬理試験である C10-003 試験（中央判定）並びに各臨床試験（ベースライン及びエンドポイントの各時点で記録）で実施した心電図の結果を解析した。

4.2.1　成人の臨床試験データ

C09-001 試験ではテデュグルチド 5 mg 単回皮下投与とテデュグルチド 20 mg 単回皮下投与の再分極及び伝導に及ぼす影響をプラセボと比較した。テデュグルチドの投与による再分極

（Fridericia 補正式による補正 QT 間隔；QTcF 間隔）への影響はプラセボと同程度であった（5.3.4.1 項 C09-001 CSR Section 13）。

CL0600-022 試験は健康被験者を対象とした二重盲検、無作為化、プラセボ対照、反復投与（連続 8 日間）試験であった。治験実施計画書に定めていなかったが本試験の用量範囲の広さを鑑み、心電図の後ろ向き解析を探索的に実施し、QT 評価試験のデザインに役立つ知見を得るとともに、テデュグルチドが心電図結果の各種間隔及び時間に及ぼしうる影響に関する安全性情報を得た。結果として、プラセボ群を含む全ての投与群で投与期間全体を通じて QTcF 間隔が時間とともに短縮する傾向が認められた。QTcF 間隔の経時変化にテデュグルチドの投与量に関連する特定の傾向はなく、テデュグルチド群とプラセボ群との間に QTcF 間隔への影響について特定の相違はみられなかった。QTcF 間隔が 480 ms を超えた被験者はみられず、QTcF 間隔のベースラインからの変化が 60 ms を超えた被験者もみられなかった。テデュグルチド群とプラセボ群の比較で、心拍数、PR 間隔及び QRS 間隔の変化に関して、経時変化及び用量の違いによる差のいずれにも、特定の傾向は認められなかった。試験治療下の心電図異常はプラセボ群、テデュグルチド群ともにみられたが、その頻度は低く、用量との関連はみられず、重症度も軽度であった（5.3.3.1 項 CL0600-022 CSR Section 12.5.2）。

C10-003 試験は健康被験者を対象にテデュグルチドが胃内容排出に及ぼす影響を検討した単施設、無作為化、二重盲検、プラセボ対照、反復投与、並行群間試験であった。テデュグルチド群とプラセボ群との間で QTc 間隔への影響に、特定の傾向はみられなかった。QTcF 間隔が 480 ms 以上であった被験者はみられず、QTcF 間隔のベースラインからの変化が 60 ms 以上であった被験者もみられなかった。テデュグルチド群及びプラセボ群の比較で、心拍数、PR 間隔及び QRS 間隔の経時変化に特定の傾向は認められなかった。心電図異常はプラセボ群、テデュグルチド群ともにみられたが、その頻度は低く、重症度も軽度であった。治験責任医師が臨床的に重要と判断した異常はなかった（5.3.4.1 項 C10-003 CSR Section 12.5.3.1）。

ベースライン及びエンドポイントの心電図所見の大部分は「正常」であった。以下の項に試験別の所見を示す。

4.2.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）では、エンドポイント時の心電図所見が「臨床的に重要な異常」に分類された被験者が 2 例みられた（いずれも CL0600-020 試験のテデュグルチド 0.05 mg/kg/日群）。

被験者番号：[redacted] は長期継続投与 CL0600-021 試験に登録され、その時点で右房拡張の事象は持続していた。

被験者番号：[redacted] において、スクリーニング時と Week 24 時の間で ST 部分の形状に有意差は認められなかった。この被験者では、ベースライン時からエンドポイント時までに臨床的に重要な心電図の変化はなかったと考えられた（5.3.5.1 項 CL0600-020 CSR Section 12.5.2）。

CL0600-004 試験（5.3.5.1 項）では、テデュグルチド 0.05 mg/kg/日群の 1 例（被験者番号：[redacted]）で Week 16 に臨床的に重要な心電図所見が 1 件認められた。Week 16 時点で軽度の上

室性三段脈、心房性期外収縮が認められたが、治験薬との関連なしと判断された。この被験者は試験への参加を継続し、試験を完了した。Week 24（試験終了時）の心電図は正常であった。これ以外に臨床的に重要な臨床検査値異常は報告されず、有害事象又は重篤な有害事象として報告された心電図異常はなかった（5.3.5.1 項 CL0600-004 CSR Section 12.5）。

4.2.1.2　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）では、1 例（被験者番号：[redacted]）でベースライン時に臨床的に重要と判断された心電図異常、すなわち持続中の T 波平低が認められた（試験治療外での発現）。本事象は治験責任医師により、軽度、治験薬と関連なしと判断された。処置は行われず、異常は持続していたが、試験終了時には臨床的に重要でないと判定された。これ以外に臨床的に重要な臨床検査値異常は報告されず、有害事象又は重篤な有害事象として報告された心電図異常もなかった（5.3.5.2 項 CL0600-021 CSR Section 12.5.3）。

CL0600-005 試験（5.3.5.2 項）及び TED-C11-001 試験（5.3.5.2 項）では、臨床的に重要な臨床検査値異常は報告されず、有害事象又は重篤な有害事象として報告された心電図異常もなかった。

4.2.1.3　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）では、試験期間中に臨床的に重要な心電図異常は認められなかった。

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）では、試験期間中に臨床的に重要な心電図異常は認められなかった。ベースライン後の心電図所見を来院ごとに 5.3.5.2 項 SHP633-306 CSR Table 14.3.5 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8 Listing 16.2.8.12 に示す。

4.2.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間では、試験期間中に臨床的に重要な心電図異常は認められなかった。

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）では、試験期間中に臨床的に重要な心電図異常は認められなかった。心電図所見の来院ごとの要約を 5.3.5.2 項 SHP633-307 CSR Table 14.3.5 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-307 CSR Appendix 16.2.8 Listing 16.2.8.12 に示す。

4.2.2　小児の臨床試験データ

4.2.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）では、0.0125 mg/kg/日コホートの 1 例（被験者番号：[redacted]）において Week 16 の追跡調査時に軽度の心電図異常が認められた。この事象は臨床的に重要と判断され、有害事象として報告された。その後、心雑音疑いのため心エコー検査が実施され、結果は陰性であった。処置は行われず、事象は回復に至った。治験責任医師は本事象を治験薬と関連なしと判断した。本被験者には右腎欠損及び多動性障害の既往歴があった。併用薬はメチルフェニデートであった。これ以外に臨床的に重要な心電図異常は認められなかった（5.3.5.2 項 TED-C13-003 CSR Section 12.5.3）。

TED-C14-006 試験（5.3.5.2 項）では、臨床的に重要な心電図の変化は認められなかった。ベースライン時、Week 12、Week 24、及び試験終了時来院のいずれの時点でも、臨床的に重要な心電図異常はみられなかった。

4.2.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）では、心電図の検査を行わなかった。

4.2.2.3　乳児を対象とした海外試験

実施中の SHP633-301 試験（5.3.5.2 項）では、心電図の検査を行わなかった。

4.2.2.4　小児及び乳児を対象とした国内第 3 相コア試験

SHP633-302 試験（5.3.5.2 項）では、臨床的に重要な心電図異常は認められなかった。ベースライン後の心電図所見の要約を 5.3.5.2 項 SHP633-302 CSR Table 14.3.5 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-302 CSR Appendix 16.2.9 Listing 16.2.8.12 に示す。

4.2.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）では、心電図の検査を行わなかった。

4.3　抗体

4.3.1　　成人の臨床試験データ

成人を対象とした臨床試験における抗体のデータは統合されなかったため、全て試験別に示す。

4.3.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）について、過敏症を示唆する臨床的に重要な免疫関連事象又はその他の臨床的に意味のある病理所見は認められなかった。抗テデュグルチド抗体の結果の要約をそれぞれ 5.3.5.1 項 CL0600-020 CSR Table 14.3.4.1 及び Table 14.3.4.2 に示す。

CL0600-004 試験（5.3.5.1 項）では、血漿検体を用いて抗テデュグルチド抗体を測定し、CL0600-005 試験のベースライン値とした（本概要 4.3.1.2）。

4.3.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）について、抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 CL0600-021 CSR Table 14.3.4.19 に、被験者ごとの一覧を 5.3.5.2 項 CL0600-021 CSR Appendix 16.2 Listing 16.2.8.7 に示す。注射部位反応及び／又は過敏症反応が 7 例に認められ、うち 3 例は抗テデュグルチド抗体陰性、残る 4 例は陽性であった（5.3.5.2 項 CL0600-021 CSR Appendix 16.2 Listing 16.2.8.7、Listing 16.2.7.1）。

CL0600-005 試験（5.3.5.2 項）（CL0600-004 試験の継続投与試験）における抗テデュグルチド抗体の結果を、CL0600-005 Immunoanalytical Report（5.3.1.4 項 Analytical Report TNJR07-368）に示す。抗テデュグルチド抗体を検出するように設計された ECL リガンド結合アッセイを用いて、244 検体をスクリーニングした。ベースラインの 62 検体は CL0600-004 試験のものであり、可能な限り投与後検体と同じプレート上で解析する。スクリーニングされた 244 検体のうち、27 検体が陽性であった。確認解析を行ったところ、27 検体全てが非特異的抗体であった。

TED-C11-001 試験（5.3.5.2 項）について、抗テデュグルチド抗体の結果一覧を 5.3.5.2 項 TED-C11-001 CSR Listing 16.2.7.6 に示す。抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.4.19 に示す。注射部位反応及び／又は過敏症反応が認められた被験者のうち、2 例が抗テデュグルチド抗体陰性（被験者番号：[redacted]［PT：注射部位反応］及び被験者番号：[redacted]［PT：注射部位血腫及びそう痒性皮疹］）、残る 1 例が陽性（被験者番号：[redacted]［PT：発疹］）であった（5.3.5.2 項 TED-C11-001 CSR、Listing 16.2.6.1、Listing 16.2.6.2）。被験者番号：[redacted] の注射部位反応は CL0600-021 試験から持続中であり、本試験中に初めて発現したものではなかった。5.3.1.4 項 Analytical Report TNJS12-027 を参照のこと。

4.3.1.3　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）の安全性解析対象集団における抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 SHP633-306 CSR Table 14.3.3.6 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8, Listing 16.2.8.6 に示す。使用した生物分析法及び抗体の生物分析結果は、5.3.1.4 項 A10772M SHP633 に記載した。試験期間中のいずれかの時点で抗テデュグルチド抗体陽性であった被験者は 1 例（14.3%、被験者番号：[redacted]、Week 24/投与終了時）で、中和抗体が認められた。抗テデュグルチド抗体価は非常に低かった（20）。本被験者は試験期間を通じてテデュグルチドに奏効を示さなかった。この被験者では過敏症反応又は注射部位反応に一致する徴候又は症状はみられなかった（5.3.5.2 項 SHP633-306 CSR, Appendix 16.2.7, Listing 16.2.7）。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む）での抗テデュグルチド抗体の要約を 5.3.5.2 項 TED-C14-004 CSR Section 12.5.6 に示す。試験期間中のいずれかの時点で抗テデュグルチド抗体陽性であった被験者は 4 例（36.4%）であり、ステージ 2 終了後（6 ヵ月間投与後）に新たに抗テデュグルチド抗体陽性となった被験者はいなかった（5.3.5.2 項 TED-C14-004 CSR Appendix 16.2.8 Listing 16.2.8.6F）。テデュグルチド投与開始後 30 ヵ月時点では、7 例全例（100.0%）が抗テデュグルチド抗体陰性であり、その後も陰性のままであった。抗テデュグルチド抗体陽性であった被験者 4 例に、過敏症反応の徴候及び症状は認められなかった（5.3.5.2 項 TED-C14-004 CSR Appendix 16.2.7 Listing 16.2.7.1、Appendix 16.2.8 Listing 16.2.8.6F）。注射部位反応は、抗テデュグルチド抗体陽性の検査結果が得られる前に 4 例中 2 例で報告され、抗テデュグルチド抗体陰性の 7 例では報告されなかった（5.3.5.2 項 TED-C14-004 CSR Appendix 16.2.7 Listing 16.2.7.1、Appendix 16.2.8 Listing 16.2.8.6F）。2 例に認められた注射部位反応は軽度であり、処置はとられなかった。これらの事象は治験責任医師により治験薬と関連ありと判断された。

4.3.1.4　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）について、安全性解析対象集団における抗体の結果の要約を 5.3.5.2 項 SHP633-307 CSR Table 14.3.3.6 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-307 CSR Appendix 16.2.8 Listing 16.2.8.6 に示す。ベースライン時、いずれの被験者も抗テデュグルチド抗体及び中和抗体陰性であった。総投与 12 ヵ月時点で、SHP633-306 試験から移行した被験者 2 例（50%）で抗テデュグルチド抗体陽性となり、うち 1 例（25%）に中和抗体が認められた。総投与 39 ヵ月時点で、TED-C14-004 試験から移行した 2 例（40%）で抗テデュグルチド抗体陽性及び中和抗体がみられた。総投与 57 ヵ月時点で、TED-C14-004 試験から移行した 1 例（100%）で抗テデュグルチド抗体陽性であった。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間については、本概要 4.3.1.3 を参照のこと。

4.3.2　小児の臨床試験データ

4.3.2.1　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、来院日別の抗体の結果の要約を 5.3.5.3 項 Pediatric ISS Table 19.1 に示す。

Week 12 時点で、テデュグルチド群では、抗テデュグルチド抗体陽性の被験者はいなかった。Week 24 時点で、0.025 mg/kg/日群の 3/24 例（12.5%）及び 0.05 mg/kg/日群の 5/26 例（19.2%）に抗テデュグルチド抗体陽性が認められた。過敏症の事象は認められず、注射部位反応の事象は全て軽度、非重篤であり、中止に至った事象はなかった（5.3.5.2 項 TED-C13-003 CSR Appendix 16.2.7.1 Listing 16.2.7.1、Listing 16.2.8.6、5.3.5.2 項 TED-C14-006 CSR Appendix 16.2.7 Listing 16.2.7.1、5.3.5.3 項 Pediatric ISS Table 58.1）。

中和抗体は、0.025 mg/kg/日群の 1/24 例（4.2%）及び 0.05 mg/kg/日群の 2/26 例（7.7%）に認められた。これら 3 例のうち 1 例は、被験者日誌データ及び医師処方データの両方に基づき、投与終了時点において体重で標準化した PS 量が 20%以上減少したレスポンダーであった。他の 2 例はいずれも被験者日誌又は医師処方データに基づくレスポンダーではなかった（5.3.5.2 項 TED-C14-006 CSR 12.5.4.5 項）。

これら 2 試験における来院日別の抗体について、年齢（5.3.5.3 項 Pediatric ISS Table 33.1）、性別（5.3.5.3 項 Pediatric ISS Table 39.1）、人種（5.3.5.3 項 Pediatric ISS Table 45.1）、地域（5.3.5.3 項 Pediatric ISS Table 51.1）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 57.1）に基づく各部分集団別の要約も示した。一部の部分集団では症例数が極めて少なかったものの、抗体の発現頻度に部分集団による傾向は認められなかった。

4.3.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データにおいて、NTT/TED 群では、2 例ともに、いずれの時点でも抗テデュグルチド抗体及び中和抗体陰性であった（5.3.5.3 項 Pediatric ISS Table 19.2）。TED/TED 群では、6/59 例（10.2%）が Cycle 1 Day 1、19/39 例（48.7%）が Cycle 1 の Week 24、3/13 例（23.1%）が Cycle 1 Week 28、5/20 例（25.0%）が Cycle 2 Day 1 において抗テデュグルチド抗体陽性となった（5.3.5.3 項 Pediatric ISS Table 19.2）。過敏症の事象は認められず、注射部位反応は全て軽度、非重篤であり、中止に至った事象はなく、1 例（2.6%）が Cycle 1 Week 24 で中和抗体陽性であった（5.3.5.2 項 SHP633-303 CSR Appendix 16.2.7 Listing 16.2.7.1、5.3.5.2 項 SHP633-304 Appendix 16.2.7 Listing 16.2.7.1、5.3.5.3 項 Pediatric ISS Table 58.2.2）。

これら試験の投与サイクル中における来院日別の抗体について、年齢（5.3.5.3 項 Pediatric ISS Table 33.2）、性別（5.3.5.3 項 Pediatric ISS Table 39.2）、人種（5.3.5.3 項 Pediatric ISS Table 45.2）、地域（5.3.5.3 項 Pediatric ISS Table 51.2）、及びベースライン時の PS 量（5.3.5.3 項 Pediatric ISS Table 57.2）に基づく各部分集団別の要約も示した。一部の部分集団では症例数が極めて少なかったものの、抗体の発現頻度に部分集団による傾向は認められなかった。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

4.3.2.3　　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）について、中間解析での抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.6.1 に示す。データカットオフ時点で、Week 12 又は Week 28 に抗テデュグルチド抗体陽性が認められた被験者はいなかった。

最終解析での抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.6.1 に示す。Week 12 及び Week 28（EOS）の来院時に検査を行ったテデュグルチド群の 3 例で、抗テデュグルチド抗体陽性であった被験者はいなかった。被験者別の抗テデュグルチド抗体の臨床検査結果を 5.3.5.2 項 SHP633-301 Final CSR Appendix 16.2.8、Listing 16.2.8.5 に示す。

4.3.2.4　　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）について、抗テデュグルチド抗体の結果の要約を 5.3.5.2 項 SHP633-302 CSR Section 12.5.5.3 に示す。抗テデュグルチド抗体陽性がみられた被験者は小児コホートの 2 例であった。うち 1 例は、Week 24 に抗テデュグルチド抗体陽性であったが、4 週後の試験終了時では陰性であった。別の 1 例では、Week 24 では陰性であったが、試験終了時（投与終了時の 4 週後）に陽性であった。いずれも中和抗体であった。テデュグルチド抗体陽性であった小児被験者 2 例のうち 1 例が、試験期間を通じて注射部位反応を発現し、治験責任医師により治験薬と関連ありと評価された。陰性の被験者 3 例も試験期間を通じて注射部位反応を発現した。アナフィラキシーの有害事象を発現した被験者は抗テデュグルチド抗体陰性であった。

乳児被験者は 2 例ともに、投与終了時及び試験終了時の両時点で、抗テデュグルチド抗体陽性であった。投与終了時及び試験終了時いずれも、1 例は中和抗体陽性、残る 1 例は中和抗体陰性であった。

4.3.2.5　　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）について、データカットオフ時点までの抗テデュグルチド抗体検査の結果を 5.3.5.2 項 SHP633-305 CSR Section 12.5.4.3 に要約する。本試験の投与開始前である Cycle 1 Day 1 に小児被験者 1 例及び乳児被験者 1 例で抗テデュグルチド抗体が認められた。これらの被験者では Week 24 まで抗テデュグルチド抗体が継続して認められた。うち、乳児被験者では注射部位反応が発現したが治験薬との関連は否定された（5.3.5.2 項 SHP633-305 CSR Listing 16.2.7）。本乳児はデータカットオフ時点で Week 28 に到達していなかった。一方、小児被験者では投与に起因する免疫原性反応はみられず、Week 28 時点では抗テデュグルチド抗体陰性であり、PS 量減少を維持していた。Cycle 1 Day 1 に抗テデュグルチド抗体が認められなかった被験者では、Week 12 で小児被験者 2 例及び乳児被験

者 1 例に抗テデュグルチド抗体及び中和抗体が認められ、Week 24 で小児被験者 2 例に抗テデュグルチド抗体が認められた。小児被験者 1 例及び乳児被験者 1 例で、テデュグルチド無投与での追跡調査期間の終了時（Week 28）まで、抗テデュグルチド抗体が認められた（いずれも Cycle 1 Day 1 時点で陽性であった 2 例とは異なる被験者）（5.3.5.2 項 SHP633-305 CSR Table 28、Listing 16.2.8.5）。平均すると、抗テデュグルチド抗体が認められた被験者（中和抗体が認められた被験者も含む）では、ベースラインからの PS 量の減少が持続しており、抗テデュグルチド抗体陽性と有効性の欠如に関連性は認められなかった（5.3.5.2 項 SHP633-305 CSR Table 14.3.3.7.1）。データカットオフ時点で、乳児被験者 2 例ともに Cycle 1 のみ完了していたが、小児被験者では最長 Cycle 5 まで完了している（5.3.5.2 項 SHP633-305 CSR Table 28）。

抗テデュグルチド抗体が認められた被験者において、テデュグルチドに関連した過敏症反応の報告はない。したがって、抗テデュグルチド抗体陽性と過敏症反応に関連は認められなかった。また、抗テデュグルチド抗体陽性と有効性との関連も認められなかった。抗体検査の結果について、5.3.5.2 項 SHP633-305 CSR Table 14.3.3.7 にサイクル及び来院別に要約し、被験者別の抗体検査結果の一覧を 5.3.5.2 項 SHP633-305 CSR Listing 16.2.8.5 に示す。

4.4　体重及び体格指数

4.4.1　　成人の臨床試験データ

4.4.1.1　　成人を対象とした海外第 3 相コア試験

CL0600-020 試験（5.3.5.1 項）及び CL0600-004 試験（5.3.5.1 項）では、テデュグルチド群におけるベースライン時からエンドポイントまでの変化量（平均値又は中央値）は小さく、臨床的に重要ではなかったが、用量依存的な体重増加が示唆された。ベースライン時からエンドポイントまでの増加量（平均値）は、0.05 mg/kg/日群で 0.96 kg、0.10 mg/kg/日群で 1.3 kg であった（5.3.5.3 項 Adult ISS Table 11.2.2）。

4.4.1.2　　成人を対象とした海外第 3 相継続投与試験

CL0600-021 試験（5.3.5.2 項）及び CL0600-005 試験（5.3.5.2 項）では、データは統合せず、本項に試験別に示す。

CL0600-021 試験（5.3.5.2 項）について、体重（平均値）及び BMI のベースラインからの変化量の要約を 5.3.5.2 項 CL0600-021 CSR Table 14.3.6.4 に示す。これらのデータの詳細を 5.3.5.2 項 CL0600-021 CSR Appendix 16.2 Listing 16.2.8.9 に示す。試験終了時、65 例（73.9%）におけるベースラインからの体重変動は±5 kg であり、これは 2 年間にわたる変化として臨床的に容認される範囲であると考えられる。全体として、5.3.5.2 項 CL0600-021 CSR Figure 12-2 に示すように、試験期間中、体重（平均値）は一定であった。体重減少が認められた被験者における有害事象の詳細を 5.3.5.2 項 CL0600-021 CSR Appendix 16.2 Listing 16.2.7.1 及び Listing 16.2.8.9 に示す。

CL0600-005 試験（5.3.5.2 項）について、体重のベースラインからの変化量の要約を 5.3.5.2 項 CL0600-005 CSR Table 14.2.1.1.10 及び Table 14.2.1.1.11 に示し、投与群で層別化したベースラインからの変化量を 5.3.5.2 項 CL0600-005 CSR Table 14.2.1.2.5 に、来院日別の変化率を 5.3.5.2 項 CL0600-005 CSR Table 14.2.1.3.5 に示す。ベースラインから Week 28 までの体重の変化量（平均値）は全体で 0.7 kg の増加であり、6 ヵ月実薬群と 1 年実薬群で同程度であった（5.3.5.2 項 CL0600-005 CSR Table 14.2.1.1.11）。

TED-C11-001 試験（5.3.5.2 項）について、体重及び BMI（平均値）のベースラインからの変化量の来院日別及び最終投与日の要約を 5.3.5.2 項 TED-C11-001 CSR Table 14.3.6.4 に示す。これらのデータの詳細を 5.3.5.2 項 TED-C11-001 CSR Appendix 16.2.8 Listing 16.2.7.8 に示す。体重及び BMI（平均値）はベースラインから試験終了時まで安定していた。

4.4.1.3　　成人を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-306 試験（5.3.5.2 項）では、試験期間中に臨床的に意味のある体重又は BMI の変化は認められなかった。本試験におけるバイタルサイン、体重及び BMI 及びベースラインからの変化量を 5.3.5.2 項 SHP633-306 CSR Table 14.3.4 に要約し、被験者ごとの一覧を 5.3.5.2 項 SHP633-306 CSR Appendix 16.2.8 Listing 16.2.8.11 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）（継続投与期間を含む、下記参照）では、試験期間中に臨床的に意味のある体重又は BMI の変化は認められなかった。体重及び BMI 値並びにベースラインからの変化量を来院別に 5.3.5.2 項 TED-C14-004 CSR Table 14.3.5.1 に示す。

4.4.1.4　　成人を対象とした国内第 3 相継続投与試験

日本人被験者を対象とした SHP633-307 試験（5.3.5.2 項）について、体重及び BMI に臨床的に意味のある変化は認められなかった。バイタルサイン、体重及び BMI の実測値及びベースラインからの変化量を 5.3.5.2 項 SHP633-307 CSR Table 14.3.4 に示す。

日本人被験者を対象とした TED-C14-004 試験（5.3.5.2 項）の継続投与期間については、本概要 4.4.1.3 を参照のこと。

4.4.2　　小児の臨床試験データ

4.4.2.1　　小児を対象とした海外第 3 相コア試験

TED-C13-003 試験（5.3.5.2 項）及び TED-C14-006 試験（5.3.5.2 項）の統合データについて、試験期間中、体重、身長、及び BMI の Z スコアに臨床的に意味のある変化は認められなかった。体重、身長、及び BMI の Z スコア及びベースラインからの変化量を 5.3.5.3 項 Pediatric ISS Table 21.1 に示す。

4.4.2.2　小児を対象とした海外第 3 相継続投与試験

SHP633-304 試験（5.3.5.2 項）及び SHP633-303 試験（5.3.5.2 項）（前向き期間のみ）の統合データの Cycle 1 において、体重、身長、及び BMI の Z スコアに臨床的に意味のある変化は認められなかった。テデュグルチド投与開始前、テデュグルチド投与サイクル中、及び休薬期間中における体重、身長、及び BMI の Z スコア並びにベースラインからの変化量をそれぞれ 5.3.5.3 項 Pediatric ISS Table 21.2.1、ISS Table 21.2.2.1、及び ISS Table 21.2.2.2 に示す。

4.4.2.3　乳児を対象とした海外試験

SHP633-301 試験（5.3.5.2 項）の中間解析について、体重、身長、体重／身長比、頭囲の Z-スコアの変化は、被験者の年齢群において予想される範囲内であった。体重、身長、体重／身長比、頭囲 Z スコア及びベースラインからの来院時までの変化量の要約を 5.3.5.2 項 SHP633-301 Interim CSR Table 14.3.5.2 に示す。

最終解析について、体重、身長、体重／身長比の Z-スコアの変化は、被験者の年齢群において予想される範囲内であった。テデュグルチド投与群と比較して、標準治療群で認められた頭囲 Z スコアは、経時的にさらに低下すると考えられた。体重、身長、体重／身長比、頭囲 Z スコア及びベースラインからの来院時までの変化量の要約を 5.3.5.2 項 SHP633-301 Final CSR Table 14.3.5.2 に示す。

4.4.2.4　小児及び乳児を対象とした国内第 3 相コア試験

日本人被験者を対象とした SHP633-302 試験（5.3.5.2 項）において、小児コホートで体重、身長、BMI 及び頭囲の Z スコアに臨床的に意味のある変化は認められなかった。乳児コホートでは、顕著な体重増加がみられ、このことは PS カロリー量の減少以上に小腸での栄養吸収能が改善したことを示す。年齢に対する体重、身長、BMI 及び頭囲の Z スコア（平均値）、並びにベースラインから各時点における変化量を 5.3.5.2 項 SHP633-302 CSR Table14.3.4.1 に、被験者ごとの一覧を 5.3.5.2 項 SHP633-302 CSR Listing 16.2.8.10、Listing 16.2.8.11 に示す。

4.4.2.5　小児及び乳児を対象とした国内第 3 相継続投与試験

実施中の日本人被験者を対象とした継続投与試験 SHP633-305 試験（5.3.5.2 項）において、データカットオフ時点で、小児コホートでは体重、身長、BMI、頭囲の Z スコアを含む成長パラメータに臨床的に意味のある変化はみられず、このことは PS 量が被験者の栄養必要量に応じて正しく調整されていたことを示唆している。乳児では体重増加が認められた。投与期間及び NTT 期間における、体重、身長、BMI 及び頭囲の年齢比 Z スコア（平均値）並びにパーセンタイル値を 5.3.5.2 項 SHP633-305 CSR Table 14.3.4.1、Table14.3.4.2 にそれぞれ示し、被験者ごとの一覧を 5.3.5.2 項 SHP633-305 CSR Listing 16.2.8.10 に示す。体重、身長、BMI 及び頭囲の年齢比 Z スコアのサイクル及び来院ごとの変化を 5.3.5.2 項 SHP633-305 CSR Figure 14.3.4.1 に示す。

5.　特別な患者集団及び状況下における安全性

本概要 1.1.1.1 で述べたように、テデュグルチドに対する 2014 年の初回の製造販売承認申請のために、成人患者を対象とした臨床試験 17 試験の安全性データを統合した。この統合解析（Adult ISS）には、海外の成人を対象としたコア試験及び継続投与試験が含まれており、本項では特別な患者集団及び状況下における安全性の評価に利用する。本項に記載した部分集団解析における患者背景及びベースライン特性については、5.3.5.3 項 Adult ISS Table 3.1.6 及び Table 4.1.2 を参照のこと。Adult ISS SAP は 5.3.5.3 項に格納されている。

5.1　内因性要因

本文書に示した海外成人安全性データの一部は統合されている（本概要 1.1.1 及び 1.1.1.1 参照）。本項では、Overseas adult SESS IDB の安全性データの探索的な部分集団解析を要約する。

- 性別
- 年齢
- 人種
- 肝機能障害
- 腎機能障害
- 結腸の連続性
- クローン病歴
- ストーマの有無

テデュグルチドの開発プログラムの多くの試験で、臨床検査値の顕著な異常及び抗テデュグルチド抗体について、多くの試験で年齢、性別、人種、地域、及びベースライン時の PS 量（疾患重症度を反映）に基づく部分集団解析を行った。データを入手可能な場合は本概要 3 及び 4 又は第 5 項の個々の試験結果に示す。

5.1.1　　性別

Overseas adult SESS IDB の 232 例について、性別の部分集団解析（5.3.5.3 項 Adult ISS Table 3.1.6、5.3.5.3 項 Adult ISS SAP）を探索的に実施した。被験者 232 例のうち、女性は 128 例（テデュグルチド群 95 例）、男性は 104 例（テデュグルチド群 78 例、5.3.5.3 項 Adult ISS Table 9.2.1）であった。

性別ごとの有害事象の概要は、5.3.5.3 項 Adult ISS Table 9.2.1 に示す。有害事象の発現頻度は女性で 98.9%、男性で 93.6%であり、重篤な有害事象の発現頻度は女性で 60.0%、男性で 56.4%であった。中止に至った有害事象の発現頻度も女性でやや高かった（それぞれ 22.1%及び 16.7%、5.3.5.3 項 Adult ISS Table 9.2.1）。

テデュグルチド群において発現した、腹痛、悪心、消化管ストーマ合併症、嘔吐、尿路感染及び水分過負荷の発現頻度は、女性が男性より 10%以上高かった（5.3.5.3 項 Adult ISS Table 9.5.1）。

国内における成人を対象とした試験の被験者数は少なかったものの、安全性については海外で実施された試験の結果と同様であり、新たな安全性上の懸念は認められなかった。

5.1.2　年齢

5.1.2.1　小児患者

1～17 歳の海外小児 SBS 患者に対するテデュグルチドの安全性については、海外第 3 相試験 2 試験（完了）及びその継続投与試験（実施中）において最長 24 週間にわたり検討されている。これらの試験の安全性データは本概要及び関連 CSR により示したため、ここでは繰り返さない。全体として、SBS を有する海外小児集団におけるテデュグルチドの安全性プロファイルは、SBS を有する成人被験者を対象とした臨床試験の結果と同様であった。本被験者集団において、新たな安全性のリスクやシグナルは認められなかった。

1 歳未満の小児 SBS 患者に対するテデュグルチドの安全性について、海外第 3 相試験 SHP633-301 試験（5.3.5.2 項）において検討した。本試験の安全性データは本概要及び関連 CSR により示したため、ここでは繰り返さない。全体として、SBS を有する海外乳児集団におけるテデュグルチドの安全性プロファイルは、SBS を有する成人被験者を対象とした臨床試験の結果と同様であった。本被験者集団において、新たな安全性のリスクやシグナルは認められなかった。

1～17 歳の日本人小児 SBS 患者に対するテデュグルチドの安全性については、国内第 3 相試験 1 試験（完了）及び継続投与試験（実施中、24 週間投与の結果）で検討されている。これらの試験の安全性データは本概要及び関連 CSR により示したため、ここでは繰り返さない。国内における小児を対象とした試験の被験者数は少なかったものの、安全性については海外で実施された試験の結果と同様であり、新たな安全性上の懸念は認められなかった。

5.1.2.2　高齢患者

Overseas Adult SESS IDB の 232 例について、年齢別の部分集団解析（5.3.5.3 項 Adult ISS Table 3.1.6、Table 4.1.2、5.3.5.3 項 Adult ISS SAP）を探索的に実施した。

被験者 232 例のうち 65 歳未満であったのは、テデュグルチド群 86.7%（150/173 例）及びプラセボ群 86.4%（51/59 例）であり、65 歳以上であったのは、テデュグルチド群 13.3%（23/173 例）及びプラセボ群 13.6%（8/59 例）であった。このうち、75 歳以上の被験者は 9 例（テデュグルチド群 6 例、プラセボ群 3 例）であった（本概要 5.1.2.1、5.3.5.3 項 Adult ISS Table 9.2.2）。

Adult ISS における 65 歳未満及び 65 歳以上の有害事象の概要は、5.3.5.3 項 Adult ISS Table 9.2.2 に示す。テデュグルチド群では、有害事象、重篤な有害事象又は中止に至った有害事象の発現頻度は、65 歳未満と 65 歳以上で同程度であった。

Adult ISS においてテデュグルチド群の被験者の 5%以上に発現した有害事象の要約を、65 歳未満及び 65 歳以上の年齢別に 5.3.5.3 項 Adult ISS Table 9.2.2 に、テデュグルチド群の年齢別の有害事象の要約を 5.3.5.3 項 Adult ISS Table 9.5.2 に示す。

テデュグルチド群において上気道感染の発現頻度は、65 歳未満の被験者が 65 歳以上と比較して 10%以上高かった。またテデュグルチド群で体重減少、食欲障害、消化管ストーマ合併症、消化管狭窄・閉塞、無力状態、注射部位反応、認知障害・注意力障害、うつ病性障害、睡眠障害、胆道障害（いずれもグループ化 PT）の発現頻度は、65 歳以上の被験者が 65 歳未満と比較して 10%以上高かった。なお、65 歳以上の被験者数（23 例）は比較的少なかったことから、これらの結果については慎重に評価する必要がある（5.3.5.3 項 Adult ISS Table 9.5.2、Table 9.15.01）。

概して、65 歳未満と 65 歳以上の被験者で安全性プロファイルに臨床的に意味のある差は認められなかった。

国内における成人を対象とした試験の被験者数は少なかったものの、安全性については海外で実施された試験の結果と同様であり、新たな安全性上の懸念は認められなかった。

5.1.3　人種

Overseas Adult SESS IDB の 232 例について、人種別の部分集団解析（5.3.5.3 項 Adult ISS Table 3.1.6、Table 4.1.2、5.3.5.3 項 Adult ISS SAP）を探索的に行った。

被験者 232 例のうち、テデュグルチド群において、白人 94.2%（163/173 例）、黒人 4.6%（8/173 例）及びその他の人種 1.2%（2/173 例）であった。プラセボ群において、白人 94.9%（56/59 例）、黒人 3.4%（2/59 例）及びその他の人種 1.7%（1/59 例）であった（5.3.5.3 項 Adult ISS Table9.2.3）。

人種別の有害事象の要約を 5.3.5.3 項 Adult ISS Table 9.2.3 に示す。テデュグルチド群の被験者について人種別の有害事象の要約を 5.3.5.3 項 Adult ISS Table 9.5.3、Table 9.15.01 に示す。黒人又はその他の人種の被験者数が限られているため、これらの部分集団解析からは、テデュグルチドの有害事象発現プロファイルが人種によって影響を受けるか否か結論を出すことはできなかった。

本項では、国内試験の安全性データを単独で記載しているため、記載を省略する。国内における成人を対象とした試験の被験者数は少なかったものの、安全性については海外で実施された試験の結果と同様であり、新たな安全性上の懸念は認められなかった。

5.1.4　肝機能障害

中等度の肝機能障害患者にテデュグルチド 20 mg を単回皮下投与したときのテデュグルチドの PK を被験者 24 例の非盲検試験により検討した（CL0600-017 試験、5.3.3.3 項）。治験実施計画書に基づき、中等度の肝機能障害を有する被験者（Child-Pugh 分類 B）と、性別、年齢、腎機能及び BMI の分布が類似した健康被験者をマッチさせた。テデュグルチド 20 mg を単回皮下投与したときの最大曝露量及び総曝露量は、健康対照群と比較して中等度の肝機能障害被験者でわずか

に低かった（10～15%）。C_{max}、$AUC_{0\text{-}inf}$及び$AUC_{0\text{-}t}$の幾何平均値の比（%GMR）の 90%信頼区間は 80～125%の範囲内に含まれなかったが、テデュグルチドの曝露量が低いことから、肝機能障害を有する被験者に投与した際に用量調節が必要となるような異常な蓄積性の問題が生じる可能性は低いと考えられた（5.3.3.3 項 CL0600-017 CSR Table 11.4.1.2.1）。

Child-Pugh 分類 B の被験者を対象とした試験に基づき、軽度及び中等度の肝機能障害患者に対する用量調節は必要ない。重度の肝機能障害患者を対象としたテデュグルチドの正式な試験は実施していない。

テデュグルチドの PK 評価については 2.7.2 項を参照のこと。

5.1.5　腎機能障害

様々な重症度の腎機能障害を有する被験者にテデュグルチド 10 mg を単回皮下投与したときのテデュグルチドの PK を検討した CL0600-018 試験（5.3.3.3 項）は、中等度腎機能障害（クレアチニンクリアランス 30～50mL/min）、重度腎機能障害（クレアチニンクリアランス 30 mL/min 未満）及び透析を要する末期腎不全の各 6 例からなる 3 群を、腎機能が正常で年齢、性別及び BMI が一致した健康被験者 6 例からなる 3 群と比較する、計 36 例を対象とした非盲検試験であった。本試験から、腎機能障害の重症度の悪化に伴いテデュグルチドの総曝露量（C_{max}及び$AUC_{0\text{–}inf}$）の増加が示された。血漿中テデュグルチド濃度の平均値は腎機能障害を有する被験者で高かった。テデュグルチドの主要な PK パラメータは、健康被験者と比較して、末期腎不全患者では$AUC_{0\text{-}inf}$が 2.6 倍、C_{max}が 2.1 倍であった。以上より、中等度及び重度の腎機能障害及び末期腎不全を有する被験者では、用量調節が必要であることが示唆された（5.3.3.3 項 CL0600-018 CSR Table 2-2）。

中等度及び重度の腎機能障害（クレアチニンクリアランスが 50 mL/min 未満）及び末期腎不全を有する患者では、テデュグルチドを 50%減量すること。軽度腎機能障害患者では用量調節の必要はない。

テデュグルチドの PK 評価については 2.7.2 項を参照のこと。

5.1.6　結腸の連続性

Overseas Adult SESS IDB の 232 例について、結腸の連続性の有無別の部分集団解析（5.3.5.3 項 Adult ISS Table 6.1.1、Table 6.1.2、5.3.5.3 項 Adult ISS SAP）を探索的に行った。

被験者 232 例のうち、結腸の連続性がみられた被験者は、テデュグルチド群 63.0%（109/173 例、5.3.5.3 項 Adult ISS Table 6.1.2）及びプラセボ群 57.6%（34/59 例、5.3.5.3 項 Adult ISS Table 6.1.1）であった。

Adult ISS で報告された有害事象の概要を結腸の連続性の有無別に 5.3.5.3 項 Adult ISS Table 9.2.4 に示す。テデュグルチド群において、結腸の連続性がみられた被験者では、結腸の連続性がみられない被験者と比較して、有害事象（それぞれ 92.7%、101/109 例及び 100%、64/64 例）又は中止に至った有害事象（それぞれ 13.8%、15/109 例及び 23.4%、15/64 例）を発現した被験

者の割合が少なかった。重篤な有害事象を発現した被験者の割合は、結腸の連続性がみられた被験者と結腸の連続性がみられない被験者でほぼ同じであった。プラセボ群でも同様の傾向が認められた。

テデュグルチド群の被験者において結腸の連続性の有無別の有害事象の概要を 5.3.5.3 項 Adult ISS Table 9.2.4 に示し、テデュグルチド群の被験者について結腸の連続性の有無別の有害事象一覧を 5.3.5.3 項 Adult ISS Table 9.5.4 に示す。

テデュグルチド群において、腹痛、悪心、腹部膨満、消化管ストーマ合併症、嘔吐、脱水、消化管の狭窄及び消化管の閉塞の発現頻度は、結腸の連続性がみられない被験者では結腸の連続性がみられた被験者と比較して 10%以上高かった。プラセボ群でも、これらの有害事象のうち、腹痛、嘔吐及び消化管ストーマ合併症は、結腸の連続性がみられない被験者では結腸の連続性がみられた被験者と比較して高かった（5.3.5.3 項 Adult ISS Table 9.5.4）。

概して、日本人 SBS 患者におけるテデュグルチドの安全性プロファイルを結腸の連続性の有無で解析した結果は、海外の SBS 患者を対象とした臨床試験で得られた安全性の結果と一致していると考えられた。この部分集団解析において、新たな安全性の問題は特定されなかった。

5.1.7　クローン病病歴

Overseas Adult Core IDB の 168 例について、クローン病の既往別の部分集団解析を探索的に行った（5.3.5.3 項 Adult ISS SAP）。

被験者 168 例のうち、テデュグルチド群の 30.3%（33/109 例）及びプラセボ群の 25.4%（15/59 例）にクローン病の既往があった（5.3.5.3 項 Adult ISS Table 6.1.1）。

5.3.5.3 項 Adult ISS Table 9.2.5 に、クローン病の既往歴別に、Overseas Adult SESS IDB で報告された有害事象の概要を示す。テデュグルチド群では、クローン病の病歴がある被験者で、ない被験者と比較して有害事象（100%, 51/51 例、95.1%, 116/122 例）及び中止に至った有害事象（29.4%, 15/51 例、15.6%, 19/122 例）の発現頻度がそれぞれ高かったが、重篤な有害事象を発現した被験者の割合は、クローン病の病歴がある被験者とない被験者で同程度であった。プラセボ群では、クローン病の既往歴のある被験者で、ない被験者と比較して有害事象の発現頻度が高かった。一方、重篤な有害事象及び中止に至った有害事象を発現した被験者の割合は、クローン病の既往歴のある被験者で、ない被験者と比較して少なかった。

有効性及び安全性を検討した試験において、テデュグルチド群の 5%以上に発現した有害事象をクローン病の既往歴の有無別に 5.3.5.3 項 Adult ISS Table 9.5.5 に、テデュグルチド群で発現した有害事象の一覧をクローン病の既往歴の有無別に 5.3.5.3 項 Adult ISS Table 9.5.5 に示す。腹痛、上気道感染、悪心、頭痛、注射部位反応、腹部膨満、消化管ストーマ合併症、嘔吐、過敏症、食欲障害のそれぞれの発現率は、テデュグルチド群においてクローン病の既往がある被験者で、ない被験者と比較して 10%以上高かった。プラセボ群では、腹痛、腹部膨満及び注射部位反応を除き、これらの有害事象はいずれも、クローン病の既往歴のある被験者で、ない被験者と比較して割合が高かった。

全体として、日本人 SBS 患者におけるクローン病の既往歴別のテデュグルチドの安全性プロファイルは、海外の SBS 患者を対象とした試験の結果と一致していると考えられた。この部分集団解析において、新たな安全性の問題は特定されなかった。

5.1.8　ストーマの有無

Overseas Adult Core IDB の 168 例について、ストーマの有無別の部分集団解析を探索的に行った（5.3.5.3 項 Adult ISS SAP）。

被験者 168 例のうち、テデュグルチド群の被験者の 41.3%（45/109 例）及びプラセボ群の被験者の 37.3%（22/59 例）がストーマを有していた（5.3.5.3 項 Adult ISS Table 6.1.1）。

