2.7.1 の略号等一覧

略号（略称）	内　容
%CV	Percent coefficient of variance／変動係数
%CVb	Percent between-participant geometric coefficient of variation／被験者間の幾何変動係数
%RE	Percent relative error／相対誤差
2R/6R	2 mL/6 mL injection vial／2 mL/6 mL 注射バイアル
ADA	Anti-drug antibody／抗薬物抗体
ADC	Antibody-drug conjugate／抗体薬物複合体
APRIL	A proliferation-inducing ligand／増殖誘導リガンド
AUC(0-tlast)	Area under the concentration-time curve from time zero (pre-dose) to last time of quantifiable concentration／0 時間（投与前）から最終定量可能時点までの濃度－時間曲線下面積
AUC(0-x)	Area under the concentration-time curve from time zero (pre-dose) to some fixed nominal time x／0 時間（投与前）から x 時間までの濃度－時間曲線下面積
AUC(0-τ)	Area under the concentration-time curve over the dosing interval／投与間隔における濃度－時間曲線下面積
BAFF	B cell activating factor／B 細胞活性化因子
BCMA	B-cell maturation antigen／B 細胞成熟抗原
BSA	Bovine Serum Albumin／ウシ血清アルブミン
C-EOI	Concentration at the end of the infusion／静脈内投与終了時の血漿中濃度
Cmax	Maximum observed concentration／最高血漿中濃度
CPMR	Clinical pharmacology modeling report
CPSR	Clinical pharmacology study report
CSR	Clinical study report／治験総括報告書
CTD	Common Technical Document／コモン・テクニカル・ドキュメント
Ctrough	Pre-dose (trough) concentration at the end of the dosing interval／次回投与前の血漿中濃度
cys-mcMMAF	Cysteine maleimidocaproyl monomethyl auristatin F／システインマレイミドカプロイルモノメチルアウリスタチン F
DAR	Drug-antibody ratio／薬物抗体比
ECD	Extracellular domain／細胞外ドメイン
ECL	Electrochemiluminescence／電気化学発光
EDTA	Disodium edetate dihydrate／エチレンジアミン四酢酸二ナトリウム
ELISA	Enzyme-linked immunosorbent assay／酵素結合免疫吸着測定法
h	Hour(s)／時間
HC	Heavy chain／重鎖
HPLC	High-performance liquid chromatography／高速液体クロマトグラフィー
HRP	Horseradish peroxidase／西洋ワサビペルオキシダーゼ
huBCMA	Human B-cell maturation antigen／ヒト B 細胞成熟抗原
IgG	Immunoglobulin G／免疫グロブリン G
ISR	Incurred sample reanalysis
JP	Japanese Pharmacopoeia／日本薬局方
LBA	Ligand binding assay／リガンド結合法
LC-MS/MS	Liquid chromatography‐tandem with mass spectrometry／液体クロマトグラフィータンデム質量分析
LLOQ	Lower limit of quantification／定量下限

略号（略称）	内　容
LOD	Limit of detection／検出限界
LQC	Low quality control
Lyo	Lyophilized／凍結乾燥粉末剤
mAb	Monoclonal antibody／モノクローナル抗体
mcMMAF	Maleimidocaproyl monomethyl auristatin／マレイミドカプロイルモノメチルアウリスタチン F
MM	Multiple myeloma／多発性骨髄腫
MQC	Middle quality control
MRD	Minimum required dilution
NA	Not applicable／該当せず
pAb	Polyclonal antibody／ポリクローナル抗体
PD	Pharmacodynamic／薬力学
Ph. Eur.	European Pharmacopoeia
PK	Pharmacokinetic(s)／薬物動態
QC	Quality control／品質管理
QS	Sufficient quantity
sBCMA	Soluble BCMA／可溶性 BCMA
TE	Total error／全誤差
tlast	Time of last quantifiable concentration／定量可能な最終時間
TM	Test method／試験方法
tmax	Time of occurrence of Cmax／Cmax 到達時間
TNF	Tumor necrosis factor／腫瘍壊死因子
UHPLC-MS/MS	Ultra-high-performance liquid chromatography‐tandem mass spectrometry／超高速液体クロマトグラフィータンデム質量分析
ULOQ	Upper limit of quantification／定量上限
USP-NF	United States Pharmacopeia and the National Formulary
WFI	Water for injections／注射用水

2.7.1. 生物薬剤学試験及び関連する分析法

2.7.1.1. 背景及び概観

2.7.1.1.1. 緒言

ベランタマブ　マホドチン（遺伝子組換え）（以下、「ベランタマブ　マホドチン」）は、B 細胞成熟抗原（BCMA）に特異的に結合する低フコース化ヒト化免疫グロブリン G（IgG）1κ モノクローナル抗体（mAb）に微小管阻害剤であるモノメチルアウリスタチン F（MMAF）をプロテアーゼ耐性マレイミドカプロイルリンカーによって結合させた抗体薬物複合体（ADC）である。

ベランタマブ　マホドチンは細胞表面の BCMA に結合すると、速やかに細胞内に取り込まれる。腫瘍細胞内に入ると、システインマレイミドカプロイルモノメチルアウリスタチン F（cys-mcMMAF）が放出され、微小管ネットワークを阻害し、細胞周期の停止及びアポトーシスを誘導する。更に、抗体が低フコース化されていることで FcγRIIIa への結合能が高まり、免疫エフェクター細胞の動員と活性化が促進され、それにより抗体依存性細胞傷害及び抗体依存性細胞貪食によって腫瘍細胞を死滅させる。ベランタマブ　マホドチンにより誘導されたアポトーシスは、免疫原性細胞死のマーカーの放出を伴い、腫瘍細胞に対する適応免疫応答に関与する可能性がある。

BCMA の通常の機能は、2 種類の既知のリガンド［腫瘍壊死因子（TNF）ファミリーの B 細胞活性化因子（BAFF）及び増殖誘導リガンド（APRIL）］からのシグナル伝達により細胞の生存を促進することである。BCMA の発現は、分化後期の B 細胞に限られる[Darce, 2007]。BCMA は多発性骨髄腫（MM）を含む様々な B 細胞性悪性腫瘍で発現する[Tai, 2014]。このように、BCMA の発現は B 細胞系列に限定的であることから、オフターゲット作用を最小限に留めることができる理想的な治療標的といえる。

早期臨床試験ではベランタマブ　マホドチンの凍結液剤を使用し、単剤療法の BMA117159（DREAMM-1）試験、205678（DREAMM-2）試験、及び併用療法の 207497（DREAMM-6）試験において投与された。その後の製剤開発により、凍結乾燥粉末製剤は、DREAMM-2 試験における被験者 24 例からなるコホート、単剤療法の 207495（DREAMM-3）試験、209626（DREAMM-12）試験、併用療法の 207503（DREAMM-7）試験、及び 207499（DREAMM-8）試験におけるベランタマブ　マホドチン投与群の全被験者に投与された。本凍結乾燥粉末剤は本邦における市販予定製剤である。包括的な分析学的同等性／同質性評価パッケージにより、凍結液剤と凍結乾燥粉末剤は製剤学的に同等／同質であることが示されている［3.2.S.2.6.2（原薬）及び 3.2.P.2.3］。

ベランタマブ　マホドチンは静脈内投与であることから、生物薬剤学的特性を評価するための生物学的利用能、生物学的同等性及び食事の影響に関する試験は実施していない。

本項は、以下に関するデータを示す。

- ベランタマブ　マホドチンの製剤開発
- ベランタマブ　マホドチン、総 mAb、cys-mcMMAF、遊離可溶性 BCMA（sBCMA）、ボルテゾミブ、レナリドミド及びポマリドミドの臨床試験検体中濃度の測定に用いた分析法

- 免疫原性の評価に用いた分析法
- DREAMM-1 試験において検討した血漿中 cys-mcMMAF 分析法
- 凍結液剤と凍結乾燥粉末剤におけるベランタマブ　マホドチンの薬物動態（PK）の探索的比較

上記について、以下のことが示された。

- 凍結液剤から凍結乾燥製剤への品質の変更は比較的軽微であった。頑健な同等性／同質性評価パッケージに基づき、凍結液剤と凍結乾燥粉末剤は同等／同質であった。
- ノンコンパートメント PK 解析及び母集団 PK 解析の結果は、分析学的同等性／同質性評価パッケージにより示された凍結液剤及び凍結乾燥粉末剤の同等性／同質性の結論を裏付けるものであった。
- ヒト血漿中のベランタマブ　マホドチン、総 mAb、cys-mcMMAF、ボルテゾミブ及びポマリドミドの濃度の定量、ヒト血清中の遊離 sBCMA の定量及びヒト尿中の cys-mcMMAF の定量に用いた分析法は、良好な選択性、正確性及び再現性を有していた。涙液中のベランタマブ　マホドチン及び cys-mcMMAF の分析法は定性目的であり、真度及び精度の基準は設定しなかった。

2.7.1.1.2. 製剤開発

臨床試験では、これまで点滴静注用製剤として、凍結液剤及び凍結乾燥粉末剤の 2 種類の製剤が使用されている。早期臨床試験で使用された製剤は凍結液剤であり、[redacted]で保存するため、[redacted]に[redacted]が[redacted]されている必要があった。そこで、[redacted]の必要性をなくすため、保存条件が 2℃～8℃である凍結乾燥粉末剤が開発され、その後の臨床試験で使用された。凍結乾燥製剤は滅菌注射用水で溶解してから希釈を行う。

臨床試験で使用した両製剤の詳細を表 2.7.1.1.1 に示す。

表 2.7.1.1.1 ベランタマブ　マホドチンの凍結液剤及び凍結乾燥粉末剤

凍結液剤（[redacted]）	凍結乾燥製剤（100 mg）
無菌の液剤として、[redacted]で提供され、防腐剤を含まない。各バイアルには、[redacted]の溶液（[redacted]）が充填されており、[redacted]が採取可能容量となる。	無菌の凍結乾燥製剤として、栓付き単回使用[redacted]ガラスバイアルで提供され、防腐剤を含まない。各バイアルは、2 mL の滅菌注射用水で溶解することで、2 mL（50 mg/mL）が採取可能容量となる。

ベランタマブ　マホドチン凍結液剤（[redacted]）はヒト初回投与試験の DREAMM-1 試験、並びに DREAMM-2 試験及び DREAMM-6 試験で使用された。ベランタマブ　マホドチン凍結乾燥粉末剤（100 mg）は、DREAMM-2 試験の被験者 24 例からなるコホート、及び DREAMM-3 試験、DREAMM-7 試験、DREAMM-8 試験、DREAMM-12 試験のベランタマブ　マホドチン投与群の全被験者に使用された。各臨床試験で使用した製剤ロットの一覧を表 2.7.1.4.1 に示す。

[redacted]

[redacted]

凍結乾燥粉末剤は、単回使用バイアルに充填された無菌の白色～黄色の粉末剤であり、50 mg/mL の濃度のベランタマブ　マホドチン、[redacted] mM クエン酸ナトリウム／クエン酸、[redacted] mM トレハロース、[redacted] mM EDTA、[redacted]ポリソルベート 80 を含む製剤のバルク製剤溶液（pH [redacted]）から製造される。

ベランタマブ　マホドチンの凍結乾燥粉末剤及び液剤の成分及び[redacted]の詳細をそれぞれ表 2.7.1.1.2 及び表 2.7.1.1.3 に示す。

表 2.7.1.1.2　凍結乾燥粉末剤（100 mg）の[redacted]

[redacted]

表 2.7.1.1.3　凍結液剤（[redacted]）の[redacted]

[redacted]

[redacted]

2.7.1.1.3. 製剤処方開発の概要

製剤の[redacted]を[redacted]するために、凍結乾燥粉末剤が目標製品品質プロファイルに合致する理想的な製剤として見出された。ただし、早期臨床試験においては凍結液剤が使用され、[redacted]して凍結乾燥粉末剤の開発が進められた。

ベランタマブ　マホドチンの[redacted]は[redacted]を通じて開発され、凍結液剤及び凍結乾燥粉末剤は[redacted]して開発された。[redacted]を基に、[redacted]して[redacted]し、[redacted]。

[redacted]は[redacted]である。[redacted]に[redacted]を[redacted]することにより、[redacted]した。[redacted]は[redacted]が、[redacted]において[redacted]は更に[redacted]。

[redacted]では、[redacted]を考慮し、[redacted]として[redacted]を使用した。[redacted]から、[redacted]、[redacted]は、[redacted]であった［3.2.S.3.1（原薬）］。また、[redacted]から、[redacted]は[redacted]と同様に[redacted]［[redacted]］を[redacted]ことが明らかとなった［3.2.S.3.2（belantamab）及び 3.2.S.3.2（原薬）］。

上記にもかかわらず、[redacted]の[redacted]は[redacted]がある。例えば、[redacted]がある。そこで、[redacted]は[redacted]においても適していることをその後検証した（3.2.P.2.2）。[redacted]について選択した[redacted]が適切であることも、[redacted]によって確認された［3.2.S.7（原薬）及び 3.2.P.8］。

ベランタマブ　マホドチンの凍結乾燥粉末剤と凍結液剤の生物物理学的、生化学的及び機能的完全性を比較する包括的な同等性／同質性評価を実施しており、詳細は 3.2.P.2.3 に示す。本試験の結果から、凍結乾燥粉末剤と凍結液剤は製剤学的に同等／同質であることが示された。

2.7.1.1.4. 分析法

ベランタマブ　マホドチンは ADC である。血漿中ベランタマブ　マホドチン（ADC）及び cys-mcMMAF を本項に示す全臨床試験で定量した。血漿中総 mAb（mcMMAF が抗体に付加している、もしくは付加していないもの）を DREAMM-1、DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-11 及び DREAMM-12 試験で定量した。総 mAb 濃

度とベランタマブ　マホドチン濃度に高い相関があることが認められた［5.3.3.5、CPMR Amendment 1（TMF-16325848）、Section 5.1.2］ため、DREAMM-8 及び DREAMM-14 試験では総 mAb を定量しなかった。

涙液中ベランタマブ　マホドチン（ADC）及び cys-mcMMAF 濃度についても DREAMM-12 試験パート 1 で定性分析法を用いて測定し評価した。

尿中 cys-mcMMAF を DREAMM-1 及び DREAMM-12 試験で定量した。

血清中遊離 sBCMA を全臨床試験で定量した。

血漿中ボルテゾミブを DREAMM-6 試験で、血漿中ポマリドミドを DREAMM-8 試験で定量した。

臨床試験で使用した分析法のライフサイクルについては 2.7.1.4.2 に要約し、2.7.1.4.3 で各分析対象物質における分析法の性能を要約した。

2.7.1.1.4.1.　ベランタマブ　マホドチン分析法

ベランタマブ　マホドチンは、ペイロードが 1 つ以上結合した ADC（DAR>0）である。当該分析法はベランタマブ　マホドチンの sBCMA への結合の有無に関わらずベランタマブ　マホドチンを検出する。

2.7.1.1.4.1.1.　ヒト血漿中ベランタマブ　マホドチン分析法

ヒト血漿中ベランタマブ　マホドチン濃度を酵素免疫測定法（ELISA）で定量した。ベランタマブ　マホドチンを[redacted]で捕捉し、[redacted]により検出した。当該分析法は DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-8、DREAMM-11、DREAMM-12 及び DREAMM-14 試験で使用した。分析法の概要を以下及び 2.7.1.4.2（表 2.7.1.4.7、表 2.7.1.4.11 及び表 2.7.1.4.16）に示した。分析法[redacted]は DREAMM-14 試験、[redacted]は中国で実施した臨床試験、[redacted]は前述の試験を除くすべての臨床試験で得られた実試料測定に使用した。DREAMM-1 試験で使用した分析法は表 2.7.1.4.2 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Numbers 2013N186863 及び 2016N282271）。これら分析法の真度の判定基準は理論値の±20%（定量下限では±25%）以内、精度の判定基準は 20%以内（定量下限では 25%以内）であった。

ヒト血漿中ベランタマブ　マホドチン分析法バリデーション（分析法[redacted]）

ヒト血漿試料を分析前にアッセイバッファーで minimum required dilution である 50 倍に希釈した。[redacted]捕捉抗体、[redacted]検出試薬及び西洋ワサビペルオキシダーゼ（HRP）標識ストレプトアビジンを用いてベランタマブ　マホドチンを検出し、SuperSignal ELISA Femto Substrate を用いて化学発光させた。

本分析法の選択性、感度、精度、真度をヒト血漿中ベランタマブ　マホドチン濃度 500～10000 ng/mL（検量線上限変更後：500～5000 ng/mL）の範囲で確認した（表 2.7.1.1.4）。検

量線上限変更前の本分析法の精度は 6.59%以下、真度は理論値の−7.89～+5.00%の範囲であった。検量線上限変更後の本分析法の精度は 7.30%以下、真度は理論値の−12.0～−1.75%であった。

表 2.7.1.1.4 ベランタマブ　マホドチン分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2019N412690_02
Validated Range	500 to 10 000 ng/mL [redacted] v1-9 500 to 5000 ng/mL [redacted] v10
Laboratory	[redacted]
Studies Supported	DREAMM-2, DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12

通常及び多発性骨髄腫患者の血漿に対する分析法の選択性を確立し、高脂質性及び溶血性血漿においても問題なく分析できることを確認した。sBCMA が 250 ng/mL 存在する時、分析への干渉は認められなかったが、500～1000 ng/mL では判定基準を超える干渉が認められた。1000 ng/mL までの sBCMA による干渉は、実試料をブランク血漿で 5 倍又は 10 倍希釈することで回避することができた。そのため、ベランタマブ　マホドチン濃度の採否を評価する前に、分析法バリデーションで試料の希釈倍率及び sBCMA 濃度を再検討した。
sBCMA が 250 ng/mL～1000 ng/mL の場合、実試料を 2 倍、5 倍又は 10 倍に希釈した時、判定基準を満たした。

全血中のベランタマブ　マホドチンは、室温で 4 時間、氷冷下で 2 時間安定であった。ヒト血漿中では、−80°C と室温の凍結融解サイクル 8 回まで、室温で 42 時間、−80°C で 1475 日、−20°C で 1470 日安定であった。バリデーションデータは表 2.7.1.4.23 に要約した。

DREAMM-2 試験で使用した本分析法（[redacted]）と DREAMM-1 試験のパート 2 で使用した分析法（[redacted]）のクロスバリデーションを、プールした実試料を用いて実施した。クロスバリデーションの結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.24）。

ヒト血漿中ベランタマブ　マホドチン分析法バリデーション（分析法 [redacted]）

ヒト血漿試料を分析前にアッセイバッファーで minimum required dilution である 100 倍に希釈した。[redacted] 捕捉抗体、[redacted] [redacted]検出試薬及び HRP 標識ストレプトアビジンを用いてベランタマブ　マホドチンを検出し、SuperSignal ELISA Femto Substrate を用いて化学発光させた。

本分析法の選択性、感度、精度、真度をヒト血漿中ベランタマブ　マホドチン濃度 500～10000 ng/mL の範囲で確認した（表 2.7.1.1.5）。本分析法の精度は 10.2%以下、真度は理論値の−14.2～−5.3%であった。

表 2.7.1.1.5 ベランタマブ　マホドチン分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2021N468577_00 and 2021N468577_01
Validated Range	500 to 10 000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-3, DREAMM-7, DREAMM-8 (China samples)

通常の血漿における分析法の選択性を確認した。高脂質性血漿及び 0.5%までの溶血性血漿においても問題なく分析できることを確認した。sBCMA が 4000 ng/mL まで存在した場合でも分析への干渉は認められなかった。

血漿中ベランタマブ　マホドチンは、室温で 25 時間 40 分、2～8°C で 69 時間 15 分安定であった。また、−80～−60°C と室温及び−30～−10°C と室温の凍結融解サイクル 6 回まで、−80°C～−60 で 736 日、−30～−10°C で 492 日安定であった。バリデーションデータは表 2.7.1.4.25 に要約した。

中国で得られた実試料の測定に使用した本分析法（[redacted]）とその他で使用した分析法（[redacted]）のクロスバリデーションを、プールした実試料を用いて実施した。クロスバリデーションの結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.26）。

ヒト血漿中ベランタマブ　マホドチン分析法バリデーション（分析法 [redacted]）

ヒト血漿試料を分析前にアッセイバッファーで minimum required dilution である 100 倍に希釈した。[redacted] 捕捉抗体、[redacted] [redacted]検出試薬及びストレプトアビジンを用いてベランタマブ　マホドチンを検出した。

本分析法の選択性、感度、精度、真度をヒト血漿中ベランタマブ　マホドチン濃度 20～2000 ng/mL の範囲で確認した（表 2.7.1.1.6）。本分析法の精度は 8.85%以下、真度は理論値の−3.50～+7.83%であった。

表 2.7.1.1.6 ベランタマブ　マホドチン分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2022N515388
Validated Range	20 to 2000 ng/mL
Laboratory	GSK Upper Providence
Studies Supported	DREAMM-14

通常の血漿における分析法の選択性を確認し、高脂質性血漿（トリグリセリド約 300 mg/dL まで）及び 2%までの溶血性血漿においても問題なく分析できることを確認した。また、無希釈の試料では sBCMA が 1500 ng/mL まで、2 倍希釈した試料では sBCMA が 2000 ng/mL まで存在した場合でも分析への干渉は認められなかった。

血漿中ベランタマブ　マホドチンは、併用薬（[redacted]及び[redacted]）存在下／非存在下で−20°C もしくは−70°C で保存後、室温で 24 時間安定であり、また、minimum

required dilution に従い希釈した前処理後試料についても室温及び 4°C で 24 時間安定であった。また、−70°C と室温及び−20°C と室温の凍結融解サイクル 5 回まで、併用薬（[redacted]及び[redacted]）非存在下で−70°C で保存した時 412 日、併用薬存在下では−70°C で 140 日、−20°C で 204 日安定であった。バリデーションデータは表 2.7.1.4.27 に要約した。

本分析法（[redacted]）と DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-8、DREAMM-11 及び DREAMM-12 試験（中国以外で得られた試料）で使用した分析法（[redacted]）のクロスバリデーションを実施した。クロスバリデーションの結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.28）。

2.7.1.1.4.1.2. 涙液中ベランタマブ　マホドチン分析法

涙液中ベランタマブ　マホドチン濃度を Gyrolab による免疫測定法で定量した。ベランタマブ　マホドチンを[redacted]で捕捉し、[redacted]により検出した。当該分析法は DREAMM-12 試験で使用した。その概要は以下及び表 2.7.1.4.17 並びに表 2.7.1.1.7 に示し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Number 2021N491769_00）。当該分析法は定性を目的としており、真度及び精度の基準は設定しなかった。

涙液中ベランタマブ　マホドチン定性分析法バリデーション

表 2.7.1.1.7 涙液中ベランタマブ　マホドチン分析法

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2021N491769_00
Validated Range	Qualitive assay with limit of detection calibrator at 50 ng/mL
Laboratory	GSK, Stevenage
Studies Supported	DREAMM-12

バリデーションデータは表 2.7.1.4.29 に要約した。

2.7.1.1.4.2. 総モノクローナル抗体分析法

総モノクローナル抗体（mAb）は、ペイロードが結合した抗体と結合していない抗体を合わせたもの（DAR≥0）と定義した。本分析法は、1 つ以上の相補性決定領域が未結合の場合に総 mAb を検出し、標的に二価結合している抗体は検出しない。

2.7.1.1.4.2.1. ヒト血漿中総 mAb 分析法

ヒト血漿中の総 mAb 濃度を ELISA で定量した。DREAMM-1 試験初期においては、総 mAb は[redacted]で捕捉し、[redacted]で検出した。しかし、本分析法が sBCMA の循環濃度により影響を受けることが明らかとなったため、捕捉試薬を[redacted]に変更した。検出試薬は、変更前と同じ[redacted]を用いることとした。本分析法は DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-11 及び DREAMM-12 試験で使用した。概要を以下並

びに表 2.7.1.4.8 及び表 2.7.1.4.12 に示した。分析法 [redacted] は中国で実施した試験を除くすべての試験、分析法 [redacted] は中国で実施した試験で得られた実試料測定に使用した。DREAMM-1 試験で使用した分析法は表 2.7.1.4.3 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Numbers 2014N206720 及び 2015N243565）。これら分析法の真度の判定基準は理論値の±20%（定量下限では±25%）以内、精度の判定基準は 20%以内（定量下限では 25%以内）であった。

ヒト血漿中総 mAb 分析法バリデーション（分析法 [redacted]）

分析前に、ヒト血漿検体を酸性アッセイバッファー（pH4.6）で minimum required dilution である 33.3 倍に希釈した。総 mAb を[redacted]で捕捉し、HRP 標識[redacted]で検出した。SuperSignal ELISA Femto Substrate を用いて化学発光させた。

本分析法の選択性、感度、精度、真度をヒト血漿中総 mAb 500～10000 ng/mL の範囲で確認した（表 2.7.1.1.8）。本分析法の精度は 6.73%以下、真度は理論値の−4.40～−3.03%であった。

表 2.7.1.1.8 総 mAb 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2019N396866_02 and 2019N396866_01
Validated Range	500 to 10 000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-2, DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-11, and DREAMM-12

通常及び多発性骨髄腫患者の血漿に対する分析法の選択性を確認した。高脂質性血漿においては問題なく分析できることを確認したが、溶血性血漿の分析については問題があったため、溶血性試料の総 mAb 濃度は報告しなかった。sBCMA が 100 ng/mL 存在する時、分析への干渉は認められなかったが、250～1000 ng/mL では判定基準を超える干渉が認められた。sBCMA 1000 ng/mL までの干渉については試料をブランク血漿で 5 倍超に、500 ng/mL までの干渉については 2 倍に希釈することで回避することができた。そのため、試料の希釈倍率及び sBCMA 濃度を確認した後で総 mAb 濃度の採否を評価した。

全血中の総 mAb は、室温で 4 時間、氷冷下で 2 時間安定であった。ヒト血漿中では、−80°C と室温の凍結融解サイクル 8 回まで、室温で 18 時間、−80°C で 1144 日、−20°C で 734 日安定であった。バリデーションデータは表 2.7.1.4.30 に要約した。

DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-11 及び DREAMM-12 試験で使用した本分析法（[redacted]）と DREAMM-1 試験で使用した分析法（[redacted]）のクロスバリデーションを、プールした実試料を用いて実施した。クロスバリデーションの結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.31）。

ヒト血漿中総 mAb 分析法バリデーション（分析法 [redacted]）

分析前に、ヒト血漿検体を酸性アッセイバッファー（pH4.6）で minimum required dilution である 33.3 倍に希釈した。総 mAb を[redacted]で捕捉し、HRP 標識[redacted]で検出した。SuperSignal ELISA Femto Substrate を用いて化学発光させた。

本分析法の選択性、感度、精度、真度をヒト血漿中総 mAb 濃度 500～10000 ng/mL の範囲で確認した（表 2.7.1.1.9）。本分析法の精度は 7.6%以下、真度は理論値の−9.5～+2.0%であった。

表 2.7.1.1.9 総 mAb 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2021N468428_00 and 2021N468428_01
Validated Range	500 to 10 000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-3, DREAMM-7 (China samples)

通常の血漿における分析法の選択性を確立し、高脂質性血漿（トリグリセリド約 300 mg/dL まで）及び 0.5%までの溶血性血漿においても問題なく分析できることを確認した。また、sBCMA が 2000 ng/mL まで存在した場合でも分析への干渉は認められなかった。

血漿中総 mAb は、室温で 45 時間 58 分、2～8°C で 71 時間 54 分安定であった。また、−80～−60°C と室温もしくは−30～−10°C と室温の凍結融解サイクル 6 回まで、−80～−60°C で 776 日、−30～−10°C で 502 日安定であった。バリデーションデータは表 2.7.1.4.32 に要約した。

中国で得られた実試料の測定に使用した本分析法（[redacted]）とその他で使用した分析法（[redacted]）のクロスバリデーションを実施した。クロスバリデーションの結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.33）。

2.7.1.1.4.3. Cys-mcMMAF 分析法

ペイロードは ADC から cys-mcMMAF として遊離し、2 つの異性体として存在する。cys-mcMMAF の直鎖型異性体はマレイミド環で化学的に加水分解され、その後脱水されて環状異性体になる。生体試料中の cys-mcMMAF を正確に定量分析するため、直鎖型異性体は完全かつ不可逆的に環状異性体に変換した。そのため、生体試料中 cys-mcMMAF 分析法は、直鎖型異性体と環状異性体の総量を定量している。

2.7.1.1.4.3.1. ヒト血漿中 cys-mcMMAF 分析法

ヒト血漿中 cys-mcMMAF 濃度は、酸性除タンパク処理試料を超高速液体クロマトグラフィータンデム質量分析（UHPLC-MS/MS）法で定量した。当該分析法は DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-8、DREAMM-11、DREAMM-12 及び DREAMM-14 試験で使用した。その概要を以下並びに表 2.7.1.4.9 及び表 2.7.1.4.13 に示した。分析法[redacted]（[redacted]法）は DREAMM-2 及び DREAMM-6 試験の実試料測定に、[redacted]は中国で実施した臨床試験の実試料測定に、分析法[redacted]は

前述の試験を除くすべての臨床試験の実試料測定に使用した。DREAMM-1 試験で使用した分析法は表 2.7.1.4.4 に要約し、分析法バリデーション報告書に詳述している（5.3.1.4、GSK Document Number 2014N195974）。

内標準物質には[$^{15}N^{13}C_3D_3$]-cys-mcMMAF 又は[D_8]-cys-MCMMAF を用いた。これら分析法の真度の判定基準は理論値の±15%（定量下限では±20%）以内、精度の判定基準は 15%以内（定量下限では 20%以内）であった。

DREAMM-1 試験の実試料測定で用いた血漿中 cys-mcMMAF 分析法の精査

DREAMM-1 試験で得られたヒト血漿中 cys-mcMMAF 濃度は、当初、固相抽出した試料を UHPLC-MS/MS 法で定量した。測定施設の調査によりこれら旧分析法（[redacted] 法及び [redacted] 法）は、ベランタマブ　マホドチン存在下において cys-mcMMAF 濃度を実際より多く見積もっていることが明らかとなった。これは固相抽出中に ADC から cys-mcMMAF が遊離することによるもので、結果として DREAMM-1 及び DREAMM-2 試験の実試料中 cys-mcMMAF 濃度を過大評価していた。試料の前処理に酸性除タンパク法を採用することにより、ベランタマブ　マホドチン存在下でも cys-mcMMAF を正確に定量可能な分析法を開発した。DREAMM-2 試験の実試料を固相抽出（[redacted] 法）及び除タンパク（[redacted]法）の両法で前処理し比較したところ、cys-mcMMAF 濃度とベランタマブ　マホドチン濃度の間に強い相関はみられなかった一方で、両前処理法での cys-mcMMAF 濃度には強い線形相関がみられた。当初、DREAMM-2 試験の実試料は [redacted]法で測定したが、その後 [redacted] 法で再測定を実施し、最終的に [redacted] 法で得られた結果を採用した。DREAMM-1 試験の cys-mcMMAF 濃度（[redacted] 法、固相抽出法を使用）については、対応する回帰式を用いて [redacted] 法の濃度に換算した。回帰式は DREAMM 2 試験の薬物濃度測定報告書（GSK Document Number 2019N416576）に記載した。DREAMM-1 試験で使用した分析法は表 2.7.1.4.4 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Numbers 2022N505659_00、2019N405330_00、2019N415230_01）。

ヒト血漿中 cys-mcMMAF 分析法バリデーション（分析法 [redacted]）

1%ギ酸含有アセトニトリルを用いた酸性除タンパク処理により cys-mcMMAF をヒト血漿から抽出し、10%水酸化アンモニウム含有 70/30（v/v）メタノール/水混合溶液を用いて直鎖型異性体を環状異性体へ変換した。抽出物を UHPLC-MS/MS（エレクトロスプレーインターフェース及び多重反応モニタリング）で分析した。

ベランタマブ　マホドチン 150 μg/mL 共存下におけるヒト血漿中 cys-mcMMAF 分析法の選択性、感度、精度、真度を 50～10000 pg/mL の範囲で確認した（表 2.7.1.1.10 及び表 2.7.1.4.9）。本分析法の精度は 3.5%以下、真度は理論値の+1.0～+3.2%であった。