有効性及び安全性を検討した試験におけるストーマの有無別の有害事象の概要を ISS に示す。テデュグルチド群において、有害事象及び重篤な有害事象を発現した被験者の割合は、ストーマの有無にかかわらず同程度であり、ストーマのある被験者及びない被験者の有害事象発現頻度はそれぞれ 100%及び 94.3%、重篤な有害事象発現頻度はそれぞれ 61.8%及び 56.2%であった。中止に至った有害事象を発現した被験者の割合は、ストーマのある被験者で、ない被験者と比較して高かった（それぞれ 26.5%、15.2%）。プラセボ群でも同様の傾向が認められた。

テデュグルチド群の 5%以上に発現した有害事象をストーマの有無別に分類した要約を ISS に示す。腹痛、悪心、腹部膨満、尿路感染、消化管ストーマ合併症、嘔吐、筋骨格痛、食欲障害、消化管の狭窄及び消化管の閉塞の発現頻度は、テデュグルチド群の被験者において、ストーマのある被験者で、ストーマのない被験者と比較して 10%以上高かった。プラセボ群では、これらの事象のうち腹痛、腹部膨満及び注射部位反応を除き、ストーマのある被験者で、ない被験者と比較して発現頻度が高かった。

概して、ストーマの有無別に解析した日本人 SBS 患者集団におけるテデュグルチドの安全性プロファイルは、海外の SBS 患者を対象とした臨床試験の安全性の結果と一致していると考えられた。この部分集団解析において、新たな安全性の問題は特定されなかった。

5.2　外因性要因

薬物相互作用については本概要 5.3 参照。

5.3　薬物相互作用

薬物動態学的薬物相互作用試験は実施されていない。*In vitro* 試験において、テデュグルチドはシトクロム P450 を阻害しないことが示されている。テデュグルチドの薬力学的作用に基づくと、併用経口薬の吸収が増加する可能性がある。

5.4　妊娠及び授乳時の使用

5.4.1　　妊婦

妊婦へのテデュグルチドの投与に関するデータは限られている。妊婦又は発生中の胎児へのリスクは否定できない。

妊婦にテデュグルチドを使用した症例報告から得られたデータでは、重大な先天異常、流産、母体又は胎児の有害転帰のリスクは確認されていない。妊娠ラット又は妊娠ウサギを用いた動物試験では、胚・胎児発生への影響は認められていない（2.6.6.6.2 項）。

妊婦又は妊娠している可能性のある女性には、治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。

5.4.2　　授乳婦

テデュグルチドがヒトの母乳中に移行するか否かは不明である。テデュグルチドの投与中は授乳しないことが望ましい。

授乳中のラットで得られている薬物動態データから、25 mg/kg を単回皮下投与したときのテデュグルチドの乳汁／血漿中薬物濃度比は、最高で 2.9%であることが示されている（2.6.4.4.4 項）。

5.4.3　　受胎能

テデュグルチドがヒトの受胎能に及ぼす影響に関するデータはない。動物データからは、受胎能の障害は示されていない（2.6.6.6.1 項）。

5.5　過量投与

過量投与のデータは極めて限られている。TED-C14-006 試験（5.3.5.2 項）の被験者 1 例が、ベースライン来院時に約 6 倍のテデュグルチドの過量投与を受けた（5.3.5.2 項 TED-C14-006 CSR 12.5.4.6）。本被験者は、投与ミスのために割り付けられた 0.05 mg/kg ではなく、約 0.30 mg/kg のテデュグルチドを投与された。この投与過誤は直ちに発見され、被験者は翌週にわたって注意深く観察された。過量投与に伴う有害事象は認められなかった。テデュグルチドの投与は中断されず、この被験者の投与群の割付けの早期開鍵は行われなかった（5.3.5.2 項 TED-C14-006 CSR Section 12.5.4.6）。

5.6　薬物の乱用及び誤用

薬理学的特性及び非臨床データから、本剤が乱用される可能性は低いと考えられる。臨床開発プログラムで報告されたテデュグルチドの乱用又は誤用はなかった。

5.7　離脱症状及び反跳現象

SHP633-304 試験及び SHP633-303 試験の前向き期間では、一部の被験者に 28 週間を 1 サイクルとしてテデュグルチド 0.05 mg/kg/日を投与した（24 週間のテデュグルチド投与＋4 週間の追跡調査期間）。各サイクルの Week 24 における休薬は、持続的なテデュグルチド投与の必要性を評価するためにデザインされた。連続的にテデュグルチドの投与を受けた被験者はいなかったが、臨床的に必要であれば投与サイクルを繰り返すことができるものとした。テデュグルチド再投与の適格性基準は、試験の適格性基準とは独立して評価した。1 つのテデュグルチド投与サイクルから次のサイクルまでの間隔は被験者によって様々であった（NTT 期間）。一部の被験者は、これらの試験でテデュグルチドの投与を受けず、試験期間を通じて単一の NTT 期間を継続した。疾患の悪化又は疾患に関連した症状以外に、離脱症状又は反跳現象に関連した有害事象は認められなかった。

小児を対象としたコア試験でテデュグルチドの投与を受けた小児被験者の多くは、継続投与試験への登録直後にテデュグルチド投与サイクルを開始した。これらの被験者では、投与サイクル間の間隔はわずかであった。特に、データカットオフ時点で最初の 24 週間の投与期間を完了していた被験者 19 例は、テデュグルチド休薬中に栄養状態が悪化したため、4 週間の追跡調査期間を早期に終了した（2.7.3 項参照）。

NTT/NTT、NTT/TED、TED/NTT 及び TED/TED 群の定義については本概要 1.1.1.5.2.2 を参照のこと。

5.8　自動車運転及び機械操作に対する影響又は精神機能の障害

該当なし。

6. 市販後データ

6.1　承認後の使用成績

テデュグルチドは現在、40 ヵ国以上で承認されている。主な承認日は以下のとおりである：成人 SBS 患者（2012 年 8 月 30 日欧州医薬品庁、2012 年 12 月 21 日米国食品医薬品局［FDA］）、1 歳以上の小児 SBS 患者（2016 年 6 月 29 日欧州医薬品庁、2019 年 5 月 16 日 FDA）

6.2　試験以外での承認後の曝露量

テデュグルチドに対して毎年、定期的安全性最新報告（PSUR、5.3.6.1 項）が行われている。2018 年 8 月 31 日から 2019 年 8 月 30 日までの報告期間中に入手した安全性及び有効性情報の主な評価結果に基づくと、テデュグルチドの患者への累積暴露は 7256 人年と推定され、さらに、2019 年 8 月 31 日から 2020 年 8 月 30 日までの報告期間中に入手した最新の安全性及び有効性情報の主な評価結果に基づくと、テデュグルチドの患者への累積暴露は 8949 人年と推定される。この結果は、テデュグルチドが SBS 患者の治療において臨床的に意味のある有益性のあることを示唆しており、SBS 患者ではテデュグルチドの長期投与により効果の持続性が得られる。1 歳以上の SBS 患者におけるテデュグルチドのベネフィット・リスクプロファイルは良好であることが示されている。

6.3　非介入試験

本申請時点で、非介入試験 1 試験（TED-R13-002 試験［5.3.6.2 項］：SBS 患者を対象とした前向き多施設共同レジストリ試験）が実施中である。本レジストリ試験では治療の提供は行われていない。本試験に登録された成人及び小児 SBS 患者から報告されたデータの解析が年 1 回実施されている。

6.3.1　　2019 年 6 月 30 日時点の結果

本項に示す結果は、試験開始（2014 年第 2 四半期）からデータカットオフ日（2019 年 6 月 30 日）までの累積データである。

2019 年 6 月 30 日現在、11 ヵ国（アルゼンチン、カナダ、デンマーク、フランス、ドイツ、イタリア、ノルウェー、スペイン、スウェーデン、英国及び米国）の 93 施設において 947 例の成人患者が本試験に登録されている。成人患者 811 例を PP 集団とした。テデュグルチド未投与患者及びテデュグルチド投与歴のある患者をカテゴリーとした部分集団解析等、全体の解析では異なる部分集団を用いた。

主要及び副次評価項目は以下のとおり。

安全性の主要評価項目

主要評価項目は、現在テデュグルチド投与を受けている、又は過去にテデュグルチド投与を受けたことがある患者における、残存結腸を有する SBS 患者での大腸癌の発現状況である。

安全性の副次評価項目及びその他の評価項目

- その他の悪性腫瘍の発現状況
- 消化管、肝胆道系及び膵蔵の良性腫瘍の発現状況
- 結腸ポリープの発現状況
- 腸閉塞の発現状況
- 膵臓及び胆管疾患の発現状況
- 心不全等の水分過負荷の発現状況
- テデュグルチドに対するアレルギー／過敏症反応の発現状況
- テデュグルチド投与に関連する可能性のあるその他の有害事象の発現状況

成人 SBS 患者を対象に解析した追加の安全性評価項目

- その他の消化器症状の発現状況
- その他の病態の発現状況
- 中枢神経系感染症の発現状況
- 運動障害／偽性閉塞腸管障害の発現状況
- PS に伴う肝疾患の発現状況
- 腸管手術の施行状況

成人の結果

試験開始からデータカットオフ日までに、主要安全性評価項目である結腸癌（主要評価項目）の発現はなかった。テデュグルチド投与歴のある患者とテデュグルチド未投与患者で、副次的安全性評価項目の結果を比較した。患者数が少なく、特定の事象の発現頻度がまれであったことを考慮すると、テデュグルチド投与歴のある患者及びテデュグルチド未投与患者間で意味のある比較は困難であったが、いくつかの潜在的な傾向がみられた。次に示す評価項目ではテデュグルチド投与歴のある患者における発現頻度がテデュグルチド未投与患者の約 2 倍以上であった：結腸ポリープ、消化管の良性腫瘍、膵臓疾患（腫瘍を除く）、その他の消化器症状及び腸管手術。テデュグルチド投与歴のある患者ではテデュグルチド未投与患者よりもポリープの発現頻度が高かった（約 5 倍）ことは、大腸内視鏡検査の実施率が高かった（3.5 倍）ことが一因であると考えられる。テデュグルチド投与歴のある患者よりもテデュグルチド未投与患者で発現頻度が高かった副次的評価項目は、心不全及び PS に伴う肝疾患であった。

テデュグルチド投与歴のある患者 293 例（74.9%）に 1966 件の有害事象が発現し、テデュグルチド未投与患者で 286 例（68.1%）に 1569 件の有害事象が発現した。テデュグルチド投与歴のある患者（テデュグルチド投与後）において頻度の高い SOC は、「胃腸障害」（43.0%）、「感染症および寄生虫症」（35.0%）、「一般・全身障害および投与部位の状態」（24.8%）、並びに「代謝およ

び栄養障害」（23.8%）であった。テデュグルチド未投与患者で頻度の高い SOC は、「感染症および寄生虫症」（38.6%）、「胃腸障害」（24.8%）、「一般・全身障害および投与部位の状態」（21.7%）、「臨床検査」（17.6%）、並びに「代謝および栄養障害」（15.7%）であった。

重度の有害事象は、テデュグルチド投与歴のある患者（テデュグルチド投与後）で 126 例（32.2%）に 372 件、テデュグルチド未投与患者で 147 例（35.0%）に 396 件報告された。テデュグルチド投与歴のある患者とテデュグルチド未投与患者のいずれにおいても、頻度の高い重度の有害事象の SOC は、頻度の高い順に、「感染症および寄生虫症」、「胃腸障害」、並びに「一般・全身障害および投与部位の状態」であった。

重篤な有害事象はテデュグルチド投与歴のある患者の 187 例（47.8%）に 740 件、テデュグルチド未投与患者の 209 例（49.8%）に 748 件発現した。テデュグルチド投与歴のある患者とテデュグルチド未投与患者のいずれにおいても、頻度の高い重篤な有害事象の SOC は、頻度の高い順に、「感染症および寄生虫症」、「胃腸障害」、並びに「一般・全身障害および投与部位の状態」であった。本試験期間中にテデュグルチド投与歴のある患者で 21 例（5.4%）の死亡が報告され、これらに関連した重篤な有害事象が 24 件認められた。本試験期間中にテデュグルチド未投与患者のうち 33 例（7.9%）の死亡が報告され、これらに関連した重篤な有害事象が 39 件認められた。テデュグルチド投与歴のある患者（テデュグルチド投与後）で報告された死亡に至った有害事象において、テデュグルチド投与と関連ありと判断されたものはなかった。

小児の結果

試験開始からデータカットオフ日までに 236 例の小児患者が登録された。うち 151 例の小児患者を PP 集団とした。小児では結腸直腸癌の既往歴を有する患者はおらず、また試験期間中に結腸直腸癌の発現はなかった。データが不十分であったため、テデュグルチド未投与の小児患者とテデュグルチド投与歴のある小児患者を比較して議論することはできなかった。次に述べる有害事象カテゴリーの発現頻度は、テデュグルチド未投与の小児患者に比べてテデュグルチド投与歴のある小児患者で低かった：テデュグルチド未投与及び投与歴のある小児患者でそれぞれ有害事象発現頻度（62.4% vs 53.8%）、重度の有害事象発現頻度（39.2% vs 26.9%）、重篤な有害事象（52.8% vs 38.5%）。テデュグルチド投与歴のある小児患者で死亡は報告されておらず、テデュグルチド未投与の小児患者では 1 例（0.8%）で 1 件の死亡が報告された（尿路感染の重篤な有害事象と関連）。

概して、本レジストリ試験の小児患者で観察された安全性所見は、レジストリ試験全体の結果と同様であるとみられる。

全体

本レジストリ試験で観察された安全性の結果は、テデュグルチドの既知の安全性プロファイルと同様であった。試験開始からデータカットオフ日までに結腸癌の発現はなかった。認められた有害事象及び重篤な有害事象は、テデュグルチドの既知の安全性情報と同様である。

6.3.2　2020 年 6 月 30 日時点の結果

本項に示す結果は、試験開始（2014 年第 2 四半期）からデータカットオフ日（2020 年 6 月 30 日）までの累積データである。

2020 年 6 月 30 日現在、12 ヵ国（アルゼンチン、カナダ、デンマーク、フィンランド、フランス、ドイツ、イタリア、ノルウェー、スペイン、スウェーデン、英国及び米国）の 113 施設において 1144 例の成人患者及び 284 例の小児患者が本試験に登録されている。成人患者 1142 例を PP 集団とした。テデュグルチド未投与患者及びテデュグルチド投与歴のある患者をカテゴリーとした部分集団解析等、全体の解析では異なる部分集団を用いた。さらに、本レジストリ試験が開始された当時、有害事象の収集は、テデュグルチド投与歴のある患者では最初の投与日から、テデュグルチド未投与患者では試験の登録日から行っていた。本規定は後の Amendment で変更されたが、テデュグルチド投与歴のある患者は有害事象の報告期間が長い可能性が高く、テデュグルチド未投与患者及びテデュグルチド投与歴のある患者の有害事象を比較して評価する際には、このことを考慮する必要がある。

主要及び副次評価項目は以下のとおり。

主要評価項目

主要評価項目は、現在テデュグルチド投与を受けている、又は過去にテデュグルチド投与を受けたことがある患者における、残存結腸を有する SBS 患者での大腸癌の発現状況である。

副次評価項目及びその他の評価項目

- その他の悪性腫瘍の発現状況
- 消化管、肝胆道系及び膵蔵の良性腫瘍の発現状況
- 結腸ポリープの発現状況
- 腸閉塞の発現状況
- 膵臓及び胆管疾患の発現状況
- 心不全等の水分過負荷の発現状況
- テデュグルチドに対するアレルギー／過敏症反応の発現状況
- テデュグルチド投与に関連する可能性のあるその他の有害事象の発現状況
- その他の消化器症状の発現状況
- その他の病態の発現状況
- 中心静脈カテーテル感染症の発現状況

有効性評価項目

有効性の評価項目には、ベースラインから追跡調査来院までの期間における以下のパラメータを含めた。

- PS 量の変化量
- PS 量の変化率

- 週間 PS 施行日数の変化量
- 週間 PS 施行日数の変化率
- PS から完全離脱した患者の割合

主要評価項目の結果

試験開始からデータカットオフ日（2020 年 6 月 30 日）までに、主要安全性評価項目である結腸癌の発現はなかった。

副次評価項目の結果

成人の結果

結腸癌以外のあらゆる種類の新たな又は悪化した悪性腫瘍は、テデュグルチド未投与患者 675 例中 25 例（3.70%）に 27 件、テデュグルチド投与歴のある患者 467 例中 18 例（3.85%）に 19 件みられた。テデュグルチド未投与患者と比較してテデュグルチド投与歴のある患者での発現頻度が約 2 倍以上であった副次評価項目は消化器の良性腫瘍、膵臓の良性腫瘍、結腸ポリープ、膵臓疾患（腫瘍を除く）、及び大腸内視鏡検査の 5 項目であった。なお、企業中核データシートには、患者の特性に応じてモニタリングの頻度を増やす必要があるかどうか個別に評価するよう記載されている。テデュグルチド投与歴のある患者と比較してテデュグルチド未投与患者で著しく頻度の高かった副次評価項目は 2 項目であった（心不全及び中心静脈カテーテル感染）。

有害事象の件数は、テデュグルチド未投与患者と比較して、テデュグルチド投与歴のある患者で多かった。テデュグルチド投与歴のある患者で報告された有害事象は 369 例（79.0%）に 2817 件であり、テデュグルチド未投与患者で報告された有害事象は 438 例（64.9%）に 2606 件であった。発現頻度は、テデュグルチド投与歴のある患者とテデュグルチド未投与患者で、それぞれ 1000 人年当たり 2653.3 件及び 1854.1 件であった。テデュグルチド投与歴のある患者とテデュグルチド未投与患者の両方で頻度の高い有害事象（1000 人年あたり 20 件以上）は、腹痛、急性腎障害、貧血、脱水、医療機器関連感染、医療機器関連敗血症、下痢、低カリウム血症、栄養障害、敗血症、尿路感染及び血管の医療機器感染であった。テデュグルチド投与歴のある患者で頻度の高いその他の有害事象（1000 人年当たり 20 件以上）は、菌血症、クローン病、食欲減退、低マグネシウム血症、鼻咽頭炎、悪心、肺炎、嘔吐及び体重減少であった。有害事象の大部分は軽度又は中等度であった。重度の有害事象は、テデュグルチド投与歴のある患者では 176 例（37.7%）、テデュグルチド未投与患者では 221 例（32.7%）で報告された。重度の有害事象の発現頻度は、テデュグルチド投与歴のある患者及びテデュグルチド未投与患者でそれぞれ 1000 人年当たり 517.1 件及び 430.5 件であった。テデュグルチドと関連ありとされた有害事象は、テデュグルチド投与歴のある患者の 129 例（27.6%）に 289 件報告された。投与の中断又は中止に至った有害事象は、テデュグルチド投与歴のある患者の 93 例（19.9%）に 160 件報告され、主な有害事象は、腹痛（11 例［2.4%］）、菌血症（5 例［1.1%］）並びに便秘、食欲減退、腸閉塞及び悪心（各 4 例［0.9%］）であった。

重篤な有害事象を発現した患者の割合は、テデュグルチド未投与患者と比較してテデュグルチド投与歴のある患者で高く、テデュグルチド投与歴のある患者では 260 例（55.7%）に 1113 件、

テデュグルチド未投与患者では 310 例（45.9%）に 1151 件であった。重篤な有害事象の発現率はテデュグルチド投与歴のある患者及びテデュグルチド未投与患者でそれぞれ 1000 人年当たり 1048.3 件及び 818.9 件であった。テデュグルチド投与歴のある患者で報告された重篤な有害事象 1113 件のうち、78 件（42 例［9.0%］）がテデュグルチドと関連ありとされた。

テデュグルチド投与歴のある患者とテデュグルチド未投与患者の両方において頻度の高い重篤な有害事象（10 例超）は、医療機器関連感染、血管の医療機器感染、敗血症、腹痛、脱水、急性腎障害、肺炎、菌血症、医療機器関連敗血症であった。その他の頻度の高い重篤な有害事象（10 例超）は、テデュグルチド投与歴のある患者では栄養障害及び貧血であり、テデュグルチド未投与患者では、死亡、尿路感染、低カリウム血症、敗血症性ショック及び発熱であった。

本試験期間中にテデュグルチド投与歴のある患者で 27 例（5.8%）の死亡が報告され、これらに関連した重篤な有害事象が 32 件認められた。いずれもテデュグルチド投与後の死亡であったが、治験責任医師によりテデュグルチドと関連ありとされたものはなかった。テデュグルチド未投与患者では 57 例（8.4%）の死亡が報告され、これらに関連した重篤な有害事象が 66 件認められた。

小児の結果

有害事象を発現した小児患者の割合は、テデュグルチド投与歴のある小児患者及びテデュグルチド未投与の小児患者で同程度であり、それぞれ 62.5%（25 例）129 件及び 63.0%（153 例）742 件であった。有害事象の発現頻度は、テデュグルチド投与歴のある小児患者及びテデュグルチド未投与の小児患者でそれぞれ 1000 人年当たり 2057.4 件及び 1643.4 件であった。テデュグルチド投与歴のある小児患者とテデュグルチド未投与の小児患者の両方で頻度の高い有害事象（1000 人年当たり 20 件以上）は、医療機器関連合併症、医療機器破損、医療機器機能不良、医療機器関連敗血症、発熱、血管の医療機器感染、嘔吐であった。その他の有害事象で頻度の高い有害事象（1000 人年当たり 20 件以上）は、テデュグルチド投与歴のある小児患者では腹痛、気管支炎、カテーテル留置部位感染、脳性麻痺、膀胱炎、インフルエンザ、偽性腸閉塞、白血球減少症、好中球減少症及び敗血症であり、テデュグルチド未投与の小児患者では、ブドウ球菌感染及びウイルス感染であった。軽度の有害事象の発現率は、テデュグルチド投与歴のある小児患者でより高かった。重度の有害事象はテデュグルチド投与歴のある小児患者 11 例（27.5%）で 46 件、テデュグルチド未投与の小児患者 66 例（27.2%）で 263 件報告された。テデュグルチドの中断又は投与中止に至った有害事象は、テデュグルチド投与歴のある小児患者で 3 例（7.5%）に 5 件認められ、内訳は、発熱が 1 例に 2 件並びに偽性腸閉塞、過量投与及び嘔吐が各 1 例に 1 件であった。

重篤な有害事象が発現した患者の割合は、テデュグルチド投与歴のある小児患者とテデュグルチド未投与の小児患者で同程度であり、それぞれ 50.0%（20 例）に 79 件及び 46.9%（114 例）に 485 件発現した。重篤な有害事象の発現頻度はテデュグルチド投与歴のある小児患者とテデュグルチド未投与の小児患者で 1000 人年当たりそれぞれ 1260.0 件及び 1074.2 件であった。テデュグルチド投与歴のある小児患者で 5 例以上に発現した重篤な有害事象は、発熱（6 例、15.0%）であった。テデュグルチド未投与の小児患者で 5 例以上に発現した重篤な有害事象は、血管の医療

機器感染（40 例、16.5%）、発熱（34 例、14.0%）、医療機器関連敗血症（17 例、7.0%）、医療機器機能不良（11 例、4.5%）、医療機器に関連した合併症（9 例、3.7%）、医療機器破損及びインフルエンザ（各 8 例、3.3%）並びにブドウ球菌感染（7 例、2.9%）であった。テデュグルチド投与歴のある小児患者にみられた重篤な有害事象 79 件のうち、3 件（3 例、7.5%）がテデュグルチドと関連ありとされた。

死亡に至った重篤な有害事象は、テデュグルチド投与歴のある小児患者では認められず、テデュグルチド未投与の小児患者では 3 例（1.2%）に 3 件認められた。

全体

本レジストリ試験で観察された安全性の結果は、テデュグルチドの既知の安全性プロファイルと同様であった。試験開始からデータカットオフ日（2020 年 6 月 30 日）までに結腸癌の発現はなかった。認められた有害事象及び重篤な有害事象は、テデュグルチドの既知の安全性情報と同様である。本レジストリ試験に新たな安全シグナルは確認されていない。テデュグルチドのベネフィット・リスクは依然良好である。

7. 引用文献

Burrin DG, Stoll B, Guan X, Cui L, Chang X, Hadsell D. GLP-2 rapidly activates divergent intracellular signaling pathways involved in intestinal cell survival and proliferation in neonatal piglets. Am J Physiol Endocrinol Metab. 2007;292(1):E281-91.(5.4.12)

Burrin DG, Stoll B, Guan X, Cui L, Chang X, Holst JJ. Glucagon-like peptide 2 dose-dependently activates intestinal cell survival and proliferation in neonatal piglets. Endocrinology. 2005;146(1):22-32. (5.4.13)

Burrin DG, Stoll B, Jiang R, Petersen Y, Elnif J, Buddington RK, et al. GLP-2 stimulates intestinal growth in premature TPN-fed pigs by suppressing proteolysis and apoptosis. Am J Physiol Gastrointest Liver Physiol. 2000;279(6):G1249-56. (5.4.14)

Lovshin JA, Huang Q, Seaberg R, Brubaker PL, Drucker DJ. Extrahypothalamic expression of the glucagon-like peptide-2 receptor is coupled to reduction of glutamate-induced cell death in cultured hippocampal cells. Endocrinology. 2004;145(7):3495-506. (5.4.41)

Petersen YM, Burrin DG, Sangild PT. GLP-2 has differential effects on small intestine growth and function in fetal and neonatal pigs. Am J Physiol Regul Integr Comp Physiol. 2001;281(6):R1986-93. (5.4.56)

8　付録

付録 1. 死亡に至った有害事象発現症例一覧

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse Event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 mg/kg/day	Male	6[redacted]	背部痛	-112	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃炎	49	.	Not Related	Mild	Not Serious	None	Ongoing
						喀血	71	.	Not Related	Moderate	Not Serious	None	Ongoing
						動脈硬化症	85	.	Not Related	Mild	Not Serious	None	Ongoing
						非小細胞肺癌	85	158	Not Related	Severe	Serious	Study Drug Discontinued	Fatal
						INR 増加	87	3	Not Related	Mild	Not Serious	None	Resolved
						十二指腸ポリープ	103	.	Not Related	Mild	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 mg/kg/day	Male	4[redacted]	背部痛	313	.	Not Related	Moderate	Not Serious	None	Ongoing
						腰椎骨折	323	.	Not Related	Severe	Serious	Study Drug Discontinued	Ongoing
						消化不良	323	.	Not Related	Mild	Not Serious	None	Ongoing
						転移性新生物	326	11	Related	Severe	Serious	Study Drug Discontinued	Fatal
Teduglutide / Teduglutide	[redacted]	White	0.05 mg/kg/day	Male	6[redacted]	憩室	-188	.	Not Related	Mild	Not Serious	None	Ongoing
						脳血管発作	244	7	Not Related	Mild	Serious	None	Resolved
						体重減少	407	.	Not Related	Mild	Not Serious	None	Ongoing
						低蛋白血症	407	.	Not Related	Mild	Not Serious	None	Ongoing
						低アルブミン血症	407	.	Not Related	Mild	Not Serious	None	Ongoing
						脳血管発作	620	9	Not Related	Mild	Serious	None	Resolved
						皮膚感染	625	10	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	688	9	Not Related	Severe	Serious	None	Resolved
						敗血症	688	16	Not Related	Severe	Serious	None	Fatal
						椎間板炎	688	.	Not Related	Severe	Serious	None	Ongoing

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	CTCAE Grade	Relationship to Study Drug	Action Taken with Study Treatment / Other Action Taken	Discontinued from the Study	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2017-04-02(242) /2017-04-16(256)	CONT/ SV/ R/R	GRADE 3	NR	NC/ DT	No	Y	Y
		肝胆道系障害／ 胆石症／ GALLBLADDER SLUDGE	2017-04-06(246) /ONGOING	CONT/ MO/ NRD	No		NC/ N	No	N	Y
		感染症および寄生虫症／ 眼感染／ EYE INFECTION	2017-04-27(267) /2017-08-01(363)	CONT/ MO/ R/R	No		NC/ DT	No	N	Y

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	CTCAE Grade	Relationship to Study Drug	Action Taken with Study Treatment / Other Action Taken	Discontinued from the Study	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	感染症および寄生虫症／消化管内細菌過剰増殖／SMALL BOWEL BACTERIAL OVERGROWTH INFECTION	2017-04-27(267) /2017-08-01(363)	CONT/ MO/ R/R	No	NR	NC/ DT	No	N	Y
		胃腸障害／短腸症候群／WORSENING OF SHORT BOWEL SYNDROME	2017-08-04(366) /2017-08-15(377)	CONT/ SV/ D	GRADE 4		NA/ N	Yes	Y	Y

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	神経系障害／ 頭痛／ Headache	21AUG2015:21:00:00 1/ 21AUG2015:22:00:00 1	1	No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Recovered/Resolved	Yes
				感染症および寄生虫症／ 医療機器関連感染／ Catheter related blood stream infection	24AUG2015:21:00:00 4/ 30AUG2015:15:00:00 10	7	Yes/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				感染症および寄生虫症／ カンジダ性亀頭炎／ Penis candidiasis	02SEP2015 13/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Not Recovered/Not Resolved	Yes
				代謝および栄養障害／ 栄養障害／ Malnutrition	02SEP2015:19:00:00 13/ - -		No/ Severe/ Not Related	Drug Interrupted/ Drug Treatment	Continuous/ Not Recovered/Not Resolved	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	一般・全身障害および投与部位の状態／ 浮腫／ Edema	02SEP2015 13/ - -		No/ Moderate/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Not Recovered/Not Resolved	Yes
				胃腸障害／ 腸炎／ Enterocolitis	02SEP2015:19:00:00 13/ 18SEP2015 29	17	Yes/ Severe/ Related	Drug Interrupted/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				胃腸障害／ 腸閉塞／ Intestinal obstruction	02SEP2015:19:00:00 13/ 18SEP2015 29	17	Yes/ Severe/ Related	Drug Interrupted/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				感染症および寄生虫症／ 医療機器関連感染／ Catheter related blood stream infection	02SEP2015 13/ 19SEP2015 30	18	No/ Severe/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/Resolved	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	血液およびリンパ系障害／ 貧血／ Anemia (aggravated)	03SEP2015 14/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Not Recovered/Not Resolved	Yes
				血液およびリンパ系障害／ 播種性血管内凝固／ Disseminated intravascular coagulation	05SEP2015 16/ - -		No/ Severe/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ -	Yes
				肝胆道系障害／ 急性肝不全／ Acute liver failure	05SEP2015 16/ 27OCT2015:12:40:00 68	53	Yes/ Severe/ Related	Drug Withdrawn/ Multiple	Continuous/ Fatal	Yes
				肝胆道系障害／ 高ビリルビン血症／ High bilirubinemia	06SEP2015 17/ - -		No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ -	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	感染症および寄生虫症／ 口腔ヘルペス／ Herpes labialis	07SEP2015 18/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Not Recovered/Not Resolved	Yes
				胃腸障害／ 膵炎／ Pancreatitis	07SEP2015 18/ 04OCT2015 45	28	No/ Moderate/ Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				皮膚および皮下組織障害／ そう痒症／ Skin pruritus	10SEP2015 21/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ -	Yes
				代謝および栄養障害／ 高血糖／ Hyperglycemia	11SEP2015 22/ 16SEP2015 27	6	No/ Moderate/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				胃腸障害／ 口腔内出血／ Bleeding mouth	16SEP2015 27/ - -		No/ Mild/ Not Related	Dose Not Changed/ None	Intermittent/ -	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	感染症および寄生虫症／ 敗血症／ Sepsis	20SEP2015 31/ 14OCT2015 55	25	Yes/ Severe/ Not Related	Dose Not Changed/ Multiple	Continuous/ Recovered/Resolved	Yes
				臨床検査／ 酸素飽和度低下／ Oxygen saturation low	21SEP2015 32/ - -		No/ Moderate/ Not Related	Dose Not Changed/ Non-Drug Treatment	Continuous/ -	Yes
				一般・全身障害および投与部位の状態／ 医療機器閉塞／ Central venous catheter occlusion	21SEP2015 32/ 21SEP2015 32	1	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/Resolved	Yes
				代謝および栄養障害／ 低血糖症／ Hypoglycemia	21SEP2015 32/ 21SEP2015 32	1	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/Resolved	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	胃腸障害／ 腸炎／ Enterocolitis	21SEP2015 32/ 13OCT2015 54	23	No/ Severe/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ Recovered/Resolved	Yes
				心臓障害／ 急性心不全／ Acute heart failure	22SEP2015 33/ - -		No/ Severe/ Not Related	Dose Not Changed/ Multiple	Continuous/ -	Yes
				筋骨格系および結合組織障害／ 筋肉痛／ Muscle pain	22SEP2015 33/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Intermittent/ Not Recovered/Not Resolved	Yes
				臨床検査／ 尿量減少／ Decreased urinal volume	22SEP2015 33/ - -		No/ Moderate/ Not Related	Dose Not Changed/ None	Intermittent/ -	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time Relative Day/ Stop Date and Time Relative Day	Dura-tion	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Japanese	Male	3[redacted]	呼吸器、胸郭および縦隔障害／ 呼吸不全／ Acute lung failure	22SEP2015 33/ 13OCT2015 54	22	No/ Severe/ Not Related	Dose Not Changed/ Non-Drug Treatment	Continuous/ Recovered/Resolved	Yes
				眼障害／ 眼球浮腫／ Eye edema	23SEP2015 34/ - -		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ -	Yes
				感染症および寄生虫症／ 口腔カンジダ症／ Oral candida	23SEP2015 34/ - -		No/ Moderate/ Not Related	Dose Not Changed/ Drug Treatment	Continuous/ -	Yes
				一般・全身障害および投与部位の状態／ 低体温／ Hypothemia	24SEP2015 35/ 24SEP2015 35	1	No/ Mild/ Not Related	Dose Not Changed/ None	Intermittent/ Recovered/Resolved	Yes
				腎および尿路障害／ 急性腎不全／ Acute renal failure	22OCT2015 63/ 27OCT2015:12:40:00 68	6	Yes/ Severe/ Not Related	Dose Not Changed/ None	Intermittent/ Fatal	Yes

Note: Treatment emergent adverse events (TEAEs) are defined as any adverse events whose onset occurs, severity worsens or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 17.1.
[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14004¥report¥adhoc¥l-ae-dth.sas　Output: l-ae-dth.rtf　29JAN2020 17:13

付録 2. 重篤な有害事象発現症例一覧

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Cohort AR - Teduglutide	[redacted]	White	Teduglutide 20 Mg/Dose With Formulation 50 Mg/Ml	Male	2[redacted]	腹痛	2	9	Related	Mild	Not Serious	None	Recovered/Resolved
						顔面骨骨折	10	4	Not Related	Severe	Serious	None	Recovered/Resolved

Notes: Teduglutide Treatment Groups: Cohort A - 20 mg qd sc 20mg/mL formulation; All other cohorts used sc 50 mg/mLformulation at following doses: Cohort AR - 20 mg qd; Cohort C - 25 mg qd; Cohort D - 10 mg qd; Cohort E - 15 mg qd;Cohort F - 30 mg qd; Cohort H - 50 mg qd; Cohort J - 80 mg qd
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 9.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-2-ae-sae-600022.sas　　Output Generated On: 23OCT2016 1:18

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10 Mg/Kg/Day With Bid Rechallenge	[redacted]	White	Teduglutide 0.10 Mg/Kg/Day With Bid Rechallenge	Female	5[redacted]	カテーテル敗血症	-2	10	Not Related	Moderate	Not Serious	None	Recovered/Resolved
						消化管ストーマ合併症	3	22	Related	Moderate	Not Serious	None	Recovered/Resolved
						脱水	342	7	Not Related	Mild	Serious	None	Recovered/Resolved
						消化管ストーマ合併症	344	25	Related	Moderate	Not Serious	None	Recovered/Resolved
						排尿困難	346	8	Not Related	Mild	Not Serious	None	Recovering/Resolving
						末梢性浮腫	350	8	Related	Mild	Not Serious	None	Recovered/Resolved
Teduglutide 0.15 Mg/Kg/Day	[redacted]	White	Teduglutide 0.15 Mg/Kg/Day	Female	4[redacted]	注射部位紅斑	3	20	Related	Moderate	Not Serious	None	Recovered/Resolved
						インフルエンザ様疾患	11	8	Not Related	Moderate	Not Serious	None	Recovered/Resolved
						敗血症	23	12	Not Related	Severe	Serious	None	Recovered/Resolved
						脱水	23	12	Not Related	Severe	Serious	None	Recovered/Resolved
Teduglutide 0.15 Mg/Kg/Day	[redacted]	White	Teduglutide 0.15 Mg/Kg/Day	Male	6[redacted]	カテーテル敗血症	11	12	Not Related	Moderate	Serious	None	Recovered/Resolved
						カテーテル敗血症	11	12	Not Related	Moderate	Serious	None	Recovered/Resolved
						浮腫	14	13	Not Related	Mild	Not Serious	None	Recovered/Resolved
						消化管ストーマ合併症	18	9	Related	Mild	Not Serious	None	Recovered/Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-14-ae-sae-92001.sas

Output Generated On: 21OCT2016 1:00

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.15 Mg/Kg/Day With Bid Rechallenge	[redacted]	White	Teduglutide 0.15 Mg/Kg/Day With Bid Rechallenge	Female	4[redacted]	消化管ストーマ合併症	7	18	Related	Mild	Not Serious	None	Recovered/Resolved
						末梢性浮腫	14	8	Related	Mild	Not Serious	None	Recovered/Resolved
						消化管ストーマ合併症	185	21	Related	Mild	Not Serious	None	Recovered/Resolved
						頭痛	185	1	Not Related	Mild	Not Serious	None	Recovered/Resolved
						食欲減退	189	1	Not Related	Mild	Not Serious	None	Recovered/Resolved
						医療機器変更	192	4	Not Related	Mild	Serious	None	Recovered/Resolved

* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-14-ae-sae-92001.sas

Output Generated On: 21OCT2016 1:00

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	Caucasian	Placebo	Female	2[redacted]	注射部位出血	9	4	Related	Mild	Not Serious	None	Resolved
						鼻漏	34	.	Not Related	Mild	Not Serious	None	Resolved
						疲労	42	.	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル敗血症	45	15	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル合併症	46	14	Not Related	Severe	Serious	None	Resolved
						カテーテル敗血症	90	5	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル敗血症	149	20	Not Related	Severe	Serious	Study Drug Discontinued	Resolved
Placebo	[redacted]	Caucasian	Placebo	Female	7[redacted]	発熱	-83	9	Not Related	Moderate	Not Serious	None	Resolved
						高カリウム血症	-65	141	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	-51	1	Not Related	Mild	Not Serious	None	Resolved
						眼外傷	3	3	Not Related	Moderate	Not Serious	None	Severity/Frequency Increased
						眼外傷	6	2	Not Related	Severe	Serious	None	Resolved
						四肢痛	21	6	Not Related	Moderate	Not Serious	None	Resolved
						疼痛	46	1	Not Related	Moderate	Not Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	Caucasian	Placebo	Female	7[redacted]	体温上昇	49	3	Not Related	Mild	Not Serious	None	Severity/Frequency Increased
						背部痛	66	4	Not Related	Moderate	Not Serious	None	Severity/Frequency Increased
						四肢痛	66	8	Not Related	Severe	Not Serious	None	Resolved
						背部痛	70	4	Not Related	Severe	Serious	None	Resolved
						鼻出血	80	1	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	84	86	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	86	7	Not Related	Severe	Serious	None	Resolved
						椎間板炎	86	7	Not Related	Severe	Serious	None	Resolved
						カテーテル菌血症	93	59	Not Related	Moderate	Not Serious	None	Resolved
						椎間板炎	93	59	Not Related	Moderate	Not Serious	None	Resolved
						女性陰部そう痒症	101	3	Not Related	Moderate	Not Serious	None	Resolved
						過量投与	101	1	Not Related	Severe	Not Serious	None	Resolved
						皮膚乾燥	169	.	Not Related	Moderate	Not Serious	None	Ongoing
Placebo	[redacted]	Caucasian	Placebo	Female	5[redacted]	医療用具故障	19	3	Not Related	Mild	Serious	None	Resolved
						血中マグネシウム減少	92	.	Not Related	Mild	Not Serious	None	Ongoing

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	Caucasian	Placebo	Male	5[redacted]	直腸ポリープ	-33	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	85	6	Not Related	Mild	Serious	None	Resolved
Placebo	[redacted]	Caucasian	Placebo	Female	3[redacted]	排卵痛	-9	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	-2	9	Not Related	Mild	Not Serious	None	Resolved
						低カリウム血症	2	57	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	42	16	Not Related	Moderate	Serious	None	Resolved
						排卵痛	43	1	Not Related	Moderate	Not Serious	None	Resolved
						気胸	45	6	Not Related	Moderate	Serious	None	Resolved
						鼻咽頭炎	67	4	Not Related	Mild	Not Serious	None	Resolved
						そう痒症	70	14	Not Related	Mild	Not Serious	None	Resolved
						リンパ節症	75	14	Not Related	Mild	Not Serious	None	Resolved
						圧痛	75	14	Not Related	Mild	Not Serious	None	Resolved
						低マグネシウム血症	82	4	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	3[redacted]	関節痛	.	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部膨満	-98	4	Not Related	Mild	Not Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	3[redacted]	薬物不耐性	-88	15	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	-78	5	Not Related	Mild	Not Serious	None	Resolved
						悪心	-78	5	Not Related	Mild	Not Serious	None	Resolved
						ウイルス性胃腸炎	-71	4	Not Related	Mild	Not Serious	None	Resolved
						錯感覚	-68	3	Not Related	Mild	Not Serious	None	Resolved
						骨盤痛	-14	43	Not Related	Mild	Not Serious	None	Resolved
						消化器痛	3	15	Related	Mild	Not Serious	None	Resolved
						悪心	3	15	Related	Mild	Not Serious	None	Resolved
						インフルエンザ	19	2	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	20	9	Not Related	Mild	Not Serious	None	Resolved
						紅斑性皮疹	25	1	Not Related	Mild	Not Serious	None	Resolved
						錯感覚	28	1	Not Related	Mild	Not Serious	None	Resolved
						発熱	44	7	Not Related	Mild	Serious	None	Resolved
						歯肉感染	66	1	Not Related	Mild	Not Serious	None	Resolved
						うつ病	79	.	Not Related	Mild	Not Serious	None	Ongoing

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	3[redacted]	関節痛	114	.	Not Related	Mild	Not Serious	None	Ongoing
						歯痛	115	1	Not Related	Mild	Not Serious	None	Resolved
						歯痛	122	1	Not Related	Mild	Not Serious	None	Resolved
						注射部位腫脹	129	1	Related	Mild	Not Serious	None	Resolved
						尿路感染	151	10	Not Related	Mild	Not Serious	None	Resolved
						斑状皮疹	154	2	Not Related	Mild	Not Serious	None	Resolved
						創傷	160	1	Not Related	Mild	Not Serious	None	Resolved
						関節痛	160	1	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	副鼻腔炎	-84	8	Not Related	Mild	Not Serious	None	Resolved
						関節痛	-75	1	Not Related	Mild	Not Serious	None	Resolved
						頭痛	-71	24	Not Related	Mild	Not Serious	None	Resolved
						背部痛	-61	5	Not Related	Severe	Not Serious	None	Resolved
						発熱	-61	1	Not Related	Mild	Not Serious	None	Resolved
						疼痛	-56	9	Not Related	Severe	Not Serious	None	Resolved
						悪心	-56	1	Not Related	Mild	Not Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	挫傷	-41	13	Not Related	Severe	Not Serious	None	Resolved
						鼻咽頭炎	-19	3	Not Related	Mild	Not Serious	None	Resolved
						腸管ストーマ合併症	1	.	Related	Mild	Not Serious	None	Ongoing
						腹痛	1	.	Related	Mild	Not Serious	None	Ongoing
						食欲不振	1	.	Related	Mild	Not Serious	None	Ongoing
						腹部膨満	1	16	Related	Severe	Not Serious	None	Resolved
						悪心	1	.	Related	Mild	Not Serious	None	Ongoing
						咽喉頭疼痛	2	4	Not Related	Mild	Not Serious	None	Resolved
						注射部位挫傷	26	.	Related	Mild	Not Serious	None	Ongoing
						浮動性めまい	47	5	Not Related	Mild	Not Serious	None	Resolved
						四肢損傷	52	1	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	54	3	Not Related	Mild	Not Serious	None	Resolved
						皮膚裂傷	91	1	Not Related	Mild	Not Serious	None	Resolved
						急性胆嚢炎	103	2	Not Related	Severe	Not Serious	None	Severity/Frequency Increased
						胆嚢穿孔	103	2	Not Related	Severe	Not Serious	None	Severity/Frequency Increased

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version[redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	急性胆嚢炎	105	10	Not Related	Severe	Serious	None	Resolved
						胆嚢穿孔	105	10	Not Related	Severe	Serious	None	Resolved
						術後感染	106	15	Not Related	Moderate	Not Serious	None	Resolved
						処置後痛	106	22	Not Related	Moderate	Not Serious	None	Resolved
						頭痛	147	.	Not Related	Mild	Not Serious	None	Ongoing
						小腸閉塞	156	8	Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						腹痛	163	8	Related	Mild	Not Serious	None	Resolved
						疲労	168	1	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	2[redacted]	腹痛	-22	3	Not Related	Mild	Not Serious	None	Resolved
						下痢	-21	8	Not Related	Severe	Not Serious	None	Resolved
						発疹	55	66	Not Related	Mild	Not Serious	None	Resolved
						伝染性単核症	.	.	Not Related	Moderate	Serious	None	Resolved
						頭痛	62	.	Not Related	Mild	Not Serious	None	Ongoing
						胃腸不快感	70	.	Not Related	Moderate	Not Serious	Study Drug Dose Interrupted	Ongoing
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	嘔吐	-8	5	Not Related	Mild	Not Serious	None	Resolved

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Note: All adverse events were coded using MedDRA version [redacted].
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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	胸痛	-5	.	Not Related	Mild	Not Serious	None	Resolved
						背部痛	-5	.	Not Related	Mild	Not Serious	None	Resolved
						悪心	2	2	Not Related	Mild	Not Serious	None	Resolved
						白血球数増加	2	8	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	3	.	Not Related	Mild	Not Serious	None	Resolved
						上腹部痛	10	.	Not Related	Moderate	Not Serious	None	Resolved
						下腹部痛	10	.	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	24	1	Not Related	Mild	Not Serious	None	Resolved
						肋骨脊柱角圧痛	26	1	Not Related	Moderate	Not Serious	None	Resolved
						下腹部痛	26	1	Not Related	Moderate	Not Serious	None	Resolved
						下腹部痛	58	1	Not Related	Moderate	Not Serious	None	Resolved
						胸痛	69	1	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	81	2	Not Related	Severe	Not Serious	None	Resolved
						腹痛	86	5	Not Related	Severe	Not Serious	Study Drug Dose Interrupted	Resolved
						無力症	132	7	Not Related	Moderate	Not Serious	None	Resolved

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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	短小腸症候群	157	42	Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						痔出血	159	3	Related	Moderate	Serious	Study Drug Discontinued	Resolved
						痔核	159	3	Not Related	Moderate	Not Serious	None	Resolved
						血中カリウム減少	202	3	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	カテーテル敗血症	10	4	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						尿路感染	10	4	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル菌血症	10	4	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						尿路感染	16	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル敗血症	16	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル菌血症	16	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						ヘマトクリット減少	50	.	Not Related	Moderate	Not Serious	None	Ongoing
						ヘモグロビン減少	50	.	Not Related	Moderate	Not Serious	None	Ongoing
						頭痛	61	.	Not Related	Moderate	Not Serious	None	Ongoing
						敗血症	87	11	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						尿路感染	87	11	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved

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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	髄膜炎	87	11	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						尿路感染	117	9	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル敗血症	117	9	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						真菌血症	161	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						敗血症	161	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						発熱	161	13	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	浮動性めまい	-37	1	Not Related	Mild	Not Serious	None	Resolved
						便秘	3	59	Related	Moderate	Not Serious	Study Drug Discontinued	Resolved
						鼻咽頭炎	40	4	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	52	8	Not Related	Severe	Serious	None	Resolved
						カテーテル敗血症	60	3	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル敗血症	117	11	Not Related	Severe	Serious	None	Resolved
						カテーテル敗血症	173	14	Not Related	Moderate	Serious	None	Resolved
						カテーテル敗血症	194	11	Not Related	Moderate	Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	鉄欠乏性貧血	.	.	Not Related	Mild	Not Serious	None	Ongoing

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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	注射部位紅斑	4	2	Related	Mild	Not Serious	None	Resolved
						関節痛	32	82	Not Related	Mild	Not Serious	None	Resolved
						腹部不快感	51	1	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	51	1	Not Related	Mild	Not Serious	None	Resolved
						紅斑	55	31	Related	Mild	Not Serious	None	Resolved
						紅斑	61	25	Not Related	Mild	Not Serious	None	Resolved
						齲歯	.	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部不快感	94	1	Not Related	Mild	Not Serious	None	Resolved
						関節痛	140	.	Not Related	Mild	Not Serious	None	Resolved
						頭痛	142	1	Not Related	Mild	Not Serious	None	Resolved
						胆嚢炎	143	3	Related	Moderate	Not Serious	None	Resolved
						胆嚢炎	145	9	Related	Severe	Serious	None	Resolved
						胆嚢炎	153	15	Related	Mild	Serious	None	Resolved
Teduglutide 0.05	[redacted]	Black	0.05 mg/kg/day	Female	5[redacted]	錯感覚	-60	62	Not Related	Mild	Not Serious	None	Resolved
						咳嗽	1	.	Not Related	Mild	Not Serious	None	Resolved

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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Black	0.05 mg/kg/day	Female	5[redacted]	カテーテル留置部位感染	51	27	Not Related	Moderate	Serious	None	Resolved
						無力症	84	29	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	6[redacted]	転倒	-11	1	Not Related	Mild	Not Serious	None	Resolved
						薬物濃度増加	.	.	Related	Severe	Serious	Study Drug Discontinued	Resolved
						過眠症	8	3	Related	Severe	Serious	Study Drug Discontinued	Resolved
						昏睡	10	7	Related	Moderate	Serious	Study Drug Discontinued	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	4[redacted]	皮膚裂傷	-7	1	Not Related	Mild	Not Serious	None	Resolved
						失神	-7	1	Not Related	Mild	Not Serious	None	Resolved
						脱水	-7	1	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	-3	32	Not Related	Mild	Not Serious	None	Resolved
						悪心	1	7	Related	Mild	Not Serious	None	Resolved
						心拍数増加	16	2	Not Related	Mild	Serious	None	Resolved
						不安	16	.	Not Related	Mild	Not Serious	None	Ongoing
						浮動性めまい	16	2	Not Related	Mild	Serious	None	Resolved
						頻脈	35	50	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	4[redacted]	咳嗽	40	10	Not Related	Moderate	Not Serious	None	Resolved
						肺炎	57	10	Not Related	Mild	Not Serious	None	Resolved
						悪心	67	.	Not Related	Mild	Not Serious	None	Resolved
						悪心	84	29	Not Related	Mild	Not Serious	None	Resolved
						筋痙攣	.	.	Not Related	Mild	Not Serious	None	Resolved
						胸壁痛	109	.	Not Related	Mild	Not Serious	None	Ongoing
						血中マグネシウム減少	112	3	Not Related	Mild	Not Serious	None	Resolved
						腹痛	137	15	Related	Moderate	Not Serious	Study Drug Dose Interrupted	Resolved
						肺炎	150	10	Not Related	Mild	Not Serious	None	Resolved
						腹痛	152	3	Related	Moderate	Serious	None	Resolved
						腹痛	155	.	Not Related	Moderate	Not Serious	None	Ongoing
						肺炎	161	10	Not Related	Mild	Not Serious	None	Resolved
						肺炎	180	8	Not Related	Mild	Serious	None	Resolved
						胸痛	180	2	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	尿路感染	-75	10	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	血中マグネシウム減少	-61	.	Not Related	Mild	Not Serious	None	Ongoing
						不安	-51	.	Not Related	Mild	Not Serious	None	Ongoing
						血中マグネシウム減少	-51	.	Not Related	Mild	Not Serious	None	Ongoing
						カルシウム欠乏	-51	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル敗血症	-49	6	Not Related	Mild	Serious	None	Resolved
						カテーテル留置	-48	1	Not Related	Mild	Not Serious	None	Resolved
						貧血	-47	1	Not Related	Mild	Not Serious	None	Resolved
						細菌感染	-44	7	Not Related	Mild	Not Serious	None	Resolved
						発熱	-29	7	Not Related	Mild	Serious	None	Resolved
						C-反応性蛋白増加	-29	7	Not Related	Mild	Serious	None	Resolved
						脱水	8	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	8	12	Not Related	Moderate	Serious	None	Resolved
						ビタミン K 欠乏	14	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	45	9	Not Related	Moderate	Serious	None	Resolved
						胃腸管瘻	85	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	カテーテル敗血症	132	8	Not Related	Moderate	Serious	None	Resolved
						ビタミン D 欠乏	142	.	Not Related	Mild	Not Serious	None	Ongoing
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	尿路感染	-34	32	Not Related	Mild	Not Serious	None	Resolved
						子宮頚部スミア異常	85	.	Not Related	Moderate	Not Serious	None	Ongoing
						うっ血性心不全	98	7	Related	Severe	Serious	Study Drug Discontinued	Resolved
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	4[redacted]	神経根炎	-105	28	Not Related	Mild	Not Serious	None	Resolved
						頭痛	-92	1	Not Related	Moderate	Not Serious	None	Resolved
						血中アルカリホスファターゼ増加	-85	.	Not Related	Moderate	Not Serious	None	Ongoing
						発疹	-53	4	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	1	28	Not Related	Moderate	Serious	None	Resolved
						ウイルス性上気道感染	103	7	Not Related	Moderate	Not Serious	None	Resolved
						膵炎	113	.	Not Related	Moderate	Serious	None	Ongoing
						アラニン・アミノトランスフェラーゼ増加	113	37	Not Related	Moderate	Not Serious	None	Resolved
						膵感染	145	13	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	4[redacted]	耐糖能障害	147	.	Not Related	Moderate	Not Serious	None	Ongoing
						血中ブドウ糖増加	147	.	Not Related	Moderate	Not Serious	None	Ongoing
						プレアルブミン減少	149	.	Not Related	Mild	Not Serious	None	Ongoing
						C-反応性蛋白増加	149	.	Not Related	Mild	Not Serious	None	Ongoing
						プレアルブミン減少	149	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	168	8	Not Related	Moderate	Not Serious	None	Resolved
						結腸狭窄	176	10	Not Related	Moderate	Serious	None	Resolved
						医療用具合併症	177	.	Not Related	Moderate	Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	7[redacted]	注射部位挫傷	2	.	Related	Mild	Not Serious	None	Ongoing
						注射部位反応	2	1	Not Related	Mild	Not Serious	None	Resolved
						挫傷	.	.	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	93	10	Not Related	Mild	Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	痔核	-65	.	Not Related	Mild	Not Serious	None	Ongoing
						発疹	-65	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル敗血症	-62	2	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	カテーテル敗血症	-60	8	Not Related	Moderate	Serious	None	Resolved
						低カルシウム血症	-56	1	Not Related	Mild	Not Serious	None	Resolved
						単純ヘルペス	-31	3	Not Related	Mild	Not Serious	None	Resolved
						羞明	6	.	Not Related	Moderate	Not Serious	None	Ongoing
						注射部位挫傷	6	8	Related	Mild	Not Serious	None	Resolved
						流涙増加	6	30	Related	Mild	Not Serious	None	Resolved
						眼の炎症	12	25	Not Related	Moderate	Not Serious	None	Resolved
						眼痛	12	25	Not Related	Moderate	Not Serious	None	Resolved
						消化不良	13	.	Not Related	Mild	Not Serious	None	Ongoing
						痔出血	18	.	Not Related	Mild	Not Serious	None	Ongoing
						感覚減退	26	1	Not Related	Mild	Not Serious	None	Resolved
						関節捻挫	28	29	Related	Mild	Not Serious	None	Resolved
						圧痛	28	29	Not Related	Mild	Not Serious	None	Resolved
						悪心	29	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部膨満	29	1	Not Related	Mild	Not Serious	None	Resolved
						下痢	29	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	嘔吐	29	.	Not Related	Mild	Not Serious	None	Ongoing
						処置後合併症	38	.	Not Related	Mild	Not Serious	None	Ongoing
						乾性角結膜炎	38	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	49	1	Not Related	Mild	Not Serious	None	Resolved
						鼓腸	50	2	Not Related	Mild	Not Serious	None	Resolved
						注射部位挫傷	51	.	Related	Mild	Not Serious	None	Ongoing
						咽喉頭疼痛	54	1	Not Related	Mild	Not Serious	None	Resolved
						感覚減退	78	1	Not Related	Mild	Not Serious	None	Resolved
						痔核	102	1	Not Related	Moderate	Not Serious	None	Resolved
						錯感覚	113	1	Not Related	Mild	Not Serious	None	Resolved
						咳嗽	116	7	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	146	1	Not Related	Mild	Not Serious	None	Resolved
						筋痙縮	146	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部ヘルニア	169	.	Related	Mild	Not Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	尿路感染	-15	23	Not Related	Moderate	Not Serious	None	Resolved

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Note: All adverse events were coded using MedDRA version [redacted].
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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	浮腫	.	.	Related	Moderate	Not Serious	None	Resolved
						医療用具故障	36	2	Not Related	Mild	Serious	None	Resolved
						腹痛	50	.	Not Related	Moderate	Not Serious	None	Resolved
						悪心	54	.	Not Related	Mild	Not Serious	None	Ongoing
						ストーマ部反応	62	.	Related	Moderate	Not Serious	None	Resolved
						うつ病	.	.	Not Related	Mild	Not Serious	None	Ongoing
						腸管ストーマ合併症	.	.	Related	Moderate	Not Serious	None	Resolved
						疼痛	.	.	Related	Mild	Not Serious	None	Resolved
						尿路感染	94	29	Not Related	Moderate	Not Serious	None	Resolved
						関節腫脹	108	.	Not Related	Moderate	Not Serious	None	Ongoing
						高血圧	146	.	Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	ウイルス性胃腸炎	-65	27	Not Related	Moderate	Not Serious	None	Resolved
						卵巣嚢胞	-49	.	Not Related	Moderate	Not Serious	None	Ongoing
						小腸閉塞	8	3	Related	Severe	Serious	Study Drug Discontinued	Resolved
						膵炎	8	68	Related	Moderate	Not Serious	Study Drug Discontinued	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version [redacted].
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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	インフルエンザ	34	11	Not Related	Moderate	Not Serious	None	Resolved
						咽喉頭疼痛	74	.	Not Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	関節痛	-14	29	Not Related	Moderate	Not Serious	None	Resolved
						鼡径部痛	-14	29	Not Related	Moderate	Not Serious	None	Resolved
						注射部位紅斑	9	1	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	11	34	Related	Moderate	Not Serious	None	Resolved
						腹部不快感	11	118	Related	Moderate	Not Serious	None	Resolved
						腹部圧痛	11	118	Related	Moderate	Not Serious	None	Resolved
						悪心	11	34	Related	Moderate	Not Serious	None	Resolved
						食欲減退	11	34	Related	Moderate	Not Serious	None	Resolved
						筋痙攣	14	2	Not Related	Moderate	Not Serious	None	Resolved
						疲労	29	.	Related	Mild	Not Serious	None	Resolved
						腸管閉塞	49	2	Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						悪心	.	.	Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	83	38	Not Related	Mild	Not Serious	None	Resolved

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Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	薬物不耐性	99	8	Not Related	Moderate	Not Serious	None	Resolved
						下痢	99	8	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	138	5	Related	Moderate	Not Serious	None	Resolved
						悪心	138	5	Related	Moderate	Not Serious	None	Resolved
						腹部不快感	138	5	Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	153	12	Not Related	Moderate	Not Serious	None	Resolved
						γ－グルタミルトランスフェラーゼ増加	175	.	Related	Mild	Not Serious	None	Ongoing
						血中アルカリホスファターゼ増加	175	.	Related	Mild	Not Serious	None	Ongoing
						膀胱不快感	384	.	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	気管支炎	-53	.	Not Related	Mild	Not Serious	None	Ongoing
						注射部位疼痛	1	1	Related	Mild	Not Serious	None	Resolved
						カテーテル関連感染	56	59	Not Related	Mild	Serious	None	Resolved
						関節痛	168	8	Not Related	Mild	Not Serious	None	Resolved
						頭痛	168	.	Not Related	Mild	Not Serious	None	Ongoing
						無力症	169	.	Not Related	Mild	Not Serious	None	Ongoing

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Note: All adverse events were coded using MedDRA version [redacted].
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	易刺激性	169	2	Not Related	Moderate	Not Serious	None	Resolved
						静脈穿刺部位挫傷	169	.	Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	腸管ポリープ	-21	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	29	4	Not Related	Severe	Serious	None	Resolved
						関節痛	29	.	Not Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	2[redacted]	尿路感染	36	7	Not Related	Mild	Not Serious	None	Resolved
						悪心	40	13	Related	Moderate	Not Serious	Study Drug Dose Interrupted	Resolved
						嘔吐	40	13	Related	Moderate	Not Serious	Study Drug Dose Interrupted	Resolved
						プレアルブミン減少	64	26	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	77	8	Not Related	Mild	Serious	None	Resolved
						非心臓性胸痛	79	2	Not Related	Mild	Not Serious	None	Resolved
						貧血	80	2	Not Related	Mild	Not Serious	None	Resolved
						四肢痛	81	4	Not Related	Mild	Not Serious	None	Resolved
						四肢痛	85	5	Not Related	Mild	Serious	None	Resolved
						四肢痛	89	4	Not Related	Mild	Not Serious	None	Resolved

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Note: All adverse events were coded using MedDRA version [redacted].
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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	2[redacted]	カテーテル敗血症	126	13	Not Related	Mild	Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	インフルエンザ	-7	1	Not Related	Mild	Not Serious	None	Resolved
						気管支炎	2	6	Not Related	Mild	Not Serious	None	Severity/Frequency Increased
						気管支炎	7	2	Not Related	Moderate	Serious	None	Resolved
						腸管ストーマ合併症	84	2	Not Related	Moderate	Serious	None	Resolved
						腹痛	113	.	Not Related	Moderate	Not Serious	None	Ongoing
						カテーテル敗血症	118	11	Not Related	Mild	Serious	None	Resolved
						口腔真菌感染	120	8	Not Related	Mild	Not Serious	None	Resolved
						アレルギー性皮膚炎	127	2	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	3[redacted]	腸管ポリープ	-38	21	Not Related	Mild	Serious	None	Resolved
						カテーテル合併症	-30	8	Not Related	Moderate	Serious	None	Resolved
						カテーテル合併症	80	3	Not Related	Mild	Serious	None	Resolved
						背部痛	.	.	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	99	6	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	113	29	Not Related	Mild	Not Serious	None	Resolved

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Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	カテーテル合併症	-36	3	Not Related	Mild	Serious	None	Resolved
						カテーテル合併症	4	5	Not Related	Mild	Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	頭痛	-108	2	Not Related	Severe	Not Serious	None	Resolved
						脂肪肝	-105	172	Not Related	Moderate	Serious	None	Resolved
						関節痛	-84	1	Not Related	Moderate	Not Serious	None	Resolved
						ウイルス性上気道感染	-84	3	Not Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	133	5	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	3[redacted]	血中アルカリホスファターゼ増加	-64	99	Not Related	Mild	Not Serious	None	Resolved
						倦怠感	-31	6	Not Related	Moderate	Not Serious	None	Resolved
						下痢	-31	6	Not Related	Moderate	Not Serious	None	Resolved
						吻合部潰瘍	.	.	Not Related	Moderate	Not Serious	None	Ongoing
						小腸狭窄	1	.	Not Related	Moderate	Not Serious	None	Ongoing
						C-反応性蛋白増加	1	36	Not Related	Mild	Not Serious	None	Resolved
						腸管ストーマ合併症	2	63	Related	Mild	Not Serious	None	Resolved

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Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	3[redacted]	腹痛	23	3	Not Related	Moderate	Not Serious	None	Resolved
						水様便	23	3	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル敗血症	39	13	Not Related	Severe	Serious	Study Drug Discontinued	Resolved
						カテーテル留置部位出血	47	.	Not Related	Mild	Not Serious	None	Ongoing
						静脈カテーテル留置	61	3	Not Related	Moderate	Serious	None	Resolved

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Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-6-ae-sae-600004.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	5[redacted]	ヘマトクリット減少	-73	38	Not Related	Mild	Not Serious	None	Resolved
						敗血症	-64	17	Not Related	Severe	Serious	None	Resolved
						血中カリウム減少	-62	2	Not Related	Mild	Not Serious	None	Resolved
						血中トリグリセリド増加	-50	65	Not Related	Mild	Not Serious	None	Resolved
						血中アミラーゼ増加	-50	8	Not Related	Mild	Not Serious	None	Resolved
						血中コレステロール増加	-43	58	Not Related	Mild	Not Serious	None	Resolved
						尿中白血球エステラーゼ陽性	-43	36	Not Related	Mild	Not Serious	None	Resolved
						蜂巣炎	-37	6	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	-22	10	Not Related	Mild	Not Serious	None	Resolved
						口腔咽頭痛	1	14	Not Related	Mild	Not Serious	None	Resolved
						血中カルシウム減少	14	15	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位分泌物	56	29	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	56	29	Not Related	Mild	Not Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	5[redacted]	ラ音	56	29	Not Related	Mild	Not Serious	None	Resolved
						尿中白血球エステラーゼ陽性	56	29	Not Related	Mild	Not Serious	None	Resolved
						血中トリグリセリド増加	56	.	Not Related	Mild	Not Serious	None	Ongoing
						血中コレステロール増加	84	29	Not Related	Mild	Not Serious	None	Resolved
						血中アミラーゼ増加	84	29	Not Related	Mild	Not Serious	None	Resolved
						血中ビリルビン減少	84	29	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位関連反応	112	31	Not Related	Mild	Not Serious	None	Resolved
						尿中白血球陽性	112	31	Not Related	Mild	Not Serious	None	Resolved
						尿中白血球エステラーゼ陽性	112	31	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位関連反応	112	31	Not Related	Mild	Not Serious	None	Resolved
						ヘマトクリット減少	112	31	Not Related	Mild	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Female	3[redacted]	関節痛	20	16	Not Related	Moderate	Not Serious	None	Resolved
						尿路感染	40	9	Not Related	Mild	Serious	None	Resolved
						カテーテル関連感染	83	11	Not Related	Moderate	Serious	None	Resolved

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	3[redacted]	腹痛	148	.	Not Related	Moderate	Not Serious	None	Ongoing
Placebo	[redacted]	White	Placebo	Male	2[redacted]	菌血症	8	13	Not Related	Moderate	Serious	None	Resolved
						肛門カンジダ症	13	.	Not Related	Mild	Not Serious	None	Ongoing
						回転性めまい	19	2	Not Related	Mild	Not Serious	None	Resolved
						低カリウム血症	20	1	Not Related	Moderate	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Female	6[redacted]	尿路感染	-68	22	Not Related	Moderate	Not Serious	None	Resolved
						気管支炎	51	9	Not Related	Moderate	Not Serious	None	Resolved
						菌血症	101	9	Not Related	Moderate	Serious	None	Resolved
						体重減少	112	.	Not Related	Mild	Not Serious	None	Ongoing
Placebo	[redacted]	White	Placebo	Male	5[redacted]	敗血症	-30	8	Not Related	Severe	Serious	None	Resolved
						中心静脈カテーテル感染	-22	9	Not Related	Moderate	Not Serious	None	Resolved
						体重増加	12	.	Related	Mild	Not Serious	None	Ongoing
						筋痙縮	24	.	Not Related	Mild	Not Serious	None	Ongoing
						消化管ストーマ合併症	26	.	Related	Mild	Not Serious	None	Ongoing

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

reatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Male	5[redacted]	鉄欠乏	36	.	Not Related	Mild	Not Serious	None	Ongoing
						頭痛	37	26	Not Related	Mild	Not Serious	None	Resolved
						上気道感染	79	20	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	92	1	Not Related	Mild	Not Serious	None	Resolved
						肺炎	164	.	Not Related	Mild	Not Serious	None	Ongoing
Placebo	[redacted]	White	Placebo	Male	6[redacted]	腹痛	2	1	Related	Mild	Not Serious	None	Resolved
						体重増加	28	29	Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	65	8	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						中心静脈カテーテル感染	73	11	Not Related	Mild	Not Serious	None	Resolved
						蜂巣炎	106	14	Not Related	Mild	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Male	2[redacted]	鼻咽頭炎	-24	18	Not Related	Mild	Not Serious	None	Resolved
						坐骨神経痛	-22	21	Not Related	Moderate	Not Serious	None	Resolved
						感覚鈍麻	15	12	Not Related	Mild	Not Serious	None	Resolved
						注射部位発疹	26	8	Related	Mild	Not Serious	None	Resolved

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Male	2[redacted]	直腸分泌物	26	39	Related	Moderate	Not Serious	None	Resolved
						腹痛	36	29	Related	Moderate	Not Serious	None	Resolved
						悪心	36	29	Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	36	36	Related	Moderate	Not Serious	None	Resolved
						発熱	42	23	Related	Mild	Not Serious	None	Resolved
						頭痛	42	23	Related	Moderate	Not Serious	None	Resolved
						便量増加	42	23	Related	Moderate	Not Serious	Study Drug Discontinued	Resolved
						疼痛	42	23	Related	Moderate	Not Serious	None	Resolved
						嗜眠	50	15	Related	Moderate	Not Serious	None	Resolved
						体重減少	50	15	Related	Moderate	Not Serious	None	Resolved
						中心静脈カテーテル感染	75	3	Not Related	Severe	Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Male	7[redacted]	腹部膨満	5	6	Not Related	Mild	Not Serious	None	Resolved
						歯膿瘍	5	25	Not Related	Severe	Not Serious	None	Resolved
						腹部膨満	36	7	Not Related	Severe	Not Serious	None	Resolved

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Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Male	7[redacted]	腎結石症	54	1	Not Related	Mild	Not Serious	None	Resolved
						腎結石症	70	1	Not Related	Mild	Not Serious	None	Resolved
						代謝性アシドーシス	71	11	Not Related	Mild	Not Serious	None	Resolved
						背部痛	80	2	Not Related	Moderate	Not Serious	None	Resolved
						肺損傷	139	.	Not Related	Mild	Not Serious	None	Ongoing
						頚椎骨折	139	34	Not Related	Mild	Not Serious	None	Resolved
						開放創	139	13	Not Related	Moderate	Not Serious	None	Resolved
						転倒・転落	139	5	Not Related	Severe	Serious	None	Resolved
						肋骨骨折	139	.	Not Related	Severe	Not Serious	None	Ongoing
						γ-グルタミルトランスフェラーゼ増加	151	26	Not Related	Moderate	Not Serious	None	Resolved
						胸水	164	.	Not Related	Severe	Serious	None	Ongoing
						体重減少	176	.	Not Related	Moderate	Not Serious	None	Ongoing
Placebo	[redacted]	White	Placebo	Female	4[redacted]	表在性血栓性静脈炎	-41	15	Not Related	Moderate	Not Serious	None	Resolved
						眼瞼浮腫	-10	3	Not Related	Moderate	Not Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	4[redacted]	鼻出血	-7	1	Not Related	Moderate	Not Serious	None	Resolved
						異常高熱	-4	2	Not Related	Moderate	Not Serious	None	Resolved
						鼻出血	3	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻出血	5	1	Not Related	Moderate	Not Serious	None	Resolved
						便量減少	6	.	Not Related	Moderate	Not Serious	None	Ongoing
						悪心	6	6	Not Related	Moderate	Not Serious	None	Resolved
						抱合ビリルビン増加	15	.	Not Related	Moderate	Not Serious	None	Ongoing
						黄疸眼	15	.	Not Related	Mild	Not Serious	None	Ongoing
						異常高熱	28	1	Not Related	Moderate	Not Serious	None	Resolved
						片頭痛	29	.	Not Related	Severe	Not Serious	None	Ongoing
						眼窩周囲浮腫	29	90	Not Related	Severe	Not Serious	None	Resolved
						末梢性浮腫	35	1	Not Related	Mild	Not Serious	None	Resolved
						粘膜擦過傷	36	8	Not Related	Mild	Not Serious	None	Resolved
						血中ビリルビン増加	43	.	Not Related	Moderate	Not Serious	None	Ongoing

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Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	4[redacted]	嘔吐	44	75	Not Related	Moderate	Not Serious	None	Resolved
						悪心	44	75	Not Related	Moderate	Not Serious	None	Resolved
						脱水	49	7	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	55	2	Not Related	Moderate	Not Serious	None	Resolved
						体重増加	55	6	Not Related	Moderate	Not Serious	None	Resolved
						異常高熱	59	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻出血	60	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻出血	80	1	Not Related	Moderate	Not Serious	None	Resolved
						口渇	83	10	Not Related	Moderate	Not Serious	None	Resolved
						γ－グルタミルトランスフェラーゼ増加	85	.	Not Related	Moderate	Not Serious	None	Ongoing
						血中アルカリホスファターゼ増加	85	.	Not Related	Moderate	Not Serious	None	Ongoing
						鼻出血	85	1	Not Related	Moderate	Not Serious	None	Resolved
						アスパラギン酸アミノトランスフェラーゼ増加	85	81	Not Related	Moderate	Not Serious	None	Resolved
						アラニン・アミノトランスフェラーゼ増加	85	81	Not Related	Moderate	Not Serious	None	Resolved

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	4[redacted]	体重減少	85	8	Not Related	Severe	Not Serious	None	Resolved
						血小板数減少	85	.	Not Related	Moderate	Not Serious	None	Ongoing
						口渇	103	15	Not Related	Moderate	Not Serious	None	Resolved
						医療機器破損	112	10	Not Related	Moderate	Serious	None	Resolved
						体重減少	117	29	Not Related	Moderate	Not Serious	None	Resolved
						上腹部痛	117	39	Not Related	Moderate	Not Serious	None	Resolved
						肝硬変	118	.	Not Related	Severe	Not Serious	None	Ongoing
						悪心	118	.	Related	Mild	Not Serious	None	Ongoing
						平滑筋抗体陽性	120	.	Not Related	Moderate	Not Serious	None	Ongoing
						貧血	124	22	Not Related	Moderate	Not Serious	None	Resolved
						医療機器位置異常	129	1	Not Related	Severe	Not Serious	None	Resolved
						カテーテル留置部位出血	133	1	Not Related	Severe	Not Serious	None	Resolved
						カテーテル留置部位出血	139	1	Not Related	Severe	Not Serious	None	Resolved
						胆汁うっ滞性肝炎	146	.	Not Related	Severe	Serious	None	Ongoing

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	4[redacted]	医療機器位置異常	146	10	Not Related	Moderate	Serious	None	Resolved
						眼瞼浮腫	161	2	Not Related	Mild	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Female	4[redacted]	口渇	-62	35	Not Related	Mild	Not Serious	None	Resolved
						上腹部痛	-42	15	Not Related	Mild	Not Serious	None	Resolved
						疲労	-42	15	Not Related	Mild	Not Serious	None	Resolved
						悪心	-42	15	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	-42	15	Not Related	Mild	Not Serious	None	Resolved
						頭痛	-42	15	Not Related	Mild	Not Serious	None	Resolved
						下痢	-31	3	Not Related	Mild	Not Serious	None	Resolved
						口腔咽頭痛	-23	10	Not Related	Mild	Not Serious	None	Resolved
						咳嗽	-23	10	Not Related	Mild	Not Serious	None	Resolved
						頭痛	-23	10	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	-23	12	Not Related	Mild	Not Serious	None	Resolved
						発熱	-21	8	Not Related	Mild	Not Serious	None	Resolved

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Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	4[redacted]	中心静脈カテーテル感染	-16	5	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	-9	1	Not Related	Mild	Not Serious	None	Resolved
						食欲減退	-9	6	Not Related	Mild	Not Serious	None	Resolved
						下痢	-9	6	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	-9	6	Not Related	Mild	Not Serious	None	Resolved
						腹痛	-9	6	Not Related	Moderate	Not Serious	None	Resolved
						発熱	-8	2	Not Related	Mild	Not Serious	None	Resolved
						鼓腸	4	21	Related	Moderate	Not Serious	None	Resolved
						肛門周囲痛	4	26	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	4	21	Related	Moderate	Not Serious	None	Resolved
						排便回数増加	4	21	Related	Moderate	Not Serious	Study Drug Discontinued	Resolved
						筋骨格痛	17	.	Not Related	Moderate	Not Serious	None	Ongoing
						インフルエンザ性肺炎	36	15	Not Related	Severe	Serious	None	Resolved
						副鼻腔炎	36	15	Not Related	Moderate	Not Serious	None	Resolved

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Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Male	1[redacted]	不安	-35	37	Not Related	Mild	Serious	None	Resolved
						呼吸困難	-35	31	Not Related	Mild	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Male	8[redacted]	中心静脈カテーテル感染	-32	19	Not Related	Severe	Serious	None	Resolved
						大腸穿孔	-26	14	Not Related	Severe	Serious	None	Resolved
						赤血球数減少	-24	12	Not Related	Severe	Not Serious	None	Resolved
						医療機器不具合	153	2	Not Related	Moderate	Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Female	7[redacted]	腹痛	1	16	Related	Mild	Not Serious	None	Resolved
						注射部位変色	4	.	Related	Mild	Not Serious	None	Ongoing
						菌血症	36	9	Not Related	Severe	Serious	None	Resolved
						埋込み部位血管外漏出	56	2	Not Related	Severe	Serious	None	Resolved
						医療機器機能不全	87	15	Not Related	Severe	Serious	None	Resolved
						発熱	95	2	Not Related	Mild	Not Serious	None	Resolved
						腹痛	101	40	Not Related	Mild	Not Serious	None	Resolved
						悪心	101	40	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo	[redacted]	White	Placebo	Female	7[redacted]	下痢	101	34	Not Related	Mild	Not Serious	None	Resolved
						軟部組織感染	132	11	Not Related	Moderate	Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Male	5[redacted]	体重減少	-8	23	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	23	9	Not Related	Mild	Serious	None	Resolved
						体重減少	42	43	Not Related	Mild	Not Serious	None	Resolved
						自殺企図	43	1	Not Related	Mild	Serious	None	Resolved
						うつ病	94	.	Not Related	Mild	Not Serious	None	Ongoing
						気分変調性障害	94	.	Not Related	Mild	Not Serious	None	Ongoing
						頭痛	122	47	Related	Mild	Not Serious	None	Resolved
						筋痙縮	133	36	Not Related	Mild	Not Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Male	5[redacted]	吻合部潰瘍	-22	15	Not Related	Moderate	Not Serious	None	Resolved
						胃腸出血	-22	5	Not Related	Moderate	Serious	None	Resolved
Placebo	[redacted]	White	Placebo	Female	5[redacted]	医療機器位置異常	154	2	Not Related	Mild	Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	関節痛	-30	5	Not Related	Severe	Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	血中カリウム増加	1	15	Not Related	Mild	Not Serious	None	Resolved
						腹痛	1	31	Related	Mild	Not Serious	None	Resolved
						悪心	1	31	Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	5	27	Related	Mild	Not Serious	None	Resolved
						腹部膨満	12	11	Related	Mild	Not Serious	None	Resolved
						腹部膨満	22	10	Related	Severe	Not Serious	Study Drug Discontinued	Resolved
						嘔吐	26	3	Related	Mild	Not Serious	None	Resolved
						尿路感染	32	5	Not Related	Moderate	Serious	None	Resolved
						脱水	32	5	Not Related	Mild	Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	注射部位変色	1	15	Related	Mild	Not Serious	None	Resolved
						体重増加	2	8	Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	2	8	Related	Mild	Not Serious	None	Resolved
						呼吸困難	4	6	Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	8	.	Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	腹部膨満	29	8	Related	Mild	Not Serious	None	Resolved
						疲労	29	8	Related	Mild	Not Serious	None	Resolved
						急性胆嚢炎	30	105	Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						軽躁	78	98	Related	Moderate	Not Serious	None	Resolved
						術後創感染	102	14	Not Related	Moderate	Not Serious	None	Resolved
						創傷感染	136	40	Not Related	Mild	Not Serious	None	Resolved
						うっ血性心不全	138	4	Not Related	Mild	Not Serious	None	Resolved
						高カリウム血症	139	6	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	口腔ヘルペス	-145	11	Not Related	Mild	Not Serious	None	Resolved
						不安	-119	50	Not Related	Moderate	Not Serious	None	Resolved
						菌血症	-90	21	Not Related	Severe	Serious	None	Resolved
						細菌の過剰繁殖	11	3	Not Related	Moderate	Not Serious	None	Resolved
						細菌の過剰繁殖	30	3	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	52	62	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	悪心	52	97	Not Related	Mild	Not Serious	None	Resolved
						縫合関連合併症	56	2	Not Related	Moderate	Not Serious	None	Resolved
						不眠症	56	2	Not Related	Mild	Not Serious	None	Resolved
						バレット食道	94	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃炎	94	.	Not Related	Moderate	Not Serious	None	Ongoing
						細菌の過剰繁殖	111	3	Not Related	Moderate	Not Serious	None	Resolved
						大腸炎	112	34	Not Related	Moderate	Not Serious	None	Resolved
						口腔ヘルペス	117	2	Not Related	Mild	Not Serious	None	Resolved
						上気道うっ血	118	1	Not Related	Mild	Not Serious	None	Resolved
						細菌の過剰繁殖	126	5	Not Related	Moderate	Not Serious	None	Resolved
						不安	127	22	Not Related	Moderate	Not Serious	None	Resolved
						血中アミラーゼ増加	148	29	Not Related	Mild	Not Serious	None	Resolved
						リパーゼ増加	148	29	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	瘻孔	1	15	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	消化管ストーマ合併症	5	182	Related	Mild	Not Serious	None	Resolved
						直腸膿瘍	8	3	Not Related	Moderate	Serious	None	Resolved
						多汗症	15	72	Not Related	Mild	Not Serious	None	Resolved
						上気道感染	37	24	Not Related	Mild	Not Serious	None	Resolved
						咳嗽	37	.	Not Related	Mild	Not Serious	None	Ongoing
						疲労	43	167	Not Related	Mild	Not Serious	None	Resolved
						関節痛	46	.	Not Related	Mild	Not Serious	None	Ongoing
						関節痛	46	.	Not Related	Mild	Not Serious	None	Ongoing
						疲労	60	.	Not Related	Mild	Not Serious	None	Ongoing
						睡眠時無呼吸症候群	114	.	Not Related	Mild	Not Serious	None	Ongoing
						体重増加	143	.	Related	Severe	Not Serious	None	Ongoing
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	カテーテル敗血症	63	6	Not Related	Severe	Serious	None	Resolved
						カテーテル敗血症	69	42	Not Related	Moderate	Not Serious	None	Resolved
						埋込み部位硬結	166	.	Not Related	Moderate	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	悪心	8	77	Related	Moderate	Not Serious	None	Resolved
						注射部位紅斑	8	28	Related	Mild	Not Serious	None	Resolved
						腹痛	13	1	Related	Moderate	Not Serious	None	Resolved
						潮紅	98	.	Related	Moderate	Not Serious	None	Ongoing
						カテーテル関連感染	155	7	Not Related	Moderate	Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	腹壁血腫	-33	63	Not Related	Mild	Not Serious	None	Resolved
						裂肛	-7	37	Not Related	Mild	Not Serious	None	Resolved
						腹壁血腫	1	29	Not Related	Mild	Not Serious	None	Resolved
						アデノウイルス感染	31	10	Not Related	Moderate	Serious	None	Resolved
						鼓腸	114	63	Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	鼓腸	5	111	Related	Moderate	Not Serious	None	Resolved
						咽頭炎	100	16	Not Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	100	16	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	148	10	Not Related	Mild	Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	不眠症	149	3	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	鼻咽頭炎	-69	9	Not Related	Mild	Not Serious	None	Resolved
						医療機器位置異常	-56	1	Not Related	Moderate	Not Serious	None	Resolved
						悪心	-55	3	Not Related	Moderate	Not Serious	None	Resolved
						鼓腸	6	.	Related	Mild	Not Serious	None	Ongoing
						悪心	9	3	Not Related	Moderate	Not Serious	None	Resolved
						疲労	34	77	Not Related	Moderate	Not Serious	None	Resolved
						悪心	70	41	Not Related	Mild	Not Serious	None	Resolved
						脱水	79	11	Not Related	Mild	Not Serious	None	Resolved
						カテーテル関連感染	99	28	Not Related	Moderate	Serious	None	Resolved
						発熱	152	2	Not Related	Moderate	Not Serious	None	Resolved
						鼻炎	167	.	Not Related	Moderate	Not Serious	None	Ongoing
						腹痛	167	.	Not Related	Mild	Not Serious	None	Ongoing
						心電図 QT 延長	168	.	Related	Mild	Not Serious	None	Ongoing

Continued next page

* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	鼻咽頭炎	-84	57	Not Related	Moderate	Not Serious	None	Resolved
						背部痛	-84	57	Not Related	Moderate	Not Serious	None	Resolved
						発熱	-8	122	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	21	44	Not Related	Moderate	Not Serious	None	Resolved
						注射部位血腫	39	4	Related	Mild	Not Serious	None	Resolved
						坐骨神経痛	57	.	Not Related	Severe	Not Serious	None	Ongoing
						腹痛	66	42	Not Related	Mild	Not Serious	None	Resolved
						悪心	66	42	Not Related	Mild	Not Serious	None	Resolved
						夜間頻尿	134	21	Not Related	Mild	Not Serious	None	Resolved
						呼吸困難	134	21	Not Related	Mild	Not Serious	None	Resolved
						埋込み部位血管外漏出	153	8	Not Related	Moderate	Serious	None	Resolved
						血腫	160	.	Not Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	カテーテル合併症	-21	2	Not Related	Mild	Not Serious	None	Resolved
						インフルエンザ	57	9	Not Related	Severe	Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	医療機器破損	60	5	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	歯膿瘍	-88	12	Not Related	Mild	Not Serious	None	Resolved
						貧血	-23	2	Not Related	Severe	Serious	None	Resolved
						尿路感染	-11	19	Not Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	14	.	Related	Mild	Not Serious	None	Ongoing
						上気道感染	44	10	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	68	5	Not Related	Severe	Serious	None	Resolved
						カテーテル留置部位感染	72	20	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	73	10	Not Related	Moderate	Not Serious	None	Resolved
						小腸狭窄	120	5	Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						小腸狭窄	125	2	Related	Moderate	Not Serious	None	Resolved
						尿路感染	133	15	Not Related	Mild	Not Serious	None	Resolved
						小腸狭窄	144	6	Related	Moderate	Not Serious	None	Resolved

Continued next page

* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	尿路感染	-56	12	Not Related	Mild	Not Serious	None	Resolved
						蛋白尿	-56	.	Not Related	Mild	Not Serious	None	Ongoing
						股関節部骨折	-27	4	Not Related	Moderate	Serious	None	Resolved
						股関節部骨折	-23	60	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	1	13	Not Related	Mild	Not Serious	None	Resolved
						悪心	107	2	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	107	2	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	113	47	Not Related	Mild	Not Serious	None	Resolved
						寝汗	126	5	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	ウイルス感染	101	7	Not Related	Mild	Serious	None	Resolved
						発熱	101	7	Not Related	Mild	Not Serious	None	Resolved
						肉芽腫	167	.	Not Related	Moderate	Not Serious	None	Ongoing
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	腸管ポリープ	1	1	Not Related	Mild	Not Serious	None	Resolved
						腹痛	134	2	Not Related	Moderate	Not Serious	None	Resolved

Continued next page

* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	発熱	134	2	Not Related	Severe	Not Serious	None	Resolved
						呼吸困難	134	1	Not Related	Mild	Not Serious	None	Resolved
						肺炎	134	16	Not Related	Moderate	Serious	None	Resolved
						カテーテル関連感染	134	4	Not Related	Moderate	Serious	None	Resolved
						下痢	155	22	Not Related	Mild	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	浮動性めまい	10	29	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	51	6	Not Related	Moderate	Serious	None	Resolved
						カテーテル関連感染	114	6	Not Related	Moderate	Serious	None	Resolved
						カテーテル関連感染	119	13	Not Related	Moderate	Not Serious	None	Resolved
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	全身性浮腫	29	29	Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	87	.	Related	Mild	Not Serious	None	Ongoing
						カテーテル関連感染	91	22	Not Related	Severe	Serious	None	Resolved
						鎖骨下静脈血栓症	98	15	Not Related	Severe	Serious	None	Resolved
						中心静脈カテーテル感染	133	43	Not Related	Moderate	Serious	None	Resolved

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* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide 0.05 Mg/Kg/Day	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	感染性血栓症	133	43	Not Related	Severe	Serious	None	Resolved
						顔面浮腫	185	.	Related	Mild	Not Serious	None	Ongoing
						末梢性浮腫	185	.	Related	Mild	Not Serious	None	Ongoing

* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-4-ae-sae-600020.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	4[redacted]	注射部位挫傷	-1	5	Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	19	3	Not Related	Mild	Not Serious	None	Resolved
						血中カルシウム減少	22	21	Not Related	Mild	Not Serious	None	Resolved
						血中リン減少	22	21	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	22	21	Not Related	Severe	Serious	None	Resolved
						低カリウム血症	22	21	Related	Mild	Not Serious	None	Resolved
						血中マグネシウム減少	22	21	Not Related	Mild	Not Serious	None	Resolved
						失神	45	1	Not Related	Mild	Not Serious	None	Resolved
						食欲減退	56	3	Not Related	Mild	Not Serious	None	Resolved
						無力症	56	3	Not Related	Mild	Not Serious	None	Resolved
						交通事故	60	1	Not Related	Moderate	Not Serious	None	Resolved
						血液培養陽性	60	1	Not Related	Mild	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	4[redacted]	嘔吐	95	1	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	126	.	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	195	4	Not Related	Mild	Not Serious	None	Resolved
						背部痛	195	18	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	197	2	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	199	14	Not Related	Severe	Serious	None	Resolved
						血中マグネシウム減少	203	1	Not Related	Mild	Not Serious	None	Resolved
						膀胱不快感	225	.	Not Related	Mild	Not Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	腹痛	-170	212	Related	Severe		None	Severity/Frequency Increased
						記憶障害	.	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル敗血症	12	33	Not Related	Mild	Not Serious	None	Resolved
						先天性心房中隔欠損症	31	.	Not Related	Mild	Not Serious	None	Ongoing

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	処置後痛	35	.	Not Related	Mild	Not Serious	None	Resolved
						腹痛	41	70	Related	Moderate	Not Serious	None	Resolved
						脱水	76	.	Not Related	Mild	Not Serious	None	Ongoing
						倦怠感	89	13	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	102	9	Not Related	Mild	Not Serious	None	Resolved
						イレウス	111	5	Not Related	Moderate	Serious	Study Drug Dose Interrupted	Resolved
						カテーテル敗血症	111	5	Not Related	Moderate	Serious	Study Drug Dose Interrupted	Resolved
						低カリウム血症	114	2	Not Related	Mild	Not Serious	None	Resolved
						腹痛	116	.	Related	Mild	Not Serious	None	Ongoing
						カテーテル敗血症	116	13	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	140	3	Not Related	Mild	Not Serious	None	Resolved
						インフルエンザ	151	7	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	163	16	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	187	11	Not Related	Mild	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	カテーテル敗血症	199	9	Not Related	Mild	Not Serious	None	Severity/Frequency Increased
						カテーテル敗血症	208	10	Not Related	Moderate	Serious	None	Resolved
						カテーテル敗血症	218	.	Not Related	Moderate	Not Serious	None	Ongoing
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	6[redacted]	口渇感減少	.	.	Related	Severe		None	Resolved
						注射部位反応	-81	286	Related	Severe		None	Resolved
						尿路感染	-1	14	Not Related	Moderate	Not Serious	None	Resolved
						蕁麻疹	9	12	Not Related	Moderate	Not Serious	None	Resolved
						全身性皮疹	9	12	Not Related	Moderate	Not Serious	None	Resolved
						抜歯	20	1	Not Related	Moderate	Not Serious	None	Resolved
						低血圧	21	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位紅斑	86	54	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル留置部位そう痒感	86	54	Not Related	Moderate	Not Serious	None	Resolved
						結腸閉塞	134	1	Not Related	Mild	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	6[redacted]	カテーテル留置	139	1	Not Related	Moderate	Not Serious	None	Resolved
						結腸閉塞	179	1	Not Related	Mild	Not Serious	None	Resolved
						悪心	180	2	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位そう痒感	186	5	Not Related	Mild	Not Serious	None	Resolved
						腸管ストーマ合併症	203	13	Related	Moderate	Not Serious	None	Resolved
						腸管閉塞	205	5	Related	Severe	Serious	None	Resolved
						全身性皮疹	221	.	Not Related	Mild	Not Serious	None	Ongoing
0.05/0.05	[redacted]	Black	0.05 mg/kg/day	Male	6[redacted]	急性胆嚢炎	10	6	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						胆嚢炎	16	88	Not Related	Mild	Not Serious	None	Severity/Frequency Increased
						急性胆嚢炎	104	4	Not Related	Mild	Serious	Study Drug Dose Interrupted	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	期外収縮	25	203	Not Related	Mild	Not Serious	None	Resolved
						斑状出血	25	.	Not Related	Mild	Not Serious	None	Resolved
						痔核	117	2	Not Related	Severe	Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	インフルエンザ様疾患	121	.	Not Related	Severe	Not Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	高血糖	-165	17	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	56	6	Not Related	Moderate	Serious	Study Drug Dose Interrupted	Resolved
						クロストリジウム性大腸炎	57	5	Not Related	Mild	Serious	Study Drug Dose Interrupted	Resolved
						クロストリジウム性大腸炎	62	128	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	62	18	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	174	3	Not Related	Mild	Not Serious	None	Resolved
						悪心	174	3	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	187	4	Not Related	Moderate	Serious	Study Drug Dose Interrupted	Resolved
						低酸素症	187	1	Not Related	Mild	Not Serious	None	Resolved
						ビタミン D 欠乏	189	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	191	11	Not Related	Mild	Not Serious	None	Resolved
0.05/0.05	[redacted]	Black	0.05 mg/kg/day	Male	4[redacted]	筋痙攣	28	.	Not Related	Mild	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Black	0.05 mg/kg/day	Male	4[redacted]	腎仙痛	80	12	Not Related	Severe	Serious	Study Drug Dose Interrupted	Resolved
						抜歯	87	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位炎症	126	17	Not Related	Mild	Not Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	4[redacted]	肺炎	58	8	Not Related	Mild	Serious	None	Resolved
						肺炎	113	8	Not Related	Mild	Serious	None	Resolved
						肺炎	182	7	Not Related	Moderate	Not Serious	None	Resolved
						肺炎	189	16	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	227	3	Not Related	Mild	Not Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	6[redacted]	カテーテル敗血症	1	9	Not Related	Moderate	Serious	None	Resolved
						下痢	10	7	Not Related	Mild	Not Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	5[redacted]	カテーテル敗血症	11	15	Not Related	Mild	Serious	None	Resolved
						腹痛	29	5	Not Related	Moderate	Not Serious	Study Drug Discontinued	Resolved
						カテーテル敗血症	31	7	Not Related	Mild	Serious	None	Resolved

Continued next page

Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	3[redacted]	カテーテル合併症	78	2	Not Related	Mild	Serious	None	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	2[redacted]	頭痛	-1	.	Not Related	Moderate	Not Serious	None	Ongoing
						結腸腺腫	9	5	Not Related	Mild	Serious	Study Drug Discontinued	Resolved
0.05/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Male	4[redacted]	血中アルカリホスファターゼ増加	-266	492	Related	Severe		None	Resolved
						結腸狭窄	-6	11	Related	Severe		None	Resolved
						医療用具合併症	-5	15	Related	Severe		None	Resolved
						血中重炭酸塩減少	87	41	Not Related	Mild	Not Serious	None	Resolved
						結腸狭窄	164	1	Not Related	Moderate	Serious	None	Resolved
						腹痛	178	55	Not Related	Mild	Not Serious	None	Resolved
						体重減少	207	47	Not Related	Moderate	Not Serious	None	Resolved
						医療用具合併症	220	2	Not Related	Moderate	Serious	None	Resolved
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	8[redacted]	注射部位腫脹	28	.	Related	Mild	Not Serious	None	Ongoing
						注射部位紅斑	28	.	Related	Mild	Not Serious	None	Ongoing

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	8[redacted]	カテーテル敗血症	33	5	Not Related	Mild	Serious	None	Resolved
						発疹	.	.	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	.	.	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	.	.	Not Related	Mild	Not Serious	None	Ongoing
						頭痛	159	1	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	159	1	Not Related	Mild	Not Serious	None	Resolved
						皮膚肥厚	199	.	Related	Moderate	Not Serious	None	Ongoing
						紅斑	199	.	Related	Moderate	Not Serious	None	Ongoing
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	注射部位挫傷	-85	309	Related	Severe		None	Resolved
						カテーテル敗血症	18	13	Not Related	Mild	Not Serious	None	Resolved
						筋挫傷	38	14	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	125	13	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	170	15	Not Related	Mild	Not Serious	None	Resolved

Continued next page

Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	カテーテル敗血症	185	13	Not Related	Moderate	Serious	None	Resolved
						胸膜痛	195	3	Not Related	Mild	Not Serious	None	Resolved
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	2[redacted]	咳嗽	.	.	Not Related	Mild	Not Serious	Study Drug Discontinued	Resolved
						血尿	30	.	Not Related	Mild	Not Serious	None	Ongoing
						貧血	34	2	Not Related	Mild	Serious	None	Resolved
						嘔吐	58	36	Related	Moderate	Not Serious	Study Drug Discontinued	Resolved
						悪心	58	36	Related	Mild	Not Serious	Study Drug Discontinued	Resolved
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	腹痛	-56	85	Related	Severe		None	Severity/Frequency Increased
						医療用具故障	3	1	Not Related	Mild	Serious	None	Resolved
						腹痛	29	.	Related	Moderate	Not Serious	Study Drug Discontinued	Ongoing
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	2[redacted]	カテーテル菌血症	38	19	Not Related	Severe	Serious	None	Resolved
						真菌血症	38	19	Not Related	Severe	Serious	None	Resolved
						肝機能異常	41	14	Not Related	Severe	Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	3[redacted]	肝機能検査値異常	59	39	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	59	16	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	97	.	Not Related	Mild	Not Serious	None	Ongoing
						尿管閉塞	149	13	Not Related	Severe	Serious	None	Resolved
0.10/0.10	[redacted]	Black	0.10 mg/kg/day	Female	5[redacted]	膀胱炎	57	35	Not Related	Mild	Not Serious	None	Resolved
						腎盂腎炎	195	27	Not Related	Severe	Serious	None	Resolved
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	6[redacted]	脳血管発作	59	18	Not Related	Severe	Serious	Study Drug Discontinued	Resolved
						心房細動	60	1	Not Related	Moderate	Not Serious	None	Resolved
0.10/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	注射部位硬結	.	.	Related	Severe		None	Resolved
						腎仙痛	16	1	Not Related	Mild	Not Serious	None	Resolved
						一過性黒内障	18	1	Not Related	Moderate	Serious	Study Drug Dose Interrupted	Resolved
Placebo/0.05	[redacted]	Black	0.05 mg/kg/day	Female	5[redacted]	軟便	-9	3	Not Related	Moderate	Not Serious	None	Resolved
						背部痛	22	16	Not Related	Moderate	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas
Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo/0.05	[redacted]	Black	0.05 mg/kg/day	Female	5[redacted]	挫傷	92	.	Related	Mild	Not Serious	None	Ongoing
						気道うっ血	92	3	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	173	16	Not Related	Moderate	Serious	None	Resolved
						挫傷	173	.	Not Related	Mild	Not Serious	None	Ongoing
						腟真菌症	175	24	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル敗血症	203	7	Not Related	Severe	Serious	None	Resolved
Placebo/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	カテーテル留置部位感染	.	.	Not Related	Mild	Not Serious	None	Resolved
						閉経期症状	37	.	Not Related	Moderate	Not Serious	None	Ongoing
						うつ病	40	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル留置部位感染	102	3	Not Related	Mild	Serious	None	Resolved
						尿路感染	121	3	Not Related	Mild	Not Serious	None	Resolved
						アレルギー性皮膚炎	121	42	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	200	2	Not Related	Mild	Not Serious	None	Severity/Frequency Increased

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo/0.05	[redacted]	Caucasian	0.05 mg/kg/day	Female	5[redacted]	カテーテル菌血症	202	10	Not Related	Moderate	Serious	None	Resolved
Placebo/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	5[redacted]	鼓腸	2	22	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	2	22	Not Related	Mild	Not Serious	None	Resolved
						疲労	.	.	Related	Moderate	Not Serious	None	Ongoing
						頭痛	47	1	Not Related	Mild	Not Serious	None	Resolved
						排尿困難	.	.	Not Related	Mild	Not Serious	None	Resolved
						排尿困難	.	.	Not Related	Mild	Not Serious	None	Resolved
						体重増加	.	.	Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	.	.	Related	Mild	Not Serious	None	Resolved
						軟便	105	5	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	120	1	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル合併症	138	3	Not Related	Moderate	Serious	None	Resolved
						直腸ポリープ	189	1	Not Related	Mild	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	7[redacted]	皮膚乾燥	-1	31	Related	Severe		None	Resolved
						腸管ストーマ合併症	25	199	Related	Mild	Not Serious	None	Resolved
						うつ病	29	.	Not Related	Moderate	Not Serious	None	Ongoing
						四肢痛	45	2	Not Related	Moderate	Not Serious	None	Resolved
						舌水疱形成	49	4	Not Related	Mild	Not Serious	None	Resolved
						悪寒	50	20	Not Related	Moderate	Not Serious	None	Resolved
						発熱	50	20	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	70	4	Not Related	Severe	Serious	None	Resolved
						発熱	100	3	Not Related	Moderate	Not Serious	None	Resolved
						悪寒	100	3	Not Related	Moderate	Not Serious	None	Resolved
						背部痛	102	1	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	103	5	Not Related	Severe	Serious	None	Resolved
						処置後痛	105	2	Not Related	Moderate	Not Serious	None	Resolved

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Female	7[redacted]	低マグネシウム血症	114	14	Not Related	Mild	Not Serious	None	Resolved
						坐骨神経痛	170	4	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	171	27	Not Related	Severe	Serious	Study Drug Discontinued	Resolved
						胸水	175	23	Not Related	Severe	Serious	None	Resolved
						胃腸出血	178	1	Not Related	Moderate	Serious	None	Resolved
						横隔膜下膿瘍	178	20	Not Related	Severe	Serious	None	Resolved
						低カリウム血症	180	12	Not Related	Moderate	Not Serious	None	Resolved
						クロストリジウム性大腸炎	186	15	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	198	24	Not Related	Moderate	Not Serious	None	Resolved
						胸水	198	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃潰瘍	205	11	Not Related	Severe	Serious	None	Resolved
						低カリウム血症	208	4	Not Related	Moderate	Not Serious	None	Resolved
						消化性潰瘍	216	.	Not Related	Moderate	Not Serious	None	Ongoing

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Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas

Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Placebo/0.10	[redacted]	Caucasian	0.10 mg/kg/day	Male	5[redacted]	腹痛	32	169	Not Related	Mild	Not Serious	None	Resolved
						気管支炎	135	7	Not Related	Mild	Serious	None	Resolved
						胆嚢炎	153	12	Not Related	Moderate	Serious	None	Resolved
						慢性膵炎	153	12	Not Related	Moderate	Serious	None	Resolved
						直腸ポリープ	190	1	Not Related	Mild	Not Serious	None	Resolved

Note: Placebo/0.05: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.05mg/kg/d teduglutide in Study 005
Placebo/0.10: Subjects were randomized to placebo in Study 004 and were rerandomized to 0.10mg/kg/d teduglutide in Study 005
0.05/0.05: Subjects were randomized to 0.05mg/kg/d teduglutide in Study 004 and continued on 0.05mg/kg/d teduglutide in Study 005
0.10/0.10: Subjects were randomized to 0.10mg/kg/d teduglutide in Study 004 and continued on 0.10mg/kg/d teduglutide in Study 005
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 7.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-7-ae-sae-600005.sas
Output Generated On: 21OCT2016 0:53

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	緑内障	-127	.	Not Related	Moderate	Not Serious	None	Ongoing
						不整脈	-77	.	Not Related	Mild	Not Serious	None	Ongoing
						顔面浮腫	-45	62	Not Related	Mild	Not Serious	None	Resolved
						静脈閉塞	1	.	Not Related	Severe	Not Serious	None	Ongoing
						静脈閉塞	1	.	Not Related	Severe	Not Serious	None	Ongoing
						労作性呼吸困難	1	16	Not Related	Mild	Not Serious	None	Resolved
						悪心	2	59	Related	Mild	Not Serious	None	Resolved
						下痢	8	13	Not Related	Mild	Not Serious	None	Resolved
						頻脈	15	9	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						慢性閉塞性肺疾患	15	16	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						肺炎	15	14	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved

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Note: Not Treated, Placebo/Teduglutide = subjects who were eligible for randomization in Study CL0600-020 but qualified after the enrollment number was satisfied and entered Study CL0600-021 directly, and those who participated in Study CL0600-020 and received placebo.
Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	肺高血圧症	17	76	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						INR 増加	17	1	Related	Moderate	Not Serious	None	Resolved
						うっ血性心不全	17	14	Not Related	Mild	Serious	Drug Dose Interrupted	Resolved
						食欲減退	17	27	Not Related	Moderate	Not Serious	None	Resolved
						顔面浮腫	17	27	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						味覚減退	17	27	Not Related	Moderate	Not Serious	None	Resolved
						肺水腫	17	76	Not Related	Mild	Serious	Drug Dose Interrupted	Resolved
						呼吸困難	17	14	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						末梢性浮腫	18	26	Not Related	Mild	Not Serious	None	Resolved
						低カリウム血症	23	2	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						三尖弁閉鎖不全症	25	.	Not Related	Moderate	Not Serious	None	Ongoing
						おくび	43	422	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	食欲減退	59	184	Not Related	Moderate	Not Serious	None	Resolved
						労作性呼吸困難	166	.	Not Related	Moderate	Not Serious	None	Ongoing
						末梢性浮腫	166	32	Not Related	Mild	Not Serious	None	Resolved
						無力症	166	559	Not Related	Moderate	Not Serious	None	Resolved
						体重増加	176	51	Not Related	Moderate	Not Serious	None	Resolved
						心房細動	193	.	Not Related	Moderate	Not Serious	None	Ongoing
						造影剤アレルギー	197	1	Not Related	Severe	Not Serious	None	Resolved
						肺高血圧症	224	19	Not Related	Severe	Serious	None	Resolved
						不眠症	225	18	Not Related	Mild	Not Serious	None	Resolved
						体重減少	253	106	Not Related	Severe	Not Serious	None	Resolved
						食欲減退	290	435	Not Related	Severe	Not Serious	None	Resolved
						尿路感染	291	74	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	悪心	302	65	Not Related	Moderate	Not Serious	None	Resolved
						創し開	309	42	Not Related	Mild	Not Serious	None	Resolved
						クッシング様	337	.	Not Related	Mild	Not Serious	None	Ongoing
						味覚異常	337	49	Not Related	Mild	Not Serious	None	Resolved
						過小食	347	132	Not Related	Moderate	Not Serious	None	Resolved
						尿量減少	355	60	Not Related	Severe	Not Serious	None	Resolved
						ビタミン D 欠乏	358	.	Not Related	Moderate	Not Serious	None	Ongoing
						うっ血性心不全	358	59	Not Related	Moderate	Not Serious	None	Resolved
						うつ病	358	367	Not Related	Mild	Not Serious	None	Resolved
						脱水	358	.	Not Related	Moderate	Not Serious	None	Ongoing
						低血圧	358	386	Not Related	Moderate	Not Serious	None	Resolved
						嗜眠	358	367	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	末梢性浮腫	359	7	Not Related	Mild	Not Serious	None	Resolved
						呼吸困難	359	7	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	393	332	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	393	.	Not Related	Moderate	Not Serious	None	Ongoing
						口腔カンジダ症	393	11	Not Related	Moderate	Not Serious	None	Resolved
						呼吸困難	414	36	Not Related	Moderate	Not Serious	None	Resolved
						体液貯留	414	36	Not Related	Moderate	Not Serious	None	Resolved
						血中クレアチニン増加	456	71	Not Related	Moderate	Not Serious	None	Resolved
						血中尿素増加	456	176	Not Related	Moderate	Not Serious	None	Resolved
						下痢	522	12	Not Related	Moderate	Not Serious	None	Resolved
						鉄欠乏	533	.	Not Related	Moderate	Not Serious	None	Ongoing
						埋込み部位膿疱	680	4	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	非心臓性胸痛	729	3	Not Related	Moderate	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	腹膜嚢胞	-132	.	Not Related	Moderate	Not Serious	None	Ongoing
						眼瞼嚢胞	-117	.	Not Related	Mild	Not Serious	None	Ongoing
						ヘマトクリット減少	1	.	Not Related	Moderate	Not Serious	None	Ongoing
						ヘモグロビン減少	1	90	Not Related	Severe	Not Serious	None	Resolved
						腹痛	1	6	Related	Mild	Not Serious	None	Resolved
						背部痛	1	6	Related	Mild	Not Serious	None	Resolved
						悪心	2	4	Related	Mild	Not Serious	None	Resolved
						筋攣縮	4	2	Not Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	4	171	Related	Mild	Not Serious	None	Resolved
						無力症	8	30	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	14	4	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	C-反応性蛋白増加	14	17	Not Related	Moderate	Not Serious	None	Resolved
						赤血球数減少	14	1	Not Related	Mild	Not Serious	None	Resolved
						食欲減退	20	7	Not Related	Moderate	Not Serious	None	Resolved
						便量減少	20	2	Not Related	Moderate	Not Serious	None	Resolved
						偶発的過量投与	20	1	Not Related	Mild	Not Serious	None	Resolved
						傾眠	20	2	Not Related	Moderate	Not Serious	None	Resolved
						動悸	20	1	Not Related	Mild	Not Serious	None	Resolved
						腹痛	21	3	Related	Moderate	Not Serious	None	Resolved
						悪寒	21	3	Not Related	Moderate	Not Serious	None	Resolved
						発熱	21	2	Not Related	Moderate	Not Serious	None	Resolved
						クローン病	22	5	Not Related	Moderate	Serious	None	Resolved
						無力症	23	4	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	INR 増加	24	3	Not Related	Moderate	Not Serious	None	Resolved
						静脈炎	25	11	Not Related	Mild	Not Serious	None	Resolved
						ほてり	29	77	Not Related	Moderate	Not Serious	None	Resolved
						脱水	30	1	Not Related	Moderate	Not Serious	None	Resolved
						尿浸透圧上昇	30	1	Not Related	Mild	Not Serious	None	Resolved
						低カルシウム血症	63	29	Not Related	Mild	Not Serious	None	Resolved
						紫斑	77	51	Not Related	Mild	Not Serious	None	Resolved
						関節痛	85	43	Not Related	Moderate	Not Serious	None	Resolved
						体液貯留	85	21	Not Related	Mild	Not Serious	None	Resolved
						全身性そう痒症	85	7	Not Related	Mild	Not Serious	None	Resolved
						尿量減少	85	21	Not Related	Mild	Not Serious	None	Resolved
						ヘモグロビン減少	91	.	Not Related	Mild	Not Serious	None	Ongoing

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	腹痛	99	4	Not Related	Moderate	Not Serious	None	Resolved
						頭痛	109	4	Not Related	Severe	Not Serious	None	Resolved
						疲労	109	26	Not Related	Moderate	Not Serious	None	Resolved
						無力症	109	26	Not Related	Moderate	Not Serious	None	Resolved
						意識変容状態	112	1	Not Related	Moderate	Not Serious	None	Resolved
						発熱	113	22	Not Related	Mild	Not Serious	None	Resolved
						上気道感染	120	8	Not Related	Moderate	Not Serious	None	Resolved
						動悸	124	2	Not Related	Moderate	Not Serious	None	Resolved
						INR 増加	136	2	Not Related	Mild	Not Serious	None	Resolved
						INR 増加	144	2	Not Related	Mild	Not Serious	None	Resolved
						好中球減少症	183	.	Not Related	Mild	Not Serious	None	Ongoing
						リンパ球数減少	183	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	好中球数増加	183	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	185	15	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	188	1	Not Related	Mild	Not Serious	None	Resolved
						クローン病	190	10	Not Related	Mild	Not Serious	None	Resolved
						上腹部痛	196	4	Not Related	Severe	Not Serious	None	Resolved
						食欲減退	197	7	Not Related	Mild	Not Serious	None	Resolved
						便量減少	197	7	Not Related	Moderate	Not Serious	Drug Dose Interrupted	Resolved
						早期満腹	197	7	Not Related	Moderate	Not Serious	None	Resolved
						腹部膨満	197	7	Not Related	Mild	Not Serious	None	Resolved
						異常便	197	364	Related	Moderate	Not Serious	None	Resolved
						側腹部痛	197	3	Not Related	Severe	Not Serious	None	Resolved
						胃腸の炎症	199	6	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	消化管運動障害	199	6	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved
						クローン病	199	6	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						回腸狭窄	199	6	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved
						側腹部痛	199	6	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved
						消化管浮腫	199	6	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved
						消化管ストーマ合併症	213	348	Related	Moderate	Not Serious	None	Resolved
						体重減少	218	35	Not Related	Moderate	Not Serious	None	Resolved
						クッシング様	218	158	Not Related	Mild	Not Serious	None	Resolved
						尿量減少	218	35	Not Related	Mild	Not Serious	None	Resolved
						眼瞼痙攣	221	107	Not Related	Mild	Not Serious	None	Resolved
						眼充血	221	107	Not Related	Mild	Not Serious	None	Resolved
						疲労	223	30	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	疼痛	223	27	Not Related	Moderate	Not Serious	None	Resolved
						ビタミン D 減少	238	.	Not Related	Severe	Not Serious	None	Ongoing
						カテーテル留置部位分泌物	259	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位紅斑	260	8	Not Related	Mild	Not Serious	None	Resolved
						霧視	267	167	Not Related	Mild	Not Serious	None	Resolved
						リパーゼ増加	295	64	Not Related	Mild	Not Serious	None	Resolved
						血中アミラーゼ増加	295	.	Not Related	Mild	Not Serious	None	Ongoing
						呼吸困難	296	14	Not Related	Mild	Not Serious	None	Resolved
						倦怠感	296	138	Not Related	Moderate	Not Serious	None	Resolved
						多汗症	296	14	Not Related	Moderate	Not Serious	None	Resolved
						胸痛	296	14	Not Related	Mild	Not Serious	None	Resolved
						胸痛	296	14	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	寝汗	296	14	Not Related	Moderate	Not Serious	None	Resolved
						心膜炎	296	14	Not Related	Mild	Not Serious	None	Resolved
						胸部不快感	296	14	Not Related	Moderate	Not Serious	None	Resolved
						ヘモジデリン沈着症	300	.	Not Related	Moderate	Not Serious	None	Ongoing
						鉄過剰	300	.	Not Related	Moderate	Not Serious	None	Ongoing
						無力症	316	.	Not Related	Moderate	Not Serious	None	Ongoing
						左室肥大	323	.	Not Related	Mild	Not Serious	None	Ongoing
						左房拡張	323	.	Not Related	Mild	Not Serious	None	Ongoing
						上腹部痛	387	14	Not Related	Severe	Not Serious	None	Resolved
						上気道感染	400	17	Not Related	Moderate	Not Serious	None	Resolved
						無力症	442	82	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	442	20	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	関節痛	.	.	Not Related	Moderate	Not Serious	None	Resolved
						全身性そう痒症	470	15	Not Related	Moderate	Not Serious	None	Resolved
						食欲不振	511	57	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	517	23	Not Related	Severe	Not Serious	Drug Dose Interrupted	Resolved
						消化不良	517	74	Not Related	Severe	Not Serious	None	Resolved
						悪心	524	44	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	524	67	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	524	16	Not Related	Moderate	Not Serious	None	Resolved
						無力症	524	44	Not Related	Moderate	Not Serious	None	Resolved
						体重減少	524	52	Not Related	Moderate	Not Serious	None	Resolved
						裂孔ヘルニア	525	66	Not Related	Mild	Not Serious	None	Resolved
						腹部圧痛	525	66	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	腸閉塞	540	28	Not Related	Moderate	Not Serious	None	Resolved
						腸管狭窄	540	51	Not Related	Severe	Not Serious	None	Resolved
						呼吸困難	542	15	Not Related	Severe	Not Serious	None	Resolved
						脱水	547	18	Not Related	Moderate	Not Serious	None	Resolved
						栄養障害	547	29	Not Related	Moderate	Not Serious	None	Resolved
						疼痛	550	7	Not Related	Moderate	Not Serious	None	Resolved
						胸痛	550	4	Not Related	Moderate	Not Serious	None	Resolved
						感覚鈍麻	550	7	Not Related	Moderate	Not Serious	None	Resolved
						頭痛	550	7	Not Related	Severe	Not Serious	None	Resolved
						嘔吐	550	18	Not Related	Moderate	Not Serious	None	Resolved
						低カリウム血症	553	1	Not Related	Moderate	Not Serious	None	Resolved
						関節痛	.	.	Not Related	Moderate	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	腸閉塞	590	10	Not Related	Severe	Serious	Drug Dose Interrupted	Resolved
						膀胱不快感	594	31	Not Related	Moderate	Not Serious	None	Resolved
						切開部位感染	599	32	Not Related	Moderate	Not Serious	Drug Dose Interrupted	Resolved
						アルカローシス	631	5	Not Related	Moderate	Not Serious	None	Resolved
						低カリウム血症	631	5	Not Related	Moderate	Not Serious	None	Resolved
						筋骨格不快感	.	.	Not Related	Mild	Not Serious	None	Ongoing
						寝汗	.	.	Not Related	Moderate	Not Serious	None	Resolved
						上気道感染	707	18	Not Related	Moderate	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	関節痛	-97	.	Not Related	Moderate	Not Serious	None	Ongoing
						上気道感染	-22	29	Not Related	Moderate	Not Serious	None	Resolved
						不規則月経	1	64	Related	Mild	Not Serious	None	Resolved
						ウイルス感染	30	18	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	ウイルス感染	62	4	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	103	44	Not Related	Mild	Not Serious	None	Resolved
						胆石症	171	1	Not Related	Moderate	Not Serious	None	Resolved
						肝嚢胞感染	304	9	Not Related	Severe	Serious	None	Resolved
						ウイルス感染	394	7	Not Related	Mild	Not Serious	None	Resolved
						ウイルス感染	434	10	Not Related	Moderate	Not Serious	None	Resolved
						細菌の過剰繁殖	444	.	Not Related	Mild	Not Serious	None	Ongoing
						不眠症	494	.	Related	Moderate	Not Serious	None	Ongoing
						注入部位感染	494	15	Not Related	Severe	Not Serious	None	Resolved
						胆管狭窄	598	1	Not Related	Moderate	Not Serious	None	Resolved
						結腸ポリープ	728	1	Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	体重増加	1	.	Related	Severe	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	注射部位腫脹	9	2	Related	Mild	Not Serious	None	Resolved
						注射部位そう痒感	9	2	Related	Mild	Not Serious	None	Resolved
						注射部位紅斑	9	2	Related	Mild	Not Serious	None	Resolved
						ほてり	37	.	Not Related	Moderate	Not Serious	None	Ongoing
						食欲減退	37	.	Related	Mild	Not Serious	None	Ongoing
						カテーテル留置部位出血	38	1	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	44	52	Related	Moderate	Not Serious	None	Resolved
						腹痛	60	.	Related	Moderate	Not Serious	None	Ongoing
						消化管ストーマ合併症	77	.	Related	Mild	Not Serious	None	Ongoing
						処置後出血	77	16	Related	Mild	Not Serious	None	Resolved
						腹部膨満	95	2	Related	Moderate	Not Serious	None	Resolved
						注射部位血腫	110	88	Related	Severe	Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	腹痛	4	72	Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	35	15	Not Related	Mild	Not Serious	None	Resolved
						外陰腟真菌感染	54	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	.	.	Not Related	Moderate	Not Serious	None	Ongoing
						中心静脈カテーテル感染	250	11	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						脱水	263	1	Not Related	Moderate	Not Serious	None	Resolved
						悪心	263	.	Not Related	Mild	Not Serious	None	Ongoing
						鼻咽頭炎	763	3	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	ワクチン接種部位紅斑	17	7	Not Related	Moderate	Not Serious	None	Resolved
						下痢	29	.	Related	Moderate	Not Serious	None	Ongoing
						末梢性浮腫	29	.	Related	Mild	Not Serious	None	Ongoing
						血尿	44	7	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	無力症	50	4	Related	Severe	Not Serious	Drug Discontinued	Resolved
						悪液質	50	4	Related	Severe	Not Serious	Drug Discontinued	Resolved
						敗血症	50	4	Not Related	Moderate	Serious	Drug Discontinued	Resolved
						電解質失調	50	4	Related	Severe	Not Serious	Drug Discontinued	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	血圧上昇	-127	.	Not Related	Mild	Not Serious	None	Ongoing
						頻脈	-127	.	Not Related	Mild	Not Serious	None	Ongoing
						体重減少	59	34	Not Related	Mild	Not Serious	None	Resolved
						無力症	59	34	Not Related	Mild	Not Serious	None	Resolved
						発熱	172	1	Not Related	Moderate	Not Serious	None	Resolved
						咳嗽	173	16	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル敗血症	177	12	Not Related	Moderate	Serious	None	Resolved
						肺炎	177	12	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	消化器カンジダ症	180	15	Not Related	Mild	Not Serious	None	Resolved
						鼓腸	714	.	Not Related	Moderate	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	腹痛	2	5	Related	Mild	Not Serious	None	Resolved
						鼓腸	2	.	Related	Moderate	Not Serious	None	Ongoing
						医療機器破損	93	3	Not Related	Mild	Serious	None	Resolved
						腹痛	252	.	Not Related	Moderate	Not Serious	None	Ongoing
						腎仙痛	722	7	Not Related	Moderate	Serious	None	Resolved
						胸水症	730	1	Not Related	Mild	Serious	None	Resolved
						筋緊張低下	730	1	Not Related	Mild	Not Serious	None	Resolved
						咳嗽	731	10	Not Related	Moderate	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	上腹部痛	1	33	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	274	13	Not Related	Moderate	Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	カンジダ症	276	57	Not Related	Mild	Not Serious	None	Resolved
						膣感染	279	52	Not Related	Mild	Not Serious	None	Resolved
						発熱	428	3	Not Related	Mild	Not Serious	None	Resolved
						カテーテル菌血症	430	17	Not Related	Mild	Serious	None	Resolved
						眼感染	.	.	Not Related	Mild	Not Serious	None	Resolved
						膣感染	523	5	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	帯状疱疹	-7	23	Not Related	Mild	Not Serious	None	Resolved
						背部痛	2	2	Related	Moderate	Not Serious	None	Resolved
						腹痛	2	2	Related	Moderate	Not Serious	None	Resolved
						四肢痛	23	42	Not Related	Mild	Not Serious	None	Resolved
						関節痛	84	59	Not Related	Moderate	Not Serious	None	Resolved
						坐骨神経痛	98	45	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	関節炎	118	26	Not Related	Moderate	Serious	None	Resolved
						足変形	119	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル菌血症	162	11	Not Related	Moderate	Serious	None	Resolved
						軟部組織の炎症	225	17	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						軟部組織の炎症	406	24	Not Related	Mild	Not Serious	None	Resolved
						発熱	456	18	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	457	35	Not Related	Moderate	Serious	None	Resolved
						伝染病病原体キャリアー	460	32	Not Related	Mild	Not Serious	None	Resolved
						クロストリジウム感染	460	32	Not Related	Moderate	Serious	None	Resolved
						下痢	545	14	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	2[redacted]	肛門カンジダ症	-156	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル菌血症	247	11	Not Related	Moderate	Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	2[redacted]	発熱	443	3	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル菌血症	445	14	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						急性胆嚢炎	458	13	Not Related	Severe	Serious	Drug Dose Interrupted	Resolved
						カテーテル菌血症	548	12	Not Related	Mild	Serious	None	Resolved
						細菌性疾患キャリアー	549	.	Not Related	Mild	Not Serious	None	Ongoing
						薬物過敏症	551	.	Not Related	Mild	Not Serious	None	Ongoing
						発熱	632	16	Not Related	Moderate	Serious	None	Resolved
						発熱	708	16	Not Related	Moderate	Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	背部痛	-112	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃炎	49	.	Not Related	Mild	Not Serious	None	Ongoing
						喀血	71	.	Not Related	Moderate	Not Serious	None	Ongoing
						動脈硬化症	85	.	Not Related	Mild	Not Serious	None	Ongoing

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	非小細胞肺癌	85	158	Not Related	Severe	Serious	Drug Discontinued	Fatal
						INR 増加	87	3	Not Related	Mild	Not Serious	None	Resolved
						十二指腸ポリープ	103	.	Not Related	Mild	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	2[redacted]	発熱	3	8	Not Related	Mild	Serious	None	Resolved
						真菌感染	10	14	Not Related	Mild	Not Serious	None	Resolved
						伝染病病原体キャリアー	181	25	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位蜂巣炎	181	12	Not Related	Moderate	Serious	None	Resolved
						急性膵炎	359	30	Not Related	Severe	Serious	None	Resolved
						カテーテル留置部位蜂巣炎	552	28	Not Related	Moderate	Serious	None	Resolved
						発疹	556	24	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Male	6[redacted]	痔核	-174	.	Not Related	Mild	Not Serious	None	Ongoing
						季節性アレルギー	1	1	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Male	6[redacted]	脱水	15	15	Not Related	Mild	Not Serious	None	Resolved
						脱水	45	63	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル留置部位紅斑	56	35	Not Related	Moderate	Not Serious	None	Resolved
						滴下投与部位そう痒感	56	35	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル留置部位分泌物	56	1	Not Related	Moderate	Not Serious	None	Resolved
						腎結石症	83	245	Not Related	Mild	Not Serious	None	Resolved
						水尿管症	83	245	Not Related	Mild	Not Serious	None	Resolved
						胸水	83	.	Not Related	Mild	Not Serious	None	Ongoing
						腎結石症	83	1	Not Related	Moderate	Not Serious	None	Resolved
						胆石症	83	.	Not Related	Mild	Not Serious	None	Ongoing
						腎嚢胞	83	.	Not Related	Moderate	Not Serious	None	Ongoing
						腹部膨満	83	101	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Male	6[redacted]	水腎症	83	245	Not Related	Mild	Not Serious	None	Resolved
						胸痛	88	2	Not Related	Moderate	Not Serious	None	Resolved
						発熱	88	10	Not Related	Moderate	Not Serious	None	Resolved
						中心静脈カテーテル感染	91	10	Not Related	Severe	Serious	None	Resolved
						頚静脈血栓症	95	11	Not Related	Severe	Serious	None	Resolved
						発熱	176	1	Not Related	Moderate	Not Serious	None	Resolved
						回転性めまい	176	13	Not Related	Moderate	Not Serious	None	Resolved
						細菌感染	184	12	Not Related	Severe	Not Serious	None	Resolved
						熱射病	374	1	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	409	41	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル合併症	449	6	Not Related	Mild	Not Serious	None	Resolved
						筋骨格痛	526	.	Not Related	Mild	Not Serious	None	Ongoing

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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Male	6[redacted]	季節性アレルギー	594	205	Not Related	Mild	Not Serious	None	Resolved
						下痢	687	3	Not Related	Mild	Not Serious	None	Resolved
						脱水	687	113	Not Related	Mild	Not Serious	None	Resolved
						貧血	687	.	Not Related	Mild	Not Serious	None	Ongoing
						血中重炭酸塩減少	730	50	Not Related	Mild	Not Serious	None	Resolved
						関節痛	799	.	Not Related	Mild	Not Serious	None	Ongoing
						関節腫脹	799	.	Not Related	Mild	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Female	4[redacted]	高血圧	-183	.	Not Related	Severe	Not Serious	None	Ongoing
						眼部腫脹	1	3	Not Related	Mild	Not Serious	None	Resolved
						悪心	2	12	Not Related	Mild	Not Serious	None	Resolved
						カルシウム欠乏	7	.	Not Related	Moderate	Not Serious	None	Ongoing
						筋骨格硬直	11	236	Not Related	Mild	Not Serious	None	Resolved

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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Female	4[redacted]	嘔吐	18	1	Not Related	Mild	Not Serious	None	Resolved
						四肢の結節	57	7	Not Related	Mild	Not Serious	None	Resolved
						下腹部痛	59	1	Not Related	Severe	Not Serious	None	Resolved
						下痢	59	1	Not Related	Severe	Not Serious	None	Resolved
						眼痛	62	6	Not Related	Mild	Not Serious	None	Resolved
						呼吸困難	85	6	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	85	91	Not Related	Severe	Not Serious	None	Resolved
						四肢痛	85	6	Not Related	Severe	Not Serious	None	Resolved
						便秘	86	5	Not Related	Mild	Not Serious	None	Resolved
						深部静脈血栓症	86	5	Not Related	Severe	Serious	None	Resolved
						下痢	88	8	Not Related	Severe	Not Serious	None	Resolved
						下腹部痛	88	8	Not Related	Severe	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Female	4[redacted]	悪心	90	6	Not Related	Mild	Not Serious	None	Resolved
						無力症	92	85	Not Related	Mild	Not Serious	None	Resolved
						疲労	92	85	Not Related	Mild	Not Serious	None	Resolved
						四肢不快感	92	155	Not Related	Mild	Not Serious	None	Resolved
						錯感覚	92	99	Not Related	Moderate	Not Serious	None	Resolved
						体重増加	92	85	Not Related	Moderate	Not Serious	None	Resolved
						下痢	156	35	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	176	14	Not Related	Severe	Not Serious	None	Resolved
						末梢性浮腫	190	169	Not Related	Moderate	Not Serious	None	Resolved
						月経困難症	190	8	Not Related	Moderate	Not Serious	None	Resolved
						筋痙縮	357	1	Not Related	Mild	Not Serious	None	Resolved
						低カルシウム血症	365	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Female	4[redacted]	下痢	432	2	Not Related	Moderate	Not Serious	None	Resolved
						乳酸アシドーシス	434	3	Not Related	Moderate	Serious	None	Resolved
						脱水	434	3	Not Related	Moderate	Not Serious	None	Resolved
						下痢	455	1	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	456	85	Not Related	Mild	Not Serious	None	Resolved
						低カリウム血症	485	.	Not Related	Moderate	Not Serious	None	Ongoing
						筋痙縮	540	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	540	.	Not Related	Mild	Not Serious	None	Ongoing
						頭痛	570	4	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	570	4	Not Related	Mild	Not Serious	None	Resolved
						悪心	570	4	Not Related	Mild	Not Serious	None	Resolved
						下痢	570	4	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	Black	0.05 Mg/Kg/Day	Female	4[redacted]	下痢	581	87	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	582	86	Not Related	Mild	Not Serious	None	Resolved
						悪心	582	86	Not Related	Severe	Not Serious	None	Resolved
						筋痙縮	594	5	Not Related	Severe	Not Serious	None	Resolved
						血中重炭酸塩減少	594	74	Not Related	Moderate	Not Serious	None	Resolved
						浮動性めまい	603	65	Not Related	Mild	Not Serious	None	Resolved
						腹痛	641	2	Not Related	Mild	Not Serious	None	Resolved
						脱水	641	2	Not Related	Mild	Not Serious	None	Resolved
						頭痛	641	2	Not Related	Mild	Not Serious	None	Resolved
						クロストリジウム・ディフィシレ大腸炎	650	11	Not Related	Mild	Not Serious	None	Resolved
						振戦	653	.	Not Related	Mild	Not Serious	None	Ongoing
						乳酸アシドーシス	687	8	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	高血圧	-99	.	Not Related	Mild	Not Serious	None	Ongoing
						嘔吐	1	26	Related	Moderate	Not Serious	None	Resolved
						悪心	23	7	Not Related	Mild	Not Serious	None	Resolved
						口内乾燥	58	27	Not Related	Mild	Not Serious	None	Resolved
						腹痛	78	3	Not Related	Moderate	Not Serious	None	Resolved
						悪心	86	.	Not Related	Mild	Not Serious	None	Ongoing
						皮膚のつっぱり感	86	91	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	.	.	Not Related	Moderate	Not Serious	None	Ongoing
						カテーテル合併症	123	90	Not Related	Mild	Not Serious	None	Resolved
						インフルエンザ	210	3	Not Related	Mild	Not Serious	None	Resolved
						ほてり	267	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル合併症	.	.	Not Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	消化管ストーマ合併症	358	358	Not Related	Mild	Not Serious	None	Resolved
						胃腸音異常	358	358	Not Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	378	25	Not Related	Moderate	Not Serious	None	Resolved
						静脈閉塞	402	.	Not Related	Mild	Not Serious	None	Ongoing
						便量増加	513	42	Not Related	Mild	Not Serious	None	Resolved
						腹部不快感	513	14	Not Related	Mild	Not Serious	None	Resolved
						脱水	517	6	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	631	25	Not Related	Moderate	Not Serious	None	Resolved
						高ビリルビン血症	.	.	Not Related	Mild	Not Serious	None	Resolved
						血腫	.	.	Not Related	Moderate	Not Serious	None	Resolved
						菌血症	670	31	Not Related	Moderate	Serious	None	Resolved
						結膜蒼白	715	.	Not Related	Mild	Not Serious	None	Ongoing