表 2.7.1.1.10 cys-mcMMAF 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2019N411691_03
Validated Range	50 to 10000 pg/mL
Laboratory	GSK Upper Providence
Studies Supported	DREAMM-2, DREAMM-6

本分析法は、高脂質性血漿（トリグリセリド約 300 mg/dL まで）、2%までの溶血性血漿、及びレナリドミド／デキサメタゾン（1800／1800 ng/mL）及びボルテゾミブ／デキサメタゾン（450/900 ng/mL）共存下においても問題なく分析できることを確認した。血漿からの cys-mcMMAF の回収率は 81.1%以上であった。

全血中 cys-mcMMAF は氷冷及びベランタマブ　マホドチン 150 µg/mL 共存下で 2 時間安定であった。

血漿中 cys-mcMMAF は、ベランタマブ　マホドチン 150 µg/mL 共存下で、−20°C と氷冷の凍結融解サイクル 6 回まで、−70°C と氷冷の凍結融解サイクル 8 回まで安定であった。ベランタマブ　マホドチン非存在下では、−20°C 又は−70°C と氷冷の凍結融解サイクル 8 回まで安定であった。また、血漿中 cys-mcMMAF は、ベランタマブ　マホドチン 150 µg/mL 共存下において、氷冷下で 7 時間安定であり（−70°C と氷冷の凍結融解サイクル 2 回を含む）、ベランタマブ　マホドチン 80 µg/mL 共存下で、−20°C で 217 日、−70°C で 566 日安定であった。

バリデーションデータは表 2.7.1.4.34 に要約した。

ヒト血漿中 cys-mcMMAF 分析法バリデーション（分析法 [redacted]）

ベランタマブ　マホドチン 300 µg/mL 共存下におけるヒト血漿中 cys-mcMMAF 分析法の選択性、感度、精度、真度を 50～10000 pg/mL の範囲で確認した（表 2.7.1.1.11）。本分析法の精度は 8.5%以下、真度は理論値の 0.0～+3.8%であった。

表 2.7.1.1.11 cys-mcMMAF 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2022N519749_00, 01 and 02
Validated Range	50 to 10000 pg/mL
Laboratory	[redacted]
Studies Supported	DREAMM-3, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12, and DREAMM-14

本分析法は、高脂質性血漿、2%までの溶血性血漿、及び併用薬（レナリドミド 1000 ng/mL、デキサメタゾン 1000 ng/mL、ボルテゾミブ 500 ng/mL 及びポマリドミド 200 ng/mL）共存下においても問題なく分析できることを確認した。血漿からの cys-mcMMAF の回収率は 93.9～111.1%であった。

全血中 cys-mcMMAF は 300 µg/mL までのベランタマブ　マホドチン共存下もしくは非共存下において、室温又は氷冷で 2 時間安定であった。

血漿中 cys-mcMMAF は、氷冷下で 21 時間、−70°C と氷冷の凍結融解サイクル 4 回まで安定であった。ベランタマブ　マホドチン 300 µg/mL 共存下では、氷冷下で 13 時間、−70°C と氷冷の凍結融解サイクル 4 回まで安定であった。一方、ベランタマブ　マホドチン 150 µg/mL 共存下では−70°C で 795 日安定であった。併用薬（レナリドミド 1000 ng/mL、デキサメタゾン 1000 ng/mL、ボルテゾミブ 500 ng/mL 及びポマリドミド 200 ng/mL）共存下におい

ては、氷冷下で 13 時間、−70°C と氷冷の凍結融解サイクル 4 回まで、−70°C で 470 日安定であった。バリデーションデータは表 2.7.1.4.35 に要約した。

プールした実試料を用いて、本分析法（[redacted]）と DREAMM-2 及び DREAMM-6 試験で使用した分析法（[redacted]）のクロスバリデーションを実施した。その結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.36）。

ヒト血漿中 cys-mcMMAF 分析法バリデーション（分析法 [redacted]）

ベランタマブ　マホドチン 300 µg/mL 共存下におけるヒト血漿中 cys-mcMMAF 分析法の選択性、感度、精度、真度を 50～10000 pg/mL の範囲で確認した（表 2.7.1.1.12）。本分析法の精度は 10.2%以下、真度は理論値の−2.0～+5.3%であった。

表 2.7.1.1.12 cys-mcMMAF 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2020N448658_00, 01 and 02
Validated Range	50 to 10000 pg/mL
Laboratory	[redacted]
Studies Supported	DREAMM-3, DREAMM-7, DREAMM-8 (China samples)

本分析法は、高脂質性血漿（トリグリセリド 300 mg/dL まで）、2%までの溶血性血漿、及び併用薬（ボルテゾミブ 500 ng/mL、レナリドミド 1200 ng/mL、ポマリドミド 400 ng/mL、ニロガセスタット 1600 ng/mL、及びデキサメタゾン 1200 ng/mL）共存下においても問題なく分析できることを確認した。血漿からの cys-mcMMAF の回収率は 120.9%であった。

全血中 cys-mcMMAF は 300 µg/mL までのベランタマブ　マホドチン共存下において、氷冷で 2 時間安定であった。150 µg/mL までのベランタマブ　マホドチン共存下においては、室温で 1 時間安定であった。

血漿中 cys-mcMMAF は、ベランタマブ　マホドチン 300 µg/mL 共存下及び非共存下において、氷冷下で 21 時間、−80～−60°C と氷冷、もしくは−30～−10°C と氷冷の凍結融解サイクル 5 回まで安定であった。また、血漿中 cys-mcMMAF は、ベランタマブ　マホドチン非共存下において、−80～−60°C で 714 日、ベランタマブ　マホドチン 300 µg/mL 共存下では、−80～−60°C で 467 日、ベランタマブ　マホドチン 300 µg/mL 共存下及び非共存下において−30～−10°C で 87 日安定であった。バリデーションデータは表 2.7.1.4.37 に要約した。

プールした実試料を用いて、中国で得られた実試料測定に使用した本分析法（[redacted]）とその他の試験で使用した分析法（[redacted]）のクロスバリデーションを実施した。その結果、プールした実試料の 67%超で乖離度は 30%以内であり判定基準を満たした（表 2.7.1.4.38）。

2.7.1.1.4.3.2.　ヒト尿中 cys-mcMMAF 分析法

DREAMM-1 試験で得られたヒト尿中 cys-mcMMAF 濃度は、固相抽出した試料を UHPLC-MS/MS 法により定量した。ベランタマブ　マホドチンは高分子であり尿中に排泄される可

能性が低いことから、固相抽出時のベランタマブ　マホドチンからの cys-mcMMAF の遊離は尿の分析には影響しないと考えられた。分析法は表 2.7.1.4.5 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Number 2014N201539）。

DREAMM-12 試験で得られたヒト尿中 cys-mcMMAF 濃度は、酸性除タンパク処理試料を UHPLC-MS/MS 法で定量した。分析法は表 2.7.1.4.15 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Number 2023N535699_00）。

ヒト尿中 cys-mcMMAF 分析法バリデーション（分析法 [redacted]）

ヒト尿中 cys-mcMMAF 分析法の選択性、感度、精度及び真度を 50～10000 pg/mL の範囲で確認した（表 2.7.1.1.13）。本分析法の精度は 11.3%以下、真度は理論値の−3.3～+13.6%であった。尿からの cys-mcMMAF の回収率は 107.9%であった。

表 2.7.1.1.13 cys-mcMMAF 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2023N535702_00
Validated Range	50 to 10000 pg/mL
Laboratory	[redacted]
Studies Supported	DREAMM-12

尿中 cys-mcMMAF は、−80°C 又は−20°C と氷冷の凍結融解サイクル 4 回まで、室温で 24 時間、氷冷下で 18 時間、−80°C で 579 日、−20°C で 31 日安定であった。バリデーションデータは表 2.7.1.4.39 に要約した。

2.7.1.1.4.3.3. 涙液中 cys-mcMMAF 分析法

涙液中 cys-mcMMAF 濃度は、LC-MS/MS 法により定量した（5.3.1.4、GSK Document Number 2022N525055_00）。当該分析法は DREAMM-12 試験で使用した。表 2.7.1.4.19 に要約し、分析法バリデーション報告書に詳述した（5.3.1.4、GSK Document Number 2021N485434_00）。当該分析法は定性を目的としており、真度及び精度の基準は設定しなかった。

涙液中 cys-mcMMAF 分析法バリデーション

表 2.7.1.1.14 cys-mcMMAF 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2021N485434_00 and 2020N458494_00
Validated Range	Limit of detection calibrators at 1.25, 2.5 and 5 pg/mL
Laboratory	GSK, Stevenage
Studies Supported	DREAMM-12

バリデーションデータは表 2.7.1.4.40 に要約した。

2.7.1.1.4.4. 遊離 sBCMA 分析法

ヒト血清中遊離 sBCMA（バリデーション及び実試料測定報告書では free BCMA と記載）濃度を電気化学発光分析法で定量した。ヒト血清試料を分析前にアッセイバッファーで minimum required dilution である 20 倍に希釈した。ヒト血清中遊離 sBCMA を[redacted]（[redacted]）で捕捉し、[redacted]（[redacted]）で検出した。DREAMM-1 試験で用いた分析法は表 2.7.1.4.6 に要約した。DREAMM-14 試験で用いた分析法は 2.7.1.1.4.4.1 及び表 2.7.1.4.18 に要約した。DREAMM-2、DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-8、DREAMM-11 及び DREAMM-12 試験で使用した分析法は、2.7.1.1.4.4.2 及び 2.7.1.1.4.4.3 並びに表 2.7.1.4.10 及び表 2.7.1.4.14 に要約した。これら分析法の真度の判定基準は理論値の±20%（定量下限では±25%）以内、精度の判定基準は 20%以内（定量下限では 25%以内）であった。

2.7.1.1.4.4.1. ヒト血清中遊離 sBCMA 分析法バリデーション（分析法 [redacted]）

ヒト血清中遊離 sBCMA 分析法の選択性、感度、精度、真度を 1.95～1000 ng/mL の範囲で確認した（表 2.7.1.1.15）。本分析法の精度は 28.21%以下、真度は理論値の-2.60～+8.67%であった。バリデーションデータは表 2.7.1.4.44 に要約した。

表 2.7.1.1.15 遊離 sBCMA 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2023N527200_00
Validated Range	1.95 to 1000 ng/mL
Laboratory	GSK Upper Providence
Studies Supported	DREAMM-14

2.7.1.1.4.4.2. ヒト血清中遊離 sBCMA 分析法バリデーション（分析法 [redacted]）

ヒト血清中遊離 sBCMA 分析法の選択性、感度、精度、真度を 1.95～1000 ng/mL の範囲で確認した（表 2.7.1.1.16）。本分析法の精度は 18.3%以下、真度は理論値の-3.5～+0.3%であった。血清中 sBCMA は、室温及び 4°C で 25 時間、−70°C と室温の凍結融解サイクル 6 回まで、−20°C で 136 日、−70°C で 1333 日安定であった（内因性遊離 sBCMA）。バリデーションデータは表 2.7.1.4.41 に要約した。

表 2.7.1.1.16 遊離 sBCMA 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2018N393390_00, 01, 02, 03, and 04
Validated Range	1.95 to 1000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-2, DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12

2.7.1.1.4.4.3. ヒト血清中遊離 sBCMA 分析法バリデーション（分析法 [redacted]）

ヒト血清中遊離 sBCMA 分析法の選択性、感度、精度、真度を 1.95～1000 ng/mL の範囲で確認した（表 2.7.1.1.17）。本分析法の精度は 10.9%以下、真度は理論値の-0.2～+4.0%であ

った。血清中 sBCMA は、2～8°C で 72 時間 7 分、室温で 24 時間 5 分、又は−80～−60°C と室温もしくは−30～−10°C と室温の凍結融解サイクル 6 回まで安定であった。また、−80～−60°C で 741 日、−30～−10°C で 185 日安定であった。バリデーションデータは表 2.7.1.4.42 に要約した。

表 2.7.1.1.17 遊離 sBCMA 分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2021N468639_00, 01, and 02
Validated Range	1.95 to 1000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-3, DREAMM-7, DREAMM-8 (China samples)

中国で得られた実試料測定に使用した本分析法（[redacted]）とその他の試験で使用した分析法（[redacted]）のクロスバリデーションを実施した。主にベースライン後の実試料を用いた最初の 2 回のクロスバリデーションは、判定基準を満たさなかった。ベースライン試料のみを用いた 3 回目の評価では、判定基準を満たした（表 2.7.1.4.43）。[redacted] 社と [redacted] 社間では 30 試料すべてが判定基準を満たし、[redacted] 社と GSK 間では 30 試料中 28 試料が判定基準を満たした。

2.7.1.1.4.5. その他薬剤の分析法

2.7.1.1.4.5.1. ボルテゾミブ分析法

ヒト血漿中ボルテゾミブ濃度は、UPLC-MS/MS 法で定量した（5.3.1.4、GSK Document Numbers 2019N413318 及び 2023N546218）。ヒト血漿を除タンパク処理後、抽出試料を UPLC-MS/MS で分析した。分析法は表 2.7.1.4.20 に要約した。これら分析法の真度の判定基準は理論値の±15%（定量下限では±20%）以内、精度の判定基準は 15%以内（定量下限では 20%以内）であった。

ヒト血漿中ボルテゾミブ UPLC-MS/MS 分析法バリデーション

ヒト血漿中ボルテゾミブ分析法の選択性、感度、精度及び真度を 0.1～100 ng/mL の範囲で確認した（表 2.7.1.1.18）。本分析法の分析単位内精度は 12.8%以下、真度は理論値の−0.535%～+12.6%であった。血漿中ボルテゾミブは、氷冷下で 27.33 時間、−80°C もしくは−25°C と氷冷の凍結融解サイクル 5 回まで、−80°C で 1032 日安定であった。バリデーションデータは表 2.7.1.4.46 に要約した。

表 2.7.1.1.18 ボルテゾミブ分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2019N413318 and 2023N546218
Validated Range	0.1 to 100 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-6

分析法の選択性評価にはコントロール血漿を用い、デキサメタゾン 500 ng/mL 共存下での特異性も確認した。

2.7.1.1.4.5.2. レナリドミド分析法

ヒト血漿中レナリドミド濃度は、UPLC-MS/MS 法で定量した（5.3.1.4、GSK Document Number 2023N533133）。ヒト血漿を除タンパク処理後、抽出試料を UPLC-MS/MS で分析した。分析法は表 2.7.1.4.21 に要約した。これら分析法の真度の判定基準は理論値の±15%（定量下限では±20%）以内、精度の判定基準は 15%以内（定量下限では 20%以内）であった。

ヒト血漿中レナリドミド UPLC-MS/MS 分析法バリデーション

ヒト血漿中レナリドミド分析法の選択性、感度、精度及び真度を 2.50～1000 ng/mL の範囲で確認した（表 2.7.1.1.19）。本分析法の分析単位内精度は 5.01%以下、真度は理論値の−2.31%～+0.69%であった（表 2.7.1.4.48）。血漿中レナリドミドは、室温で 3 時間 26 分、−80°C もしくは−20°C と室温の凍結融解サイクル 4 回まで、−20°C で 4 日、−80°C で 516 日安定であった。バリデーションデータは表 2.7.1.4.48 に要約した。

表 2.7.1.1.19 レナリドミド分析法 [redacted]

Method Name	[redacted]
GSK Report Number	5.3.1.4, 2023N533133
Validated Range	2.50 to 1000 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-6

2.7.1.1.4.5.3. ポマリドミド分析法

ヒト血漿中ポマリドミド濃度は、UPLC-MS/MS 法で定量した（5.3.1.4、GSK Document Number 2023N527155）。ヒト血漿を液液抽出後、UPLC-MS/MS で分析した。分析法は表 2.7.1.4.22 に要約した。これら分析法の真度の判定基準は理論値の±15%（定量下限では±20%）以内、精度の判定基準は 15%以内（定量下限では 20%以内）であった。

ヒト血漿中ポマリドミド UPLC-MS/MS 分析法バリデーション

ヒト血漿中ポマリドミド分析法の選択性、感度、精度及び真度を 0.5～200 ng/mL の範囲で確認した（表 2.7.1.1.20）。本分析法の分析単位内精度は 7.59%以下、真度は理論値の−5.79%～−1.49%であった（表 2.7.1.4.49）。