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	体重減少	-57	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	14	23	Not Related	Mild	Not Serious	None	Resolved
						瘢痕ヘルニア	75	17	Not Related	Severe	Serious	None	Resolved
						頭痛	355	.	Not Related	Moderate	Not Serious	None	Ongoing
						高アミラーゼ血症	453	.	Not Related	Moderate	Not Serious	None	Ongoing
						高リパーゼ血症	453	.	Not Related	Moderate	Not Serious	None	Ongoing
						胆石症	553	.	Not Related	Mild	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	血中リン減少	92	.	Not Related	Mild	Not Serious	None	Ongoing
						統合失調症、妄想型	181	.	Not Related	Moderate	Not Serious	None	Ongoing
						体重減少	181	376	Not Related	Moderate	Not Serious	None	Resolved
						妄想性障害、詳細不明	181	.	Not Related	Moderate	Not Serious	None	Ongoing
						妄想性障害、詳細不明	427	70	Not Related	Severe	Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	カテーテル合併症	427	77	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	455	9	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	背部痛	313	.	Not Related	Moderate	Not Serious	None	Ongoing
						腰椎骨折	323	.	Not Related	Severe	Serious	Drug Discontinued	Ongoing
						消化不良	323	.	Not Related	Mild	Not Serious	None	Ongoing
						転移性新生物	326	11	Related	Severe	Serious	Drug Discontinued	Fatal
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	体重増加	-160	527	Related	Mild	Not Serious	None	Resolved
						筋痙縮	-148	.	Not Related	Mild	Not Serious	None	Ongoing
						消化管ストーマ合併症	-146	148	Related	Mild	Not Serious	None	Severity/ Frequency Increased
						鉄欠乏	-136	.	Not Related	Mild	Not Serious	None	Ongoing
						肺炎	-8	40	Not Related	Mild	Not Serious	None	Resolved
						腹痛	2	.	Related	Mild	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	消化管ストーマ合併症	2	.	Related	Moderate	Not Serious	None	Ongoing
						上気道感染	25	7	Not Related	Mild	Not Serious	None	Resolved
						血中トリグリセリド増加	60	.	Related	Mild	Not Serious	None	Ongoing
						カテーテル留置部位感染	89	92	Not Related	Mild	Not Serious	None	Resolved
						メレナ	221	3	Not Related	Moderate	Serious	None	Resolved
						上気道感染	240	.	Not Related	Mild	Not Serious	None	Resolved
						疲労	312	69	Not Related	Mild	Not Serious	None	Resolved
						敗血症	333	5	Not Related	Moderate	Serious	None	Resolved
						レンサ球菌性咽頭炎	337	10	Not Related	Mild	Not Serious	None	Resolved
						ほてり	.	.	Not Related	Mild	Not Serious	None	Resolved
						アナフィラキシー反応	373	1	Not Related	Moderate	Not Serious	None	Resolved
						中心静脈カテーテル感染	422	8	Not Related	Moderate	Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	鼻咽頭炎	486	465	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	492	8	Not Related	Moderate	Serious	None	Resolved
						中心静脈カテーテル感染	523	6	Not Related	Moderate	Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	腹痛	10	5	Related	Moderate	Not Serious	Drug Dose Interrupted	Resolved
						悪心	11	2	Not Related	Mild	Not Serious	None	Resolved
						血中重炭酸塩減少	14	19	Not Related	Moderate	Not Serious	None	Resolved
						敗血症	57	7	Not Related	Severe	Serious	None	Resolved
						中心静脈カテーテル感染	64	8	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	肋骨骨折	-37	.	Not Related	Severe	Not Serious	None	Ongoing
						肺損傷	-37	.	Not Related	Mild	Not Serious	None	Ongoing
						胸水	-12	44	Not Related	Severe	Serious	None	Resolved
						体重減少	1	485	Not Related	Moderate	Not Serious	None	Severity/ Frequency Increased

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	鼓腸	9	18	Not Related	Moderate	Not Serious	None	Resolved
						血中重炭酸塩減少	15	80	Not Related	Mild	Not Serious	None	Resolved
						鼓腸	36	25	Not Related	Mild	Not Serious	None	Resolved
						異常高熱	47	1	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	47	15	Not Related	Moderate	Not Serious	None	Resolved
						高血圧	92	.	Not Related	Moderate	Not Serious	None	Ongoing
						血中重炭酸塩減少	95	272	Not Related	Moderate	Not Serious	None	Resolved
						下痢	271	3	Not Related	Moderate	Not Serious	None	Resolved
						注射部位発疹	348	3	Related	Mild	Not Serious	None	Resolved
						注射部位腫脹	348	3	Related	Mild	Not Serious	None	Resolved
						注射部位腫脹	354	3	Related	Mild	Not Serious	None	Resolved
						注射部位発疹	354	3	Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	腎結石症	362	1	Not Related	Severe	Not Serious	None	Resolved
						貧血	366	92	Not Related	Mild	Not Serious	None	Resolved
						血中クレアチニン増加	366	14	Not Related	Mild	Not Serious	None	Severity/ Frequency Increased
						急性腎不全	380	.	Not Related	Moderate	Not Serious	None	Ongoing
						血中重炭酸塩減少	380	78	Not Related	Moderate	Not Serious	None	Resolved
						血中クレアチニン増加	380	.	Not Related	Moderate	Not Serious	None	Ongoing
						尿路閉塞	380	.	Not Related	Moderate	Not Serious	None	Ongoing
						良性前立腺肥大症	437	.	Not Related	Mild	Not Serious	None	Ongoing
						下痢	457	14	Not Related	Moderate	Not Serious	None	Resolved
						体重減少	486	15	Not Related	Severe	Not Serious	None	Resolved
						下痢	500	.	Not Related	Mild	Not Serious	None	Ongoing
						血中重炭酸塩減少	500	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	貧血	542	91	Not Related	Moderate	Not Serious	None	Resolved
						膀胱結石	586	.	Not Related	Moderate	Not Serious	None	Ongoing
						腎結石症	623	2	Not Related	Moderate	Not Serious	None	Resolved
						腎結石症	630	1	Not Related	Mild	Not Serious	None	Resolved
						慢性腎不全	688	.	Not Related	Severe	Serious	Drug Discontinued	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	便量減少	-160	324	Not Related	Moderate	Not Serious	None	Resolved
						抱合ビリルビン増加	-151	243	Not Related	Moderate	Not Serious	None	Resolved
						黄疸眼	-151	243	Not Related	Mild	Not Serious	None	Resolved
						片頭痛	-137	.	Not Related	Severe	Not Serious	None	Ongoing
						血中ビリルビン増加	-123	187	Not Related	Moderate	Not Serious	None	Resolved
						血中アルカリホスファターゼ増加	-81	.	Not Related	Moderate	Not Serious	None	Ongoing
						γ-グルタミルトランスフェラーゼ増加	-81	.	Not Related	Moderate	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	血小板数減少	-81	.	Not Related	Moderate	Not Serious	None	Ongoing
						肝硬変	-48	.	Not Related	Severe	Not Serious	None	Ongoing
						悪心	-48	.	Related	Mild	Not Serious	None	Ongoing
						平滑筋抗体陽性	-46	.	Not Related	Moderate	Not Serious	None	Ongoing
						胆汁うっ滞性肝炎	-20	.	Not Related	Severe	Serious	None	Ongoing
						腹痛	4	134	Related	Severe	Not Serious	None	Resolved
						消化管ストーマ合併症	5	.	Related	Mild	Not Serious	None	Ongoing
						消化管ストーマ合併症	5	.	Related	Moderate	Not Serious	None	Ongoing
						異常高熱	9	1	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	39	1	Related	Severe	Not Serious	None	Resolved
						嘔吐	49	1	Related	Severe	Not Serious	None	Resolved
						嘔吐	58	1	Related	Severe	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	細菌性尿路感染	63	24	Not Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	64	1	Related	Moderate	Not Serious	None	Resolved
						嘔吐	75	1	Related	Moderate	Not Serious	None	Resolved
						片頭痛	76	3	Not Related	Severe	Not Serious	None	Resolved
						眼部腫脹	76	4	Not Related	Moderate	Not Serious	None	Resolved
						嘔吐	78	1	Related	Moderate	Not Serious	None	Resolved
						鼻出血	82	2	Not Related	Moderate	Not Serious	None	Resolved
						注射部位腫脹	91	122	Related	Mild	Not Serious	None	Resolved
						注射部位発疹	91	192	Related	Moderate	Not Serious	None	Resolved
						処置後出血	137	32	Not Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	146	23	Related	Moderate	Not Serious	None	Resolved
						貧血	164	19	Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	口渇	164	6	Not Related	Moderate	Not Serious	None	Resolved
						便量増加	164	6	Not Related	Moderate	Not Serious	None	Resolved
						下痢	176	4	Not Related	Moderate	Not Serious	None	Resolved
						異常高熱	177	2	Not Related	Moderate	Not Serious	None	Resolved
						白血球減少症	182	.	Not Related	Moderate	Not Serious	None	Ongoing
						消化管ストーマ合併症	183	12	Related	Moderate	Serious	Drug Discontinued	Resolved
						処置による疼痛	184	9	Not Related	Severe	Not Serious	None	Resolved
						消化管ストーマ合併症	184	1	Related	Moderate	Not Serious	None	Resolved
						術後膿瘍	191	10	Not Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	209	1	Related	Mild	Not Serious	None	Resolved
						腹痛	209	.	Related	Moderate	Not Serious	None	Ongoing
						便量増加	213	10	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	便量増加	224	11	Not Related	Moderate	Not Serious	None	Severity/ Frequency Increased
						消化管ストーマ合併症	225	1	Related	Mild	Not Serious	None	Resolved
						血中重炭酸塩減少	227	96	Not Related	Moderate	Not Serious	None	Resolved
						カンジダ症	228	11	Not Related	Moderate	Not Serious	None	Resolved
						便量増加	234	.	Not Related	Severe	Not Serious	None	Ongoing
						消化管ストーマ合併症	235	1	Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	241	8	Related	Severe	Not Serious	None	Resolved
						末梢性浮腫	248	15	Not Related	Moderate	Not Serious	None	Resolved
						貧血	249	26	Related	Moderate	Not Serious	None	Resolved
						低アルブミン血症	249	26	Not Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	259	2	Related	Moderate	Not Serious	Drug Dose Interrupted	Resolved
						異常高熱	262	6	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	末梢性浮腫	266	.	Not Related	Mild	Not Serious	None	Ongoing
						便量増加	274	8	Not Related	Severe	Serious	None	Resolved
						消化管ストーマ合併症	274	8	Related	Moderate	Serious	Drug Discontinued	Resolved
						門脈圧亢進症	276	.	Related	Moderate	Not Serious	Drug Dose Interrupted	Ongoing
						処置後出血	281	1	Not Related	Moderate	Not Serious	None	Resolved
						消化管ストーマ合併症	305	1	Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	319	1	Related	Mild	Not Serious	None	Resolved
						無力症	322	.	Not Related	Moderate	Not Serious	None	Ongoing
						筋肉痛	322	.	Not Related	Moderate	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	血中ビリルビン増加	178	148	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						血中アルカリホスファターゼ増加	178	148	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						アラニン・アミノトランスフェラーゼ増加	178	148	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	γ-グルタミルトランスフェラーゼ増加	178	148	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						アスパラギン酸アミノトランスフェラーゼ増加	178	148	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						胆石症	206	101	Not Related	Severe	Serious	Drug Discontinued	Resolved
						アスパラギン酸アミノトランスフェラーゼ増加	345	.	Not Related	Mild	Not Serious	Drug Discontinued	Ongoing
						γーグルタミルトランスフェラーゼ増加	345	.	Not Related	Mild	Not Serious	Drug Discontinued	Ongoing
						血中ビリルビン増加	345	.	Not Related	Mild	Not Serious	Drug Discontinued	Ongoing
						アラニン・アミノトランスフェラーゼ増加	345	.	Not Related	Mild	Not Serious	Drug Discontinued	Ongoing
						血中アルカリホスファターゼ増加	345	.	Not Related	Mild	Not Serious	Drug Discontinued	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	8[redacted]	胆嚢炎	16	12	Related	Severe	Serious	Drug Dose Interrupted	Resolved
						腸閉塞	16	12	Related	Severe	Serious	Drug Dose Interrupted	Resolved
						消化管ストーマ合併症	16	12	Related	Severe	Serious	Drug Discontinued	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	8[redacted]	門脈圧亢進症	16	12	Related	Severe	Serious	Drug Dose Interrupted	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	高血圧	-88	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル関連感染	191	7	Not Related	Moderate	Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	Asian	0.05 Mg/Kg/Day	Female	4[redacted]	浮動性めまい	-276	.	Not Related	Mild	Not Serious	None	Ongoing
						血尿	20	6	Not Related	Mild	Not Serious	None	Resolved
						背部痛	20	32	Not Related	Mild	Not Serious	None	Resolved
						下腹部痛	20	30	Not Related	Mild	Not Serious	None	Resolved
						副鼻腔炎	55	15	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	79	11	Not Related	Mild	Not Serious	None	Resolved
						発熱	109	3	Not Related	Severe	Serious	None	Resolved
						尿路感染	155	16	Related	Mild	Not Serious	None	Resolved
						尿路感染	225	15	Not Related	Moderate	Not Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	Asian	0.05 Mg/Kg/Day	Female	4[redacted]	尿路感染	370	14	Not Related	Severe	Not Serious	None	Resolved
						四肢痛	605	15	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	7[redacted]	注射部位変色	-199	201	Related	Mild	Not Serious	None	Resolved
						悪心	5	27	Related	Mild	Not Serious	None	Resolved
						インフルエンザ様疾患	5	27	Related	Mild	Not Serious	None	Resolved
						疲労	5	27	Related	Mild	Not Serious	None	Resolved
						腹痛	5	27	Related	Mild	Not Serious	None	Resolved
						血腫	31	62	Related	Mild	Not Serious	None	Resolved
						悪寒	50	43	Not Related	Mild	Not Serious	None	Resolved
						発熱	50	392	Not Related	Mild	Not Serious	None	Resolved
						回転性めまい	101	20	Not Related	Mild	Not Serious	None	Resolved
						発熱	165	8	Not Related	Mild	Serious	None	Resolved
						発熱	210	4	Not Related	Mild	Serious	None	Resolved

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Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	7[redacted]	発熱	217	15	Not Related	Mild	Serious	None	Resolved
						リンパ節炎	233	55	Not Related	Mild	Not Serious	None	Severity/Frequency Increased
						体重減少	276	274	Not Related	Mild	Not Serious	None	Resolved
						リンパ節炎	288	10	Not Related	Mild	Serious	None	Resolved
						リンパ節炎	298	.	Not Related	Mild	Not Serious	None	Ongoing
						脱毛症	316	50	Not Related	Mild	Not Serious	None	Resolved
						呼吸困難	317	49	Not Related	Mild	Not Serious	None	Resolved
						嚥下障害	365	77	Not Related	Mild	Not Serious	None	Resolved
						無力症	410	1	Not Related	Moderate	Not Serious	None	Resolved
						結核	441	2	Not Related	Moderate	Serious	None	Resolved
						結核	443	.	Not Related	Moderate	Not Serious	None	Ongoing
						悪心	456	49	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	7[redacted]	回転性めまい	456	49	Not Related	Mild	Not Serious	None	Resolved
						高血圧	603	.	Not Related	Moderate	Not Serious	None	Ongoing
						うつ病	610	127	Not Related	Moderate	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	うつ病	-130	.	Not Related	Mild	Not Serious	None	Ongoing
						気分変調性障害	-130	.	Not Related	Mild	Not Serious	None	Ongoing
						鼻咽頭炎	2	14	Not Related	Mild	Not Serious	None	Resolved
						筋痙縮	30	49	Related	Mild	Not Serious	None	Resolved
						自殺企図	106	6	Not Related	Severe	Serious	None	Resolved
						筋痙縮	272	.	Not Related	Mild	Not Serious	None	Ongoing
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	鎖骨下静脈血栓症	148	6	Not Related	Moderate	Serious	None	Resolved
						脱水	149	4	Not Related	Mild	Not Serious	None	Resolved
						低カリウム血症	151	2	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	頭痛	151	1	Not Related	Mild	Not Serious	None	Resolved
						カテーテル合併症	406	2	Not Related	Severe	Not Serious	None	Resolved
						医療機器合併症	478	2	Not Related	Mild	Not Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	鼓腸	22	11	Related	Mild	Not Serious	None	Resolved
						カテーテル敗血症	231	12	Not Related	Moderate	Serious	None	Resolved
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	8[redacted]	下痢	-166	.	Not Related	Mild	Not Serious	None	Ongoing
						悪心	-105	.	Related	Mild	Not Serious	None	Ongoing
						腹部圧痛	-70	94	Related	Mild	Not Serious	None	Resolved
						頚部痛	23	.	Not Related	Moderate	Not Serious	None	Ongoing
						腹部膨満	39	.	Related	Mild	Not Serious	None	Ongoing
						うつ病	131	.	Not Related	Mild	Not Serious	None	Ongoing
						ウイルス感染	274	2	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Not Treated, Placebo / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	8[redacted]	尾骨骨折	315	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃食道逆流性疾患	361	33	Not Related	Mild	Not Serious	None	Resolved
						関節炎	493	.	Not Related	Mild	Not Serious	None	Ongoing
						胃食道逆流性疾患	631	16	Related	Mild	Not Serious	None	Resolved
						カテーテル菌血症	667	47	Not Related	Severe	Serious	None	Resolved
						尿路感染	667	6	Not Related	Moderate	Not Serious	None	Resolved
						口腔ヘルペス	669	15	Not Related	Moderate	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	消化管ストーマ合併症	-195	.	Related	Mild	Not Serious	None	Ongoing
						体液貯留	261	16	Related	Moderate	Not Serious	None	Resolved
						体液貯留	295	30	Related	Moderate	Not Serious	None	Resolved
						中心静脈カテーテル感染	315	67	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						食欲不振	360	73	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	筋痙縮	385	1	Not Related	Moderate	Not Serious	None	Resolved
						体重減少	386	.	Not Related	Mild	Not Serious	None	Ongoing
						脱水	386	22	Not Related	Moderate	Not Serious	None	Resolved
						筋痙縮	392	248	Not Related	Mild	Not Serious	None	Resolved
						無力症	625	15	Not Related	Moderate	Not Serious	None	Resolved
						脱水	625	15	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	バレット食道	-82	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃炎	-82	.	Not Related	Moderate	Not Serious	None	Ongoing
						注射部位血腫	1	175	Related	Moderate	Not Serious	None	Resolved
						注射部位蕁麻疹	1	175	Related	Moderate	Not Serious	None	Resolved
						悪心	15	72	Not Related	Severe	Not Serious	None	Resolved
						振戦	28	1	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	2[redacted]	血液培養陽性	30	14	Not Related	Mild	Not Serious	None	Resolved
						発熱	30	4	Not Related	Moderate	Not Serious	None	Resolved
						上腹部痛	40	31	Related	Moderate	Serious	None	Resolved
						中耳滲出液	87	89	Not Related	Mild	Not Serious	None	Resolved
						咽喉刺激感	87	89	Not Related	Mild	Not Serious	None	Resolved
						鼓腸	88	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	95	11	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	埋込み部位硬結	1	.	Not Related	Moderate	Not Serious	None	Ongoing
						カテーテル留置部位感染	281	7	Not Related	Severe	Serious	None	Resolved
						カテーテル留置部位感染	352	6	Not Related	Severe	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	消化管ストーマ合併症	-161	.	Related	Severe	Not Serious	None	Ongoing
						腹痛	-148	199	Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	注射部位感染	16	14	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	50	341	Related	Moderate	Not Serious	None	Resolved
						皮膚潰瘍	100	93	Not Related	Moderate	Not Serious	None	Resolved
						四肢痛	267	63	Not Related	Moderate	Not Serious	None	Resolved
						血中コレステロール増加	330	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	390	37	Related	Severe	Serious	Drug Dose Interrupted	Resolved
						直腸炎	407	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	427	.	Related	Moderate	Not Serious	None	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	腹部膨満	-165	.	Related	Mild	Not Serious	None	Ongoing
						消化管ストーマ合併症	-163	.	Related	Moderate	Not Serious	None	Ongoing
						悪心	-27	.	Related	Moderate	Not Serious	None	Ongoing
						甲状腺機能低下症	27	324	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	四肢痛	75	.	Not Related	Moderate	Not Serious	None	Ongoing
						筋痙縮	301	.	Not Related	Moderate	Not Serious	None	Ongoing
						甲状腺機能低下症	351	.	Not Related	Moderate	Not Serious	None	Ongoing
						血中ビリルビン増加	461	173	Related	Moderate	Serious	None	Resolved
						カテーテル関連感染	493	33	Not Related	Severe	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	消化管ストーマ合併症	-161	.	Related	Moderate	Not Serious	None	Ongoing
						末梢性浮腫	-84	.	Related	Moderate	Not Serious	None	Ongoing
						カテーテル留置部位紅斑	-52	.	Not Related	Mild	Not Serious	None	Ongoing
						体液貯留	1	15	Related	Moderate	Not Serious	None	Resolved
						体液貯留	162	56	Not Related	Mild	Not Serious	None	Resolved
						頭痛	162	102	Not Related	Moderate	Not Serious	None	Resolved
						脳浮腫	162	112	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	脳膿瘍	162	102	Not Related	Severe	Serious	Drug Discontinued	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	7[redacted]	体重減少	89	.	Not Related	Moderate	Not Serious	None	Ongoing
						カテーテル敗血症	256	22	Not Related	Moderate	Serious	None	Resolved
						鼓腸	333	.	Not Related	Mild	Not Serious	None	Ongoing
						喀血	379	.	Not Related	Moderate	Not Serious	None	Ongoing
						結核	403	110	Not Related	Moderate	Not Serious	None	Resolved
						低カリウム血症	410	2	Not Related	Mild	Not Serious	None	Resolved
						肺扁平上皮癌、病期不明	535	.	Not Related	Severe	Serious	Drug Discontinued	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	無力症	.	.	Not Related	Mild	Not Serious	None	Resolved
						下痢	-42	58	Not Related	Mild	Not Serious	None	Resolved
						眼部化学熱傷	52	16	Not Related	Moderate	Serious	None	Resolved
						ウイルス感染	263	3	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	体重減少	.	.	Not Related	Moderate	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	無力症	51	44	Not Related	Moderate	Not Serious	None	Resolved
						便秘	51	.	Not Related	Moderate	Not Serious	None	Ongoing
						腸管吻合合併症	60	13	Not Related	Moderate	Serious	None	Resolved
						尿路感染	63	9	Not Related	Mild	Not Serious	None	Resolved
						大球性貧血	338	.	Not Related	Moderate	Not Serious	None	Ongoing
						無力症	338	29	Not Related	Mild	Not Serious	None	Resolved
						尿路感染	353	14	Not Related	Moderate	Serious	None	Resolved
						発熱	372	12	Not Related	Moderate	Serious	None	Resolved
						尿路感染	471	10	Not Related	Mild	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	裂肛	-178	.	Not Related	Moderate	Not Serious	None	Ongoing
						鼓腸	-166	.	Related	Mild	Not Serious	None	Ongoing

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	関節痛	-30	.	Not Related	Mild	Not Serious	None	Ongoing
						鼻炎	3	12	Not Related	Mild	Not Serious	None	Resolved
						頻脈性不整脈	.	.	Not Related	Moderate	Not Serious	None	Ongoing
						骨痛	247	.	Not Related	Moderate	Not Serious	None	Ongoing
						四肢痛	247	.	Not Related	Moderate	Not Serious	None	Ongoing
						結膜炎	408	.	Not Related	Mild	Not Serious	None	Ongoing
						帯状疱疹	484	17	Not Related	Moderate	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	消化不良	1	173	Not Related	Mild	Not Serious	None	Resolved
						挫傷	1	15	Not Related	Mild	Not Serious	None	Resolved
						下痢	1	15	Not Related	Mild	Not Serious	None	Resolved
						心電図 T 波振幅減少	1	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部膨満	1	15	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	おくび	2	.	Not Related	Mild	Not Serious	None	Ongoing
						カテーテル合併症	10	1	Not Related	Mild	Not Serious	None	Resolved
						副腎機能不全	14	160	Not Related	Mild	Not Serious	None	Resolved
						上気道うっ血	15	22	Not Related	Mild	Not Serious	None	Resolved
						高血圧	15	1	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	15	50	Not Related	Moderate	Not Serious	None	Resolved
						高血圧	21	3	Related	Severe	Serious	None	Resolved
						急性胆嚢炎	21	153	Not Related	Mild	Not Serious	None	Resolved
						腎動脈閉塞	23	.	Not Related	Mild	Not Serious	None	Ongoing
						腎萎縮	23	.	Not Related	Mild	Not Serious	None	Ongoing
						節足動物咬傷	31	1	Not Related	Mild	Not Serious	None	Resolved
						腹腔内血腫	61	32	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	蛋白尿	64	393	Not Related	Moderate	Not Serious	None	Resolved
						腹部膨満	73	11	Not Related	Moderate	Not Serious	None	Resolved
						ビタミン B12 欠乏	92	.	Not Related	Mild	Not Serious	None	Ongoing
						紅斑	92	204	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	92	204	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	159	1	Not Related	Moderate	Not Serious	None	Resolved
						肺炎	165	9	Not Related	Severe	Serious	None	Resolved
						腸骨動脈閉塞	165	.	Not Related	Mild	Not Serious	None	Ongoing
						高血圧	166	145	Not Related	Mild	Not Serious	None	Resolved
						うつ病	166	.	Not Related	Mild	Not Serious	None	Ongoing
						過角化	196	261	Not Related	Mild	Not Serious	None	Resolved
						皮膚乾燥	197	260	Not Related	Mild	Not Serious	None	Resolved

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* Age at study informed consent date.
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Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	悪心	260	.	Not Related	Mild	Not Serious	None	Ongoing
						関節腫脹	281	15	Not Related	Mild	Not Serious	None	Resolved
						医療機器合併症	294	283	Not Related	Moderate	Not Serious	None	Resolved
						挫傷	302	9	Not Related	Mild	Not Serious	None	Resolved
						腹痛	303	8	Not Related	Moderate	Not Serious	None	Resolved
						発熱	310	3	Not Related	Moderate	Not Serious	None	Resolved
						急性腎不全	310	3	Not Related	Severe	Serious	None	Resolved
						疼痛	310	.	Not Related	Moderate	Not Serious	None	Ongoing
						低血圧	310	1	Not Related	Mild	Not Serious	None	Resolved
						高カリウム血症	310	3	Not Related	Severe	Not Serious	None	Resolved
						高血圧	318	.	Not Related	Moderate	Not Serious	None	Ongoing
						骨粗鬆症	332	.	Not Related	Severe	Not Serious	None	Ongoing

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	ほてり	335	.	Not Related	Mild	Not Serious	None	Ongoing
						体重減少	336	121	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル合併症	357	7	Not Related	Mild	Not Serious	None	Resolved
						疲労	372	.	Not Related	Mild	Not Serious	None	Ongoing
						紅斑	453	95	Not Related	Mild	Not Serious	None	Resolved
						斑状出血	453	95	Not Related	Mild	Not Serious	None	Resolved
						嘔吐	508	1	Not Related	Mild	Not Serious	None	Resolved
						片頭痛	508	1	Not Related	Moderate	Not Serious	None	Resolved
						イレウス	508	38	Not Related	Mild	Not Serious	None	Resolved
						腹痛	508	1	Not Related	Mild	Not Serious	None	Resolved
						下痢	508	7	Not Related	Mild	Not Serious	None	Resolved
						寝汗	547	.	Not Related	Mild	Not Serious	None	Ongoing

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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	片頭痛	599	1	Not Related	Moderate	Not Serious	None	Resolved
						背部痛	641	11	Not Related	Severe	Not Serious	None	Resolved
						鎖骨下静脈血栓症	652	3	Not Related	Mild	Serious	None	Resolved
						カテーテル合併症	652	3	Not Related	Moderate	Not Serious	None	Resolved
						埋込み部位滲出液	673	7	Not Related	Mild	Not Serious	None	Resolved
						処置による疼痛	707	16	Not Related	Moderate	Not Serious	None	Resolved
						術後創感染	716	7	Not Related	Mild	Not Serious	None	Resolved
						栄養障害	738	.	Not Related	Mild	Not Serious	None	Ongoing
						嘔吐	738	1	Not Related	Mild	Not Serious	None	Resolved
						下痢	738	21	Not Related	Moderate	Not Serious	None	Resolved
						血中重炭酸塩減少	743	62	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	758	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	悪心	801	2	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	801	5	Not Related	Moderate	Serious	None	Resolved
						下痢	801	2	Not Related	Mild	Not Serious	None	Resolved
						下痢	804	.	Not Related	Mild	Not Serious	None	Ongoing
						ビタミン D 欠乏	811	.	Not Related	Mild	Not Serious	None	Ongoing
						血液量増加症	811	.	Not Related	Moderate	Not Serious	None	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	骨粗鬆症	-71	.	Not Related	Mild	Not Serious	None	Ongoing
						腹部ヘルニア	-7	.	Not Related	Mild	Not Serious	None	Ongoing
						ほてり	-7	52	Not Related	Mild	Not Serious	None	Resolved
						結膜蒼白	15	22	Not Related	Mild	Not Serious	None	Resolved
						腹痛	15	176	Not Related	Mild	Not Serious	None	Resolved
						腹部ブルイ	15	9	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	鼻咽頭炎	19	24	Not Related	Moderate	Not Serious	None	Resolved
						口腔咽頭痛	19	11	Not Related	Moderate	Not Serious	None	Resolved
						鼻漏	19	24	Not Related	Moderate	Not Serious	None	Resolved
						下痢	56	37	Not Related	Moderate	Not Serious	None	Resolved
						腹部不快感	64	29	Not Related	Moderate	Not Serious	None	Resolved
						うつ病	78	44	Not Related	Moderate	Not Serious	None	Resolved
						腟出血	81	1	Not Related	Mild	Not Serious	None	Resolved
						細菌性尿路感染	92	631	Not Related	Moderate	Not Serious	None	Resolved
						細菌性上気道感染	94	28	Not Related	Mild	Not Serious	None	Resolved
						気管支炎	94	28	Not Related	Moderate	Not Serious	None	Resolved
						胸水	115	.	Not Related	Mild	Not Serious	None	Ongoing
						上大静脈狭窄	122	57	Not Related	Severe	Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	低アルブミン血症	158	6	Not Related	Moderate	Not Serious	None	Resolved
						全身性浮腫	158	33	Not Related	Moderate	Not Serious	None	Resolved
						貧血	162	1	Not Related	Moderate	Not Serious	None	Resolved
						処置による疼痛	169	10	Not Related	Mild	Not Serious	None	Resolved
						処置による悪心	169	10	Not Related	Mild	Not Serious	None	Resolved
						処置後合併症	169	10	Not Related	Mild	Not Serious	None	Resolved
						悪液質	170	63	Not Related	Mild	Not Serious	None	Resolved
						甲状腺新生物	172	.	Not Related	Mild	Not Serious	None	Ongoing
						高血糖	176	3	Not Related	Moderate	Not Serious	None	Resolved
						大静脈血栓症	179	.	Not Related	Moderate	Not Serious	None	Ongoing
						筋骨格系胸痛	189	44	Not Related	Moderate	Not Serious	None	Resolved
						末梢性浮腫	190	176	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	下痢	232	16	Not Related	Moderate	Not Serious	None	Resolved
						下痢	295	71	Not Related	Mild	Not Serious	None	Resolved
						処置による疼痛	402	3	Not Related	Mild	Not Serious	None	Resolved
						気管支炎	406	7	Not Related	Mild	Not Serious	None	Resolved
						副甲状腺機能亢進症	456	92	Not Related	Mild	Not Serious	None	Resolved
						表在性異物	479	7	Not Related	Mild	Not Serious	None	Resolved
						処置後局所反応	505	134	Not Related	Mild	Not Serious	None	Resolved
						悪心	547	92	Not Related	Mild	Not Serious	None	Resolved
						末梢性浮腫	562	77	Not Related	Mild	Not Serious	None	Resolved
						溶血性貧血	574	10	Not Related	Moderate	Not Serious	None	Resolved
						尿路感染	574	23	Not Related	Moderate	Serious	None	Resolved
						医療機器位置異常	637	2	Not Related	Mild	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	6[redacted]	末梢性浮腫	675	.	Not Related	Moderate	Not Serious	None	Ongoing
						視力障害	691	32	Not Related	Mild	Not Serious	None	Resolved
						浮動性めまい	715	.	Not Related	Mild	Not Serious	None	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	鼓腸	-171	167	Related	Mild	Not Serious	None	Resolved
						鼻炎	-10	3	Not Related	Moderate	Not Serious	None	Resolved
						腹痛	-10	26	Not Related	Mild	Not Serious	None	Resolved
						心電図 QT 延長	-9	86	Related	Mild	Not Serious	None	Resolved
						悪心	16	75	Not Related	Mild	Not Serious	None	Resolved
						腹部不快感	16	.	Not Related	Moderate	Not Serious	None	Ongoing
						四肢痛	18	12	Not Related	Moderate	Not Serious	None	Resolved
						食欲不振	18	32	Not Related	Mild	Not Serious	None	Resolved
						発熱	19	10	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	疲労	.	.	Not Related	Moderate	Not Serious	None	Resolved
						脱水	.	.	Not Related	Moderate	Not Serious	None	Resolved
						発熱	43	14	Not Related	Moderate	Not Serious	None	Resolved
						食欲不振	50	.	Not Related	Mild	Not Serious	None	Resolved
						中心静脈カテーテル感染	118	12	Not Related	Moderate	Serious	None	Resolved
						背部痛	.	.	Not Related	Moderate	Not Serious	None	Resolved
						発熱	203	.	Not Related	Moderate	Not Serious	None	Resolved
						血性水疱	.	.	Not Related	Moderate	Not Serious	None	Resolved
						骨痛	351	.	Not Related	Mild	Not Serious	None	Ongoing
						高リパーゼ血症	362	.	Related	Moderate	Not Serious	Drug Dose Interrupted	Ongoing
						体重減少	.	.	Not Related	Mild	Not Serious	None	Resolved
						カテーテル留置部位感染	448	52	Not Related	Severe	Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	4[redacted]	治癒不良	448	50	Not Related	Moderate	Not Serious	None	Resolved
						高血圧	.	.	Not Related	Moderate	Not Serious	None	Ongoing
						鎖骨下静脈血栓症	497	.	Not Related	Moderate	Not Serious	None	Ongoing
						大静脈血栓症	497	.	Not Related	Moderate	Not Serious	None	Ongoing
						胃腸感染	540	92	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	5[redacted]	カテーテル関連感染	410	9	Not Related	Severe	Serious	None	Resolved
						大静脈血栓症	413	.	Not Related	Moderate	Not Serious	None	Ongoing
						医療機器位置異常	448	5	Not Related	Moderate	Not Serious	None	Resolved
						低リン酸血症	550	88	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	7[redacted]	γ-グルタミルトランスフェラーゼ増加	14	.	Not Related	Moderate	Not Serious	None	Ongoing
						体重減少	14	260	Not Related	Mild	Not Serious	None	Resolved
						便秘	18	.	Not Related	Mild	Not Serious	None	Ongoing

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	7[redacted]	血中アルカリホスファターゼ増加	63	.	Not Related	Moderate	Not Serious	None	Ongoing
						アスパラギン酸アミノトランスフェラーゼ増加	88	.	Not Related	Moderate	Not Serious	None	Ongoing
						尿路感染	182	9	Not Related	Mild	Not Serious	None	Resolved
						胆汁うっ滞	197	2	Not Related	Mild	Serious	None	Resolved
						無力症	204	7	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル関連感染	208	31	Not Related	Severe	Serious	None	Resolved
						カテーテル留置部位感染	448	.	Not Related	Mild	Not Serious	None	Ongoing
						腎仙痛	528	6	Not Related	Moderate	Not Serious	None	Resolved
						高リパーゼ血症	539	.	Not Related	Moderate	Not Serious	None	Ongoing
						高アミラーゼ血症	539	.	Not Related	Moderate	Not Serious	None	Ongoing
						ファーター乳頭狭窄	659	2	Not Related	Severe	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	肺炎	85	10	Not Related	Moderate	Serious	None	Resolved

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Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	体重減少	123	425	Not Related	Mild	Not Serious	None	Resolved
						腹痛	435	2	Not Related	Mild	Not Serious	None	Resolved
						消化管ストーマ合併症	547	176	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	消化管ストーマ合併症	-148	.	Related	Mild	Not Serious	None	Ongoing
						血中クロモグラニン A 増加	6	.	Related	Mild	Not Serious	None	Ongoing
						舌痛	30	.	Not Related	Mild	Not Serious	None	Ongoing
						空腸狭窄	30	.	Related	Mild	Not Serious	None	Ongoing
						筋痙縮	87	.	Not Related	Mild	Not Serious	None	Ongoing
						切迫性尿失禁	160	.	Not Related	Mild	Not Serious	None	Ongoing
						体重増加	181	.	Not Related	Mild	Not Serious	None	Ongoing
						中心静脈カテーテル感染	195	3	Not Related	Moderate	Serious	None	Resolved
						カテーテル関連感染	267	14	Not Related	Moderate	Not Serious	None	Resolved

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	尿路感染	267	31	Not Related	Mild	Not Serious	None	Resolved
						頻脈	.	.	Not Related	Mild	Not Serious	None	Ongoing
						声帯肥厚	461	168	Not Related	Moderate	Not Serious	None	Resolved
						貧血	471	.	Not Related	Moderate	Not Serious	None	Ongoing
						貧血	721	2	Not Related	Severe	Serious	None	Resolved
						血中マグネシウム減少	722	.	Not Related	Mild	Not Serious	None	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	蛋白尿	-217	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	59	11	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	87	.	Not Related	Mild	Not Serious	None	Resolved
						胃腸炎	105	3	Not Related	Moderate	Serious	None	Resolved
						憩室炎	127	29	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						ポリープ	137	1	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	敗血症症候群	145	5	Not Related	Moderate	Serious	Drug Dose Interrupted	Resolved
						心筋症	150	.	Not Related	Moderate	Not Serious	None	Ongoing
						憩室炎	167	4	Not Related	Moderate	Serious	None	Resolved
						失神	248	2	Not Related	Moderate	Serious	None	Resolved
						憩室	249	.	Not Related	Mild	Not Serious	None	Ongoing
						尿路感染	270	5	Not Related	Mild	Not Serious	None	Resolved
						インフルエンザ	338	23	Not Related	Moderate	Not Serious	None	Resolved
						尿路感染	338	23	Not Related	Mild	Not Serious	None	Resolved
						副鼻腔炎	430	12	Not Related	Moderate	Not Serious	None	Resolved
						血中重炭酸塩減少	449	.	Not Related	Mild	Not Serious	None	Ongoing
						血中トリグリセリド増加	449	94	Not Related	Mild	Not Serious	None	Resolved
						体重減少	449	.	Not Related	Moderate	Not Serious	None	Ongoing

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	5[redacted]	血中カルシウム減少	449	.	Not Related	Mild	Not Serious	None	Ongoing
						腹痛	.	.	Not Related	Moderate	Not Serious	None	Resolved
						注射部位反応	.	.	Related	Mild	Not Serious	None	Ongoing
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Female	3[redacted]	肉芽腫	1	103	Not Related	Moderate	Not Serious	None	Resolved
						注入部位腫瘤	1	99	Not Related	Moderate	Not Serious	None	Resolved
						骨粗鬆症	18	.	Not Related	Mild	Not Serious	None	Ongoing
						発熱	75	2	Not Related	Mild	Not Serious	None	Resolved
						口腔咽頭痛	76	6	Not Related	Mild	Not Serious	None	Resolved
						感染	99	5	Not Related	Mild	Serious	None	Resolved
						肉芽腫	103	7	Not Related	Moderate	Not Serious	None	Resolved
						カテーテル留置部位紅斑	303	4	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	水腎症	2	1	Not Related	Severe	Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	皮膚硬結	2	55	Not Related	Mild	Not Serious	None	Resolved
						四肢痛	2	55	Not Related	Mild	Not Serious	None	Resolved
						四肢痛	2	27	Not Related	Mild	Not Serious	None	Resolved
						腎結石症	2	1	Not Related	Severe	Serious	None	Resolved
						頭痛	12	1	Not Related	Moderate	Not Serious	None	Resolved
						高トリグリセリド血症	14	15	Not Related	Mild	Not Serious	None	Resolved
						頭痛	37	7	Not Related	Mild	Not Serious	None	Resolved
						腎仙痛	37	5	Not Related	Moderate	Not Serious	None	Resolved
						腎仙痛	43	1	Not Related	Moderate	Not Serious	None	Resolved
						腎仙痛	51	4	Not Related	Moderate	Not Serious	None	Resolved
						腎仙痛	63	1	Not Related	Mild	Not Serious	None	Resolved
						腎仙痛	77	3	Not Related	Moderate	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

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Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	鼻咽頭炎	131	4	Not Related	Mild	Not Serious	None	Resolved
						腎仙痛	135	4	Not Related	Moderate	Not Serious	None	Resolved
						腎仙痛	165	1	Not Related	Mild	Not Serious	None	Resolved
						冷汗	.	.	Not Related	Mild	Not Serious	None	Resolved
						腹部膨満	183	463	Related	Moderate	Not Serious	None	Resolved
						高トリグリセリド血症	183	92	Not Related	Mild	Not Serious	None	Resolved
						痔核	229	16	Not Related	Moderate	Not Serious	None	Resolved
						蕁麻疹	330	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	394	32	Not Related	Mild	Not Serious	None	Resolved
						皮下血腫	464	2	Related	Mild	Not Serious	None	Resolved
						腎仙痛	518	2	Not Related	Mild	Not Serious	None	Resolved
						鼻咽頭炎	520	25	Not Related	Mild	Not Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
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Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	3[redacted]	腎仙痛	.	.	Not Related	Mild	Not Serious	None	Resolved
						上顆炎	646	.	Not Related	Moderate	Not Serious	None	Ongoing
						関節痛	646	.	Not Related	Mild	Not Serious	None	Ongoing
						痔核	715	1	Not Related	Moderate	Not Serious	None	Resolved
						鼻咽頭炎	722	11	Not Related	Moderate	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	顔面浮腫	13	4	Not Related	Moderate	Not Serious	None	Resolved
						中心静脈カテーテル感染	227	4	Not Related	Moderate	Serious	None	Resolved
						胃腸炎	292	4	Not Related	Severe	Serious	None	Resolved
						中心静脈カテーテル感染	460	8	Not Related	Moderate	Serious	None	Resolved
						中心静脈カテーテル感染	609	15	Not Related	Moderate	Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	直腸分泌物	121	24	Related	Mild	Not Serious	Drug Dose Interrupted	Resolved
						大腸炎	155	.	Related	Moderate	Not Serious	None	Ongoing

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
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Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	創部分泌	158	.	Not Related	Mild	Not Serious	Drug Dose Interrupted	Ongoing
						血中クレアチニン増加	185	4	Not Related	Mild	Not Serious	None	Resolved
						クローン病	285	21	Related	Moderate	Serious	Drug Discontinued	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	4[redacted]	末梢性浮腫	-103	.	Related	Mild	Not Serious	None	Ongoing
						末梢性浮腫	-5	21	Related	Mild	Not Serious	None	Resolved
						顔面浮腫	-5	7	Related	Mild	Not Serious	None	Resolved
						肋骨骨折	69	12	Not Related	Moderate	Serious	None	Resolved
						血腫	69	12	Not Related	Moderate	Serious	None	Resolved
						鎖骨骨折	69	12	Not Related	Moderate	Serious	None	Resolved
						口唇血腫	269	97	Not Related	Mild	Not Serious	None	Resolved
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	憩室	-188	.	Not Related	Mild	Not Serious	None	Ongoing
						脳血管発作	244	7	Not Related	Mild	Serious	None	Resolved

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas

Output Generated On: 21OCT2016 14:57

Treatment group	Subject ID	Race	Dose	Sex	Age*	Adverse event	Day of onset	Duration (Days)	Causality	Severity	Serious /Not serious	Action taken	Outcome
Teduglutide / Teduglutide	[redacted]	White	0.05 Mg/Kg/Day	Male	6[redacted]	低アルブミン血症	407	.	Not Related	Mild	Not Serious	None	Ongoing
						低蛋白血症	407	.	Not Related	Mild	Not Serious	None	Ongoing
						体重減少	407	.	Not Related	Mild	Not Serious	None	Ongoing
						脳血管発作	620	9	Not Related	Mild	Serious	None	Resolved
						皮膚感染	625	10	Not Related	Mild	Not Serious	None	Resolved
						椎間板炎	688	.	Not Related	Severe	Serious	None	Ongoing
						尿路感染	688	9	Not Related	Severe	Serious	None	Resolved
						敗血症	688	16	Not Related	Severe	Serious	None	Fatal

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Teduglutide/Teduglutide = subjects already exposed to active treatment with teduglutide for 24 weeks in Study CL0600-020
* Age at study informed consent date.
Note: All adverse events were coded using MedDRA version 12.0.
Note: Day of onset is counted from the day of the first administration inclusive.
Program: l-3-5-ae-sae-600021.sas
Output Generated On: 21OCT2016 14:57

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term	Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	Duration (days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Asian	Female	4[redacted]	胃腸障害／ 腹部膨満／ Bloating	15DEC2018 (5)/ 27DEC2018 (17)	13	No/ Mild/ Related	Dose Not Changed/ None	Intermittent/ Recovered/ Resolved	Yes
				生殖系および乳房障害／ 月経過多／ Prolonged Menstruation	15JAN2019 (36)/ Ongoing		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Intermittent/ Not Recovered/ Not Resolved	Yes
				感染症および寄生虫症／ 上咽頭炎／ Common Cold	16JAN2019 (37)/ 19JAN2019 (40)	4	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved	Yes
				感染症および寄生虫症／ 医療機器使用部位感染／ Suspected Catheter Site Infection	01FEB2019 (53)/ 15FEB2019: 10:00 (67)	15	Yes/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Recovered/ Resolved	Yes
				血液およびリンパ系障害／ 貧血／ Anemia	04FEB2019 (56)/ Ongoing		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Not Recovered/ Not Resolved	Yes
				代謝および栄養障害／ 低亜鉛血症／ Hypozincemia	04FEB2019 (56)/ Ongoing		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Not Recovered/ Not Resolved	Yes

Note: Treatment emergent AEs (TEAEs) are defined as AEs whose onset occurs, severity worsens, or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 21.0.
Note: Reported terms are collected on the eCRFs.