表 2.7.1.1.20 ポマリドミド分析法 [redacted]

Method Name	[redacted] and [redacted]
GSK Report Number	5.3.1.4, 2023N527155 and 2023N527169
Validated Range	0.5 to 200 ng/mL
Laboratory	[redacted]
Studies Supported	DREAMM-8

分析法の選択性評価にはコントロール血漿を用い、ボルテゾミブ（100 ng/mL）、cys-mcMMAF（10 ng/mL）及びデキサメタゾン（1800 ng/mL）共存下での特異性も確認した。

血漿中ポマリドミドは、室温で 2 時間 2 分、4°C で 24 時間 25 分、−80°C もしくは−20°C と室温の凍結融解サイクル 4 回まで、−20°C で 10 日、−80°C で 525 日安定であった。バリデーションデータは表 2.7.1.4.49 に要約した。

2.7.1.1.4.6. 実試料分析における QC 試料測定の要約

GSK、[redacted] 及び [redacted] で実施した実試料中ベランタマブ　マホドチン及び総 mAb 測定の各分析単位には QC 試料を含めており、別途調製した検量線用試料を用いて定量した。分析結果の判定基準は、理論値から 20%を超えて逸脱している QC 試料が 1/3 以下であり、かつ各濃度の 50%以上の QC 試料が理論値の 20%以内であることとした。

涙液中ベランタマブ　マホドチン（ADC）定性分析法における QC 試料については、繰り返し分析した時、検出限界試料のレスポンスの平均値を上回るか（陽性対照）、又は下回るか（陰性対照）を判定基準とした。

GSK、[redacted] 及び [redacted] で実施した実試料中 cys-mcMMAF 測定の各分析単位には QC 試料を含めており、別途調製した検量線用試料を用いて定量した。分析結果の判定基準は、理論値から 15%を超えて逸脱している QC 試料が 1/3 以下であり、かつ各濃度の 50%以上の QC 試料が理論値の 15%以内であることとした。

涙液中 cys-mcMMAF 定性分析法における QC 試料の判定基準については、各分析単位におけるシグナル対ノイズ比に基づき設定した。

GSK、[redacted] 及び [redacted] で実施した実試料中遊離 sBCMA 測定の各分析単位には QC 試料を含めており、別途調製した検量線用試料を用いて定量した。分析結果の判定基準は、理論値から 20%を超えて逸脱している QC 試料が 1/3 以下であり、かつ各濃度の 50%以上の QC 試料が理論値の 20%以内であることとした。

[redacted] で実施した、DREAMM-6 試験における実試料中ボルテゾミブ測定の各分析単位には QC 試料を含めており、別途調製した検量線用試料を用いて定量した。分析結果の判定基準は、理論値から 15%を超えて逸脱している QC 試料が 1/3 以下であり、かつ各濃度の 50%以上の QC 試料が理論値の 15%以内であることとした。

[redacted] で実施した、DREAMM-8 試験における実試料中ポマリドミド測定の各分析単位には QC 試料を含めており、別途調製した検量線用試料を用いて定量した。分析結果の判定基準は、理論値から 15%を超えて逸脱している QC 試料が 1/3 以下であり、かつ各濃度の 50%以上の QC 試料が理論値の 15%以内であることとした。

報告したすべての分析結果は、あらかじめ規定した判定基準を満たした。QC 試料の分析結果は 2.7.1.4.3 に示した。

2.7.1.1.4.7. 分析性能

実試料中ベランタマブ　マホドチン、総 mAb、cys-mcMMAF、遊離 sBCMA、ボルテゾミブ及びポマリドミド濃度測定には、あらかじめ規定した判定基準を満たすよう妥当性が確認された分析法を用いた。真度及び精度データ（2.7.1.4.3）が示す通り、十分な分析性能を有していた。

2.7.1.1.4.8. 試料中安定性

分析対象物質の試料中安定性については上述（2.7.1.1.4.1～2.7.1.1.4.5.3）した。

2.7.1.1.4.9. ベランタマブ　マホドチン分析法における DAR の影響

バリデーションにおいて、実試料の DAR によりベランタマブ　マホドチンの分析に偏りが生じることが示された。標準物質より低い DAR を有する試料は負に偏り、高い DAR を有する試料は正に偏っていた。報告した濃度データは、DAR が 4.1 の標準物質を用いた検量線に基づくものであった（5.3.1.4、GSK Document Number 2016N282271）。ベランタマブ　マホドチンのすべての分析において同じ捕捉抗体（2.7.1.1.4.1）を使用したため、DAR による影響は同等であった。

2.7.1.1.4.10. 分析法の結論

ヒト血漿中ベランタマブ　マホドチン、総 mAb、cys-mcMMAF、ボルテゾミブ及びポマリドミドの定量、ヒト血清中遊離 sBCMA の定量、並びにヒト尿中 cys-mcMMAF の定量に用いた分析法の選択性、真度及び再現性を確認した。涙液中ベランタマブ　マホドチン及び cys-mcMMAF の定量に用いた分析法は定性目的であり、真度及び精度の基準は設定しなかったが、当該分析法は選択的であった。

2.7.1.1.5. 免疫原性の評価に用いた分析法の概要

血清中抗ベランタマブ　マホドチン抗体（ADA）の分析には、Meso Scale Discovery（MSD）プラットフォームを使用した電気化学発光免疫測定法（ブリッジング法を用いたホモジーニアス ECL）を用いた。[redacted]。発光強度は試料中の ADA 量に比例した。

中和抗体（NAb）の分析には MSD プラットフォームを使用し、酸解離を伴う競合リガンド結合法を用いた。[redacted]。発光強度は試料中の NAb 量に反比例した。

ADA 分析法は第 1（Gen 1）及び第 2 世代（Gen 2）からなり、Gen 1 分析法は、[redacted]を使用した。最新ガイダンスに準拠し、かつ[redacted]目的で Gen 2 分析法を開発してバリデートした。Gen 2 分析法は[redacted]。Gen 2 分析法は、ベランタマブ　マホドチンのすべ

てのドメイン［GSK2857916（ADC）、GSK2857914（mAb）及びモノメチルアウリスタチンF］に特異的な ADA を検出可能であった。

臨床試験の増加及び中国で実施される試験に対応するため、Gen 2 分析法及び NAb 分析法を GSK から [redacted] 及び [redacted] に移管し、クロスバリデーションを実施した。クロスバリデーションは、全測定施設で同じ試料を使用して行われ、各測定施設間及び全測定施設間において、あらかじめ設定したクロスバリデーションの判定基準を満たした。

各臨床試験で用いた分析法は表 2.7.1.1.21 に示した。また、分析法の詳細は Integrated Summary of Immunogenicity（5.3.5.3）に示した。

表 2.7.1.1.21 各臨床試験で用いた分析法

Study	Phase	Study Design	ADA Validation Report	NAb Validation Report
Monotherapy studies				
BMA117159 DREAMM-1	Phase 1	FTIH, open label, dose escalation (Part 1) and dose expansion (Part 2)	2014N196391 Gen 1 Assay, GSK	Not Analyzed
205678 DREAMM-2	Phase 2	Randomized, multicenter, open label, 2 arm	2019N398576 Gen 2 Assay, GSK	2019N410762 GSK
207495 DREAMM-3	Phase 3	Randomized, multicenter, controlled, open label	2022N498991 [redacted] 2021N480912 [redacted]	2022N498992 [redacted] 2021N494602 [redacted]
207504 DREAMM-11 (Part 1)	Phase 1	Open label, dose escalation	2019N398576 Gen 2 Assay, GSK	Not Analyzed
Combination studies				
207497 DREAMM-6	Phase 1/2	Open label, dose escalation and expansion	2019N398576 Gen 2 Assay, GSK	2019N410762 GSK
207503 DREAMM-7	Phase 3	Multicenter, open label, randomized	2022N498991 [redacted] 2021N480912 [redacted]	2022N498992 [redacted] 2021N494602 [redacted]
207499 DREAMM-8	Phase 3	Multicenter, open label, randomized	2022N498991 [redacted] 2021N480912 [redacted]	2022N498992 [redacted] 2021N494602 [redacted]
207504 DREAMM-11 (Part 2)	Phase 1	Open label, dose escalation	2019N398576 Gen 2 Assay, GSK	Not Analyzed

2.7.1.2. 個々の試験結果の要約

ベランタマブ　マホドチンは静脈内投与であることから、生物薬剤学的特性を検討するための生物学的利用能、生物学的同等性及び食事の影響に関する試験は実施していない。

2.7.1.3. 全試験を通しての結果の比較と解析

2.7.1.3.1. 血漿中 cys-mcMMAF 分析法

DREAMM-1 試験及び DREAMM-2 試験で採取した PK 用血漿検体中の cys-mcMMAF 濃度は、それぞれ分析法 [redacted] 法及び [redacted] 法にて測定した。DREAMM-2 試験の血漿検体を分析した [redacted] 法は、2.7.1.1.4.3.1 で示すように、ベランタマブ　マホドチンの存在下における cys-mcMMAF 濃度が実際よりも高く推定される可能性があることが示された。そこで、新たに [redacted] 法を開発してバリデーションを行ったところ、この方法ではベランタマブ　マホドチンの存在下で cys-mcMMAF 濃度が実際よりも高く推定されるというエビデンスは認められなかった。

DREAMM-1 試験で採取した cys-mcMMAF 濃度測定用血漿検体の [redacted] 法による再分析は、同検体の保管期間が影響して実施不可能であった。DREAMM-2 試験のデータに基づくと [redacted] 法と [redacted] 法による分析結果は線形の相関関係にあるが、[redacted] 法と [redacted] 法の固相抽出方法は同一であることから、[redacted] 法と [redacted] 法の間でも [redacted] 法と [redacted] 法の間と同様の相関関係が存在すると合理的に考えられる。したがって、線形回帰分析に基づく以下の関係式を利用して、[redacted] 法にて測定した DREAMM-1 試験の血漿中 cys-mcMMAF 濃度を補正することで、[redacted] 法による血漿中 cys-mcMMAF 濃度を推定することとした。

$$Cys-mcMMAF_{\blacksquare} = \frac{(Cys-mcMMAF_{\blacksquare} + 8.360)}{1.486}$$

このように推定した [redacted] 法による DREAMM-1 試験における血漿中 cys-mcMMAF 濃度を、主要な PK 解析及び PK/薬力学（PD）解析に含めることとした。ノンコンパートメント法にて求めた DREAMM-1 試験の [redacted] 法及び [redacted] 法による PK パラメータを表 2.7.1.4.50 に要約する。cys-mcMMAF の PK パラメータより、[redacted] 法と [redacted] 法で血漿中 cys-mcMMAF 濃度に差異があることが示された。平均すると、[redacted] 法の最高血漿中濃度（Cmax）及び静脈内投与終了時の血漿中濃度（C-EOI）は、[redacted] 法によるそれぞれの値よりも約 30%低値であった。したがって、当初の [redacted] 法による cys-mcMMAF の PK パラメータを、[redacted] 法による PK パラメータに差し替えることとした。

2.7.1.3.2. ベランタマブ　マホドチン製剤間の薬物動態の比較

ベランタマブ　マホドチンの臨床試験では、1）点滴静注用の凍結液剤（[redacted]に[redacted]が必要）、及び 2）点滴静注用の凍結乾燥粉末剤（[redacted]の必要性をなくすために開発）の 2 種類の製剤が使用された。早期臨床試験においては、凍結液剤が使用された。

DREAMM-2 試験では、主要な試験対象集団に凍結液剤を投与した一方で、凍結乾燥粉末剤の臨床使用経験を得るため、追加の被験者 24 例からなる別のコホートにおいて凍結乾燥粉末剤を投与した。なお、同等性の統計学的評価は行わなかった。DREAMM-3 試験では、ベランタマブ　マホドチン投与群に凍結乾燥粉末剤を投与した。

DREAMM-2 試験の凍結液剤投与群（2.5 mg/kg 及び 3.4 mg/kg）、凍結乾燥粉末剤投与群（3.4 mg/kg）、及び DREAMM-3 試験の凍結乾燥粉末剤投与群（2.5 mg/kg）における、サイクル 1 のベランタマブ　マホドチン、総 mAb 及び cys-mcMMAF の PK パラメータを、それぞれ表 2.7.1.3.1、表 2.7.1.3.2 及び表 2.7.1.3.3 に示す。ベランタマブ　マホドチン、総 mAb 及び cys-mcMMAF の PK パラメータから、凍結液剤投与後と凍結乾燥製剤投与後の PK は、2.5 mg/kg 及び 3.4 mg/kg のいずれの用量においても類似していることが示された。

表 2.7.1.3.1 ベランタマブ　マホドチンの凍結液剤及び凍結乾燥粉末剤を投与した時のサイクル 1 におけるベランタマブ　マホドチンの PK パラメータ（DREAMM-2 試験及び DREAMM-3 試験）

	DREAMM-3 Treatment Group		DREAMM-2 Treatment Group					
	2.5 mg/kg Lyophile (N=217)		2.5 mg/kg Frozen Liquid (N=95)		3.4 mg/kg Lyophile (N=24)		3.4 mg/kg Frozen Liquid (N=99)	
Parameter	n	Value	n	Value	n	Value	n	Value
AUC(0-τ) (μg·h/mL)	66	4200 (39.7)	30	4666 (46)	22	5946 (37)	20	5678 (40)
C-EOI (μg/mL)	202	44.9 (36.1)	91	39.6 (48)	23	49.5 (18)	97	49.8 (36)
Cmax (μg/mL)	102	44.0 (35.6)	32	42.5 (26)	22	51.3 (18)	21	52.0 (20)
tmax (h)	102	1.64 (0.500, 24.0)	32	0.78 (0.42, 2.50)	22	0.75 (0.48, 2.88)	21	0.70 (0.43, 2.15)
Ctrough (μg/mL)	148	2.09 (80.2)	69	2.43 (52)	20	3.41 (76)	71	2.54 (88)

Source: 5.3.5.2, DREAMM-2 CSR Table 4.0040; 5.3.5.1, DREAMM-3 CSR Table 81
Note: Data presented as geometric mean (%CVb), except tmax, presented as median, (minimum, maximum).

表 2.7.1.3.2 ベランタマブ　マホドチンの凍結液剤及び凍結乾燥粉末剤を投与した時のサイクル 1 における総 mAb の PK パラメータ（DREAMM-2 試験及び DREAMM-3 試験）

	DREAMM-3 Treatment Group		DREAMM-2 Treatment Group					
	2.5 mg/kg Lyophile (N=217)		2.5 mg/kg Frozen Liquid (N=95)		3.4 mg/kg Lyophile (N=24)		3.4 mg/kg Frozen Liquid (N=99)	
Parameter	n	Value	n	Value	n	Value	n	Value
AUC(0-τ) (μg·h/mL)	78	6650 (48.7)	29	7305 (42)	19	9029 (40)	18	9566 (42)
C-EOI (μg/mL)	198	42.7 (32.1)	88	43.5 (49)	22	56.4 (21)	91	56.4 (39)

	DREAMM-3 Treatment Group		DREAMM-2 Treatment Group					
	2.5 mg/kg Lyophile (N=217)		2.5 mg/kg Frozen Liquid (N=95)		3.4 mg/kg Lyophile (N=24)		3.4 mg/kg Frozen Liquid (N=99)	
Parameter	**n**	**Value**	**n**	**Value**	**n**	**Value**	**n**	**Value**
Cmax (μg/mL)	102	43.1 (32.2)	30	48.9 (30)	20	60.1 (18)	19	61.1 (27)
tmax (h)	102	1.77 (0.500, 24.3)	30	1.75 (0.42, 2.50)	20	0.65 (0.48, 2.17)	19	1.87 (0.50, 24.50)
Ctrough (μg/mL)	163	5.52 (86.1)	66	5.27 (83)	18	8.13 (101)	71	5.98 (87)

Source: 5.3.5.2, DREAMM-2 CSR Table 4.0050; 5.3.5.1, DREAMM-3 CSR Table 82
Note: Data presented as geometric mean (%CVb), except tmax, presented as median, (minimum, maximum).

表 2.7.1.3.3 ベランタマブ　マホドチンの凍結液剤及び凍結乾燥粉末剤を投与した時のサイクル 1 における cys-mcMMAF の PK パラメータ（DREAMM-2 試験及び DREAMM-3 試験）

	DREAMM-3 Treatment Group		DREAMM-2 Treatment Group					
	2.5 mg/kg Lyophile (N=217)		2.5 mg/kg Frozen Liquid (N=95)		3.4 mg/kg Lyophile (N=24)		3.4 mg/kg Frozen Liquid (N=99)	
Parameter	**n**	**Value**	**n**	**Value**	**n**	**Value**	**n**	**Value**
AUC(0-168) (ng·h/mL)	76	104 (51.4)	14	84.3 (59)	7	81.6 (58)	12	109.4 (55)
AUC(0-tlast) (ng·h/mL)	103	95.3 (64.3)	27	79.3 (61)	19	100.4 (52)	20	113.6 (58)
tlast (days)	109	6.98 (0.07, 22.98)	27	7.78 (2.78, 12.89)	19	6.93 (2.91, 10.89)	20	7.90 (2.64, 20.96)
C-EOI (pg/mL)	191	430 (62.1)	90	316 (63)	22	386 (45)	97	449 (67)
Cmax (pg/mL)	105	1131 (65.5)	27	903 (64)	19	1017 (61)	20	1148 (65)
tmax (h)	105	23.7 (0.500, 68.0)	27	22.83 (1.92, 65.63)	19	24.08 (0.97, 69.47)	20	23.84 (17.38, 72.65)

Source: 5.3.5.2, DREAMM-2 CSR Table 4.0060; 5.3.5.1, DREAMM-3 CSR Table 4.0060
Note: Data presented as geometric mean, (%CVb), except tmax and tlast, presented as median, (minimum, maximum).

母集団 PK モデルから得られたベランタマブ　マホドチンの曝露量を、DREAMM-3 試験の凍結乾燥粉末剤 2.5 mg/kg 投与群と DREAMM-2 試験の凍結液剤 2.5 mg/kg 投与群で比較した［5.3.3.5、CPMR Amendment 1（TMF-16325848）］。母集団 PK モデルにおいて、製剤はベランタマブ　マホドチンの PK に対して有意な共変量ではなかった。

以上のことから、凍結液剤及び凍結乾燥製剤におけるベランタマブ　マホドチン、総 mAb 及び cys-mcMMAF の PK は、類似していることが示された。

2.7.1.4. 付録

2.7.1.4.1. 臨床試験で使用した製剤ロット一覧

表 2.7.1.4.1 臨床試験で使用した製剤ロット一覧

Study Reference No.	Drug Product Batch No.	Dosage Form	Input Drug Substance Batch (Belantamab Mafodotin)	CTD Report Location
DREAMM-1	[redacted]	Liquid	[redacted]	5.3.3.2
	[redacted]	Liquid	[redacted]	
DREAMM-2	[redacted]	Liquid	[redacted]	5.3.5.2
	[redacted]	Liquid	[redacted]	
	[redacted] ([redacted])[a]	Lyo	[redacted]	
	[redacted] ([redacted])[a]	Lyo	[redacted]	
DREAMM-3	[redacted]	Lyo	[redacted]	5.3.5.1
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted] [redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
DREAMM-6	[redacted]	Liquid	[redacted]	5.3.5.2
	[redacted]	Liquid	[redacted]	
	[redacted]	Liquid	[redacted]	
	[redacted]	Liquid	[redacted]	
	[redacted]	Liquid	[redacted]	
DREAMM-7	[redacted]	Lyo	[redacted] [redacted]	5.3.5.1

Study Reference No.	Drug Product Batch No.	Dosage Form	Input Drug Substance Batch (Belantamab Mafodotin)	CTD Report Location
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
DREAMM-8	[redacted]	Lyo	[redacted]	5.3.5.1
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
DREAMM-11	[redacted] ([redacted])[a]	Lyo	[redacted]	5.3.3.2
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	

Study Reference No.	Drug Product Batch No.	Dosage Form	Input Drug Substance Batch (Belantamab Mafodotin)	CTD Report Location
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
DREAMM-12	[redacted]	Lyo	[redacted]	5.3.3.3
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	
	[redacted]	Lyo	[redacted]	

a. Batch number in parenthesis is the GSK site batch number.

2.7.1.4.2. 分析法のライフサイクル

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Study	Measure	Table
DREAMM-1	Belantamab mafodotin	表 2.7.1.4.2
	Total mAb	表 2.7.1.4.3
	Cys-mcMMAF	表 2.7.1.4.4
	Cys-mcMMAF (urine)	表 2.7.1.4.5
	Free sBCMA	表 2.7.1.4.6
DREAMM-2	Belantamab mafodotin[a]	表 2.7.1.4.7
	Total mAb[b]	表 2.7.1.4.8
	Cys-mcMMAF[c]	表 2.7.1.4.9
	Free sBCMA[d]	表 2.7.1.4.10
DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12	Belantamab mafodotin[a]	表 2.7.1.4.11
DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-11, DREAMM-12	Total mAb[b]	表 2.7.1.4.12
DREAMM-3, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12, DREAMM-14	Cys-mcMMAF[c]	表 2.7.1.4.13
DREAMM-3, DREAMM-6, DREAMM-7, DREAMM-8, DREAMM-11, DREAMM-12	Free sBCMA[d]	表 2.7.1.4.14
DREAMM-6	Cys-mcMMAF	表 2.7.1.4.9
DREAMM-12	Cys-mcMMAF (urine)	表 2.7.1.4.15
DREAMM-14	Belantamab mafodotin	表 2.7.1.4.16
DREAMM-14	Free sBCMA[d]	表 2.7.1.4.18
DREAMM-12	Belantamab mafodotin (tear fluid)	表 2.7.1.4.17
DREAMM-12	Cys-mcMMAF (tear fluid)	表 2.7.1.4.19
DREAMM-6	Bortezomib	表 2.7.1.4.20
DREAMM-6	Lenalidomide	表 2.7.1.4.21
DREAMM-8	Pomalidomide	表 2.7.1.4.22

Note: Total mAb data were not collected for DREAMM-8 or DREAMM-14.

a. The method used to measure the analyte is the same, but analyses were conducted in different laboratories.
b. The method used to measure the analyte is the same, but analyses were conducted in different laboratories.
c. The method used to measure the analyte is the same, but analyses were conducted in different laboratories.
d. The method used to measure the analyte is the same, but analyses were conducted in different laboratories.

表 2.7.1.4.2 血漿中ベランタマブ マホドチン濃度分析法のライフサイクル要約（DREAMM-1 試験）

	Method Validation #1	Method Validation #2	DREAMM-1
Analyte	Belantamab mafodotin	Belantamab mafodotin	Belantamab mafodotin
Validation type	Full	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US
Matrix	Plasma		
Platform	ELISA		
Format	A validated sandwich format using [redacted] for capture and either [redacted] ([redacted]) or [redacted] ([redacted]) for detection		
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021
Calibration range (LLOQ-ULOQ) and levels validated	100 to 5000 ng/mL 100, 250, 500, 1000, 2500, 5000 ng/mL	200 to 10 000 ng/mL 200, 500, 750, 1000, 2500, 5000, 10 000 ng/mL	100 to 5000 ng/mL ([redacted]) 200 to 10 000 ng/mL ([redacted]) 100, 250, 500, 1000, 2500, 5000 ng/mL ([redacted]) 200, 500, 750, 1000, 2500, 5000, 10 000 ng/mL ([redacted])
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2013N186863_00	2016N282271_01	2019N400688_00

	Method Validation #1	Method Validation #2	DREAMM-1
Amendment history	NA	2016N282271_01 contains data on the cross-validation to the methods in 2013N186863 and 2019N412690; further evaluation of the tolerance to circulating BCMA, data on conjugation selectivity and drug load selectivity; further long-term stability data.	NA

表 2.7.1.4.3 血漿中総 mAb 濃度分析法のライフサイクル要約（DREAMM-1 試験）

	Method Validation #1	Method Validation #2	DREAMM-1
Analyte	Total mAb	Total mAb	Total mAb
Validation type	Full	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US
Matrix	Plasma		
Platform	ELISA		
Format	A validated sandwich format using either [redacted] ([redacted]) or [redacted] ([redacted]) for capture and a [redacted] for detection		
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021
Calibration range (LLOQ-ULOQ) and levels validated	100 to 5000 ng/mL 100, 250, 500, 1000, 2500, 5000 ng/mL	200 to 10 000 ng/mL 200, 500, 750, 1000, 2500, 5000, 10 000 ng/mL	100 to 5000 ng/mL ([redacted]) 200 to 10 000 ng/mL ([redacted]) 100, 250, 500, 1000, 2500, 5000 ng/mL ([redacted]) 200, 500, 750, 1000, 2500, 5000, 10 000 ng/mL ([redacted])
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2014N206720_00	2015N243565_01	2019N400688_00

	Method Validation #1	Method Validation #2	DREAMM-1
Amendment history	NA	2015N243565_01 contains data on the cross-validation to the method 2019N396866; further evaluation of the tolerance to circulating BCMA, data on conjugation selectivity and drug load selectivity; further long-term stability data.	NA

表 2.7.1.4.4 血漿中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM-1 試験）

	Method Validation #1	DREAMM-1
Analyte	Cys-mcMMAF	Cys-mcMMAF
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US
Matrix	Plasma	
Platform	Mass spectrometry	
Format	Solid phase extraction followed by LC-MS/MS	
Stock reference and lot (expiry)	Cys-mcMMAF Lot no.: 1202426090 Expiry date: October 2016	Cys-mcMMAF Lot no.: 1202426090 Expiry date: October 2016 Lot no.: 1409436190 Expiry date: October 2018
Calibration range (LLOQ-ULOQ) and levels validated	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2014N195974_01	2019N400688_00
Amendment history	2014N195974_01 contains further long-term stability data.	NA

表 2.7.1.4.5 尿中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM-1 試験）

	Method Validation #1	DREAMM-1
Analyte	Cys-mcMMAF	Cys-mcMMAF
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US
Matrix	Urine	
Platform	Mass spectrometry	
Format	Solid phase extraction followed by LC-MS/MS	
Stock reference and lot (expiry)	Cys-mcMMAF Lot no.: 1202426090 Expiry date: October 2016 Lot no.: 1409436190 Expiry date: October 2018	Cys-mcMMAF Lot no.: 1202426090 Expiry date: October 2016 Lot no.: 1409436190 Expiry date: October 2018
Calibration range (LLOQ-ULOQ) and levels validated	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL
Matrix/clinical study population	Control urine	Urine from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2014N201539_00	2019N400688_00
Amendment history	NA	NA

表 2.7.1.4.6 血清中遊離 sBCMA 濃度分析法のライフサイクル要約（DREAMM-1 試験）

	Method Validation	DREAMM-1
Analyte	Free BCMA	Free BCMA
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US
Matrix	Serum	
Platform	MSD (ECL)	
Format	A validated sandwich format using [redacted] for capture and [redacted] for detection	
Stock reference and lot (expiry)	Glycosylated huBCMA Lot no.: GRITS48017 Expiry date: 07 February 2019	Glycosylated huBCMA Lot no.: GRITS48017 Expiry date: 07 February 2019
Calibration range (LLOQ-ULOQ) and levels validated	2 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.25, 62.25, 125, 250, 500, 1000 ng/mL	2 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.25, 62.25, 125, 250, 500, 1000 ng/mL
Matrix/clinical study population	Control serum and serum from multiple myeloma participants	Serum from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2014N202258_00	No report available
Amendment history	NA	NA

表 2.7.1.4.7　血漿中ベランタマブ　マホドチン濃度分析法のライフサイクル要約（DREAMM-2 試験）

	Method Validation #1	DREAMM-2
Analyte	Belantamab mafodotin	Belantamab mafodotin
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], US
Matrix	Plasma	
Platform	ELISA	
Format	A validated sandwich format using [redacted] for capture and [redacted] for detection	
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no: [redacted] Expiry date: 31 July 2021	Belantamab mafodotin Lot no.: [redacted] Expiry date: 31 July 2021
Calibration range (LLOQ-ULOQ) and levels validated	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL After calibration curve truncation: 500 to 5000 ng/mL 500, 750, 1000, 1750, 2500, 4000 and 5000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL After calibration curve truncation: 500 to 5000 ng/mL 500, 750, 1000, 1750, 2500, 4000 and 5000 ng/mL
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2019N412690_00 2019N412690_01	2018N390896_00 2018N390896_01 2018N390896_02
Amendment history	2019N412690_01 contains additional stability data; 2019N412690_02 contains partial validation data for calibration curve truncation as well as additional long-term stability data.	2018N390896_01 contains parallelism results and updates to stability information; 2018N390896_02 contains additional sample analysis and ISR runs performed after report amendment 2018N390896_01 and updates to stability information.

表 2.7.1.4.8 血漿中総 mAb 濃度分析法のライフサイクル要約（DREAMM-2 試験）

	Method Validation #1	DREAMM-2
Analyte	Total mAb	Total mAb
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], US
Matrix	Plasma	
Platform	ELISA	
Format	A validated sandwich format using [redacted] for capture and [redacted] for detection	
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021	Belantamab mafodotin Lot no.: [redacted] Expiry date: 31 July 2021
Calibration range (LLOQ-ULOQ) and levels validated	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2019N396866_00 2019N396866_01 2019N396866_02	2018N390896_00 2018N390896_01 2018N390896_02
Amendment history	2019N396866_01 contains additional long-term stability data; 2019N396866_02 contains additional long-term stability data.	2018N390896_01 contains parallelism results and updates to stability information; 2018N390896_02 contains additional sample analysis and ISR runs performed after report amendment 2018N390896_01 and updates to stability information.

表 2.7.1.4.9 血漿中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM-2 及び DREAMM-6 試験）

	Method Validation #1	Method Validation #2	DREAMM-2	DREAMM-6
Analyte	Cys-mcMMAF	Cys-mcMMAF	Cys-mcMMAF	Cys-mcMMAF
Validation type	Abbreviated	Full	Not applicable	Not applicable
CTD reference	m2.7.1	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]	[redacted]
Bioanalytical site	GSK, 709 Swedeland Road, King of Prussia, Pennsylvania 19406, US		GSK, 1250 South Collegeville Road, Collegeville, Pennsylvania 19426, US	
Matrix	Plasma			
Platform	Mass spectrometry			
Format	Solid phase extraction ([redacted]) or protein precipitation ([redacted]) followed by LC-MS/MS			
Stock reference and lot (expiry)	Cys-mcMMAF Lot no.: 1409436190 Expiry date: 18 October 2019	Cys-mcMMAF Lot no.: 1409436190 Expiry date: 18 October 2019	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2022	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2022
Calibration range (LLOQ-ULOQ) and levels validated	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL ([redacted]) 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL ([redacted])	50 to 10 000 pg/mL 50, 100, 250, 500, 1000, 2500, 5000, 10 000 pg/mL
Matrix/clinical study population	Control plasma	Control plasma and plasma from multiple myeloma participants	Plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2019N404180_00	2019N411691_03	2019N416576_00 – Interim Bioanalytical Report 2022N505659_00 – Final Bioanalytical Report	2023N530064_00

	Method Validation #1	Method Validation #2	DREAMM-2	DREAMM-6
Amendment history	Not applicable	2019N411691_01, 2019N411691_02 and 2019N411691_03 contain additional stability data.	Not applicable	Not applicable

表 2.7.1.4.10 血清中遊離 sBCMA 濃度分析法のライフサイクル要約（DREAMM-2 試験）

	Method Validation #2	DREAMM-2
Analyte	Free BCMA	Free BCMA
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], US
Matrix	Serum	
Platform	ECL	
Format	A validated sandwich format using [redacted] for capture and a biotinylated [redacted] for detection	
Stock reference and lot (expiry)	Glycosylated huBCMA Lot no.: GRITS48017 Expiry date: 07 February 2019 Lot no.: N38580-51-P1 Expiry date: 03 August 2023	Glycosylated huBCMA Lot no.: N38580-51-P1 Expiry date: 03 August 2023
Calibration range (LLOQ-ULOQ) and levels validated	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.75, 62.5, 125, 250, 500, 1000 ng/mL	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.75, 62.5, 125, 250, 500, 1000 ng/mL
Matrix/clinical study population	Control serum and serum from multiple myeloma participants	Serum from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2018N393390_00 2018N393390_01 2018N393390_02 2018N393390_03 2018N393390_04	2022N511202_00
Amendment history	2018N393390_01 contains additional stability data; 2018N393390_02 contains parallelism data; 2018N393390_03 contains additional stability data, bridging of new lot of detection reagent, and assessment of increased incubation time for both sample plating and detection steps. 2018N393390_04 contains cross-validation data.	NA