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term	Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	Duration (days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Asian	Female	4[redacted]	血管障害／ 静脈炎／ Phlebitis	16FEB2019 (68)/ 13MAR2019 (93)	26	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved	Yes
				胃腸障害／ 腹痛／ Left Abdominal Pain	14MAR2019 (94)/ 16MAR2019 (96)	3	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved	Yes
[redacted]	Asian	Male	2[redacted]	皮膚および皮下組織障害／ 皮下出血／ Subcutaneous Bleeding	25DEC2018 (15)/ 22APR2019 (133)	119	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved	Yes
				呼吸器、胸郭および縦隔障害／ 鼻出血／ Nose Bleeding	11JAN2019 (32)/ 11JAN2019 (32)	1	No/ Mild/ Not Related	Dose Not Changed/ None	Intermittent/ Recovered/ Resolved	Yes
				皮膚および皮下組織障害／ 皮膚乾燥／ Dry Skin	14FEB2019 (66)/ Ongoing		No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Not Recovered/ Not Resolved	Yes
				神経系障害／ てんかん／ Worsening Of Epilepsy	13MAR2019 (93)/ Ongoing		No/ Mild/ Not Related	Not Applicable/ Drug Treatment Given	Intermittent/ Not Recovered/ Not Resolved	Yes

Note: Treatment emergent AEs (TEAEs) are defined as AEs whose onset occurs, severity worsens, or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 21.0.
Note: Reported terms are collected on the eCRFs.

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term	Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	Duration (days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Asian	Male	2[redacted]	神経系障害／ てんかん／ Epilepsy Seizure	13MAR2019 (93)/ 13MAR2019 (93)	1	Yes/ Severe/ Not Related	Not Applicable/ Drug Treatment Given	Continuous/ Recovered/ Resolved	Yes
				神経系障害／ 頭痛／ Headache	28MAR2019 (108)/ Ongoing		No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Not Recovered/ Not Resolved	Yes
				感染症および寄生虫症／ 上咽頭炎／ Common Cold	08APR2019 (119)/ 30APR2019 (141)	23	No/ Mild/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Recovered/ Resolved	Yes
				傷害、中毒および処置合併症 ／ 脊椎圧迫骨折／ Thoracic Compression Fractures	02MAY2019 (143)/ Ongoing		Yes/ Mild/ Not Related	Not Applicable/ None	Continuous/ Recovering/ Resolving	Yes
				神経系障害／ てんかん／ Epilepsy Seizure	02MAY2019 (143)/ 02MAY2019 (143)	1	Yes/ Severe/ Not Related	Not Applicable/ Drug Treatment Given	Continuous/ Recovered/ Resolved	Yes
[redacted]	Asian	Male	4[redacted]	一般・全身障害および投与部位の状態／ 倦怠感／ Malaise	25OCT2018: 08:00 (-49)/ 01NOV2018 (-42)	8	No/ Moderate/ Not Related	Not Applicable/ Drug Treatment Given	Intermittent/ Recovered/ Resolved	No

Note: Treatment emergent AEs (TEAEs) are defined as AEs whose onset occurs, severity worsens, or intensity increases after receiving the study medication.
Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 21.0.
Note: Reported terms are collected on the eCRFs.

Site ID - Subject ID	Race	Sex	Age	System Organ Class/ Preferred Term/ Reported Term	Start Date and Time (Study Day)/ Stop Date and Time (Study Day)	Duration (days)	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?
[redacted]	Asian	Male	4[redacted]	胃腸障害／ 十二指腸炎／ Acute Duodenitis	29NOV2018 (-14)/ 04DEC2018: 08:00 (-9)	6	Yes/ Moderate/ Not Related	Not Applicable/ Multiple	Continuous/ Recovered/ Resolved	No
				胃腸障害／ 十二指腸潰瘍／ Duodenal Ulcer	29NOV2018 (-14)/ 30MAY2019 (169)	183	No/ Moderate/ Not Related	Not Applicable/ Drug Treatment Given	Continuous/ Recovered/ Resolved	No
				一般・全身障害および投与部位の状態／ 発熱／ Fever	13DEC2018: 16:10 (1)/ 16DEC2018 (4)	4	No/ Mild/ Not Related	Dose Not Changed/ None	Continuous/ Recovered/ Resolved	Yes
				感染症および寄生虫症／ 医療機器関連感染／ Central Venous Catheter Related Infection	24DEC2018: 12:00 (12)/ 01JAN2019: 00:00 (20)	9	Yes/ Moderate/ Not Related	Dose Not Changed/ Drug Treatment Given	Continuous/ Recovered/ Resolved	Yes
				血液およびリンパ系障害／ 赤血球増加症／ Polycythemia	27JUN2019 (197)/ Ongoing		No/ Mild/ Related	Not Applicable/ None	Continuous/ Not Recovered/ Not Resolved	Yes

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Note: Relationship to study treatment is based upon investigator assessment.
Note: System organ classes and preferred terms are coded using MedDRA 21.0.
Note: Reported terms are collected on the eCRFs.

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	臨床検査／ C-反応性蛋白増加／ ELEVATED CRP	07MAY2014:23:15/ 1/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		臨床検査／ 尿中細菌／ URINE BACTERIA (MANY)	08MAY2014:23:15/ 2/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		臨床検査／ 尿中白血球エステラーゼ陽性／ URINE TRACE LEUKOESTERASE	08MAY2014:23:15/ 2/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		臨床検査／ 白血球数増加／ ELEVATED WBC 15.2	08MAY2014:23:15/ 2/ 22MAY2014:05:38/ 16	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ カテーテル合併症／ NONFUNCTIONING BROVIAC CATHETER	22MAY2014:02:43/ 16/ 22MAY2014:17:12/ 16	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	臨床検査／ 血中重炭酸塩減少／ LOW BICARBONATE	29MAY2014:13:08/ 23/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
	[redacted]	感染症および寄生虫症／ 鼻咽頭炎／ COLD SYMPTOMS	15DEC2013/ -25/ 16DEC2013/ -24	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		胃腸障害／ 下痢／ DIARRHEA	17DEC2013/ -23/ 24DEC2013/ -16	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		胃腸障害／ 嘔吐／ VOMITING	17DEC2013/ -23/ 19DEC2013/ -21	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 鼻咽頭炎／ COLD	07FEB2014/ 30/ 12MAR2014/ 63	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	皮膚および皮下組織障害／ 紅斑性皮疹／ RASH	07FEB2014/ 30/ 11MAR2014/ 62	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 下痢／ WORSENING DIARRHEA	07MAR2014/ 58/ 10MAR2014/ 61	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ SEVERITY/FREQUENCY INCREASED	Yes	Treatment
		胃腸障害／ 便秘／ CONSTIPATION	08MAR2014/ 59/ 08MAR2014/ 59	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	08MAR2014/ 59/ 11MAR2014/ 62	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ ウイルス性胃腸炎／ VIRAL ILLNESS: VOMITING AND DIARRHEA	11MAR2014/ 62/ 14MAR2014/ 65	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	胃腸障害／ 嘔吐／ VOMITING	14MAR2014/ 65/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	No	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL CRAMPING	15MAR2014/ 66/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		胃腸障害／ 便秘／ CONSTIPATION	20MAR2014/ 71/ 22MAR2014/ 73	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 下痢／ WORSENING DIARRHEA	29APR2014/ 111/ 07MAY2014/ 119	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Post-treatment
		全身障害および投与局所様態／ 発熱／ FEVER	30APR2014/ 112/ 01MAY2014/ 113	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	30AUG2014/ 18/ 03SEP2014/ 22	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 易刺激性／ FUSSY	16SEP2014/ 35/ 17SEP2014/ 36	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	11OCT2014/ 60/ 11OCT2014/ 60	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	12OCT2014/ 61/ 16OCT2014/ 65	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	22OCT2014:19:00/ 71/ 26OCT2014:17:10/ 75	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
STANDARD OF CARE	[redacted]	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER RASH	23OCT2014/ 72/ 26OCT2014/ 75	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 真菌血症／ MALASSEZIA FURFUR FUNGEMIA	29OCT2014:07:00/ 78/ 17NOV2014:16:54/ 97	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 真菌血症／ MALASSEZIA FURFUR FUNGEMIA	18NOV2014/ 98/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Post-treatment
	[redacted]	感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	29JUL2014/ -15/ 03AUG2014/ -10	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 細菌性胃腸感染／ SB BACTERIAL OVERGROWTH	31AUG2014/ 19/ 01SEP2014/ 20	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.0125 MG/KG/DAY	[redacted]	呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	11FEB2014/ -2/ 20FEB2014/ 8	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		呼吸器、胸郭および縦隔障害／ 鼻漏／ RHINNORRHEA	11FEB2014/ -2/ 20FEB2014/ 8	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ アデノウイルス感染／ ADENOVIRUS INFECTION	23FEB2014/ 11/ 13MAR2014/ 29	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 肛門直腸不快感／ PERIANAL SORENESS	24FEB2014/ 12/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 耳感染／ EAR INFECTION	19MAY2014/ 96/ 02JUN2014/ 110	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.0125 MG/KG/DAY	[redacted]	全身障害および投与局所様態／ 発熱／ FEVER	18FEB2014:01:36/ -7/ 20FEB2014/ -5	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		胃腸障害／ 変色便／ FLORESCENT COLOR STOOL	28FEB2014/ 4/ 03MAR2014/ 7	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 消化管粘膜変色／ DISCOLORATION OF MOUTH	28FEB2014/ 4/ 03MAR2014/ 7	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	28FEB2014/ 4/ 03MAR2014/ 7	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		胃腸障害／ 血便排泄／ BLOOD IN STOOL	05MAR2014/ 9/ 21APR2014/ 56	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.0125 MG/KG/DAY	[redacted]	胃腸障害／ 鼓腸／ INCREASE IS IN FLATULENCE	17MAR2014/ 21/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 鼻咽頭炎／ COLD	21MAR2014/ 25/ 07APR2014/ 42	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 便量増加／ INCREASE IN STOOL OUTPUT	25MAR2014/ 29/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	27MAR2014/ 31/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中耳炎／ OTITIS MEDIA	01MAY2014/ 66/ 11MAY2014/ 76	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.0125 MG/KG/DAY	[redacted]	全身障害および投与局所様態／ カテーテル合併症／ CENTRAL LINE CLOT	01FEB2014/ -5/ 05FEB2014/ -1	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		耳および迷路障害／ 耳痛／ EAR ACHE, LEFT EAR	-----/ ---/ 03MAR2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 高血糖／ HYPERGLYCEMIA	17FEB2014/ 12/ 26FEB2014/ 21	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 高カリウム血症／ HYPERKALEMIA	17FEB2014/ 12/ 26FEB2014/ 21	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 体重減少／ WEIGHT LOSS	26FEB2014/ 21/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.0125 MG/KG/DAY	[redacted]	感染症および寄生虫症／ カテーテル関連感染／ CVL INFECTION	05MAR2014/ 28/ 19MAR2014/ 42	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	代謝および栄養障害／ 高ナトリウム血症／ HYPERNATREMIA	31DEC2013:09:56/ -6/ 06JAN2014:10:20/ 1	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ インフルエンザ／ FLU A POSITIVE	02FEB2014/ 28/ 08FEB2014/ 34	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ カテーテル合併症／ CVL MALFUNCTION	05FEB2014/ 31/ 14FEB2014/ 40	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ ビタミンＥ欠乏／ VITAMIN E DEFICIENCY	18FEB2014:09:45/ 44/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	胃腸障害／ 下痢／ LOOSE STOOL	18JUN2014/ 22/ 02JUL2014/ 36	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	18JUN2014:08:32/ 22/ 20JUN2014:17:00/ 24	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ ライノウイルス感染／ RHINOVIRUS INFECTION	18JUN2014:10:00/ 22/ 21JUN2014:16:00/ 25	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 血中クレアチニン増加／ ELEVATED CREATININE	21JUN2014:06:57/ 25/ 01JUL2014:14:28/ 35	Yes/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ アラニン・アミノトランスフェラーゼ増加／ ELEVATED ALANINE AMINOTRANSFERASE	26JUN2014:12:39/ 30/ 01JUL2014:14:28/ 35	No/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	臨床検査／ アスパラギン酸アミノトランスフェラーゼ増加／ ELEVATED ASPARTATE AMINOTRANSFERASE	26JUN2014:12:39/ 30/ 01JUL2014:14:28/ 35	No/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		神経系障害／ 浮動性めまい／ DIZZINESS	16JUL2014/ 50/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		神経系障害／ 頭痛／ HEADACHE	16JUL2014/ 50/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		呼吸器、胸郭および縦隔障害／ 扁桃肥大／ ENLARGED TONSILS, NO REDNESS	17SEP2014/ 113/ 09OCT2014/ 135	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	26MAR2014/ -23/ 09APR2014/ -9	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	血液およびリンパ系障害／ リンパ節症／ MILD BILATERAL ANTERIOR CERVICAL AND SUBMANDIBULAR LYMPHODENOPATHY	18APR2014/ 1/ 02MAY2014/ 15	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING (INCREASED FROM BASELINE)	02MAY2014/ 15/ 02MAY2014/ 15	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		血液およびリンパ系障害／ 好中球減少症／ NEUTROPENIA-WORSENING FROM BASELINE	16MAY2014:09:27/ 29/ 20MAY2014/ 33	No/ MODERATE/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		血液およびリンパ系障害／ 血小板減少症／ THROMBOCYTOPENIA-WORSENING FROM BASELINE	16MAY2014:09:27/ 29/ 20MAY2014/ 33	No/ MODERATE/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		神経系障害／ 頭痛／ HEADACHE	22MAY2014/ 35/ 22MAY2014/ 35	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	23MAY2014/ 36/ 11JUN2014/ 55	Yes/ SEVERE/ NOT RELATED	DRUG INTERRUPTED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 低血糖症／ HYPOGLYCEMIA	27MAY2014/ 40/ 10JUN2014/ 54	No/ MODERATE/ NOT RELATED	DRUG INTERRUPTED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		神経系障害／ 大発作痙攣／ GENERALIZED TONIC-CLONIC SEIZURE	27MAY2014/ 40/ 27MAY2014:21:28/ 40	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ カテーテル合併症／ CENTRAL LINE BREAK	26JUN2014/ 70/ 27JUN2014/ 71	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	16JUL2014/ 90/ 17JUL2014/ 91	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	07AUG2014:12:34/ 112/ 12AUG2014/ 117	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	全身障害および投与局所様態／ カテーテル合併症／ CENTRAL LINE DYSFUNCTION	12APR2014:00:45/ -18/ 14APR2014:22:09/ -16	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		皮膚および皮下組織障害／ 発疹／ RASH	19APR2014/ -11/ 24JUN2014/ 56	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	05MAY2014/ 6/ 20MAY2014/ 21	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		傷害、中毒および処置合併症／ 栄養補給管合併症／ FEEDING TUBE DISFUNCTION	01JUL2014/ 63/ 01JUL2014/ 63	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	神経系障害／ 筋痙直／ SPASTICITY	28JUL2014/ 90/ 28JUL2014/ 90	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	全身障害および投与局所様態／ カテーテル合併症／ REPAIR OF BROKEN LINE	14MAY2014/ -14/ 15MAY2014/ -13	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	08JUN2014/ 12/ 25JUN2014/ 29	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER RASH	25JUN2014/ 29/ 28JUN2014/ 32	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING	17JUL2014/ 51/ 17JUL2014/ 51	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	胃腸障害／ 嘔吐／ VOMITING	03AUG2014/ 68/ 04AUG2014/ 69	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		免疫系障害／ 薬物過敏症／ ALLERGIC REACTION TO IRON INFUSION	05AUG2014/ 70/ 12AUG2014/ 77	No/ MILD/ NOT RELATED	DRUG INTERRUPTED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING	06AUG2014/ 71/ 06AUG2014/ 71	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 亜鉛欠乏／ ZINC DEFICIENCY	20AUG2014/ 85/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		皮膚および皮下組織障害／ 蕁麻疹／ HIVES	24AUG2014/ 89/ 25AUG2014/ 90	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	-----/ ---/ 17SEP2014/ 113	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		胃腸障害／ 嘔吐／ VOMITING	04SEP2014/ 100/ 05SEP2014/ 101	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 発熱／ FEVER	04SEP2014/ 100/ 05SEP2014/ 101	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	胃腸障害／ 嘔吐／ VOMITING	09MAY2014/ -20/ 25JUN2014/ 28	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		臨床検査／ Ｃ－反応性蛋白増加／ ELEVATED C REACTIVE PROTEIN	29MAY2014:08:28/ 1/ 10JUL2014:10:10/ 43	No/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	臨床検査／ 尿中結晶陽性／ ELEVATED CALCIUM OXALATE	29MAY2014:08:28/ 1/ 12JUN2014:09:46/ 15	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		臨床検査／ 尿中蛋白陽性／ ELEVATED URINE PROTEIN	29MAY2014:08:28/ 1/ 12JUN2014:09:13/ 15	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		臨床検査／ 尿円柱／ ELEVATED HYALINE CAST	29MAY2014:08:28/ 1/ 12JUN2014:09:46/ 15	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		臨床検査／ 尿中白血球陽性／ ELEVATED WBC (URINE)	29MAY2014:08:28/ 1/ 12JUN2014:09:46/ 15	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		心臓障害／ 頻脈／ TACHYCARDIA	04JUN2014/ 7/ 04JUN2014/ 7	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	04JUN2014:10:57/ 7/ 12JUN2014:10:06/ 15	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		血管障害／ 血液量減少性ショック／ SHOCK AND HYPOVOLEMIC	04JUN2014:10:57/ 7/ 07JUN2014:14:25/ 10	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		血液およびリンパ系障害／ 貧血／ ANEMIA	21JUN2014/ 24/ 23JUN2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		血液およびリンパ系障害／ 骨髄機能不全／ BONE MARROW SUPPRESSION	21JUN2014/ 24/ 23JUN2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		血液およびリンパ系障害／ 好中球減少症／ NEUTROPENIA	21JUN2014/ 24/ 23JUN2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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0.025 MG/KG/DAY	[redacted]	血液およびリンパ系障害／ 血小板減少症／ THROMBOCYTOPENIA	21JUN2014/ 24/ 23JUN2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 疼痛／ PAIN	21JUN2014/ 24/ 23JUN2014/ 26	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	21JUN2014/ 24/ 22JUN2014/ 25	Yes/ MODERATE/ NOT RELATED	DRUG INTERRUPTED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		筋骨格系および結合組織障害／ 筋痙縮／ MUSCLE SPASMS	21JUN2014/ 24/ 21JUN2014/ 24	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		腎および尿路障害／ 腎結石症／ KIDNEY STONE	21JUN2014:18:18/ 24/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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0.025 MG/KG/DAY	[redacted]	胃腸障害／ 悪心／ NAUSEA	16JUL2014/ 49/ 16JUL2014/ 49	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING	18JUL2014/ 51/ 20JUL2014/ 53	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment
	[redacted]	全身障害および投与局所様態／ カテーテル合併症／ BROKEN PICC LINE	16MAY2014/ -69/ 17MAY2014/ -68	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	29MAY2014:09:50/ -56/ 09JUN2014:12:01/ -45	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		呼吸器、胸郭および縦隔障害／ 扁桃肥大／ ENLARGED TONSILS	21AUG2014:12:32/ 29/ 16OCT2014:10:34/ 85	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	胃腸障害／ レッチング／ GAGGING	29AUG2014/ 37/ 11SEP2014/ 50	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING	29AUG2014/ 37/ 11SEP2014/ 50	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		傷害、中毒および処置合併症／ 切開部位紅斑／ ERYTHEMA AROUND G-TUBE	18SEP2014:10:42/ 57/ 16OCT2014:10:34/ 85	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION	15OCT2014:15:04/ 84/ 22OCT2014:18:13/ 91	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
	[redacted]	呼吸器、胸郭および縦隔障害／ 鼻漏／ RHINORRHEA	29MAR2014/ -19/ 03APR2014/ -14	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	胃腸障害／ 嘔吐／ EMESIS	30MAR2014/ -18/ 30MAR2014/ -18	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		全身障害および投与局所様態／ 発熱／ FEVER	30MAR2014/ -18/ 03APR2014/ -14	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		胃腸障害／ 鼓腸／ GAS	22APR2014/ 6/ ---------/ ---	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		感染症および寄生虫症／ パラインフルエンザウイルス感染／ PARAINFLUENZA 3 WITH FEVER	03MAY2014/ 17/ 09MAY2014/ 23	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ ライノウイルス感染／ RHINOVIRUS WITH FEVER	03MAY2014/ 17/ 09MAY2014/ 23	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	傷害、中毒および処置合併症／ 栄養補給管合併症／ GTUBE PULLED OUT	16JUN2014/ 61/ 17JUN2014/ 62	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	09APR2014/ -42/ 20APR2014/ -31	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ 鼻咽頭炎／ COLD	20MAY2014/ -1/ 27MAY2014/ 7	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		皮膚および皮下組織障害／ 発疹／ SMALL RASH	28MAY2014/ 8/ 29MAY2014/ 9	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	04JUN2014/ 15/ 09JUN2014/ 20	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	皮膚および皮下組織障害／ 発疹／ RASH ON FACE AND ARMS	05JUN2014:11:30/ 16/ 05JUN2014/ 16	No/ MODERATE/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		皮膚および皮下組織障害／ 発疹／ RASH ON FACE	06JUN2014:11:20/ 17/ 09JUN2014/ 20	Yes/ SEVERE/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 体温上昇／ INCREASED TEMPERATURE	17JUN2014/ 28/ 17JUN2014/ 28	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	26JUN2014/ 37/ 02JUL2014/ 43	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ STAPH CENTRAL LINE INFECTION	13JUL2014:17:30/ 54/ 20JUL2014/ 61	Yes/ SEVERE/ NOT RELATED	DRUG INTERRUPTED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	呼吸器、胸郭および縦隔障害／ 鼻漏／ SBEEZING AND RUNNING NOSE	25JUL2014/ 66/ 31JUL2014/ 72	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ カテーテル合併症／ BROKEN CENTRAL LINE	29JUL2014:03:44/ 70/ 29JUL2014:09:00/ 70	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION E.COLI	11AUG2014/ 83/ 15AUG2014/ 87	Yes/ SEVERE/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	胃腸障害／ 血便排泄／ LARGE VOLUME OF BLOOD IN STOOL	21MAR2014:09:30/ -32/ 23MAR2014/ -30	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Pre-treatment
		免疫系障害／ 薬物過敏症／ REACTION TO IV IRON	28APR2014:17:00/ 7/ 28APR2014:17:01/ 7	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	全身障害および投与局所様態／ 注射部位疼痛／ LEG PAIN AFTER INJECTION SHOT	02MAY2014/ 11/ 02MAY2014/ 11	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ インフルエンザ／ FLU	10MAY2014/ 19/ 11MAY2014/ 20	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 悪心／ NAUSEA	03JUN2014/ 43/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITING	03JUN2014/ 43/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		臨床検査／ 血中重炭酸塩減少／ BICARBONATE LAB WAS LOW. BICARBONATE 17	17JUN2014/ 57/ 17JUN2014/ 57	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.025 MG/KG/DAY	[redacted]	胃腸障害／ 血便排泄／ BLOOD IN STOOL	03JUL2014:17:00/ 73/ 04JUL2014:08:00/ 74	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 血便排泄／ BLOOD IN STOOL	06JUL2014:11:00/ 76/ 07JUL2014:02:30/ 77	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment
		胃腸障害／ おくび／ MALODOROUS BURPING	26JUL2014/ 96/ 01AUG2014/ 102	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		胃腸障害／ 腹部膨満／ ABDOMINAL DISTENTION	31JUL2014/ 101/ 02AUG2014/ 103	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
0.05 MG/KG/DAY	[redacted]	胃腸障害／ 下痢／ LOOSE AND WATERY DIARRHEA	02AUG2014/ 4/ 25AUG2014/ 27	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ ウイルス性胃腸炎／ STOMACH FLU WITH VOMITTING	05AUG2014/ 7/ 06AUG2014/ 8	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 呼気臭／ SEAWEED SMELL TO BREATH	06AUG2014/ 8/ 03OCT2014/ 66	No/ MODERATE/ RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 易刺激性／ IRRITABILITY	26AUG2014/ 28/ 03OCT2014/ 66	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	--- / RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 脱水／ DEHYDRATION	27AUG2014:16:32/ 29/ 29AUG2014/ 31	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	臨床検査／ 血中重炭酸塩減少／ BICARBONATE (LOW)	24JUL2014:15:52/ 1/ 31JUL2014:10:19/ 8	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	臨床検査／ ヘマトクリット減少／ HEMATOCRIT (LOW)	31JUL2014:10:19/ 8/ 14AUG2014:10:00/ 22	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ ヘモグロビン減少／ HEMOGLOBIN (LOW)	31JUL2014:10:19/ 8/ 14AUG2014:10:00/ 22	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		筋骨格系および結合組織障害／ 関節腫脹／ SWOLLEN RIGHT WRIST	07AUG2014/ 15/ 14AUG2014/ 22	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER RASH	14AUG2014/ 22/ 13NOV2014/ 113	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 尿中細菌／ URINE BACTERIA (HIGH)	21AUG2014:08:50/ 29/ 05SEP2014:12:31/ 44	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	臨床検査／ C-反応性蛋白増加／ C REACTIVE PROTEIN (HIGH)	21AUG2014:08:50/ 29/ 18SEP2014:15:25/ 57	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 尿中蛋白陽性／ URINE PROTEIN (HIGH)	21AUG2014:08:50/ 29/ 05SEP2014:12:31/ 44	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 尿中白血球陽性／ URINE WBC (HIGH)	21AUG2014:08:50/ 29/ 05SEP2014:12:31/ 44	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ MRSA CELLULITIS WITH BACTEREMIA- CENTRAL LINE INFECTION	05SEP2014:14:59/ 44/ 09SEP2014:09:29/ 48	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		傷害、中毒および処置合併症／ 切開部位合併症／ SKIN INFLAMMATION AT G-TUBE SITE	06SEP2014:23:00/ 45/ 07SEP2014:08:30/ 46	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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0.05 MG/KG/DAY	[redacted]	心臓障害／ 頻脈／ TACHYCARDIC	25SEP2014:12:06/ 64/ 25SEP2014:12:15/ 64	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ MRSA ABSCESS - CENTRAL LINE INFECTION	25SEP2014:10:41/ 64/ 29SEP2014:15:08/ 68	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 低血糖症／ HYPOGLYCEMIA	25SEP2014/ 64/ 25SEP2014/ 64	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 血中重炭酸塩減少／ BICARBONATE (LOW)	28SEP2014/ 67/ 02OCT2014/ 71	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	No	Treatment
		呼吸器、胸郭および縦隔障害／ 鼻漏／ NASAL DISCHARGE AND CRUSTING	13NOV2014/ 113/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Post-treatment

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0.05 MG/KG/DAY	[redacted]	胃腸障害／ 腹痛／ ABDOMINAL PAIN	23SEP2014/ 28/ 26SEP2014/ 31	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	01OCT2014/ 36/ 03OCT2014/ 38	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 便量増加／ INCREASE IN STOOL OUTPUT	01OCT2014/ 36/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	27OCT2014/ 62/ 29OCT2014/ 64	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
	[redacted]	胃腸障害／ 嘔吐／ VOMITING	16JUL2014/ -12/ 16JUL2014/ -12	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	全身障害および投与局所様態／ 注射部位出血／ RIGHT UPPER ARM SMALL ECCHYMOSIS AT INJECTION SITE	26AUG2014/ 30/ 25SEP2014/ 60	No/ MILD/ RELATED	DOSE NOT CHANGED/ UNKNOWN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ LOW GRADE	11SEP2014/ 46/ 12SEP2014/ 47	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ LOW GRADE FEVER 99.7 F	18SEP2014/ 53/ 19SEP2014/ 54	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		神経系障害／ 外傷後頭痛／ HEAD ACHE FROM CAR ACCIDENT	18NOV2014:09:00/ 114/ 18NOV2014/ 114	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	胃腸障害／ 嘔吐／ VOMITTING	26JUL2014/ 4/ 26JUL2014/ 4	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	胃腸障害／ 嘔吐／ VOMITTING	02AUG2014/ 11/ 04AUG2014/ 13	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	13AUG2014:17:00/ 22/ 13AUG2014:17:05/ 22	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	15AUG2014/ 24/ 15AUG2014/ 24	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		代謝および栄養障害／ 食欲不振／ LOSS OF APPETITE	15AUG2014/ 24/ 18AUG2014/ 27	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	21AUG2014/ 30/ 21AUG2014/ 30	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 肛門膿瘍／ PERIANAL ABSCESS	24AUG2014/ 33/ 03SEP2014/ 43	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		腎および尿路障害／ 着色尿／ GREENISH URINE	25AUG2014/ 34/ 28AUG2014/ 37	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		皮膚および皮下組織障害／ 接触性皮膚炎／ CONTACT DERMATITIS	30AUG2014/ 39/ 15SEP2014/ 55	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 悪心／ NAUSEA	19SEP2014/ 59/ 30SEP2014/ 70	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	19SEP2014/ 59/ 30SEP2014/ 70	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	胃腸障害／ 悪心／ NAUSEA	04OCT2014/ 74/ 07OCT2014/ 77	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	04OCT2014/ 74/ 07OCT2014/ 77	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 悪心／ NAUSEA	10OCT2014/ 80/ 14OCT2014/ 84	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ VOMITTING	10OCT2014/ 80/ 14OCT2014/ 84	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 発熱／ FEVER	19OCT2014/ 89/ 21OCT2014/ 91	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	19OCT2014/ 89/ 21OCT2014/ 91	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		呼吸器、胸郭および縦隔障害／上気道うっ血／UPPER RESPIRATORY CONJESTION	19OCT2014/ 89/ 21OCT2014/ 91	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		感染症および寄生虫症／パラインフルエンザウイルス感染／PARAINFLUENZA VIRUS	21OCT2014/ 91/ 25OCT2014/ 95	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／カテーテル合併症／MALFUNCTIONING BROVIAC LINE	02NOV2014/ 103/ 03NOV2014/ 104	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ MULTIPLE: DRUG TREATMENT GIVEN; NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	感染症および寄生虫症／肺炎／PNEUMONIA	03JUN2014/ -36/ 16JUN2014/ -23	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ HOSPITAL ADMISSION FOR POSSIBLE LINE INFECTION	16JUN2014:15:00/ -23/ 17JUN2014:14:00/ -22	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		全身障害および投与局所様態／ 発熱／ HOSPITAL ADMISSION FOR FEVER POSSIBLE SEPSIS	22JUN2014/ -17/ 25JUN2014:17:00/ -14	Yes/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		皮膚および皮下組織障害／ 水疱／ BLISTER	23JUN2014/ -16/ 29JUN2014/ -10	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		胃腸障害／ 排便回数増加／ HOSPITAL ADMISSION FOR INCREASED STOOL FREQUENCY	08AUG2014:16:00/ 31/ 10AUG2014:12:09/ 33	Yes/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 疲労／ HOSPITAL ADMISSION FOR FATIGUE	08AUG2014:16:00/ 31/ 10AUG2014:12:09/ 33	Yes/ MILD/ NOT RELATED	DRUG INTERRUPTED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ HOSPITAL ADMISSION FOR POSSIBLE LINE INFECTION	08AUG2014:16:00/ 31/ 10AUG2014:12:09/ 33	Yes/ MILD/ NOT RELATED	DRUG INTERRUPTED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		胃腸障害／ 便秘／ CONSTIPATION	27AUG2014/ 50/ 30AUG2014/ 53	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 上気道感染／ UPPER RESPITORY INFECTION	27AUG2014/ 50/ 29AUG2014/ 52	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	12SEP2014/ 66/ 22SEP2014/ 76	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 嘔吐／ EMESIS	12SEP2014/ 66/ 12SEP2014/ 66	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	傷害、中毒および処置合併症／ 挫傷／ MINOR BRUISING TO CHEST DUE TO A CAR ACCIDENT	16OCT2014/ 100/ 18OCT2014/ 102	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
	[redacted]	眼障害／ 眼瞼浮腫／ PUFFINESS AROUND BOTH EYES	09SEP2014/ 8/ 11SEP2014/ 10	No/ MILD/ RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 排便痛／ PAIN ON OPENING BOWELS X 2	15SEP2014/ 14/ 16SEP2014/ 15	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 疲労／ TIREDNESS	03OCT2014:09:20/ 32/ 03OCT2014:11:00/ 32	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	08OCT2014:08:00/ 37/ 08OCT2014:09:00/ 37	No/ MILD/ RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	臨床検査／ 尿中結晶陽性／ URINALYSIS SHOWED MANY CALCIUM OXILATE CRYSTALS	13OCT2014/ 42/ 25NOV2014/ 85	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		全身障害および投与局所様態／ 疲労／ TIREDNESS	25OCT2014/ 54/ 04NOV2014/ 64	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		臨床検査／ 体重減少／ WEIGHT LOSS	28OCT2014/ 57/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		神経系障害／ 頭痛／ HEADACHE	04NOV2014/ 64/ 05NOV2014/ 65	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 消化不良／ HEARTBURN	06NOV2014/ 66/ 06NOV2014/ 66	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	胃腸障害／ 腹痛／ ABDOMINAL PAIN	14NOV2014:18:00/ 74/ 16NOV2014/ 76	No/ MILD/ RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	21NOV2014/ 81/ 21NOV2014/ 81	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN X 2	22NOV2014/ 82/ 23NOV2014/ 83	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN X 3	24NOV2014/ 84/ 24NOV2014/ 84	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN X 2	25NOV2014/ 85/ 25NOV2014/ 85	No/ MILD/ RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Treatment

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Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	臨床検査／ 血中カルシウム減少／ LOW CALCIUM ON ROUTINE BLOODS	25NOV2014/ 85/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Treatment
		胃腸障害／ 消化不良／ HEARTBURN	29NOV2014/ 89/ 30NOV2014/ 90	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 疲労／ TIREDNESS	30NOV2014/ 90/ 01DEC2014/ 91	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	01DEC2014/ 91/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 発熱／ FEVER	08DEC2014/ 98/ 08DEC2014/ 98	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment

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[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	全身障害および投与局所様態／ 疲労／ TIREDNESS	11DEC2014/ 101/ 12DEC2014/ 102	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION (BLOOD IN URINE)	12DEC2014/ 102/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ 尿中蛋白陽性／ PROTEIN IN URINE	12DEC2014/ 102/ 30DEC2014/ 120	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		胃腸障害／ 嘔吐／ VOMITING	14DEC2014/ 104/ 15DEC2014/ 105	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ アラニン・アミノトランスフェラーゼ増加／ INCREASED ALT LEVELS	15DEC2014/ 105/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	臨床検査／ アスパラギン酸アミノトランスフェラーゼ増加／ INCREASED AST LEVELS	15DEC2014/ 105/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ 血中重炭酸塩減少／ LOW BICARBONATE LEVELS	15DEC2014/ 105/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ 尿中血陽性／ BLOOD +++ IN URINE	15DEC2014/ 105/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ 尿中結晶陽性／ MANY CALCIUM OXALATE CRYSTALS IN URINE	15DEC2014/ 105/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	Yes	Post-treatment
		臨床検査／ 尿中赤血球陽性／ INCREASED RBC IN URINE	15DEC2014/ 105/ 30DEC2014/ 120	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	眼障害／ 霧視／ BLURRED VISION	16DEC2014:13:00/ 106/ 16DEC2014:18:00/ 106	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 疲労／ FATIGUE	16DEC2014:13:00/ 106/ 16DEC2014:18:00/ 106	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		神経系障害／ 浮動性めまい／ DIZZINESS	16DEC2014:13:00/ 106/ 16DEC2014:18:00/ 106	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		神経系障害／ 頭痛／ HEADACHE	16DEC2014:13:00/ 106/ 16DEC2014:18:00/ 106	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		神経系障害／ 浮動性めまい／ DIZZINESS	19DEC2014:18:00/ 109/ 29DEC2014/ 119	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	胃腸障害／ 消化不良／ HEARTBURN	20DEC2014:03:00/ 110/ 20DEC2014:11:00/ 110	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		胃腸障害／ 嘔吐／ VOMITING	20DEC2014:18:00/ 110/ 20DEC2014:18:30/ 110	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 疲労／ FATIGUE	20DEC2014/ 110/ ---------/ ---	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NON-DRUG TREATMENT GIVEN	INTERMITTENT/ NOT RECOVERED/NOT RESOLVED	Yes	Post-treatment
		神経系障害／ 意識レベルの低下／ REDUCED CONSCIOUSNESS, GCS OF 8	21DEC2014:00:00/ 111/ 22DEC2014/ 112	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	INTERMITTENT/ RECOVERED/RESOLVED	Yes	Post-treatment
		臨床検査／ 血中尿素減少／ LOW BLOOD UREA NITROGEN	30DEC2014/ 120/ ---------/ ---	No/ MILD/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ NOT RECOVERED/NOT RESOLVED	No	Post-treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	01SEP2014:17:00/ -17/ 06SEP2014:13:30/ -12	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Pre-treatment
		感染症および寄生虫症／ カテーテル敗血症／ LINE SEPSIS	22SEP2014:04:30/ 5/ 25SEP2014:12:58/ 8	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ LINE INFECTION	02OCT2014:14:52/ 15/ 08OCT2014:17:57/ 21	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		感染症および寄生虫症／ 中心静脈カテーテル感染／ CENTRAL LINE INFECTION	02DEC2014:20:45/ 76/ 13DEC2014:16:15/ 87	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	No	Treatment
		免疫系障害／ アナフィラキシー反応／ ANAPHYLAXIS	07DEC2014:19:00/ 81/ 07DEC2014:20:20/ 81	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Actual Treatment	Site ID - Subject ID	Body System Organ Class/ Preferred Term/ Reported Term[a]	Start Date and Time/ Relative Day/ Stop Date and Time/ Relative Day	Serious AE/ Severity/ Relationship	Action Taken/ Other Action Taken	Frequency/ Outcome	TEAE?	Study Phase[b]
0.05 MG/KG/DAY	[redacted]	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	20DEC2014/ 94/ 30DEC2014:18:37/ 104	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		全身障害および投与局所様態／ 発熱／ FEVER	26DEC2014:00:46/ 100/ 30DEC2014:18:37/ 104	Yes/ SEVERE/ NOT RELATED	DOSE NOT CHANGED/ DRUG TREATMENT GIVEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		血液およびリンパ系障害／ 汎血球減少症／ CYTOPENIA	27DEC2014:00:46/ 101/ 30DEC2014:16:11/ 104	Yes/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment
		血液およびリンパ系障害／ 汎血球減少症／ CYTOPENIA	30DEC2014:16:11/ 104/ 21JAN2015:00:55/ 126	No/ MODERATE/ NOT RELATED	DOSE NOT CHANGED/ NO OTHER ACTION TAKEN	CONTINUOUS/ RECOVERED/RESOLVED	Yes	Post-treatment

[a]: Reported terms are collected on the eCRF. Body system organ classes and preferred terms are coded using MedDRA 12.0.　Details of SAEs were not collected in this study.
[b]: Study phases are pre-treatment, treatment, and post-treatment, determined by the AE onset date.
Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-13003¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:29