表 2.7.1.4.11 血漿中ベランタマブ　マホドチン濃度分析法のライフサイクル要約（DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-8、DREAMM-11 及び DREAMM-12 試験）

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -8, -11, and -12 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Analyte	Belantamab mafodotin	Belantamab mafodotin	Belantamab mafodotin	Belantamab mafodotin
Validation type	Full	Full	Not applicable	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted] US	[redacted], China	[redacted] US	[redacted], China
Matrix	Plasma			
Platform	ELISA			
Format	A validated sandwich format using [redacted] for capture and [redacted] for detection			
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023	Belantamab mafodotin Lot no: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023	Belantamab mafodotin Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 April 2023
Calibration range (LLOQ-ULOQ) and levels validated	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL After calibration curve truncation: 500 to 5000 ng/mL 500, 750, 1000, 1750, 2500, 4000, and 5000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL After calibration curve truncation:500 to 5000 ng/mL 500, 750, 1000, 1750, 2500, 4000, and 5000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -8, -11, and -12 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Control plasma	Plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2019N412690_00 2019N412690_01 2019N412690_02	2021N468577_00 2021N468577_01	DREAMM-3: 2022N524971_00 DREAMM-6: 2023N536470_00 DREAMM-7: 2023N539579_00, 01 DREAMM-8: 2024N551059_00, 01 DREAMM-11: 2023N533324_00 DREAMM-12: 2023N536270_00	DREAMM-3: 2022N524960_00 DREAMM-7: 2023N539630_00 DREAMM-8: 2024N549478_00
Amendment history	2019N412690_01 contains additional stability data; 2019N412690_02 contains partial validation data for calibration curve truncation as well as additional long-term stability data.	2021N468577_01 contains additional stability data.	NA	NA

表 2.7.1.4.12 血漿中総 mAb 濃度分析法のライフサイクル要約（DREAMM-3、DREAMM-6、DREAMM-7、DREAMM-11 及び DREAMM-12 試験）

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -11, and -12 (Non-China Samples)	DREAMM-3 and -7 (China Samples)
Analyte	Total mAb	Total mAb	Total mAb	Total mAb
Validation type	Full	Full	Not applicable	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted] US	[redacted] China	[redacted] US	[redacted] China
Matrix	Plasma			
Platform	ELISA			
Format	A validated sandwich format using [redacted] for capture and [redacted] for detection			
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 November 2017 Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023	Belantamab mafodotin Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023	Belantamab mafodotin Lot no.: [redacted] Expiry date: 31 July 2021 Lot no.: [redacted] Expiry date: 30 April 2023
Calibration range (LLOQ-ULOQ) and levels validated	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL	500 to 10 000 ng/mL 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Control plasma	Plasma from multiple myeloma participants	Plasma from multiple myeloma participants

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -11, and -12 (Non-China Samples)	DREAMM-3 and -7 (China Samples)
Relevant reference and applicable report amendment(s) and hyperlinks	2019N396866_00 2019N396866_01 2019N396866_02	2021N468428_00 2021N468428_01	DREAMM-3: 2022N524971_00 DREAMM-6: 2023N536470_00 DREAMM-7: 2023N539579_00, 01 DREAMM-11: 2023N533324_00 DREAMM-12: 2023N536270_00	DREAMM-3: 2022N524955_00 DREAMM-7: 2023N539561_00
Amendment history	2019N396866_01 contains additional long-term stability data; 2019N396866_02 contains additional long-term stability data.	2021N468428_01 contains additional stability data.	NA	NA

表 2.7.1.4.13 血漿中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM 3、DREAMM-7、DREAMM-8、DREAMM-11、DREAMM-12 及び DREAMM-14 試験）

	Method Validation #1	Method Validation #2	DREAMM-3, -7, -8, -11, -12, and -14 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Analyte	Cys-mcMMAF	Cys-mcMMAF	Cys-mcMMAF	Cys-mcMMAF
Validation type	Full	Full	Not applicable	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], China	[redacted], US	[redacted], China
Matrix	Plasma			
Platform	Mass spectrometry			
Format	Protein precipitation followed by LC-MS/MS			
Stock reference and lot (expiry)	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023
Calibration range (LLOQ-ULOQ) and levels validated	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL
Matrix/clinical study population	Control plasma	Control plasma	Plasma from multiple myeloma participants	Plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2022N519749_00 2022N519749_01 2022N519749_02	2020N448658_00 2020N448658_01	DREAMM-3: 2022N525492_00 DREAMM-7: 2023N538470_00, 01 DREAMM-8: 2024N550649_00, 01 DREAMM-11: 2023N535795 00 DREAMM-12: 2023N535698_00 DREAMM-14: 2023N536676_00	DREAMM-3: 2022N502523_00 DREAMM-7: 2022N514277_00 DREAMM-8: 2024N550524_00

	Method Validation #1	Method Validation #2	DREAMM-3, -7, -8, -11, -12, and -14 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Amendment history	2022N519749_01 and 2022N519749_02 contain additional long-term stability data.	2020N448658_01 contains data on additional stability and co-administration drug interference assessment.	NA	NA

表 2.7.1.4.14 血清中遊離 sBCMA 濃度分析法のライフサイクル要約（DREAMM-3、DREAMM 6、DREAMM-7、DREAMM-8、DREAMM-11 及び DREAMM-12 試験）

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -8, -11, and -12 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Analyte	Free BCMA	Free BCMA	Free BCMA	Free BCMA
Validation type	Full	Full	Not applicable	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], China	[redacted], US	[redacted], China
Matrix	Serum			
Platform	ECL			
Format	A validated sandwich format using [redacted] for capture and a biotinylated [redacted] for detection			
Stock reference and lot (expiry)	Glycosylated huBCMA Lot no.: GRITS48017 Expiry date: 07 February 2019 Lot no.: N38580-51-P1 Expiry date: 03 August 2023	Glycosylated huBCMA Lot no.: E10295-B1 Expiry date: 01 February 2024	Glycosylated huBCMA Lot no.: N38580-51-P1 Expiry date: 03 August 2023	Glycosylated huBCMA Lot no.: E10295-B1 Expiry date: 01 February 2024
Calibration range (LLOQ-ULOQ) and levels validated	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.75, 62.5, 125, 250, 500, 1000 ng/mL	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.6, 31.3, 62.5, 125, 250, 500, 1000 ng/mL	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.75, 62.5, 125, 250, 500, 1000 ng/mL	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.6, 31.3, 62.5, 125, 250, 500, 1000 ng/mL
Matrix/clinical study population	Control serum and serum from multiple myeloma participants	Control serum	Serum from multiple myeloma participants	Serum from multiple myeloma participants

	Method Validation #1	Method Validation #2	DREAMM-3, -6, -7, -8, -11, and -12 (Non-China Samples)	DREAMM-3, -7, and -8 (China Samples)
Relevant reference and applicable report amendment(s) and links	2018N393390_00 2018N393390_01 2018N393390_02 2018N393390_03 2018N393390_04	2021N468639_00 2021N468639_01 2021N468639_02	DREAMM-3: 2022N523127_00 DREAMM-6: 2023N530039_00 DREAMM-7: 2023N546327_00, 01 DREAMM-8: 2024N550098_00, 01 DREAMM-11: 2023N533364_00 DREAMM-12: 2023N532337_00	DREAMM-3: 2022N525047_00 DREAMM-7: 2023N544471_00 DREAMM-8: 2024N549481_00
Amendment history	2018N393390_01 contains additional long-term stability data; 2018N393390_02 provides parallelism data; 2018N393390_03 contains data of additional long-term stability, bridging of detection reagent, and assessment of increase incubation time for sample plating and detection steps. 2018N393390_04 contains cross-validation data.	2021N468639_01 contains additional long-term stability data. 2021N468639_02 contains cross-validation data.	NA	NA

表 2.7.1.4.15 尿中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM-12 試験）

	Method Validation	DREAMM-12
Analyte	Cys-mcMMAF	Cys-mcMMAF
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], US
Matrix	Urine	
Platform	Mass spectrometry	
Format	Acidic protein precipitation followed by LC-MS/MS	
Stock reference and lot (expiry)	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023	Cys-mcMMAF Lot no.: 1409436190 Expiry date: October 2023
Calibration range (LLOQ-ULOQ) and levels validated	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL	50 to 10 000 pg/mL 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL
Matrix/clinical study population	Human urine from healthy population	Urine from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2023N535702_00	DREAMM-12: 2023N535699_00
Amendment history	NA	NA

表 2.7.1.4.16 血漿中ベランタマブ　マホドチン濃度分析法のライフサイクル要約（DREAMM-14 試験）

	Method Validation #1	DREAMM-14
Analyte	Belantamab mafodotin	Belantamab mafodotin
Validation type	Full	Not applicable
CTD reference no.	M2.7.1	M2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK 1250 South Collegeville Road, Collegeville, PA 19426, US	
Matrix	Plasma	
Platform	MSD	
Format	A validated sandwich format using [redacted] and detected through a ruthenylated [redacted] for detection	
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 April 2024	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 April 2024
Calibration range (LLOQ-ULOQ) and levels validated	20 to 2000 ng/mL 20.0, 50.0, 100, 250, 500, 1000, 1800, 2000 ng/mL	20 to 2000 ng/mL 20.0, 50.0, 100, 250, 500, 1000, 1800, 2000 ng/mL
Matrix/clinical study population	Control plasma and plasma from multiple myeloma participants	Control plasma and plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and hyperlinks	2022N515388_00	2023N538105_01
Amendment history	NA	NA

表 2.7.1.4.17 涙液中ベランタマブ　マホドチン濃度分析法のライフサイクル要約（DREAMM-12 試験）

	Method Validation #1	DREAMM-12
Analyte	Belantamab mafodotin	Belantamab mafodotin
Validation type	Abbreviated validation	Not applicable
CTD reference no.	M2.7.1	M2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY, UK	GSK, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY, UK
Matrix	Human tears	
Platform	Gyrolab	
Format	A validated immunoassay capturing with [redacted] and detected through an alexa labeled [redacted]	
Stock reference and lot (expiry)	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 April 2024	Belantamab mafodotin Lot no.: [redacted] Expiry date: 30 April 2024
Calibration range (LLOQ-ULOQ) and levels validated	Qualitive assay with limit of detection calibrator at 50 ng/mL	Qualitive assay with limit of detection calibrator at 50 ng/mL
Matrix/clinical study population	Control human tears	Control human tears
Relevant reference and applicable report amendment(s) and links	2021N491769_00	2022N522945_00
Amendment history	NA	NA

表 2.7.1.4.18 血清中遊離 sBCMA 濃度分析法のライフサイクル要約（DREAMM-14 試験）

	Method Validation	DREAMM-14
Analyte	Free BCMA	Free BCMA
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	GSK 1250 South Collegeville Road, Collegeville, PA 19426, US	GSK 1250 South Collegeville Road, Collegeville, PA 19426, US
Matrix	Serum	
Platform	MSD (ECL)	
Format	A validated sandwich format using [redacted] for capture and a biotinylated [redacted] for detection	
Stock reference and lot (expiry)	Glycosylated huBCMA Lot no.: N38580-51-P1 Expiry date: 09 August 2024 Lot no ELN114071-1 Expiry date 16 February 2028	Glycosylated huBCMA Lot no.: ELN114071-1 Expiry date: 16 February 2028
Calibration range (LLOQ-ULOQ) and levels validated	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.25, 62.25, 125, 250, 500, 1000 ng/mL	1.95 to 1000 ng/mL 1.95, 3.91, 7.81, 15.63, 31.25, 62.25, 125, 250, 500, 1000 ng/mL
Matrix/clinical study population	Control serum and serum from multiple myeloma participants	Serum from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2023N527200_00	2023N539208_00
Amendment history	NA	NA

表 2.7.1.4.19 涙液中 cys-mcMMAF 濃度分析法のライフサイクル要約（DREAMM-12 試験）

	Method Validation #1	DREAMM-12
Analyte	Cys-mcMMAF	Cys-mcMMAF
Validation type	Abbreviated validation	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	
Bioanalytical site	Stevenage, UK	
Matrix	Human tears	
Platform	LC-MS/MS	
Format	A qualitative protein precipitation method followed by evaporation, reconstitution and solid phase extraction.	
Stock reference and lot (expiry)	SGD-1362 (Cys-mcMMAF) Lot no.: 1409436190 Expiry date: 31 October 2021	SGD-1362 (Cys-mcMMAF) Lot no.: 1409436190 Expiry date: 31 October 2021
Calibration range (LLOQ-ULOQ) and levels validated	Qualitive assay with limit of detection calibrators at 1.25, 2.5 and 5 pg/mL	Qualitative assay with limit of detection calibrators at 1.25, 2.5 and 5 pg/mL
Matrix/clinical study population	Artificial and control human tears	Artificial and control human tears
Relevant reference and applicable report amendment(s) and links	2021N485434 and 2020N458494	2022N525055
Amendment history	NA	NA

表 2.7.1.4.20 ボルテゾミブ濃度分析法のライフサイクル要約（DREAMM-6 試験）

	Method Validation #1	Method Validation #2	DREAMM-6
Analyte	Bortezomib	Bortezomib	Bortezomib
Validation type	Full	Additional validation stability	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted], US	[redacted], US	[redacted], US
Matrix	Plasma		
Platform	UPLC with MS/MS		
Format	A validated protein precipitation method followed by evaporation and reconstitution		
Stock reference and lot (expiry)	Bortezomib Lot no.: 2737-007A1 Expiry date: 01 September 2020	Bortezomib Lot no.: 2737-007A1 Expiry date: 01 September 2020	Bortezomib Lot no.: 2737-007A1 Expiry date: 01 September 2020
Calibration range (LLOQ-ULOQ) and levels validated	0.1 to 100 ng/mL 0.1, 0.2, 0.4, 1.5, 6.0, 25.0,80.0 and 100.0 ng/mL	0.1 to 100 ng/mL 0.1, 0.2, 0.4, 1.5, 6.0, 25.0,80.0 and 100.0 ng/mL	0.1 to 100 ng/mL 0.1, 0.2, 0.4, 1.5, 6.0, 25.0,80.0 and 100.0 ng/mL
Matrix/clinical study population	Control plasma	Control plasma	Control plasma/plasma from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2019N413318	2023N546218	2018N389799
Amendment history	NA	NA	NA

表 2.7.1.4.21 レナリドミド濃度分析法のライフサイクル要約（DREAMM-6 試験）

	Method validation #1	DREAMM-6
Analyte	Lenalidomide	Lenalidomide
Validation type	Full	Not applicable
CTD reference no.	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]
Bioanalytical site	[redacted] Canada, [redacted]	[redacted] Canada, [redacted]
Matrix	Plasma	
Platform	LC-MS/MS	
Format	A validated liquid-liquid extraction method	
Stock reference and lot (expiry)	Lenalidomide Lot no.: TC27682 Expiry date: 11 April 2019	Lenalidomide Lot no.: TC27682 Expiry date: 04 November 2019 Recertified 27 April 2021
Calibration range (LLOQ-ULOQ) and levels validated	2.5 to 1000 ng/mL 2.5, 5.0, 50.0, 100,0, 200.0, 400.0, 800.0, 1000.0 ng/mL	2.5 to 1000 ng/mL 2.5, 5.0, 50.0, 100,0, 200.0, 400.0, 800.0, 1000.0 ng/mL
Matrix/clinical study population	Control plasma	Control plasma/from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2023N533133	2018N393429
Amendment history	NA	NA