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-16(42) /2017-01-18(44)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		呼吸器、胸郭および縦隔障害／ 鼻漏／ RUNNY NOSE	2017-02-20(77) /2017-02-27(84)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-03-10(95) /2017-03-13(98)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ パラインフルエンザウイルス感染／ PARAFLU	2017-03-31(116) /2017-04-03(119)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-06-09(186) /2017-06-30(207)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/WHITE	臨床検査／ 血中重炭酸塩減少／ DECREASED BICARBONATE	2016-06-02(-21) /2016-12-01(162)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位腫脹／ SKIN SWELLING AT INJECTION SITE	2016-06-28(6) /2016-06-28(6)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		筋骨格系および結合組織障害／ 関節痛／ RIGHT WRIST PAIN	2016-07-04(12) /2016-07-06(14)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	皮膚および皮下組織障害／ 皮膚変色／ YELLOWISH DISCOLORATION OF SKIN	2016-07-08(16) /2016-07-08(16)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 疼痛／ BODY ACHES	2016-07-20(28) /2016-07-20(28)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 悪心／ NAUSEA	2016-07-20(28) /2016-07	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 低カリウム血症／ HYPOKALEMIA	2016-07-21(29) /2016-11-29(160)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		筋骨格系および結合組織障害 ／ 四肢痛／ LEG PAIN	2016-08-06(45) /2016-12	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	胃腸障害／ 腹痛／ ABDOMINAL PAIN	2016-08-29(68) /2016-08-31(70)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ クロストリジウム・ディフィシレ大腸炎／ C DIFFICILE ENTERITIS	2016-09-01(71) /2016-09-15(85)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		製品の問題／ 医療機器位置異常／ CENTRAL LINE DISLODGED	2016-09-06(76) /2016-09-07(77)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	神経系障害／ 頭痛／ HEADACHE	2016-10-05(105) /2016-10-05(105)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 上腹部痛／ STOMACH ACHE	2016-10-28(128) /2016-10-28(128)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		代謝および栄養障害／ 低カリウム血症／ HYPOKALEMIA	2016-11-29(160) /2016-11-30(161)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	代謝および栄養障害／脱水／DEHYDRATION	2016-11-29(160) /2016-12-01(162)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		代謝および栄養障害／低ナトリウム血症／HYPONATREMIA	2016-11-29(160) /2016-12-12(173)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		代謝および栄養障害／低マグネシウム血症／HYPOMAGNESEMIA	2016-11-30(161) /2016-12-01(162)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	代謝および栄養障害／ 低カリウム血症／ HYPOKALEMIA	2016-12-12(173) /2016-12-15(176)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		傷害、中毒および処置合併症 ／ 上肢骨折／ BROKEN ARM	2017-01-07(199) /ONGOING	CONTINUOUS/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位疼痛／ PAIN AT INJECTION SITE	2016-11-05(3) /2016-11-07(5)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	免疫系障害／ 季節性アレルギー／ SEASONAL ALLERGIES	2016-11-06(4) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		神経系障害／ 頭痛／ HEADACHE	2016-11-12(10) /2016-11-12(10)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COLD	2016-12-05(33) /2016-12-07(35)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	筋骨格系および結合組織障害／ 四肢痛／ EXTREMITY PAIN	2016-12-15(43) /2016-12	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 注射部位内出血／ BRUISING AT INJECTION SITE	2016-12-30(58) /2017-01	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位疼痛／ PAIN AT INJECTION SITE	2016-12-30(58) /2017-01	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ 全身性そう痒症／ GENERAL BODY ITCHINESS	2017-01-12(71) /2017-01	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	代謝および栄養障害／ アシドーシス／ ACIDOSIS	2017-02-16(106) /2017-02-20(110)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題／ 医療機器閉塞／ CENTRAL LINE OCCULSION	2017-03-15(133) /2017-03-16(134)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		臨床検査／ ヒトメタニューモウイルス検査陽性／ HMPV TEST POSITIVE	2017-03-15(133) /2017-03-17(135)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ イレウス／ ILEUS	2017-03-15(133) /2017-03-17(135)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	RELATED	No	DRUG INTERRUPTED/ NONE	Y	Y
		筋骨格系および結合組織障害 ／ 筋痙縮／ LEG CRAMPS, BILATERAL	2017-03-15(133) /2017-03	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE BLOODSTREAM INFECTION	2017-04-13(162) /2017-04-17(166)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE BLOODSTREAM INFECTION	2017-05-16(195) /2017-05-21(200)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		傷害、中毒および処置合併症／ ストーマ部発疹／ RASH AROUND G-TUBE	2017-05-16(195) /2017-05-21(200)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-05-16(195) /2017-05-21(200)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ アラニンアミノトランスフェラーゼ増加／ ALT INCREASED	2017-05-18(197) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 腹痛／ ABDOMINAL PAIN	2017-01-05(10) /2017-01-05(10)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 鼓腸／ ABDOMINAL GAS	2017-01-05(10) /2017-01-05(10)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 精巣炎／ EPIDIDYMOORCHITIS	2017-01-20(25) /2017-03	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 腹痛／ BELLY PAIN	2017-01-29(34) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS NO MORE INFORMATION	2017-02-02(38) /2017-02-03(39)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題／ 医療機器閉塞／ CATHETER BLOCKAGE	2017-02-16(52) /2017-02-16(52)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 蜂巣炎／ CELLULITIS OF THE GROIN	2017-02-19(55) /2017-03-06(70)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-02-23(59) /2017-03-07(71)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 尿路感染／ RECURRENT URINARY TRACT INFECTION	2017-03-10(74) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 細菌感染／ BACTERIAL INFECTION	2017-03-24(88) /ONGOING	INTERMITTENT/ MODERATE	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		腎および尿路障害／ 膀胱ポリープ／ BLADDER POLYP	2017-03-24(88) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 膿疱性皮疹／ TINY PUSTULE IN GROIN INCISION	2017-03-24(88) /2017-03-24(88)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	生殖系および乳房障害／ 精巣上体嚢胞／ LEFT EPIDIDYMAL CYST	2017-03-29(93) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		胃腸障害／ 便量増加／ INCREASE IN STOOL OUTPUT	2017-04 /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 精巣炎／ INFECTION LEFT TESTICLE	2017-05-23(148) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-07-02(188) /2017-07-09(195)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注入部位疼痛／ INFUSION SITE TENDERNESS	2016-12-27(1) /2016-12	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位紅斑／ INJECTION SITE ERYTHEMA	2016-12-27(1) /2016-12	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中重炭酸塩減少／ BICARB LOW	2017-01-26(31) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2017-01-29(34) /2017-01-31(36)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		製品の問題／ 医療機器位置異常／ CVC CUFF EXPOSURE	2017-03-06(70) /2017-03-14(78)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		傷害、中毒および処置合併症 ／ 下肢骨折／ LEG FRACTURE	2017-03-16(80) /2017-06-09(165)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON- DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ インフルエンザ／ INFLUENZA B	2017-03-26(90) /2017-03-29(93)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		臨床検査／ プロトロンビン時間延長／ ELEVATED PROTIME	2017-03-26(90) /2017-04-10(105)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 胃炎／ GASTRITIS	2017-04-24(119) /ONGOING	CONTINUOUS/ MILD	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2017-02-26(46) /2017-02-27(47)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	DRUG INTERRUPTED/ NON-DRUG TREATMENT	Y	Y
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	2017-03-01(49) /2017-03-02(50)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 好中球数減少／ LOW NEUTROPHIL	2017-03-08(56) /2017-03-17(65)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	呼吸器、胸郭および縦隔障害＼ 鼻出血＼ BLOODY NOSE	2017-04-18(97) /2017-04-18(97)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題＼ 医療機器破損＼ BROKEN CENTRAL LINE	2017-05-25(134) /2017-05-26(135)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		製品の問題＼ 医療機器破損＼ BROKEN CENTRAL LINE	2017-06-28(168) /2017-06-28(168)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 上腹部痛／ STOMACH PAIN	2016-12-26(21) /2016-12-26(21)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH PAIN	2016-12-30(25) /2016-12-30(25)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-01-03(29) /2017-01-03(29)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-01-16(42) /2017-01-16(42)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-01-16(42) /2017-01-16(42)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-01-17(43) /2017-01-17(43)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	肝胆道系障害／ 胆石症／ GALLSTONES	2017-01-19(45) /ONGOING	CONTINUOUS/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ アラニンアミノトランスフェラーゼ増加／ CLINICALLY SIGNIFICANT INCREASED ALT CHEMPATH	2017-01-19(45) /2017-02-14(71)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ アスパラギン酸アミノトランスフェラーゼ増加／ CLINICALLY SIGNIFICANT INCREASED AST CHEMPATH	2017-01-19(45) /2017-02-14(71)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-01-27(53) /2017-02-01(58)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-02-19(76) /2017-02-20(77)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		傷害、中毒および処置合併症 ／ ストーマ部過剰肉芽／ GRANULOMA AT GASTROSTOMY SITE	2017-03-10(95) /2017-04-06(122)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ 水痘／ CHICKEN POX	2017-03-18(103) /2017-04-10(126)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 嘔吐／ VOMITING 3X DAILY	2017-03-20(105) /2017-03-26(111)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 胃脱出／ GASTRIC PROLAPSE THROUGH A GASTROSTOMY TRACT	2017-03-31(116) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 嘔吐／ VOMITING 2X DAILY	2017-04-02(118) /2017-04-05(121)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ 1X VOMIT	2017-04-04(120) /2017-04-04(120)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 下痢／ DIARRHOEA	2017-04-06(122) /2017-05-01(147)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	代謝および栄養障害／ 脱水／ DEHYDRATION REQUIRING HOSPITALISATION	2017-04-18(134) /2017-04-30(146)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	DRUG INTERRUPTED/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ ウイルス性胃腸炎／ VIRAL GASTROENTERITIS	2017-04-18(134) /2017-05-01(147)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	DRUG INTERRUPTED/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	臨床検査／ リンパ節触知／ SHOTTY CERVICAL AND AXILLARY LYMPH NODES	2017-05-02(148) /2017-06-21(198)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ ADMISSION TO HOSPITAL - VOMITING	2017-05-06(152) /2017-05-10(156)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	DRUG INTERRUPTED/ NONE	Y	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-06-13(190) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	胃腸障害／ 下痢／ DIARRHOEA	2017-01-02(14) /2017-01-03(15)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-01-02(14) /2017-01-03(15)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	2017-01-06(18) /2017-01-06(18)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	胃腸障害／ 嘔吐／ VOMITING	2017-01-06(18) /2017-01-06(18)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-01-10(22) /2017-01-10(22)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-01-17(29) /2017-01-17(29)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	胃腸障害／ 嘔吐／ VOMITING	2017-01-24(36) /2017-01-24(36)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 鼻炎／ CORYZAL	2017-01-27(39) /2017-05-15(147)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ リンパ節触知／ SHOTTY CERVICAL LYMPH NODES	2017-01-30(42) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	一般・全身障害および投与部位の状態／ 注射部位内出血／ BRUISE AT INJECTION SITE	2017-02-09(52) /2017-02-15(58)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題／ 医療機器内血栓／ BLOOD CLOT IN CENTRAL LINE	2017-02-27(70) /2017-02-27(70)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	皮膚および皮下組織障害／ おむつ皮膚炎／ NAPPY RASH	2017-03-09(80) /2017-03-15(86)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ NAPPY RASH	2017-03-24(95) /2017-03-26(97)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		耳および迷路障害／ 耳痛／ EAR ACHE	2017-03-29(100) /2017-04-03(105)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	皮膚および皮下組織障害／ おむつ皮膚炎／ NAPPY RASH	2017-04-06(108) /2017-04-10(112)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 粘液便／ MUCOUS IN STOOL	2017-04-18(120) /2017-04-21(123)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ NAPPY RASH	2017-04-18(120) /2017-04-21(123)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	一般・全身障害および投与部位の状態／ 注射部位内出血／ BRUISE TO INJECTION SITE ON ABDO	2017-04-24(126) /2017-04-26(128)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION - URTI	2017-04-28(130) /2017-04-30(132)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	呼吸器、胸郭および縦隔障害／ 鼻漏／ SNOTTY NOSE WITH GREEN MUCOUS	2017-04-28(130) /2017-06-14(177)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ NAPPY RASH	2017-05-19(151) /2017-05-25(157)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	一般・全身障害および投与部位の状態／ 発熱／ PYREXIA	2017-06-30(193) /2017-07-02(195)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	F/[redacted]/NALLW	肝胆道系障害／ 脂肪肝／ HEPATIC STEATOSIS	2016-12-14(-15) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	
		一般・全身障害および投与部位の状態／ カテーテル留置部位発疹／ RASH UNDERNEATH CENTRAL LINE DRESSING	2017-02-02(36) /2017-02-15(49)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/NALLW	臨床検査／ 血中尿素増加／ CLINICALLY SIGNIFICANT HIGH UREA	2017-02-23(57) /2017-02-23(57)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中重炭酸塩減少／ CLINICALLY SIGNIFICANT LOW BICARB	2017-03-08(70) /2017-03-23(85)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 下腹部痛／ RIGHT SIDED ILEAC FOSSA PAIN	2017-03-16(78) /2017-03-17(79)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/NALLW	感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS, TIRED AND WEAK	2017-03-19(81) /2017-03-20(82)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	2017-03-20(82) /2017-03-26(88)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 脱水／ CLINICAL DEHYDRATION	2017-04-12(105) /2017-04-17(110)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/NALLW	臨床検査／ 血中尿素増加／ HIGH UREA	2017-04-18(111) /2017-04-23(116)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		代謝および栄養障害／ 脱水／ CLINICAL DEHYDRATION REQUIRING HOSPITALISATION	2017-04-18(111) /2017-04-23(116)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		代謝および栄養障害／ 代謝性アシドーシス／ METABOLIC ACIDOSIS	2017-04-18(111) /2017-04-23(116)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/NALLW	神経系障害／ 頭痛／ HEADACHE	2017-04-30(123) /2017-05-02(125)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 頭痛／ HEADACHE	2017-05-16(139) /2017-05-22(145)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 代謝性アシドーシス／ D LACTIC ACIDOSIS	2017-05-23(146) /ONGOING	CONTINUOUS/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2017-01-29(34) /2017-02-01(37)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／鼻閉／NASAL CONGESTED	2017-01-30(35) /2017-02-01(37)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	眼障害／ 眼充血／ RED EYES	2017-01-30(35) /2017-02-01(37)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ インフルエンザ／ INFLUENZA	2017-02-08(44) /2017-02-10(46)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		臨床検査／ リパーゼ増加／ LIPASE INCREASE	2017-03-08(72) /2017-03-23(87)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 下痢／ DIAHHREA	2017-04-09(104) /2017-04-09(104)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITTED	2017-04-09(104) /2017-04-09(104)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ 湿疹／ ECZEMA RASH	2017-05-14(139) /ONGOING	INTERMITTENT/ MODERATE/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-05-29(154) /2017-05-31(156)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-12-29(10) /2017-01-10(22)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COLD	2016-12-29(10) /2017-01-10(22)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／結膜炎／CONJUNCTIVITIS	2017-01-01(13) /2017-01-10(22)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		臨床検査／血中重炭酸塩減少／LOW BICARB	2017-01-04(16) /2017-01-18(30)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／γ－グルタミルトランスフェラーゼ増加／INCREASED GAMMA GLUTAMYL TRANSFERASE LAB	2017-01-04(16) /2017-01-18(30)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ 血小板数減少／ LOW PLATELETS	2017-01-04(16) /2017-01-18(30)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION	2017-01-10(22) /2017-01-10(22)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		代謝および栄養障害／ 脱水／ DEHYDRATION	2017-01-10(22) /2017-01-10(22)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 嘔吐／ VOMITTING	2017-01-17(29) /2017-01-17(29)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITTING	2017-01-20(32) /2017-01-20(32)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 下痢／ DIARRHEA	2017-02-01(44) /2017-02-04(47)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ カンジダ性おむつ皮疹／ YEAST DIAPER RASH	2017-02-05(48) /2017-02-10(53)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		先天性、家族性および遺伝性障害／ 尿道下裂／ HYPOSPADIAS REPAIR SURGERY	2017-03-03(74) /2017-03-03(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 便秘／ CONSTIPATION	2017-03-11(82) /2017-03-16(87)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 疼痛／ PAIN	2017-03-14(85) /2017-03-14(85)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITTING	2017-03-25(96) /2017-03-25(96)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ ヘモグロビン減少／ DECREASED HEMOGLOBIN	2017-04-05(107) /2017-05-17(149)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス性胃腸炎／ STOMACH FLU	2017-04-21(123) /2017-04-25(127)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		代謝および栄養障害／ アシドーシス／ VIRAL ACIDOSIS	2017-04-26(128) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ ウイルス性下痢／ VIRAL DIARRHEA	2017-04-26(128) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		臨床検査／ 血中重炭酸塩減少／ LOW BICARBONATE	2017-04-26(128) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中カリウム減少／ DECREASED POTASSIUM	2017-04-26(128) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2017-05-08(140) /2017-05-12(144)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／鼻漏／RUNNY NOSE	2017-05-08(140) /2017-05-12(144)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／血中トリグリセリド増加／ELEVATED TRIGLYCERIDES	2017-07-05(198) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	肝胆道系障害／ 肝障害／ LIVER COMPLICATION NO FURTHER INFORMATION	2017-07-05(198) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
			2017-07-05(198) /2017-07-05(198)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ アラニンアミノトランスフェラーゼ増加／ POTENTIAL LIVER INJURY DUE TO HIGH ALT	2017-02-24(29) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ アスパラギン酸アミノトランスフェラーゼ増加／ POTENTIAL LIVER INJURY-HIGH AST	2017-02-24(29) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ 抱合ビリルビン増加／ SUSPECTED LIVER COMPLICATIONS DUE TO HIGH DIRECT BILIRUBIN	2017-02-24(29) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中ビリルビン増加／ SUSPECTED LIVER COMPLICATIONS DUE TO HIGH TOTAL BILIRUBIN	2017-02-24(29) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ 血中マグネシウム増加／ CLINICALLY SIGNIFICANT HIGH MAGNESIUM - ELECTROLYTE IMBALANCE	2017-02-24(29) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中尿酸減少／ CLINICALLY SIGNIFICANT LOW URIC ACID - UNKNOWN DIAGNOSIS	2017-02-24(29) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ C-反応性蛋白増加／ SUSPECTED INFLAMMATION DUE TO HIGH CRP	2017-02-24(29) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中アルブミン減少／ CLINICALLY SIGNIFICANT LOW ALBUMIN - INDICATION OF INFLAMMATION	2017-02-24(29) /2017-08-18(204)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ 血中アルカリホスファターゼ増加／ BILE DUCT OBSTRUCTION DUE TO HIGH ALKALINE PHOS	2017-02-24(29) /2017-08-18(204)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中カルシウム減少／ LOW CALCIUM	2017-02-24(29) /2017-08-18(204)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ 血中リン減少／ CLINICALLY SIGNIFICANT LOW PHOSPHORUS - UNKNOWN DIAGNOSIS	2017-02-24(29) /2017-08-18(204)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 脱水／ SUSPECTED DEHYDRATION DUE TO HIGH SODIUM	2017-02-24(29) /2017-08-18(204)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	胃腸障害／ 悪心／ NAUSEA	2017-03-06(39) /2017-03-06(39)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 脱水／ CLINICALLY SIGNIFICANT ELEVATED SODIUM - DEHYDRATION	2017-03-10(43) /2017-08-18(204)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	肝胆道系障害／ 胆汁うっ滞／ CHOLESTASIS	2017-05-12(106) /ONGOING	CONTINUOUS/ MODERATE	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		感染症および寄生虫症／ 結膜炎／ PINK EYE	2017-05-12(106) /2017-05-15(109)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		臨床検査／ 血中トリグリセリド増加／ ELEVATED TRIGLYCERIDES	2017-06-10(135) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	臨床検査／ γ－グルタミルトランスフェラーゼ増加／ ELEVATED GGT INDICATING LIVER DAMAGE	2017-06-24(149) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-07-13(168) /2017-07-13(168)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/BLACK	心臓障害／ 心室肥大／ ABNORMAL EKG LEFT VENTRICULAR HYPERTROPHY, POSSIBLE BIVENTRICULAR HYPERTROPHY, EARLY REPOLARIZATION	2016-07-20(-14) /2016-08-02(-1)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-08-04(2) /2016-08-04(2)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/BLACK	感染症および寄生虫症／ 蜂巣炎／ CELLULITIS ON LEFT LEG	2016-08-30(28) /2016-09-06(35)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		傷害、中毒および処置合併症／ 節足動物咬傷／ BUG BITE	2016-08-30(28) /2016-09-06(35)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 末梢性浮腫／ PERIPHERAL EDEMA	2016-09-17(46) /2016-10-12(71)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/BLACK	感染症および寄生虫症／ 蜂巣炎／ CELLULITIS	2016-10-06(65) /2016-10-18(77)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 医療機器関連敗血症／ CENTRAL LINE ASSOCIATED SEPSIS	2016-12-04(124) /2016-12-08(128)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		胃腸障害／ 下痢／ DIARRHEA	2016-12-12(132) /2016-12-16(136)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/BLACK	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-07(158) /2017-01-09(160)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		一般・全身障害および投与部位の状態／ 発熱／ LOW-GRADE FEVER	2017-01-23(174) /2017-01-23(174)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 下腹部痛／ LOWER ABDOMINAL PAIN	2017-01-23(174) /2017-01-24(175)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/BLACK	胃腸障害／ 嘔吐／ VOMITTING	2017-01-24(175) /2017-01-24(175)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 脱水／ DEHYDRATION	2017-01-30(181) /2017-02-02(184)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
[redacted]	M/[redacted]/WHITE	心臓障害／ 頻脈／ TACHYCARDIA	2017-01-23(15) /2017-07-24(197)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED WITH SEQUELAE	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 下痢／ DIARRHEA	2017-02-02(25) /2017-02-03(26)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		呼吸器、胸郭および縦隔障害 ／ 湿性咳嗽／ PHLEGM	2017-02-02(25) /2017-02-03(26)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		臨床検査／ 体重減少／ WEIGHT REDUCTION	2017-02-06(29) /2017-02-20(43)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 下痢／ DIARRHEA	2017-02-26(49) /2017-02-27(50)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 無力症／ ASTHENIA	2017-02-27(50) /2017-02-27(50)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 平衡障害／ POOR CONTROL OF BALANCE	2017-02-27(50) /2017-02-27(50)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 嘔吐／ VOMIT	2017-04-30(112) /2017-04-30(112)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス性胃腸炎／ INTESTINAL FLU	2017-05-04(116) /2017-05-25(137)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 糞塊／ FAECALOMA	2017-05-31(143) /2017-06-06(149)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 糞塊／ SUB OCCLUSION EPISODE WITH FECAL IMPACTION	2017-05-31(143) /2017-06-06(149)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ UNKNOWN	Y	Y
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ 接触皮膚炎／ CONTACT DERMATITIS	2016-11-17(1) /2016-11-18(2)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-11-18(2) /2017-01-13(58)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-11-27(11) /2016-11-28(12)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2016-12-11(25) /2016-12-18(32)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2016-12-19(33) /2016-12-25(39)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2016-12-27(41) /2016-12-29(43)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2016-12-30(44) /2017-01-03(48)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-02(47) /2017-01-02(47)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		耳および迷路障害／ 耳漏／ OTORRHEA	2017-01-02(47) /2017-01-10(55)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-01-02(47) /2017-01-13(58)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-01-05(50) /2017-01-09(54)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-01-15(60) /2017-01-17(62)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-01-21(66) /2017-01-22(67)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-01-26(71) /2017-01-30(75)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-02-05(81) /2017-02-08(84)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-02-12(88) /2017-02-16(92)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-02-26(102) /2017-02-28(104)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		耳および迷路障害／ 耳漏／ OTORRHEA	2017-03-04(108) /2017-03-08(112)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-03-11(115) /2017-03-11(115)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-03-11(115) /2017-03-23(127)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		一般・全身障害および投与部位の状態／ カテーテル留置部位皮膚炎／ BROVIAC DERMATITIS	2017-03-11(115) /2017-03-25(129)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-03-12(116) /2017-03-14(118)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-04-23(158) /2017-04-27(162)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-05-02(167) /2017-05-11(176)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.025 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/OTHER	皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-05-10(175) /2017-05-11(176)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／ おむつ皮膚炎／ DIAPER DERMATITIS	2017-05-16(181) /2017-05-17(182)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-05-28(193) /2017-06-20(216)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	精神障害／ 激越／ AGITATION	2016-09-14(42) /ONGOING	CONTINUOUS/ MODERATE	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2016-09-16(44) /ONGOING	INTERMITTENT/ MILD	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-09-16(44) /2016-09-22(50)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	胃腸障害／ 腹痛／ ABDOMINAL PAIN	2016-10-13(71) /ONGOING	INTERMITTENT/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 感染性腸炎／ SMALL INTESTINE INFECTION	2016-10-13(71) /2016-10-20(78)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		腎および尿路障害／ 水腎症／ HYDRONEPHROSIS	2016-11-01(90) /ONGOING	CONTINUOUS/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	腎および尿路障害／ 腎結石症／ KIDNEY STONE	2016-11-01(90) /ONGOING	INTERMITTENT/ MODERATE/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害 ／ 咳嗽／ COUGH	2016-11-24(113) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-11-24(113) /2016-11-27(116)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2016-12-03(122) /2016-12-03(122)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		一般・全身障害および投与部位の状態／発熱／FEVER	2017-01-27(177) /2017-01-27(177)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題／医療機器破損／BROKEN CENTRAL LINE	2017-01-31(181) /2017-01-31(181)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害＼ 鼻出血＼ NOSE BLEEDS	2017-01-12(16) /2017-01-19(23)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症＼ 鼻咽頭炎＼ COLD LIKE SYMPTOMS	2017-01-12(16) /2017-01-20(24)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題＼ 医療機器の問題＼ CENTRAL LINE CONTAMINATION	2017-01-25(29) /2017-01-26(30)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害＼ 咳嗽＼ COUGH	2017-04-15(109) /2017-05-19(143)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害＼ 血便排泄＼ BLOOD IN STOOL	2017-04-21(115) /2017-04-22(116)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		血液およびリンパ系障害＼ リンパ節症＼ LYMPHADENOPATHY	2017-05-24(148) /2017-05-30(154)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 異常便／ ABNORMAL STOOLS	2017-05-25(149) /2017-06-01(156)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/WHITE	血管障害／ 上大静脈症候群／ SVC OBSTRUCTION	2017-01-27(44) /2017-01-28(45)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 耳感染／ EAR INFECTION	2017-05-26(163) /2017-06-04(172)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害＼ 咳嗽＼ COUGH	2017-05-26(163) /2017-06-07(175)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症＼ 結膜炎＼ PINK EYE	2017-05-28(165) /2017-06-01(169)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症＼ 医療機器関連感染＼ CENTRAL LINE INFECTION	2017-06-08(176) /2017-06-12(180)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 腹痛／ ABDOMINAL PAIN	2016-07-07(1) /2016-07-07(1)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	2016-07-24(18) /2016-07-24(18)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-08-01(26) /2016-08-03(28)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	製品の問題／ 医療機器閉塞／ OCCLUDED CENTRAL LINE	2016-08-12(37) /2016-08-14(39)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON-DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-08-29(54) /2016-09-21(77)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		免疫系障害／ 季節性アレルギー／ SEASONAL ALLERGY	2016-09-01(57) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	呼吸器、胸郭および縦隔障害＼ 湿性咳嗽＼ PRODUCTIVE COUGH	2016-10-15(101) /2016-10-17(103)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症＼ 鼻咽頭炎＼ COMMON COLD	2016-11-11(128) /2016-11-12(129)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		神経系障害＼ 頭痛＼ HEADACHE	2016-12-11(158) /2016-12-14(161)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ メタニューモウイルス感染／ HMPV INFECTION	2016-12-12(159) /2016-12-14(161)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位内出血／ BRUISING FROM INJECTION NEEDLE	2017-01-25(1) /2017-01-25(1)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 医療機器関連損傷／ SCRATCH FROM INJECTION NEEDLE	2017-01-25(1) /2017-01-25(1)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 疲労／ TIREDNESS	2017-01-25(1) /2017-04-26(92)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 気道感染／ RESPIRATORY INFECTION	2017-02-03(10) /2017-02-12(19)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ＲＳウイルス感染／ RSV INFECTION	2017-02-09(16) /2017-02-12(19)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ コロナウイルス感染／ CORONAVIRUS INFECTION	2017-02-09(16) /2017-03-12(47)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		胃腸障害／ 嘔吐／ INCREASE IN VOMITING	2017-03-12(47) /2017-03-22(57)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 頭痛／ HEADACHE	2017-03-27(62) /2017-04	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ 嘔吐／ VOMITING	2017-04-04(70) /2017-04-30(96)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH PAIN	2017-04-14(80) /2017-05-01(97)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ カテーテル留置部位紅斑／ REDNESS AT CVC SITE	2017-04-24(90) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 気道感染／ RESPIRATORY INFECTION	2017-05-02(98) /2017-05-31(127)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 頭痛／ HEAD ACHE	2017-05-10(106) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	2017-05-16(112) /2017-06-19(146)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ 腹痛／ BELLY PAIN	2017-07-20(177) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-07-20(177) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	2017-07-24(181) /2017-08-01(189)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 医療機器使用部位疼痛／ PAIN AT GTUBE SITE	2017-08-07(195) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	F/[redacted]/WHITE	呼吸器、胸郭および縦隔障害／ 呼吸障害／ RESPIRATORY ILLNESS NOT FURTHER INFORMATION	2017-01 /2017-01-22(5)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 注射部位変色／ SLIGHT PINK MARK AT INJECTION SITE	2017-01-18(1) /2017-01	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		製品の問題／ 医療機器破損／ BROKEN CVC	2017-01-30(13) /2017-01-31(14)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER WITH CENTRAL LINE	2017-02-02(16) /2017-02-07(21)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 気道感染／ RESPIRATORY INFECTION	2017-04-30(103) /2017-05	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	製品の問題／ 医療機器破損／ CRACKED G-J TUBE	2017-06 /2017-06-27(161)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-06-22(156) /2017-07-08(172)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		精神障害／ 注意欠陥多動性障害／ Attention deficit/hyperactivity disorder	2017-07-21(185) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ 好酸球性結腸炎／ EOSINOPHILIC COLITIS	2017-07-26(190) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ 血中尿酸増加／ CLINICALLY SIGNIFICANT HIGH URIC ACID	2017-08-02(197) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	呼吸器、胸郭および縦隔障害＼／鼻閉／NASAL CONGESTION	2017-08-02(197) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2016-11-23(7) /2016-11-25(9)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-11-23(7) /2016-11	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-02-16(92) /2017-02-18(94)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 肺炎／ PNEUMONIA	2017-02-16(92) /2017-03-04(108)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	M/[redacted]/BLACK	代謝および栄養障害／ 脱水／ DEHYDRATION	2016-06-17(-42) /2016-06-18(-41)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	
		感染症および寄生虫症／ カテーテル留置部位感染／ CATHETER SITE INFECTION	2016-06-30(-29) /2016-07-10(-19)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED WITH SEQUELAE	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON- DRUG TREATMENT	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	感染症および寄生虫症／ ブドウ球菌性菌血症／ STAPHYLOCOCCAL EPIDERMIS BACTEREMIA	2016-06-30(-29) /2016-07-10(-19)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED WITH SEQUELAE	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	
		製品の問題／ 医療機器位置異常／ PATIENT ACCIDENTALLY PARTIALLY REMOVED PICC LINE	2016-07-06(-23) /2016-07-07(-22)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	感染症および寄生虫症／ インフルエンザ／ VIRAL INFLUENZA	2016-08-08(11) /2016-08-12(15)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		製品の問題／ 医療機器位置異常／ DISLODGEMENT OF BROVIAC CATHETER	2016-09-24(58) /2016-09-29(63)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 細菌性疾患キャリアー／ BACTERIAL COLONIZATION OF CENTRAL LINE	2016-11-06(101) /2016-12-16(141)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	感染症および寄生虫症／ カテーテル留置部位感染／ HICKMAN CATHETER INFECTION	2017-01-06(162) /2017-01-09(165)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	F/[redacted]/BLACK	感染症および寄生虫症／ 耳感染／ EAR INFECTION	2016-12-05(18) /2016-12-13(26)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVERS	2017-02-14(89) /2017-02-16(91)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-03-10(113) /2017-03-11(114)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		代謝および栄養障害／ 代謝性アシドーシス／ D-LACTIC ACIDOSIS	2017-05-04(168) /2017-05-07(171)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		代謝および栄養障害／ アシドーシス／ ACIDOSIS	2017-05-18(182) /2017-05-20(184)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/BLACK	呼吸器、胸郭および縦隔障害／ 低炭酸症／ HYPOCARBIA	2017-05-18(182) /2017-05-20(184)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	M/[redacted]/BLACK	製品の問題／ 医療機器位置異常／ DISLODGEMENT OF HICKMAN LINE	2016-12-09(-10) /2016-12-15(-4)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	
		血液およびリンパ系障害／ リンパ節症／ ENLARGED CERVICAL LYMPH NODES	2016-12-19(1) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	2017-01-02(15) /2017-01-16(29)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 鼻炎／ CORYZAL	2017-01-26(39) /2017-01-27(40)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION	2017-02-11(55) /2017-02-22(66)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	精神障害／ 中期不眠症／ NOT SLEEPING 0200 TO 0600 AT NIGHT	2017-02-11(55) /2017-03-23(95)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		眼障害／ 斜視／ EYE SURGERY STRATISMUS	2017-02-21(65) /2017-02-21(65)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-02-21(65) /2017-02-28(72)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	眼障害／ 眼充血／ RED LEFT EYE SINCE SURGERY	2017-02-21(65) /2017-04-21(124)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 口唇のひび割れ／ CRACKED LIP	2017-03-26(98) /2017-06-09(173)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 口唇出血／ BLEEDING LIP	2017-03-26(98) /2017-06-09(173)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	胃腸障害／ 腹部膨満／ BLOATING	2017-04-06(109) /2017-04-12(115)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-04-07(110) /2017-04-08(111)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 鼻炎／ CORYZAL	2017-04-28(131) /2017-05-09(142)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	神経系障害／ 嗜眠／ LETHARGIC	2017-04-28(131) /2017-05-17(150)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMIT X2	2017-05-05(138) /2017-05-08(141)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING AFTER MILK FEED	2017-05-08(141) /2017-05-13(146)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	代謝および栄養障害／ 低血糖／ HYPO-GLYCAEMIA	2017-06-10(174) /2017-06-10(174)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 下痢／ DIARRHOEA	2017-06-14(178) /2017-06-17(181)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	F/[redacted]/WHITE	製品の問題／ 医療機器機能不良／ CENTRALLINE MALFUNCTION	2016-12-28(-13) /2016-12-29(-12)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ 嘔吐／ EMESIS	2017-01-14(5) /2017-01-14(5)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 悪心／ NAUSEA	2017-01-14(5) /2017-01-15(6)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 頭痛／ HEADACHES	2017-01-14(5) /2017-01-15(6)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-14(5) /2017-01-15(6)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ インフルエンザ／ INFLUENZA A VIRUS INFECTION	2017-01-14(5) /2017-01-22(13)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	DRUG INTERRUPTED/ NONE	Y	Y
		胃腸障害／ 上腹部痛／ STOMACHACHES	2017-03-12(62) /2017-03-24(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	胃腸障害／ 嘔吐／ VOMITTED	2017-03-12(62) /2017-03-24(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 頭痛／ HEADACHES	2017-03-12(62) /2017-03-24(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-03-15(65) /2017-03-24(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-03-24(74) /2017-03-31(81)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		呼吸器、胸郭および縦隔障害／ ／ 咳嗽／ COUGH	2017-05-01(112) /2017-05-08(119)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-05-02(113) /2017-05-04(115)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	2017-05-31(142) /2017-06-26(168)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/WHITE	製品の問題／ 医療機器内血栓／ BROVIAC LINE CLOTTED	2016-12-20(-20) /2016-12-20(-20)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 下痢／ DIARRHEA	2016-12-20(-20) /2016-12-21(-19)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	
		製品の問題／ 医療機器内血栓／ BROVIAC LINE CLOTTED	2017-01-09(1) /2017-01-09(1)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	
		製品の問題／ 医療機器破損／ BROVIAC LINE BROKE	2017-01-19(11) /2017-01-20(12)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ 尿中結晶陽性／ URINE CALCIUM OXALATE CRYSTAL PRESENT	2017-02-27(50) /2017-07-24(197)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		呼吸器、胸郭および縦隔障害 ／ 咳嗽／ COUGH	2017-04-17(99) /2017-04-30(112)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		神経系障害／ 痙攣発作／ SEIZURES	2017-04-20(102) /2017-04-20(102)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ ウイルス感染／ VIRAL INFECTION	2017-05-18(130) /2017-05-22(134)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		胃腸障害／ 下痢／ DIAHHREA	2017-05-20(132) /2017-05-22(134)	INTERMITTENT/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		胃腸障害／ 嘔吐／ VOMIT	2017-05-23(135) /2017-06-28(171)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ 赤血球数増加／ INCREASE RBC	2017-06-05(148) /2017-06-26(169)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		腎および尿路障害／ 血尿／ HEMATURIA	2017-06-05(148) /2017-06-26(169)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
[redacted]	M/[redacted]/WHITE	血液およびリンパ系障害／ 貧血／ ANEMIA	2017-01-05(22) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 上腹部痛／ STOMACH ACHE	2017-01-10(27) /2017-01-12(29)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 便秘／ CONSTIPATION	2017-01-10(27) /2017-01-12(29)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		耳および迷路障害／ 耳痛／ EAR ACHE	2017-01-11(28) /2017-01-12(29)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-01-19(36) /2017-01-22(39)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ アラニンアミノトランスフェラーゼ増加／ INCREASED ALT	2017-02-10(58) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-02-16(64) /2017-03-11(87)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 胃腸炎／ GASTROENTERITIS	2017-03-19(95) /2017-03-21(97)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-05-17(154) /2017-05-27(164)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 肛門周囲痛／ PERIANAL SORENESS	2017-06-29(197) /ONGOING	CONTINUOUS/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ 鼻炎／ CORZYAL SYMPTOMS	2017-01-28(41) /2017-02-03(47)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-02-03(47) /2017-02-13(57)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION	2017-02-03(47) /2017-02-13(57)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 嘔吐／ VOMITING	2017-02-27(71) /2017-05-22(155)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION	2017-02-27(71) /2017-05-22(155)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ PYREXIA	2017-03-21(93) /2017-03-21(93)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ 医療機器関連敗血症／ LINE SEPSIS	2017-03-21(93) /2017-03-23(95)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 中耳炎／ OTITIS MEDIA	2017-03-21(93) /2017-03-23(95)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		呼吸器、胸郭および縦隔障害 ／ 喘息／ EXACERBATION OF ASTHMA	2017-03-21(93) /2017-04-03(106)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	一般・全身障害および投与部位の状態／ 注射部位腫瘤／ INJECTION SITE LUMPS	2017-04-07(110) /2017-04-25(128)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		血管障害／ 血腫／ HEAMATOMA	2017-04-21(124) /ONGOING	CONTINUOUS/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		皮膚および皮下組織障害／ 過剰肉芽組織／ GRANULATION TISSUE AROUND LINE SITE	2017-05-02(135) /2017-06-30(194)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／カテーテル留置部位感染／CENTRAL LINE SITE SKIN INFECTION	2017-05-15(148) /2017-05-20(153)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／皮下組織膿瘍／INCISION AND DRAINAGE OF SKIN ABCESS	2017-06-05(169) /2017-06-21(185)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas Output: l-sae.rtf 30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／皮膚細菌感染／PSEUDOMONAS SKIN INFECTION	2017-06-12(176) /ONGOING	CONTINUOUS/ MODERATE/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／医療機器関連感染／PSUEDOMONAS AERUGINOSA IN CENTRAL LINE TIP	2017-06-21(185) /2017-06-21(185)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION WITH E COLI	2017-01-21(-11) /2017-01-28(-4)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ UNKNOWN	Y	
		胃腸障害／ 悪心／ NAUSEA	2017-03-06(34) /2017-03-06(34)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 眼感染／ EYE INFECTION	2017-05-13(102) /2017-05-20(109)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 耳感染／ EAR INFECTION	2017-05-18(107) /2017-05-29(118)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-06-03(123) /2017-06-03(123)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 菌血症／ BACTEREMIA	2017-06-03(123) /2017-06-19(139)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ 血中トリグリセリド増加／ ELEVATED TRIGLYCERIDES	2017-06-26(146) /2017-07-10(160)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 医療機器関連感染／ LINE INFECTION - PLACEMENT OF NEW BROVIAC CATHETER	2017-06-30(150) /2017-06-30(150)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	胃腸障害／ 嘔吐／ VOMIT	2017-08-05(186) /2017-08-05(186)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ N NON-DRUG TREATMENT		Y
[redacted]	M/[redacted]/NALLW	皮膚および皮下組織障害／ アトピー性皮膚炎／ ATOPIC ECZEMA	2016-12-12(6) /ONGOING	INTERMITTENT/ MILD/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ N DRUG TREATMENT,NON- DRUG TREATMENT		Y
		代謝および栄養障害／ 低カリウム血症／ HYPOKALEMIA	2016-12-13(7) /2016-12-14(8)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ Y NON-DRUG TREATMENT		Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/NALLW	感染症および寄生虫症／ カテーテル留置部位感染／ CV TUNNEL INFECTION	2017-01-02(27) /2017-01-30(55)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ インフルエンザ／ FLU	2017-03-28(112) /2017-04-07(122)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-04-25(140) /2017-05-01(146)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/1[redacted]/WHITE	胃腸障害／ 嚥下障害／ SWALLOWING DIFFICULTY	2016-12 /2017-05-29(169)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ トランスアミナーゼ上昇／ ELEVATED LIVER TRANSAMINASES	2016-12-27(16) /2017-07-19(220)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		代謝および栄養障害／ 脱水／ DEHYDRATION TREATED WITH EXTRA RINGER AT HOME	2017-06-17(188) /2017-06-17(188)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	臨床検査／ アラニンアミノトランスフェラーゼ増加／ ALT INCREASED 5X ULN 208	2017-01-19(8) /2017-01-24(13)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING TWICE	2017-01-30(19) /2017-02-01(21)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2017-02-03(23) /2017-02-13(33)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	傷害、中毒および処置合併症／裂傷／LACERATION ON CHIN	2017-02-11(31) /2017-02-16(36)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y
		胃腸障害／嘔吐／VOMITED X1	2017-02-22(42) /2017-02-22(42)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		皮膚および皮下組織障害／湿疹／ECZEMA	2017-03-01(49) /2017-03-23(71)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	皮膚および皮下組織障害／ 脱毛症／ HAIR LOSS	2017-03-05(53) /2017-03-16(64)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス性胃炎／ VIRAL GASTRITIS	2017-04-28(107) /2017-05-08(117)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON-DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ ロタウイルス感染／ ROTAVIRUS INFECTION	2017-05-20(129) /2017-05-29(138)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y

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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	感染症および寄生虫症／ 鼻咽頭炎／ COLD SYMPTOMS	2017-05-28(137) /2017-06-14(154)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING X2	2017-06-12(152) /2017-06-12(152)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 鼻咽頭炎／ COLD SYMPTOMS	2017-02-01(14) /2017-02-04(17)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／倦怠感／FELLING UNWELL	2017-02-15(28) /2017-02-16(29)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／発熱／FEVER	2017-03-18(59) /2017-03-20(61)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		胃腸障害／悪心／INTERMITTENT NAUSEA	2017-04-27(99) /2017-04-27(99)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 疼痛／ INTERMITTENT GENERALIZED BODY PAIN	2017-05-06(108) /2017-06-30(163)	INTERMITTENT/ MODERATE/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COLD SYMPTOMS	2017-06-05(138) /2017-06-15(148)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL VENOUS LINE INFECTION WITH GRAM POSITIVE COAG NEG STAPH	2017-08-01(195) /2017-08-19(213)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-12-18(-43) /2016-12-20(-41)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	
		一般・全身障害および投与部位の状態／ カテーテル留置部位出血／ BLEEDING BROVIAC LINE	2016-12-31(-30) /2017-01-01(-29)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2017-01-09(-21) /2017-01-11(-19)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	
		傷害、中毒および処置合併症／裂傷／CUT ON UPPER THIGH	2017-01-30(1) /2017-01-30(1)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	
		呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2017-01-30(1) /2017-02-02(4)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-30(1) /2017-02-02(4)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	
		傷害、中毒および処置合併症 ／ 挫傷／ BRUISES ON UPPER THIGH	2017-02-06(8) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	傷害、中毒および処置合併症／人による咬傷／BITE MARK FROM SISTER	2017-02-06(8) /2017-02	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／下痢／DIARRHEA	2017-02-18(20) /2017-02-22(24)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		傷害、中毒および処置合併症／挫傷／BRUISE ON LEFT ARM	2017-03-13(43) /2017-03-20(50)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	2017-03-17(47) /2017-03	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		免疫系障害／ 季節性アレルギー／ SEASONAL ALLERGIES	2017-03-29(59) /ONGOING	INTERMITTENT/ MILD/ NOT RECOVERED/NOT RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		傷害、中毒および処置合併症／ 鼻部損傷／ CUT ON NOSE	2017-04-11(72) /2017-04	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	傷害、中毒および処置合併症／ 節足動物刺傷／ BEE STING	2017-05-01(92) /2017-05-03(94)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL INFECTION	2017-05-25(116) /2017-05-26(117)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		胃腸障害／ 肛門周囲紅斑／ PERIANAL ERYTHEMA	2017-06-14(136) /2017-06-21(143)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/[redacted]/WHITE	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-06-16(138) /2017-06-18(140)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	Y	Y
		胃腸障害／ 下痢／ DIARRHEA	2017-06-21(143) /2017-06-26(148)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		傷害、中毒および処置合併症／ ／ ストーマ部紅斑／ G-TUBE ERYTHEMA	2017-08-07(190) /2017-08-15(198)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	臨床検査／ 消化管ストーマ排液増加／ INCREASE SIZE OF JEJUNO TERMINAL STOMA	2016-09-29(2) /2017-04-11(196)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		胃腸障害／ 腹痛／ ABDOMINAL PAIN	2016-10-05(8) /2017-04-11(196)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／ 咳嗽／ COUGH	2016-10-09(12) /2016-10-23(26)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 鼻炎／ RHINITIS	2016-10-09(12) /2016-11-17(51)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		代謝および栄養障害／ 食欲減退／ LESS APPETITE	2016-10-16(19) /2017-04-11(196)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 咽頭炎／ PHARYNGITIS	2016-11-23(57) /2016-12-09(73)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	神経系障害／ 頭痛／ HEADACHE	2017-01-07(102) /2017-01-10(105)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-26(121) /2017-01-27(122)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		胃腸障害／ 吐血／ HEMATEMESIS	2017-02-06(132) /2017-02-07(133)	CONTINUOUS/ SEVERE/ RECOVERED/RESOLVED	NOT RELATED	Yes, 3	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Teduglutide 0.05 mg/kg/day

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/WHITE	感染症および寄生虫症／ 急性中耳炎／ ACUTE OTITIS RIGHT	2017-02-19(145) /2017-02-25(151)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 嘔吐／ INCREASED VOMITING	2016-11-02(43) /2016-11-06(47)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		感染症および寄生虫症／ 中耳炎／ BILATERAL OTITIS MEDIA	2016-11-07(48) /2016-11-17(58)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-11-09(50) /2016-11-25(66)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ 上気道感染／ INTERMITTENT URI	2016-12-11(82) /2016-12-19(90)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		耳および迷路障害／ 耳痛／ OTALGIA	2016-12-16(87) /2016-12-26(97)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON-DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 急性中耳炎／ ACUTE OTITIS MEDIA	2016-12-17(88) /2016-12-19(90)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON-DRUG TREATMENT	Y	Y