表 2.7.1.4.22 ポマリドミド濃度分析法のライフサイクル要約（DREAMM-8 試験）

	Method validation #1	Method validation #2	DREAMM-8
Analyte	Pomalidomide	Pomalidomide	Pomalidomide
Validation type	Full	Partial (Specificity)	Not applicable
CTD reference no.	m2.7.1	m2.7.1	m2.7.1
Method ID	[redacted]	[redacted]	[redacted]
Bioanalytical site	[redacted] Canada, [redacted]		
Matrix	Plasma		
Platform	LC-MS/MS		
Format	A validated liquid-liquid extraction method		
Stock reference and lot (expiry)	Pomalidomide Lot no.: 1787-068A1 Expiry date: 11 January 2020	Pomalidomide Batch no.: 20794 Expiry date: 10 November 2024	Pomalidomide Batch no.: 20794 Expiry date: 10 November 2024
Calibration range (LLOQ-ULOQ) and levels validated	0.50 to 200.0 ng/mL 0.5, 1.0, 4.0, 20.0, 40.0, 80.0, 160.0 and 200 ng/mL	0.50 to 200.0 ng/mL 0.5, 1.0, 4.0, 20.0, 40.0, 80.0, 160.0 and 200 ng/mL	0.50 to 200.0 ng/mL 0.5, 1.0, 4.0, 20.0, 40.0, 80.0, 160.0 and 200 ng/mL
Matrix/clinical study population	Control plasma	Control plasma	Control plasma/from multiple myeloma participants
Relevant reference and applicable report amendment(s) and links	2023N527155	2023N527169	2023N532441
Amendment history	NA	NA	NA

2.7.1.4.3. 分析法性能の要約

ヒト血漿中ベランタマブ　マホドチン分析法

表 2.7.1.4.23 血漿中ベランタマブ　マホドチン分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2019N412690_02 Validation and cross validation of a chemiluminescent immunoassay for the quantitation of GSK2857916 (antibody drug conjugate) in human K2EDTA plasma (Method reference number: [redacted])		
Method description	Belantamab mafodotin was captured in human plasma using [redacted] and detected with a biotinylated [redacted] with streptavidin conjugated to an HRP reporter tag.		
Materials used for calibration curve and concentration	Before calibration curve truncation: Belantamab mafodotin at 200 (anchor), 500, 750, 1000, 1750, 2500, 5000, and 10 000 ng/mL After calibration curve truncation: Belantamab mafodotin at 200 (anchor), 500, 750, 1000, 1750, 2500, 4000, and 5000 ng/mL		
Validated assay range	Before calibration curve truncation: 500 to 10 000 ng/mL After calibration curve truncation: 500 to 5000 ng/mL		
Material used for QCs and concentration	Before calibration curve truncation: Belantamab mafodotin at 500, 1500, 3500, 8000, and 10 000 ng/mL After calibration curve truncation: Belantamab mafodotin at 500, 1500, 2500, 3500, and 5000 ng/mL		
Minimum required dilutions	50-fold in assay buffer		
Source and lot of reagents (LBA)	Belantamab mafodotin, GSK, Lot no.: [redacted], GSK, N71496-2-1 HRP-labeled streptavidin, Thermo Fisher Scientific, Lot no.: RJ236399, SF252108, UB274936, and VG299366		
Regression model and weighting	Four parameter logistic – weighted 1/x		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	7	2019N412690_02, Table 3 and H.3
	Cumulative accuracy (%bias) from LLOQ to ULOQ	Before calibration curve truncation: –1.20% to +1.40% After calibration curve truncation: –1.50% to +1.20%	
	Cumulative precision (%CV) from LLOQ to ULOQ	Before calibration curve truncation: ≤2.04% After calibration curve truncation: ≤2.19%	

QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	Before calibration curve truncation: –7.89% to +5.00% After calibration curve truncation: –12.0% to –1.75%	2019N412690_02, Table 7 and H.7
	Inter-batch %CV	Before calibration curve truncation: ≤6.59% After calibration curve truncation: ≤7.30%	
	TE	Before calibration curve truncation: ≤14.5% After calibration curve truncation: ≤19.3%	
Selectivity and matrix effect	The selectivity of the method in normal human plasma and in plasma from multiple myeloma patients was established by analyzing 10 individual donor lots of plasma from each plasma type unspiked or spiked at the LLOQ of the assay. The precision and accuracy in 10/10 lots spiked at assay LLOQ met the acceptance criteria for both normal and multiple myeloma plasma. All unspiked samples were tested less than LLOQ.		2019N412690_02, Table 14 and 15
Interference and specificity	The ability of the method to tolerate sBCMA in human plasma was evaluated by spiking sBCMA at 25 to 1000 ng/mL into human plasma containing LQC and HQC level of belantamab mafodotin. Interference from soluble BCMA was observed at the LQC at 1000 ng/mL of BCMA and above and at the HQC at 500 ng/mL of BCMA and above. Interference from soluble BCMA was evaluated again after dilution, and the data indicate that the method can accurately quantitate belantamab mafodotin in the presence of up to 250 ng/mL sBCMA, or up to 2000 ng/mL sBCMA following 5- or 10-fold dilution or up to 3000 ng/mL sBCMA following 10-fold dilution. Sample dilutions and concentrations of sBCMA were reviewed prior to assessing the acceptability of the belantamab mafodotin concentrations.		2019N412690_02, Table 11 to 13, H.8, and H.9
Hemolysis effect	Five lots of hemolyzed human plasma were tested blank and spiked with 500 ng/mL belantamab mafodotin. The accuracy under the conditions tested was <20% in at least 80% of the samples. Blank hemolyzed plasma provided a response less than the LLOQ.		2019N412690_02, Table 16
Lipemic effect	Five lots of lipemic plasma were tested blank and spiked with 500 ng/mL belantamab mafodotin. The accuracy under the conditions tested was <20%. Blank lipemic plasma provided a response less than the LLOQ.		2019N412690_02, Table 17
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 1 000 000 ng/mL belantamab mafodotin from 8- to 8192-fold. All replicates of the 1 000 000 ng/mL belantamab mafodotin sample diluted 8- to 64-fold were greater than ULOQ and samples diluted 4096- to 8192-fold were less than LLOQ. The precision and accuracy of all the 128- to 2048-fold diluted samples was <20%. Dilution linearity was considered acceptable, and no hook effect was observed at or below 1 000 000 ng/mL belantamab mafodotin in human plasma.		2019N412690_02, Table 18

Bench-top/process stability	The stability of belantamab mafodotin at 1500 and 8000 ng/mL was assessed in human whole blood stored on wet ice for 2 hours or at ambient temperature for 4 hours, prior to processing to plasma. All samples were within 20% of similarly spiked samples in which the blood was processed to plasma immediately. The stability of belantamab mafodotin in human plasma stored at ambient temperature for 42 hours was assessed at 1500 and 8000 ng/mL. The precision and accuracy for the stored samples was <20%.	2019N412690_02, Table 19 and 23, Appendix F
Freeze-thaw stability	The stability of belantamab mafodotin in human plasma after 8 freeze-thaw cycles from –80°C to room temperature was assessed at 1500 and 8000 ng/mL. The precision and accuracy under the conditions tested was <20%.	2019N412690_02, Table 20
Long-term storage	The stability of belantamab mafodotin in human plasma stored at –20°C for 1470 days and at –80°C for 1475 days was assessed at 1500 and 8000 ng/mL. The precision and accuracy under the conditions tested was <20%.	2019N412690_02, Table 21 and 22, Appendix F, Appendix I
Parallelism	Nine samples at near Cmax from DREAMM-2 were diluted at 4 different dilution factors. Eighty percent or more of the samples tested had results within 30% of each other.	2018N390896_02, Appendix E
Carry over	Not applicable	
Method Performance in DREAMM-2 Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples. Report Number 2018N390896_02		
Assay passing rate	135/153 analytical runs met the predefined acceptance criteria	2018N390896_02, Table 2 and Table 27
Standard curve performance	For sample analysis runs from 17 December 2018 to 21 June 2019 (until interim bioanalytical report 2018N390896_01): Cumulative bias range: –0.6% to +1.0% Cumulative precision: ≤5.9%CV For sample analysis runs from 16 August 2019 to 31 March 2022 (additional runs reported in 2018N390896_02): Cumulative bias range: –0.600% to +1.00% Cumulative precision: ≤6.60%CV	2018N390896_02, Table 11 and Table 36
QC performance	For sample analysis runs from 17 December 2018 to 21 June 2019 (until interim bioanalytical report 2018N390896_01): Cumulative bias range: –6.4% to –0.7% Cumulative precision: ≤12.2%CV TE: not reported For sample analysis runs from 16 August 2019 to 31 March 2022 (additional runs reported in 2018N390896_02): Cumulative bias range: –6.40% to +0.667% Cumulative precision: ≤14.8%CV TE: not reported	2018N390896_02, Table 13 and Table 38
Method reproducibility	ISR was performed in 12.7% of clinical study samples analyzed using this method and 99.4% of samples met the pre-specified criteria.	2018N390896_02, Section 4.4
Clinical study sample analysis/ stability	Calibration standards were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt. QC samples were stored frozen at –80°C.	
Method Performance in DREAMM-3 Interim Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207495. Report Number 2022N524971_00		
Assay passing rate	108 out of 125 analytical runs met the predefined acceptance criteria	2022N524971_00, Table 2

Standard curve performance	Cumulative bias range: –1.00% to +0.800% Cumulative precision: ≤5.35 %CV	2022N524971_00, Table 11
QC performance	Cumulative bias range: –13.3% to +6.93% Cumulative precision: ≤22.6 %CV TE: not reported	2022N524971_00, Table 13
Method reproducibility	ISR was performed in 7.4% of clinical study samples analyzed using this method and 84.8% of samples met the pre-specified criteria.	2022N524971_00, Table 15
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-6 **Interim Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207497. Report Number** 2023N536470_00		
Assay passing rate	126 out of 152 analytical runs met the predefined acceptance criteria	2023N536470_00, Table 2 and 3
Standard curve performance	Standard curve: 500 – 10 000 ng/mL: Cumulative bias range: –1.00% to +2.00% Cumulative precision: ≤4.34% Truncated standard curve: 500 – 5000 ng/mL: Cumulative bias range: –1.00% to 0.800% Cumulative precision: ≤5.96%	2023N536470_00, Table 13 and 14
QC performance	Standard curve: 500 – 10 000 ng/mL Cumulative bias range: –6.88% to +2.00% Cumulative precision: ≤17.0% Truncated standard curve: 500 – 5000 ng/mL Cumulative bias range: –82.0% to +9.60% Cumulative precision: ≤132%	2023N536470_00, Table 16 and 17
Method reproducibility	ISR was performed in 7.8% of clinical study samples analyzed using this method and 68.2% of samples met the pre-specified criteria.	2023N536470_00, Table 19
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-7 **Interim Bioanalytical Report: Determination of GSK2857916 (Total mAb) and GSK2857916 (Conjugated Drug [ADC]) in Human K2EDTA Plasma Samples from Protocol 207503. Report Number:** 2023N539579_01		
Assay passing rate	167 out of 199 analytical runs met the predefined acceptance criteria	2023N539579_01, Table 2
Standard curve performance	Cumulative bias range: –1.00% to +0.800% Cumulative precision: ≤4.89%	2023N539579_01, Table 11
QC performance	Cumulative bias range: –82.0% to +0.667% Cumulative precision: ≤13.9%	2023N539579_01, Table 13
Method reproducibility	ISR was performed in 10.6% of clinical study samples analyzed using this method and 67.6% of samples met the pre-specified criteria.	2023N539579_01, Table 15
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-8 **Interim Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207499. Report Number:** 2024N551059_01		
Assay passing rate	123 out of 159 analytical runs met the predefined acceptance criteria	2024N551059_01, Table 1
Standard curve performance	Cumulative bias range: –1.50% to +1.14% Cumulative precision: ≤5.89%	2024N551059_01, Table 6
QC performance	Cumulative bias range: –10.1% to +4.27% Cumulative precision: ≤10.6%	2024N551059_01, Table 7

Method reproducibility	ISR was performed in 8.82% of clinical study samples analyzed using this method and 80.6% of samples met the pre-specified criteria.	2024N551059_01, Table 8
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-11 **Final Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207504. Report Number** 2023N533324_00		
Assay passing rate	13 out of 18 analytical runs met the predefined acceptance criteria	2023N533324_00, Table 2
Standard curve performance	Standard curve: 500 – 10 000 ng/mL: Cumulative bias range: –1.40% to +3.00% Cumulative precision: ≤5.50% Truncated standard curve: 500 – 5000 ng/mL: Cumulative bias range: –1.25% to 1.20% Cumulative precision: ≤4.28%	2023N533324_00, Table 10 and 11
QC performance	Standard curve: 500 – 10 000 ng/mL Cumulative bias range: –6.50% to +1.33% Cumulative precision: ≤16.3% Truncated standard curve: 500 – 5000 ng/mL Cumulative bias range: –17.9% to –6.80% Cumulative precision: ≤16.5%	2023N533324_00, Table 13 and 14
Method reproducibility	ISR was performed in 53.1% of clinical study samples analyzed using this method and 84.3% of samples met the pre-specified criteria.	2023N533324_00, Table 16
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-12 **Interim Bioanalytical Report: Determination of GSK2857916 (Total mAb) and GSK2857916 (Conjugated Drug [ADC]) in Human K2EDTA Plasma Samples from Protocol 209626. Report Number** 2023N536270_00		
Assay passing rate	23 out of 32 analytical runs met the predefined acceptance criteria	2023N536270_00, Table 2
Standard curve performance	Cumulative bias range: –2.50% to +4.00% Cumulative precision: ≤7.90%	2023N536270_00, Table 11
QC performance	Cumulative bias range: –12.0% to +1.33% Cumulative precision: ≤13.9%	2023N536270_00, Table 13
Method reproducibility	ISR was performed in 11% of clinical study samples analyzed using this method and 72.5% of samples met the pre-specified criteria.	2023N536270_00, Table 15
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All clinical study samples were stored frozen at –80°C on receipt.	

表 2.7.1.4.24 血漿中ベランタマブ　マホドチン分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2016N282271 The Validation of a method for the conjugated antibody (ADC) of GSK2857916 from 200 to 10 000 ng/mL in human plasma using chemiluminescent immunoassay (Method reference number: [redacted]) Report number 2019N412690_02 Validation and cross-validation of a chemiluminescent immunoassay for the quantitation of GSK2857916 (Antibody Drug Conjugate) in human K2EDTA Plasma (Method reference number: [redacted])	
Changes in method	None	
New validated assay range if any	500 to 5000 ng/mL for 2019N412690_02	
Validation parameters	Cross-validation performance	Source location
Cross-validation	A selection of samples from DREAMM-1 were grouped together to create 20 different pools across the concentration ranges of the assays. The calculated concentrations of 19 out of 20 pooled samples were within ±30% between the assays, showing that the 2 assays return results that are within acceptable equivalence.	2016N282271, Table 23 2019N412690_02, Appendix C, Table 5

表 2.7.1.4.25 血漿中ベランタマブ　マホドチン分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2021N468577_00, and 2021N468577_01 Validation of an ELISA assay for measuring GSK2857916 (ADC) in human plasma (K2EDTA) (Method reference number#: [redacted])		
Method description	Belantamab mafodotin was captured in human plasma using [redacted] and detected with a biotinylated [redacted] with streptavidin conjugated to an HRP reporter tag.		
Materials used for calibration curve and concentration	Belantamab mafodotin; 200 (anchor), 500, 750, 1000, 1750, 2500, 5000, and 10 000 ng/mL		
Validated assay range	500 to 10 000 ng/mL		
Material used for QCs and concentration	Belantamab mafodotin; 500 (LLOQ), 1500 (LQC), 3500 (MQC), 8000 (HQC), 10 000 (ULOQ) ng/mL		
Minimum required dilutions	100-fold in assay buffer		
Source and lot of reagents (LBA)	Belantamab mafodotin, GSK, Lot #No.: [redacted], [redacted], and [redacted], GSK, Lot #No.: 136414; Biotinylated [redacted], Lot no.: B06JUL2003; HRP Conjugated streptavidin, Thermo Fisher Scientific, Lot #No.: UB274936		
Regression model and weighting	Four parameter logistic – weighted 1/Y		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	7	2021N468577_00, Table 1
	Cumulative accuracy (%bias) from LLOQ to ULOQ	–2.1% to +3.2%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤4.0%	
QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	–14.2% to –5.3%	2021N468577_00, Table 3
	Inter-batch %CV	≤10.2%	
	TE	≤20.0%	
Selectivity and matrix effect	The selectivity of the method in normal human plasma was established by analyzing 10 lots of normal human plasma (gender balanced) as blank matrix as well as spiked with belantamab mafodotin at LLOQ and ULOQ. 10 out of 10 (100%) spiked samples met precision and accuracy criteria at the LLOQ, 9 out of 10 (90%) spiked samples met criteria at ULOQ, and all 10 unspiked samples were less than LLOQ. The data indicated there were no matrix effects in normal human plasma.		2021N468577_00, Table 6