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Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	一般・全身障害および投与部位の状態／医療機器使用部位疼痛／GASTROSTOMY TUBE SITE PAIN	2016-12-29(100) /2017-01-17(119)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ウイルス性上気道感染／VIRAL UPPER RESPIRATORY INFECTION	2017-02-05(138) /2017-02-07(140)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	胃腸障害／ 悪心／ NAUSEA	2017-02-07(140) /2017-02-07(140)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 尿路感染／ URINARY TRACT INFECTION	2017-02-07(140) /2017-02-10(143)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ ウイルス性上気道感染／ VIRAL UPPER RESPIRATORY INFECTION	2017-02-07(140) /2017-02-10(143)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ 細菌性尿路感染／ PROTEUS MIRABILIS URINARY TRACT INFECTION	2017-02-10(143) /2017-02-17(150)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL SYNDROME	2017-03-16(177) /2017-03-22(183)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/ASIAN	感染症および寄生虫症／ ウイルス感染／ VIRAL SYNDROME	2017-03-22(183) /2017-03-24(185)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
[redacted]	M/[redacted]/BLACK	呼吸器、胸郭および縦隔障害 ／ 鼻閉／ NASAL CONGESTION	2016-11-21(39) /2016-12-01(49)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2016-12-20(68) /2016-12-29(77)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／鼻閉／NASAL CONGESTION	2016-12-20(68) /2016-12-29(77)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-14006¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 13:05

Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	呼吸器、胸郭および縦隔障害／咳嗽／COUGH	2017-04-05(174) /2017-04-05(174)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／過換気／HYPERVENTILATION	2017-04-05(174) /2017-04-05(174)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	血液およびリンパ系障害／ リンパ節症／ RIGHT ANTERIOR CERVICAL ADENOPATHY	2017-04-05(174) /2017-04-07(176)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／ 鼻漏／ RHINORRHEA	2017-04-05(174) /2017-04-12(181)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-04-07(176) /2017-04-07(176)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ コロナウイルス感染／ CORONAVIRUS INFECTION	2017-04-07(176) /2017-04-10(179)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NON-DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 真菌血症／ MALASSEZIA FURFUR FUNGEMIA	2017-04-20(189) /2017-05-17(216)	CONTINUOUS/ MODERATE/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT,NON- DRUG TREATMENT	Y	Y

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/BLACK	胃腸障害／ 嘔吐／ INCREASED EMESIS	2017-04-25(194) /2017-04-25(194)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		肝胆道系障害／ 薬物性肝障害／ DRUG INDUCED LIVER INJURY	2017-04-26(195) /2017-04-29(198)	CONTINUOUS/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
[redacted]	M/[redacted]/OTHER	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-03-14(78) /2017-03-16(80)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	M/[redacted]/OTHER	一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-03-29(93) /2017-04-05(100)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 耳感染／ EAR INFECTION	2017-04-27(122) /2017-05-05(130)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-06-26(182) /2017-06-30(186)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/-/NALLW	感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-02 /2017-02	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		臨床検査／ トランスアミナーゼ上昇／ TRANSAMINITIS	2017-02-09(28) /ONGOING	CONTINUOUS/ MODERATE/ RECOVERING/RESOLVING	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-02-23(42) /2017-02-25(44)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
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Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/-/NALLW	皮膚および皮下組織障害／レッドマン症候群／REDMAN SYNDROME REACTION TO VANCOMYCIN	2017-03-21(68) /2017-03-21(68)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ばら疹／HOSPITALIZATION DUE TO ROSEOLA	2017-03-21(68) /2017-03-27(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
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Treatment: Standard of Care

Subject	Sex/ Age/ Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Frequency/ Severity/ Outcome	Relat. to Study Drug	Potential Dose Interrupt. Criteria (Y/N, CTCAE Grade)	Action Taken with Study Treatment/ Other Action Taken	SAE	TEAE
[redacted]	F/-/NALLW	胃腸障害／ 嘔吐／ VOMITING	2017-03-21(68) /2017-03-27(74)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY TRACT INFECTION	2017-05-14(122) /2017-05-16(124)	INTERMITTENT/ MILD/ RECOVERED/RESOLVED	NOT RELATED	No	NOT APPLICABLE/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Relat. = Relationship; Interrupt. = Interruption; TEAE = Treatment Emergent Adverse Event; SAE = Serious Adverse Event.
Note: Treatment Emergent Adverse Events (TEAEs) are defined as adverse events that started or worsened on or after the date of first dose for treatment groups and adverse events that started or worsened on or after the baseline visit of standard of care group. Adverse events with an unknown date of onset and a stop date after the start of the date of first dose or unknown are included as TEAEs.
Note: Adverse events were coded to primary SOC and preferred term using MedDRA dictionary, Version 19.1.
Note: Study day is considered to begin with the day that the subject receives the first dose of the study medication or the baseline visit for the subjects in the standard of care treatment group. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ インフルエンザ／ INFLUENZA A VIRAL INFECTION	2014-12-28 (241)/ 2014-12-30 (243)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		胃腸障害／ 小腸閉塞／ SMALL BOWEL OBSTRUCTION	2015-01-02 (246)/ 2015-01-14 (258)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 消化管運動低下／ SECONDARY SMALL BOWEL PSEUDO OBSTRUCTION	2015-04-20 (354)/ 2015-06-11 (406)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		胃腸障害／ 機能性胃腸障害／ COMPENSATED INTESTINAL FAILURE ASSOCIATED LIVER DISEASE (NO MORE INFO)	2015-07-21 (446)/ 2015-07-29 (454)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CLABSI	2016-01-08 (617)/ 2016-01-13 (622)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CLABSI	2016-01-23 (632)/ 2016-02-10 (650)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器機能不良／ CENTRAL LINE MALFUNCTION	2017-01-17 (992)/ 2017-01-20 (995)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		血液およびリンパ系障害／ 貧血／ WORSENING ANEMIA	2017-07-26 (92)/ 2017-07-28 (94)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連敗血症／CLABSI	2017-09-15 (143)/ 2017-09-26 (154)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ライノウイルス感染／RHINOVIRUS RESPIRATORY INFECTION	2017-09-16 (144)/ 2017-09-26 (154)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 腹痛／ ABDOMINAL PAIN	2017-09-21 (149)/ 2017-09-21 (149)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ DRUG TREATMENT	N	Y
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 腸球菌感染／ ENTEROCOCCUS INFECTION	2014-08-28 (197)/ 2014-09-03 (203)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／医療機器関連合併症／CENTRAL LINE COMPLICATION	2014-09-20 (220)/ 2014-09-20 (220)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	N	
		感染症および寄生虫症／細気管支炎／BRONCHIOLITIS	2015-02-19 (372)/ 2015-02-25 (378)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2015-04-29 (441)/ 2015-04-30 (442)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		皮膚および皮下組織障害 ／ 皮膚刺激／ SKIN IRRITATION	2015-06-07 (480)/ 2015-06-09 (482)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	傷害、中毒および処置合併症／ 処置後出血／ RECTAL BLEEDING(RESULTING FROM EDG PROCEDURE)	2017-03-13 (1125)/ 2017-03-13 (1125)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	神経系障害／ 嗜眠／ LETHARGY	2017-04-23 (1166)/ 2017-04-23 (1166)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	N	
		感染症および寄生虫症／ 医療機器関連感染／ MALESSEZIA CENTRAL LINE INFECTION	2017-12-08 (171)/ 2017-12-22 (185)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	肝胆道系障害／ 黄疸／ JAUNDICE	2014-12-11 (238)/ 2014-12-18 (245)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2014-12-19 (246)/ 2015-01-11 (269)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	肝胆道系障害／ 肝不全／ WORSENING OF LIVER FAILURE	2014-12-19 (246)/ ONGOING	RETROSPECTIVE	CONT/ MO/ RCG	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2015-02-11 (300)/ 2015-02-13 (302)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	胃腸障害／膵炎／PANCREATITIS FLARE	2016-03-30 (713)/ 2016-04-04 (718)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		胃腸障害／膵炎／PANCREATITIS FLARE	2017-03-25 (1073)/ 2017-03-29 (1077)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2014-12-07 (194)/ 2014-12-11 (198)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		製品の問題／医療機器破損／BROKEN CENTRAL LINE	2015-01-07 (225)/ 2015-01-07 (225)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-02-15 (264)/ 2015-02-27 (276)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		製品の問題／医療機器破損／BROKEN CENTRAL LINE	2015-03-26 (303)/ 2015-03-26 (303)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／医療機器関連合併症／CENTRAL LINE COMPLICATION	2015-11-28 (550)/ 2015-12-01 (553)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2015-11-28 (550)/ 2015-12-01 (553)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ インフルエンザ／ INFLUENZA B VIRUS INFECTION	2016-02-22 (636)/ 2016-02-23 (637)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2016-04-01 (675)/ 2016-04-04 (678)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2016-09-12 (839)/ 2016-09-13 (840)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		製品の問題／医療機器破損／BROKEN CENTRAL LINE	2016-12-21 (939)/ 2016-12-23 (941)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2017-04-28 (1067)/ 2017-04-29 (1068)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-05-01 (1070)/ 2017-05-03 (1072)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	呼吸器、胸郭および縦隔障害／呼吸不全／RESPIRATORY INSUFFICIENCY	2014-11-13 (136)/ 2014-11-18 (141)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		心臓障害／頻脈／TACHYCARDIA	2014-12-30 (183)/ 2015-02-06 (221)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	一般・全身障害および投与部位の状態／発熱／FEVER	2014-12-30 (183)/ 2015-02-06 (221)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／RS ウイルス細気管支炎／RESPIRATORY SYNCYTIAL VIRUS, BRONCHIOLITIS	2014-12-30 (183)/ 2015-02-06 (221)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	呼吸器、胸郭および縦隔障害／ 頻呼吸／ TACHYPNEA	2014-12-30 (183)/ 2015-02-06 (221)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2015-03-19 (262)/ 2015-03-20 (263)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	一般・全身障害および投与部位の状態／発熱／ FEVER	2015-06-04 (339)/ 2015-06-06 (341)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／ FEVER	2016-02-06 (586)/ 2016-02-09 (589)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	感染症および寄生虫症／ ライノウイルス感染／ RHINOVIRUS INFECTION	2016-02-06 (586)/ 2016-02-09 (589)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2016-03-06 (615)/ 2016-03-08 (617)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	一般・全身障害および投与部位の状態／発熱／FEVER	2016-09-23 (816)/ 2016-09-25 (818)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		代謝および栄養障害／脱水／DEHYDRATION	2016-10-10 (833)/ 2016-10-13 (836)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	胃腸障害／ 嘔吐／ VOMITING	2017-01-08 (923)/ 2017-01-11 (926)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER	2017-01-08 (923)/ 2017-01-11 (926)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	感染症および寄生虫症／インフルエンザ／INFLUENZA A INFECTION	2017-01-12 (927)/ 2017-01-16 (931)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2017-01-21 (936)/ 2017-01-27 (942)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ OTHER	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2017-01-21 (936)/ 2017-01-27 (942)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		呼吸器、胸郭および縦隔障害／ 喘息／ ASTHMA EXACERBATION	2017-02-19 (965)/ 2017-03-08 (982)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／パラインフルエンザウイルス感染／ PARAINFLUENZA 2	2014-10-09 (134)/ 2015-10-14 (504)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／ CENTRAL LINE INFECTION	2014-12-26 (212)/ 2015-01-01 (218)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ インフルエンザ／ INFLUENZA B	2016-02-27 (640)/ 2016-03-09 (651)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		傷害、中毒および処置合併症／ 吻合部潰瘍／ ANASTOMOTIC ULCERS	2016-03-02 (644)/ 2016-03-09 (651)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-02-11 (203)/ 2015-02-21 (213)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-06-09 (321)/ 2015-06-20 (332)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2016-02-23 (580)/ 2016-02-27 (584)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／尿路感染／UNINARY TRACT INFECTION	2016-02-23 (580)/ 2016-02-27 (584)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／全身性炎症反応症候群／SYSTEMIC INFLAMMATORY RESPONSE SYNDROME	2016-08-20 (759)/ 2016-08-22 (761)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2017-02-09 (932)/ 2017-02-21 (944)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
[redacted]	F/[redacted]/ WHITE	製品の問題／ 医療機器機能不良／ NON FUNCTIONING PICC LINE	2016-02-26 (583)/ 2016-02-29 (586)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2014-12-01 (131)/ 2014-12-12 (142)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTIOIN	2015-04-01 (252)/ 2015-04-07 (258)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／麻痺性イレウス／ADYNAMIC ILEUS	2015-04-08 (259)/ 2015-04-13 (264)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	
		感染症および寄生虫症／ロタウイルス感染／ROTAVIRUS INFECTION	2015-04-08 (259)/ 2015-04-13 (264)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2015-07-24 (366)/ 2015-07-26 (368)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NC	Y	
		胃腸障害／イレウス／ILEUS	2017-02-02 (925)/ 2017-02-04 (927)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 嘔吐／ VOMITING	2017-08-18 (65)/ 2017-08 (78)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／ 感染性クループ／ CROUP	2017-10-06 (114)/ 2017-10 (139)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-07 (31)/ 2017-08 (92)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	代謝および栄養障害／低血糖／HYPOGLYCEMIA	2017-07-03 (33)/ 2017-07-17 (47)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		代謝および栄養障害／低カルシウム血症／HYPOCALCEMIA	2017-07-24 (54)/ 2017-07-31 (61)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	代謝および栄養障害／ 低カリウム血症／ HYPOKALEMIA	2017-07-24 (54)/ 2017-07-31 (61)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 胃腸炎／ ACUTE GASTROENTERITIS	2014-09-08 (196)/	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／ FEVER WITH CENTRAL LINE	2014-10-08 (226)/ 2014-10-10 (228)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		一般・全身障害および投与部位の状態／発熱／ FEVER IN THE SETTING OF A CENTRAL LINE	2014-10-19 (237)/ 2014-10-21 (239)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／ FEVER, LIKELY VIRAL ETIOLOGY	2014-12-25 (304)/ 2014-12-28 (307)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		一般・全身障害および投与部位の状態／発熱／ FEVER WITH COUGH	2015-03-05 (374)/ 2015-03-08 (377)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2015-06-13 (474)/ 2015-06-17 (478)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		胃腸障害／膵炎／PANCREATITIS UNCLEAR ETIOLOGY	2015-09-08 (561)/ 2015-09-11 (564)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／膵炎／PANCREATITIS	2015-09-12 (565)/ 2015-09-16 (569)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		胃腸障害／小腸炎／INTESTINAL INFLAMMATION/ENTERITIS	2016-01-24 (699)/ 2016-01-29 (704)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER IN THE SETTING OF A CENTRAL LINE	2016-07-12 (869)/ 2016-07-14 (871)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		製品の問題／医療機器閉塞／CVC OCCLUSION	2016-08-12 (900)/ 2016-08-18 (906)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	外科および内科処置／ 中心静脈カテーテル留置 ／ CVC REPLACED	2016-08-19 (907)/ 2016-08-21 (909)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 骨髄炎／ OSTEOMYELITIS	2014-12-01 (229)/ 2015-02-08 (298)	RETROSPECTIVE	CONT/ MO/ R/R	No			Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 尿路性敗血症／ UREUOSEPSIS	2015-03-01 (319)/ 2015-03-20 (338)	RETROSPECTIVE	CONT/ MI/ R/R	No			Y	
		一般・全身障害および投与部位の状態／ 発熱／ FEVER WITH CVC	2016-05-14 (759)/ 2016-05-27 (772)	RETROSPECTIVE	CONT/ MI/ R/R	No			Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ STAPH AUREUS CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION	2016-07-12 (818)/ 2016-07-31 (837)	RETROSPECTIVE	CONT/ MI/ R/R	No			Y	
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ 小球菌感染／ POSITIVE BLOOD CULTURE WITH ORGANISM MICROCOCCUS	2014-10-10 (122)/ 2014-10-14 (126)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ ACUTE CENTRAL LINE INFECTION DUE TO KOCURIA VARIANS	2014-11-14 (157)/ 2014-11-18 (161)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		製品の問題／ 医療機器機能不良／ ACUTE BROVIAC CENTRAL LINE MALFUNCTION	2015-04-01 (295)/ 2015-04-02 (296)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER/BROVIAC REPLACEMENT	2016-08-07 (789)/ 2016-08-09 (791)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		感染症および寄生虫症／RS ウイルス感染／RESPIRATORY SYNCYTIAL VIRUS - RSV - UNKNOWN	2016-12-06 (910)/ 2016 (935)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／メタニューモウイルス感染／HUMAN METAPNEUMOVIRUS (ADDITIONAL INFORMATION UNKNOWN)	2017-03-08 (1002)/ 2017-03-10 (1004)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2017-04-22 (1047)/ 2017 (1300)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ アデノウイルス感染／ ADENOVIRUS NO MORE INFORMATION	2017-04-26 (1051)/ 2017 (1300)	RETROSPECTIVE	CONT/ MI/ R/R	No		NA	Y	
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／ 異常高熱／ ACUTE HYPERPYREXIA	2015-02-17 (174)/ 2015-02-18 (175)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	外科および内科処置／ カテーテル管理／ CENTRAL LINE REPAIR (NO MORE INFO)	2015-03-11 (196)/ 2015-03-12 (197)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		製品の問題／ 医療機器機能不良／ CENTRAL LINE MALFUNCTION	2015-08-24 (362)/ 2015-08-25 (363)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2015-09-07 (376)/ 2015-09-08 (377)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER IN THE SETTING OF A BROKEN CENTRAL VENOUS LINE	2015-12-12 (472)/ 2015-12-12 (472)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	外科および内科処置／中心静脈カテーテル留置／CENTRAL VENOUS LINE REMOVAL AND REPLACEMENT	2015-12-12 (472)/ 2015-12-12 (472)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		胃腸障害／小腸狭窄／PROXIMAL ANASTOMOTIC STRICTURE (NO MORE INFORMATION)	2017-04-20 (967)/ 2017-04-20 (967)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器破損／ BROKEN CENTRAL VENOUS CATHETER	2015-03-16 (202)/ 2015-03-25 (211)	RETROSPECTIVE	UNKNOWN / MI/ R/R	No	NR	NA	Y	
[redacted]	F/[redacted]/ WHITE	代謝および栄養障害／ 脱水／ DEHYDRATION	2015-03-22 (238)/ 2015-03-31 (247)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-07-03 (341)/ 2015-07-13 (351)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER, RULE OUT CENTRAL LINE INFECTION	2016-06-30 (704)/ 2016-07-01 (705)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	代謝および栄養障害／脱水／DEHYDRATION	2016-09-06 (772)/ 2016-09-18 (784)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2017-02-16 (935)/ 2017-02-23 (942)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	血液およびリンパ系障害／貧血／ANEMIA	2014-10-30 (114)/ 2014-11-06 (121)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2014-10-30 (114)/ 2014-11-06 (121)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-09-25 (444)/ 2015-10-08 (457)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		臨床検査／ブドウ球菌検査陽性／POSITIVE BLOOD CULTURE (STAPH CAPITIS)	2015-12-21 (531)/ 2015-12-22 (532)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2016-06-10 (703)/ 2016-06-13 (706)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER, RULE OUT CENTRAL LINE INFECTION	2016-08-25 (779)/ 2016-08-27 (781)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ BLACK	感染症および寄生虫症／医療機器関連感染／FEVER/LINE INFECTION	2014-12-14 (210)/ 2014-12-24 (220)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／POSITIVE BLOOD CULTURE/ LINE INFECTION	2014-12-28 (224)/ 2015-01-09 (236)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ BLACK	代謝および栄養障害／代謝性アシドーシス／LAB DERANGEMENT CONCERNING FOR BACTERIAL OVERGROWTH AND D-LACTIC ACIDOSIS	2015-03-06 (292)/ 2015-03-07 (293)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ BLACK	代謝および栄養障害／電解質失調／ELECTROLYTE ABNORMALITIES	2015-07-13 (421)/ 2015-07-14 (422)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／菌血症／BACTEREMIA	2015-12-03 (564)/ 2015-12-16 (577)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ BLACK	一般・全身障害および投与部位の状態／発熱／ FEVER IN SETTING OF CENTRAL LINE	2016-06-21 (765)/ 2016-06-28 (772)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
[redacted]	M/[redacted]/ OTHER	感染症および寄生虫症／医療機器関連感染／ CENTRAL LINE INFECTION/FEVER	2015-03-15 (299)/ 2015-03-21 (305)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ OTHER	一般・全身障害および投与部位の状態／発熱／FEVER	2015-05-11 (356)/ 2015-05-14 (359)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		製品の問題／医療機器破損／BROKEN CENTRAL LINE/ FEVER	2016-02-03 (624)/ 2016-02-05 (626)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ OTHER	一般・全身障害および投与部位の状態／発熱／ FEVER	2016-03-21 (671)/ 2016-03-23 (673)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
[redacted]	M/[redacted]/ WHITE	胃腸障害／直腸出血／ RECTAL BLEED	2015-01-14 (279)/ 2015-01-16 (281)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／細菌感染／BACTERIAL INFECTION	2015-01-17 (282)/ 2015-01-28 (293)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-03-13 (337)/ 2015-03-18 (342)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-04-09 (364)/ 2015-04-13 (368)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-11-22 (591)/ 2015-11-29 (598)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器機能不良／ MALFUNCTIONING CENTRAL LINE	2016-04-04 (725)/ 2016-04-06 (727)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		血管障害／ 上大静脈症候群／ SVC SYNDROME	2016-04-07 (728)/ 2017-02-02 (1029)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／菌血症／BACTEREMIA	2016-04-09 (730)/ 2016-04-20 (741)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		代謝および栄養障害／電解質失調／ELECTROLYTE ABNORMALITIES	2016-04-24 (745)/ 2016-04-26 (747)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器不具合／ FAILURE OF PICC LINE	2016-07-12 (824)/ 2016-07-13 (825)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
[redacted]	F/[redacted]/ BLACK	感染症および寄生虫症／ ブドウ球菌性菌血症／ MRSA BACTEREMIA	2014-05-17 (132)/ 2014-05-28 (143)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2014-06-11 (157)/ 2014-06-13 (159)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		代謝および栄養障害／体重増加不良／HOSPITAL ADMISSION FOR POOR WEIGHT GAIN	2014-08-13 (220)/ 2014-08-29 (236)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2014-10-23 (291)/ 2014-10-27 (295)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-05-23 (503)/ 2015-05-29 (509)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2015-07-20 (561)/ 2015-07-24 (565)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2015-11-07 (671)/ 2015-11-09 (673)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2015-11-13 (677)/ 2015-11-18 (682)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
[redacted]	F/[redacted]/ WHITE	傷害、中毒および処置合併症／ 足骨折／ FRACTURED 2ND METATARSAL OF LEFT FOOT	2016-07 (660)/ 2016-07 (690)	RETROSPECTIVE	CONT/ SV/ R/R	No	NR	UK	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	胃腸障害／ 下痢／ OVERNIGHT HOSPITALISATION DUE TO DIARRHOEA	2016-11-27 (809)/ 2016-11-28 (810)	RETROSPECTIVE	UNKNOWN / SV/ R/R	No	NR	UK	Y	
		胃腸障害／ 嘔吐／ OVERNIGHT HOSPITALISATION DUE TO VOMITING	2016-11-27 (809)/ 2016-11-28 (810)	RETROSPECTIVE	UNKNOWN / SV/ R/R	No	NR	UK	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
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Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	血液およびリンパ系障害／小球性貧血／MICROCYTIC ANAEMIA	2017-08-09 (2)/ 2017-08-30 (23)	PROSPECTIVE	CONT/ SV/ R/R	No	NR	NA/ NON-DRUG TREATMENT	Y	Y
		血液およびリンパ系障害／貧血／ANAEMIA	2017-08-30 (23)/ 2017-11-14 (99)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	2017-10 (55)/ 2017-11-14 (99)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／ 鼻出血／ NOSE BLEED	2017-11-14 (99)/ 2017-11-14 (99)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2015-03-08 (200)/ 2015-03-13 (205)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		胃腸障害／ 短腸症候群／ SHORT BOWEL SYNDROME REQUIRING BOWEL DILATION.	2015-04-10 (233)/ 2015-04-23 (246)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2016-01-31 (529)/ 2016-02-02 (531)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／敗血症／SEPSIS	2015-11-20 (429)/ 2015-11-25 (434)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／尿路感染／ URINARY TRACT INFECTION	2015-11-20 (429)/ 2015-11-25 (434)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／上気道感染／ FEVER/URI	2015-12-07 (446)/ 2015-12-08 (447)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	製品の問題／医療機器破損／BROKEN BROVIAC	2015-12-07 (446)/ 2015-12-08 (447)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2016-03-02 (532)/ 2016-03-09 (539)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／インフルエンザ／INFLUENZA	2016-03-02 (532)/ 2016-03-09 (539)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／ウイルス感染／VIRAL INFECTION	2016-03-02 (532)/ 2016-03-09 (539)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ ウイルス感染／ VIRAL INFECTION	2016-06-06 (628)/ 2016-06-09 (631)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2016-09-24 (738)/ 2016-09-29 (743)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／尿路性敗血症／URO SEPSIS	2016-09-24 (738)/ 2016-09-29 (743)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2017-02-15 (882)/ 2017-02-23 (890)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/NTT

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／上気道感染／URI	2017-02-15 (882)/ 2017-02-23 (890)	RETROSPECTIVE	INT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL INTRA VENOUS LINE INFECTION	2014-06-22 (189)/ 2014-06-26 (193)	RETROSPECTIVE	CONT/ SV/ R/R	No	NR	NA	Y	
		製品の問題／ 医療機器機能不良／ CENTRAL INTRA VENOUS LINE MALFUNCTION	2014-08-23 (251)/ 2014-08-29 (257)	RETROSPECTIVE	CONT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL INTRA VENOUS LINE INFECTION	2014-08-23 (251)/ 2014-09-04 (263)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ ウイルス性上気道感染／ VIRAL UPPER RESPIRATORY INFECTION	2014-11-19 (339)/ 2014-11-21 (341)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	
		胃腸障害／ イレウス／ ILEUS	2014-12-20 (370)/ 2014-12-25 (375)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2014-12-20 (370)/ 2014-12-25 (375)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／医療機器関連感染／CENTRAL INTRA VENOUS INFECTION	2015-06-06 (538)/ 2015-06-11 (543)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL INTRA VENOUS LINE INFECTION	2015-07-14 (576)/ 2015-07-22 (584)	RETROSPECTIVE	CONT/ MI/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2015-09-05 (629)/ 2015-09-07 (631)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2015-10-13 (667)/ 2015-10-16 (670)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	Y	
		一般・全身障害および投与部位の状態／発熱／FEVER	2016-02-08 (785)/ 2016-02-09 (786)	RETROSPECTIVE	INT/ MI/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	代謝および栄養障害／ アシドーシス／ ACIDOSIS	2017-04-27 (-19)/ 2017-05-01 (-15)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		臨床検査／ C-反応性蛋白増加／ C-REACTIVE PROTEIN INCREASED	2017-05-30 (15)/ 2017-06-13 (29)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 下痢／ INCREASED DIARRHEA	2017-06-16 (32)/ ONGOING	PROSPECTIVE	INT/ MI/ NRD	No	NR	NC/ NONE	N	Y
		代謝および栄養障害／ 高カリウム血症／ HYPERKALEMIA	2017-07-03 (49)/ 2017-07-10 (56)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	代謝および栄養障害／ 低クロール血症／ HYPOCHLOREMIA	2017-07-03 (49)/ 2017-07-10 (56)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		臨床検査／ C-反応性蛋白増加／ C-REACTIVE PROTEIN INCREASED	2017-07-18 (64)/ 2017-08-07 (84)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 下痢／ INCREASED DIARRHEA	2017-09-30 (138)/ 2017-10-01 (139)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-09-30 (138)/ 2017-10-01 (139)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		胃腸障害／ 胃炎／ ANTRAL GASTRITIS	2017-11-16 (185)/ ONGOING	PROSPECTIVE	CONT/ MO/ NRD	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	血液およびリンパ系障害／ 貧血／ SYMPTOMATIC ANEMIA	2017-11-30 (199)/ 2017-12-26 (225)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ NON-DRUG TREATMENT	N	Y
[redacted]	M/1[redacted]/ WHITE	臨床検査／ 体重減少／ WEIGHT LOSS	2014-10-01 (154)/ 2014-10-08 (161)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	代謝および栄養障害／電解質失調／ELECTROLYTE ABNORMALITIES	2014-10-01 (154)/ 2014-10-08 (161)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	
		代謝および栄養障害／栄養補給不耐性／FEEDING INTOLERANCE	2015-09-23 (511)/ 2015-10-16 (534)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	感染症および寄生虫症／ ウイルス性咽頭炎／ VIRAL PHARYNGITIS	2016-02-20 (661)/ 2016-02-23 (664)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	
		感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2016-04-15 (716)/ 2016-04-28 (729)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	感染症および寄生虫症／ 医療機器関連感染／ CENTRAL LINE INFECTION	2016-05-01 (732)/ 2016-05-05 (736)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	
		製品の問題／ 医療機器破損／ BROKEN CENTRAL LINE	2016-06-14 (776)/ 2016-06-15 (777)	RETROSPECTIVE	CONT/ MO/ R/R	No	NR	NC	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	皮膚および皮下組織障害／ そう痒性皮疹／ PRURITIC FACIAL RASH	2017-07-20 (64)/ 2017-08-10 (85)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		臨床検査／ 細菌検査陽性／ BACTERIA IN URINE	2017-08-10 (85)/ 2017-09-07 (113)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	臨床検査／ 尿中白血球陽性／ LEUKOCYTES IN URING	2017-08-10 (85)/ 2017-10-05 (141)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		臨床検査／ C-反応性蛋白増加／ C-REACTIVE PROTEIN INCREASED	2017-09-07 (113)/ 2017-10-05 (141)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	胃腸障害／ 口唇腫脹／ LIP SWELLING	2017-10-12 (148)/ 2017-10 (167)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		皮膚および皮下組織障害 ／ 顔面腫脹／ FACE SWELLING	2017-10-12 (148)/ 2017-10 (167)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-11 (168)/ 2017-11 (197)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		胃腸障害／ 嘔吐／ INCREASED VOMITING	2017-11 (168)/ 2017-12 (228)	PROSPECTIVE	INT/ MO/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	神経系障害／ 痙攣発作／ INCREASED SEIZURES	2017-11 (168)/ 2017-12 (228)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		精神障害／ 攻撃性／ INCREASED AGGRESSION	2017-11 (168)/ 2017-12 (228)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		臨床検査／ 体重減少／ WEIGHT LOSS	2017-11-30 (197)/ 2017-12 (228)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
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Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ WHITE	感染症および寄生虫症／せつ／ FURUNCLE	2017-12 (198)/ 2018-02-15 (274)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
[redacted]	M/[redacted]/ WHITE	胃腸障害／嘔吐／ VOMITING	2017-05-09 (-7)/ 2017-05-23 (8)	PROSPECTIVE	INT/ MO/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		製品の問題／医療機器閉塞／ CENTRAL LINE OCCLUSION	2017-06-02 (18)/ 2017-06-02 (18)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	臨床検査／ C-反応性蛋白増加／ ELEVATED CRP	2017-07-21 (67)/ 2017-08-07 (84)	PROSPECTIVE	INT/ MO/ R/R	No	NR	NC/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 疲労／ FATIGUE	2017-11-15 (184)/ 2017-11-22 (191)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	製品の問題／ 医療機器位置異常／ CENTRAL LINE DISLODGED	2017-12-20 (219)/ 2017-12-21 (220)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ NON-DRUG TREATMENT	N	Y
[redacted]	F/[redacted]/ WHITE	臨床検査／ 細菌検査陽性／ BACTERIA IN URINE	2017-09-08 (116)/ 2017-10-03 (141)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	臨床検査／ C-反応性蛋白増加／ C-REACTIVE PROTEIN INCREASED	2017-09-08 (116)/ 2017-10-03 (141)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		臨床検査／ 尿中白血球陽性／ LEUKOCYTES IN URINE	2017-09-08 (116)/ 2017-10-03 (141)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-09-25 (133)/ 2017-10-03 (141)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		血液およびリンパ系障害 ／ 貧血／ ANEMIA	2018-01-03 (233)/ 2018-01-11 (241)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ NON-DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2016-03-14 (600)/ 2016-03-16 (602)	RETROSPECTIVE	INT/ MO/ R/R	No	NR	NA	Y	
		胃腸障害／腹痛／ABDOMINAL PAIN	2016-09-17 (787)/ 2016-09-22 (792)	RETROSPECTIVE	INT/ MO/ R/R	No	R	DI	N	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 便秘／ CONSTIPATION	2016-09-17 (787)/ 2016-09-22 (792)	RETROSPECTIVE	INT/ MO/ R/R	No	R	DI	N	
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 胃腸炎／ ACUTE GASTROENTERITIS	2017-10 (56)/ 2017-10 (86)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
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Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	代謝および栄養障害／ 食欲減退／ DECREASED APPETITE	2017-10-06 (61)/ 2017-12-20 (136)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 気道感染／ RESPIRATORY INFECTION	2017-10-23 (78)/ 2018-01-15 (162)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
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Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

Program: x:¥shire_s@sgattex@adhoc¥japanaelistings¥shp633-303¥report¥adhoc¥l-sae.sas　Output: l-sae.rtf　30JAN2020 19:13

Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 肛門周囲紅斑／ REDNESS AT RECTUM	2017-10-26 (81)/ ONGOING	PROSPECTIVE	CONT/ MI/ NRD	No	NR	NC/ NONE	N	Y
[redacted]	F/[redacted]/ WHITE	呼吸器、胸郭および縦隔障害／ 鼻閉／ NASAL CONGESTION	2017-07-20 (11)/ 2017-08-17 (39)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
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Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／気道感染／RESPIRATORY INFECTION	2017-09-18 (71)/ 2017-09-30 (83)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／胃腸炎／GASTROENTERITIS	2017-10-16 (99)/ 2017-10-25 (108)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ レンサ球菌性咽頭炎／ STREPTOCOCCAL SORE THROAT	2017-11-21 (135)/ 2017-11-30 (144)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ UK	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL INFECTION	2017-11-26 (140)/ 2017-11-29 (143)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／上気道感染／ UPPER RESPIRATORY INFECTION	2017-11-30 (144)/ 2018-01-09 (184)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／中耳炎／ OTITIS MEDIA	2017-12-11 (155)/ 2017-12-14 (158)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	傷害、中毒および処置合併症／ 吻合部潰瘍／ ANASTOMOTIC ULCER	2017-08-14 (36)/ ONGOING	PROSPECTIVE	CONT/ MI/ RCG	No	NR	NC/ NON-DRUG TREATMENT	Y	Y
		胃腸障害／ 胃腸出血／ GI BLEED	2017-10-25 (108)/ ONGOING	PROSPECTIVE	CONT/ MI/ RCG	No	NR	NC/ MULTIPLE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 胃腸出血／ GI BLEED	2017-11-11 (125)/ ONGOING	PROSPECTIVE	CONT/ MI/ NRD	No	NR	NC/ MULTIPLE	Y	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-12-04 (148)/ 2017-12-18 (162)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	傷害、中毒および処置合併症／ 注入に伴う反応／ INFLIXIMAB INFUSION REACTION	2017-12-27 (171)/ 2017-12-27 (171)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ ライム病／ LYME DISEASE	2017-07-03 (-24)/ 2017-07-25 (-2)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	一般・全身障害および投与部位の状態／注射部位疼痛／PAIN AT INJECTION SITE	2017-09-11 (47)/ 2017-09-11 (47)	PROSPECTIVE	INT/ MI/ R/R	No	R	NC/ NONE	N	Y
		一般・全身障害および投与部位の状態／注射部位疼痛／PAIN AT INJECTION SITE	2017-09-20 (56)/ 2017-09-20 (56)	PROSPECTIVE	INT/ MI/ R/R	No	R	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	一般・全身障害および投与部位の状態／発熱／FEVER	2017-12-01 (128)/ 2017-12-02 (129)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	DI/ DRUG TREATMENT	Y	Y
[redacted]	M/[redacted]/ BLACK	胃腸障害／排便回数増加／INCREASE STOOL FREQUENCY	2017-06-07 (24)/ 2017-06-12 (29)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ BLACK	呼吸器、胸郭および縦隔障害／ 呼吸困難／ SHORT OF BREATHE	2017-06-12 (29)/ 2017-06-12 (29)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		胃腸障害／ 排便回数増加／ INCREASE STOOL FREQUENCY	2017-06-13 (30)/ 2017-07-05 (52)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-01-12 (-1)/ 2017-01-20 (8)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y
		胃腸障害／ 嘔吐／ VOMITING	2017-01-15 (3)/ 2017-01-15 (3)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NA/ DRUG TREATMENT	N	Y
		感染症および寄生虫症／ 上気道感染／ UPPER RESPIRATORY INFECTION	2017-01-15 (3)/ 2017-01-16 (4)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	胃腸障害／ 肛門周囲痛／ RECTAL PAIN	2017-02-01 (20)/ 2017-02-24 (43)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		神経系障害／ 頭痛／ HEADACHE	2017-02-24 (43)/ 2017-02-24 (43)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		胃腸障害／ 胃腸出血／ GI BLEED	2017-02-24 (43)/ 2017-02-27 (46)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NC/ MULTIPLE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	皮膚および皮下組織障害／ 発疹／ RASH ON NECK AND ABDOMEN	2017-04-04 (82)/ 2017-04-23 (101)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		呼吸器、胸郭および縦隔障害／ 口腔咽頭痛／ SORE THROAT	2017-04-06 (84)/ 2017-04 (108)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ ウイルス性胃腸炎／ VIRAL GASATROENTERITIS	2017-07-27 (196)/ 2017-08-15 (215)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD	2017-11-07 (299)/ 2017-11-13 (305)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	皮膚および皮下組織障害／ 顔面腫脹／ FACIAL SWELLING	2017-11-07 (299)/ 2017-11-13 (305)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y
		感染症および寄生虫症／ ウイルス性胃腸炎／ VIRAL GASTROENTERITIS	2017-12-25 (347)/ 2017-12-28 (350)	PROSPECTIVE	CONT/ MO/ R/R	No	NR	NA/ DRUG TREATMENT	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	血液およびリンパ系障害／ リンパ節症／ ANTERIOR CERVICAL LYMPHADENOPATHY	2017-09 (25)/ ONGOING	PROSPECTIVE	CONT/ MI/ RCG	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／ 鼻咽頭炎／ COMMON COLD SYNDROME	2017-09-01 (25)/ 2017-09-08 (32)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ BLACK	胃腸障害／ 嘔吐／ EMESIS	2017-09-05 (29)/ 2017-09-05 (29)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		胃腸障害／ 嘔吐／ EMESIS	2017-09-09 (33)/ 2017-09-09 (33)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／ インフルエンザ／ INFLUENZA A TEST POSITIVE	2017-12-11 (126)/ 2017-12-13 (128)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ UK	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ BLACK	製品の問題／ 医療機器位置異常／ CENTRAL LINE FELL OUT	2015-07-01 (303)/ 2015-07-03 (305)	RETROSPECTIVE	CONT/ SV/ R/R	No	NR	NA	Y	
		感染症および寄生虫症／ 医療機器関連敗血症／ CENTRAL LINE SEPSIS	2016-01-03 (489)/ 2016-01-05 (491)	RETROSPECTIVE	CONT/ SV/ R/R	No	NR	NA	Y	

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ BLACK	胃腸障害／ 腹痛／ ABDOMINAL PAIN, LEFT SIDE	2017-08-08 (-1)/ 2017-08-08 (-1)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NA/ NONE	N	Y
		胃腸障害／ 上腹部痛／ STOMACH ACHE RELATED TO LOPERAMIDE	2017-08-23 (15)/ 2017-10-09 (62)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ BLACK	神経系障害／ 嗜眠／ LETHARGY	2017-08-27 (19)/ 2017-08-27 (19)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		一般・全身障害および投与部位の状態／ 注射部位硬結／ SMALL INDURATIONS AT SITE OF INJECTION	2017-09-22 (45)/ 2017-10-09 (62)	PROSPECTIVE	CONT/ MI/ R/R	No	R	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ BLACK	臨床検査／ リンパ節触知／ CERVICAL LYMPH NODE PALPABLE	2017-09-22 (45)/ 2017-10-09 (62)	PROSPECTIVE	CONT/ MI/ R/R	No	NR	NC/ NONE	N	Y
		感染症および寄生虫症／ ウイルス感染／ VIRAL ILLNESS	2017-11-01 (85)/ 2017-11-29 (113)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/1[redacted]/ BLACK	一般・全身障害および投与部位の状態／注射部位腫脹／SWELLING AT INJECTION SITE	2017-12-28 (142)/ 2018-01-26 (171)	PROSPECTIVE	INT/ MI/ R/R	No	R	NC/ NONE	N	Y
		一般・全身障害および投与部位の状態／疲労／INCREASED TIREDNESS	2017-12-29 (143)/ 2018-02-09 (185)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ NONE	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent.　Severity: MI= Mild, MO= Moderate, SV= Severe.　Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown.　Relationship: NR = Not Related, R = Related.　Action:　NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown.　Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／医療機器関連感染／CENTRAL LINE INFECTION	2017-05-04 (-18)/ 2017-05-09 (-13)	PROSPECTIVE	INT/ SV/ R/R	No	NR	NA/ DRUG TREATMENT	Y	Y
		感染症および寄生虫症／上気道感染／UPPER RESPIRATORY INFECTION	2017-09-19 (121)/ 2017-09-23 (125)	PROSPECTIVE	INT/ MO/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
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Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	M/[redacted]/ WHITE	感染症および寄生虫症／ ウイルス性上気道感染／ UPPER RESPIRATORY VIRAL INFECTION	2017-12-25 (218)/ 2017-12-27 (220)	PROSPECTIVE	INT/ SV/ R/R	Yes: 3	NR	NC/ NONE	Y	Y
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ 細菌感染／ BACTERIAL INFECTION	2017-07-19 (59)/ 2017-08-18 (89)	PROSPECTIVE	INT/ SV/ R/R	No	NR	NC/ NONE	Y	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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Treatment: TED/TED

Subject	Sex/Age/Race	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ Stop Date (Study Day)	Retrospective/ Prospective	Frequency/ Severity/ Outcome	DIC(Y/N, CTCAE Grade)	Relationship to Study Drug	Action Taken with Study Treatment/ Other Action Taken	SAE/ Discont. AE	TEAE
[redacted]	F/[redacted]/ WHITE	感染症および寄生虫症／ 敗血症／ SEPSIS	2017-07-19 (59)/ 2017-08-18 (89)	PROSPECTIVE	INT/ SV/ R/R	No	NR	NC/ NONE	Y	Y
		製品の問題／ 医療機器閉塞／ CENTRAL LINE CLOGGED	2017-12-20 (213)/ 2017-12-21 (214)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y
		製品の問題／ 医療機器閉塞／ CENTRAL LINE CLOGGED	2018-01-02 (226)/ 2018-01-02 (226)	PROSPECTIVE	INT/ MI/ R/R	No	NR	NC/ DRUG TREATMENT	N	Y

Note: F = Female; M = Male; AIOAN = American Indian or Alaska Native; BLACK = Black or African American; ASIAN = Asian; WHITE = White; NHOPI = Native Hawaiian or Other Pacific Islander; OTHER = Other; NALLW = Not allowed based on local regulations.
Note: Reasons for SAE were not collected for this study. Frequency: CONT = Continuous, INT=Intermittent. Severity: MI= Mild, MO= Moderate, SV= Severe. Outcome: R/R=Recovered/Resolved, R/S=Recovered/Resolved with sequelae, NRD=Not Recovered/Not resolved, RCG=Recovering/Resolving, D=Fatal, UNK=Unknown. Relationship: NR = Not Related, R = Related. Action: NC=Dose Not Changed, DR=Dose Reduced, DI = Drug Interrupted, DW=Drug Withdrawn, NA= Not Applicable, UK=Unknown. Other Action: N=None, DT=Drug Treatment Given, NT=Non-drug treatment given, UK=Unknown. Discont. AE =DISC. DIC = Dose Interruption Criteria.
Note: TED/NTT - subjects who received teduglutide in the core study but not during the prospective period of this study; TED/TED - subjects who received teduglutide in the core study and during the prospective period of this study.
Note: Treatment-emergent adverse events (TEAEs) are defined as adverse events that started or worsened on or after the first dose of teduglutide treatment in the core study TED-C13-003.
Note: Adverse events were coded to primary system organ class and preferred term using MedDRA dictionary, Version 19.1.
Note: For retrospective adverse events,study day is considered to begin with the day of first teduglutide treatment in TED-C13-003. For prospective adverse events, study day is considered to begin with the start of either the first treatment on Cycle 1 Day 1 for the teduglutide treatment period or the date of informed consent for the prospective period. Study day before reference start date is negative.

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