Interference and specificity	The ability of the method to tolerate soluble BCMA in human plasma was evaluated by spiking BCMA at concentrations from 25 to 4000 ng/mL into human plasma as blank and containing belantamab mafodotin at LLOQ and ULOQ levels. A total of 2 lots of BCMA were tested, Lot# LC13NO1907 from Sino Biological and Lot# E10295-B1 from GSK. For both lots, no interference was observed at the LLOQ and ULOQ levels with soluble BCMA concentration ranging from 25 to 4000 ng/mL.	2021N468577_00, Table 9
Hemolysis effect	Five lots of hemolyzed matrix were prepared by spiking whole blood matrix into individual normal plasma matrix to get the desired percentage of hemolysis. The resultant 5 lots of hemolyzed human plasma were unspiked and spiked with belantamab mafodotin at LLOQ and ULOQ. At 2% Hemolyzed level, 5 out of 5 (100%) unspiked samples generated a result less than the LLOQ, 5 out of 5 (100%) spiked samples met precision and accuracy criteria at the ULOQ, and 1 out of 5 spiked (20%) samples met criteria at the LLOQ. At 0.5% Hemolyzed level, 5 out of 5 (100%) unspiked samples generated a result less than the LLOQ, 5 out of 5 (100%) spiked samples met criteria at the ULOQ, and 5 out of 5 (100%) spiked samples met criteria at the LLOQ. The data indicates there were no matrix effects in 0.5% hemolyzed human plasma.	2021N468577_00, Table 7-2
Lipemic effect	Five lots of lipemic plasma were tested blank and spiked with belantamab mafodotin at LLOQ and ULOQ. 5 out of 5 (100%) unspiked samples generated a result less than the LLOQ, 5 out of 5 (100%) spiked samples met precision and accuracy criteria at the LLOQ, and 4 out of 5 (80%) spiked samples met criteria at the ULOQ. The data indicates there were no matrix effects in Lipemic Human Plasma.	2021N468577_00, Table 7-1
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 500 000 ng/mL belantamab mafodotin from 10- to 2500-fold. All replicates of the 500 000 ng/mL belantamab mafodotin sample undiluted and diluted by 10-fold were tested greater than ULOQ, and samples diluted by 2500-fold were tested less than LLOQ. The precision and accuracy of all the 50- to 1000-fold diluted samples met the predefined acceptance criteria. Dilution linearity was considered acceptable, and no hook effect was observed at or below 500 000 ng/mL belantamab mafodotin in human plasma.	2021N468577_00, Table 8 and Figure 2
Ambient temperature stability	The stability of belantamab mafodotin in human plasma stored at ambient temperature for 25 hours 40 minutes was established at the LQC and the HQC of the assay.	2021N468577_00, Table 12
Refrigerator stability	The stability of belantamab mafodotin in human plasma stored at 2°C to 8°C for 69 hours 15 minutes was established at the LQC and the HQC of the assay.	2021N468577_00, Table 13

Freeze-thaw stability	The stability of belantamab mafodotin in human plasma after 6 freeze-thaw cycles from –60°C to –80°C to room temperature and from –10°C to –30°C to room temperature was established at the LQC and the HQC of the assay.	2021N468577_00, Table 11
Long-term storage	The stability of belantamab mafodotin in human plasma stored at –10°C to –30°C for 492 days and at –60°C to –80°C for 736 days was established at the LQC and the HQC of the assay.	2021N468577_01, Table 11 and 12
Whole blood stability	The stability of belantamab mafodotin in human blood was established for 2 hours 2 min at ambient temperature and 2 hours 1 min on wet ice at the LQC and the HQC of the assay.	2021N468577_01, Table 8
Parallelism	Not applicable	
Carry over	Not applicable	
Method Performance in DREAMM-3 **Interim Bioanalytical Report: Determination of GSK2857916 (ADC) in Human Plasma Samples from Clinical Study 207495. Report Number 2022N524960_00**		
Assay passing rate	12 out of 16 analytical runs met the predefined acceptance criteria (including ISR)	2022N524960_00, Table 1
Standard curve performance	Cumulative bias range: –1.3% to +1.6% Cumulative precision: ≤3.7%CV	2022N524960_00, Table 2
QC performance	Cumulative bias range: –11.4% to –6.0% Cumulative precision: ≤12.7%CV TE: not reported	2022N524960_00, Table 5
Method reproducibility	ISR was performed in 11.0% of clinical study samples analyzed using this method and 76.5% of samples met the pre-specified criteria.	2022N524960_00, Table 8
Clinical study sample analysis/stability	Calibration standards and QCs were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C on receipt.	
Method Performance in DREAMM-7 **Interim Bioanalytical Report: Determination of GSK2857916 (ADC) in Human Plasma Samples Using Chemiluminescence Assay From Clinical Study 207503. Report Number 2023N539630_00**		
Assay passing rate	15 out of 15 analytical runs met the predefined acceptance criteria. (including ISR)	2023N539630_00, Table 1
Standard curve performance	Cumulative bias range: –2.8% to 1.1% Cumulative precision: ≤3.9%CV	2023N539630_00, Table 2
QC performance	Cumulative bias range: –5.1% to –2.2% Cumulative precision: ≤8.1%CV TE: not reported	2023N539630_00, Table 4
Method reproducibility	ISR was performed in 8.3% of clinical study samples analyzed using this method and 100% of samples met the pre-specified criteria. ISR is ongoing, and the updated ISR result will be reported in the final bioanalytical report.	2023N539630_00, Table 7
Clinical study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C on receipt.	
Method Performance in DREAMM-8 **Interim Bioanalytical Report: Determination of GSK2857916 (ADC) in Human Plasma Samples Using ELISA From Clinical Study 207499. Report Number: 2024N549478_00**		
Assay passing rate	4 out of 4 analytical runs met the predefined acceptance criteria.	2024N549478_00, Table 1
Standard curve performance	Cumulative bias range: –1.7% to +1.4% Cumulative precision: ≤1.5%CV	2024N549478_00, Table 2

QC performance	Cumulative bias range: –6.3% to –5.0% Cumulative precision: ≤2.7%CV TE: not reported	2024N549478_00, Table 4
Method reproducibility	ISR has not been performed and will be reported in future reports.	NA
Clinical study sample analysis/stability	Calibration standards were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C on receipt. QC samples were stored frozen at –60°C to –80°C.	

表 2.7.1.4.26 血漿中ベランタマブ　マホドチン分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2019N412690_02 Validation and cross-validation of a chemiluminescent immunoassay for the quantitation of GSK2857916 (Antibody Drug Conjugate) in human K2EDTA plasma Report number 2021N468577_00 Validation of an ELISA assay for measuring GSK2857916 (ADC) in human plasma (K2EDTA)	
Changes in method	None	
New validated assay range if any	500 to 5000 ng/mL for 2019N412690_02	
Validation parameters	Cross-validation performance	Source location
Cross-validation	A selection of samples from DREAMM-1 were grouped together to create 20 different pools across the concentration ranges of the assays. The calculated concentrations of 19 out of 20 pooled samples were within ±30% of the mean, showing that the 2 assays return results that are within acceptable equivalence.	2019N412690_02, Table H.10 2021N468577_00, Table 10

表 2.7.1.4.27 血漿中ベランタマブ　マホドチン分析法性能の要約

（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2022N515388 The full validation of a method for the determination of GSK2857916 conjugated antibody (range 20.0 to 2000 ng/mL) in human plasma using an electrochemiluminescence immunoassay Method reference number: [redacted]		
Method description	Belantamab mafodotin was captured in human plasma using [redacted] and detected with a ruthenylated [redacted]		
Materials used for calibration curve and concentration	Belantamab mafodotin; 20.0, 50.0, 100, 250, 500, 1000, 1800, and 2000 ng/mL		
Validated assay range	20.0 to 2000 ng/mL		
Material used for QCs and concentration	Belantamab mafodotin; 20.0, 60.0, 200, 1600, 2000 ng/mL		
Minimum required dilutions	100-fold		
Source and lot of reagents (LBA)	GSK2857916, SAFC, batch [redacted] GSK2857914, SAFC, batch FG9K-AA-R [redacted], [redacted], batch PR210931A Biotinylated [redacted], GSK, batch ELX14203-A1 Ruthenylated [redacted], GSK, batch ELX14668-A1		
Regression model and weighting	4-parameter logistic-Marquardt (1/Y2)		
Validation parameters			Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2022N515388 Table 2
	Cumulative accuracy (%bias) from LLOQ to ULOQ	–1.50% to –6.00%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤12.46%	
QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	–3.50% to 7.83%	2022N515388 Table 5
	Inter-batch %CV	≤8.85%	
	TE	≤13.81%	
Selectivity and matrix effect	The selectivity of the method in human plasma was established by analyzing 10 lots of normal human plasma as blank matrix as well as spiked with belantamab mafodotin at LLOQ and HQC. 10 out of 10 spiked samples met precision and accuracy criteria at the LLOQ, 10 out of 10 (100%) spiked samples met criteria at HQC, and all 10 unspiked samples were less than LLOQ. The data indicated there were no matrix effects in multiple myeloma human plasma.		2022N515388 Table 7
	The selectivity of the method in multiple myeloma human plasma was established by analyzing 10 lots of normal multiple myeloma plasma as blank matrix as well as spiked with belantamab mafodotin at LLOQ and HQC. 9 out of 10 spiked samples met precision and accuracy criteria at the LLOQ, 10 out of 10 (100%) spiked samples met criteria at HQC, and 9 out of 10 unspiked samples were less than LLOQ. The data indicated there were no matrix effects in multiple myeloma human plasma.		2022N515388 Table 8

Interference and specificity	The ability of the method to tolerate soluble BCMA in human plasma was evaluated by spiking BCMA at concentrations up to 2000 ng/mL into human plasma containing belantamab mafodotin at LQC and HQC levels. Suitability demonstrated up to 1500 ng/mL of circulating BCMA with no dilution of the sample and up to 2000 ng/mL with a 2-fold dilution of the sample.	2022N515388 Table 11 and 12
	The ability of the method to tolerate circulating ADA in human plasma was evaluated by spiking the surrogate ADA positive control at concentrations up to 10 000 ng/mL into human plasma containing belantamab mafodotin at LQC and HQC levels. Suitability demonstrated up to 10 ng/mL of circulating ADA at the LQC and up to 1000 ng/mL at the HQC.	2022N515388 Table 13
	The ability of the method to specifically quantify conjugated drug GSK2857916 in the presence of unconjugated drug GSK2857914 was tested. The method does not quantify unconjugated drug, GSK2857914.	2022N515388 Table 15
	The ability of the method to specifically quantify conjugated drug GSK2857916 in the presence of [redacted] and [redacted]. The method is specific for GSK2857916.	2022N515388 Table 14
Hemolysis effect	Acceptable in 1 lot of 2% hemolysed human plasma	2022N515388 Table 9
Lipemic effect	Suitability demonstrated to ≤300 mg/dL triglycerides	2022N515388 Table 10
Dilution linearity and hook effect	No hook affect effect observed up to 500 µg/mL and dilution linearity confirmed to the LQC.	2022N515388 Table 16
Bench-top/process stability	24 hours at ambient temperature after storage at –70°C 24 hours at ambient temperature after storage at –20°C 24 hours at ambient temperature after storage at –70°C in the presence of co-medications ([redacted] and [redacted]) 24 hours at 4°C and at ambient temperature for processed samples (MRD dilution)	2022N515388 Table 17, 18, 19, 20
Freeze-thaw stability	5 cycles from nominally –70°C to ambient temperature 5 cycles from nominally –20°C to ambient temperature 5 cycles from nominally –70°C to ambient temperature in the presence of co-Medications ([redacted] and [redacted])	2022N515388 Table 21, 22, 23
Long-term storage	204 days at nominally –20°C 412 days at nominally –70°C 140 days at nominally –70°C in the presence of co-medications ([redacted] and [redacted])	2022N515388 Table 24, 25, 26, 27, 28, 29, 30
Parallelism	Not applicable	
Carry over	Not applicable	
Method Performance in DREAMM-14 **Bioanalytical Report: Bioanalytical Study Data for the Determination of Conjugated GSK2857916 in Human Plasma in Study 209628** **Report Number: 2023N538105_01**		
Assay passing rate	27 out of 31 analytical runs met the predefined acceptance criteria	2023N538105 Table 1
Standard curve performance	Cumulative bias range: –0.90% to +2.40% Cumulative precision: ≤5.80%	2023N538105 Table 2
QC performance	Cumulative bias range: –1.00% to +1.33% Cumulative precision: ≤7.73%	2023N538105 Table 4
Method reproducibility	ISR was performed in 10.2% of clinical study samples analyzed using this method and 100.0% of samples met the pre-specified criteria.	2023N538105 Table 7
Clinical study sample analysis/ stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All clinical study samples were stored frozen at –70°C on receipt.	

表 2.7.1.4.28 血漿中ベランタマブ　マホドチン分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2022N515388 ([redacted]) Report number 2019N412690 ([redacted])	
Changes in method	Validated Range of [redacted] (500 - 5000 ng/mL) and validated range of [redacted] (20.0 - 2000 ng/mL)	
New validated assay range if any	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	35/35 samples were within ±30% between methods [redacted] and [redacted]	2022N515388 Table 34, 35, 36

ヒト涙液中ベランタマブ　マホドチン分析法

表 2.7.1.4.29 涙液中ベランタマブ　マホドチン分析法性能の要約

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2021N491769_00 The validation of a qualitative assay for the determination of the presence/absence of GSK2857916 ADC in human tear fluid using a Gyrolab immunoassay (Method reference number: [redacted])	
Method description	Belantamab mafodotin was captured with [redacted] and detected using [redacted]	
Materials used for calibration curve and concentration	Belantamab mafodotin Limit of detection calibrator at 50 ng/mL	
Validated assay range	Qualitive assay with limit of detection calibrator at 50 ng/mL	
Material used for QCs and concentration	Belantamab mafodotin Positive control at 150 ng/mL	
Minimum required dilutions	10 fold in assay buffer	
Source and lot of reagents (LBA)	Belantamab mafodotin, GSK, Lot no.: [redacted] Biotinylated [redacted], GSK, batch #110032-153 Alexa [redacted], GSK, batch 110032-111	
Regression model and weighting	NA – qualitative assay	
Validation parameters	Method validation summary	Source location
Calibration curve performance during accuracy and precision	NA	2021N491769_00
QCs performance during accuracy and precision	NA	
Selectivity and matrix effect	Acceptable in 6 lots of individual control human tears	2021N491769_00 Table 4
Interference and specificity	NA	
Hemolysis effect	NA	
Lipemic effect	NA	
Dilution linearity and hook effect	NA	
Bench-top/process stability	6 hours on wet ice	2021N491769_00 Table 5
Freeze-thaw stability	2 cycles from –80°C to ambient temperature	2021N491769_00 Table 5
Long-term storage	365 days at nominally –80°C (on spear) 363 days at nominally –80°C (extract)	2021N491769_00 Table 10
Parallelism	NA	
Carry over	NA	

Method performance in DREAMM-12 **Bioanalytical Report: Bioanalytical Study Data for the Qualitative Determination of GSK2857916 antibody drug conjugate (ADC) in Human Tear Fluid** **Report number: 2022N522945_00**		
Assay passing rate	5 out of 5 (100%)	2022N522945_00 Table 1
Standard curve performance	NA – Limit of detection calibrator response values	2022N522945_00 Table 2
QC performance	NA – Negative control and positive control response values	2022N522945_00 Table 3 and Table 4
Method reproducibility	Incurred sample re-analysis was not performed	NA
Clinical study sample analysis/ stability	On spear: 2 cycles from –80°C to ambient plus 6 hours on wet ice 365 days nominally at –80°C Extracted sample: 2 cycles from –80°C to ambient plus 6 hours on wet ice 363 days nominally at –80°C	

ヒト血漿中総 mAb 分析法

表 2.7.1.4.30 血漿中総 mAb 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2019N396866_02 Validation and cross-validation of a chemiluminescent immunoassay for the quantitation of GSK2857916 (total antibody) in human K2EDTA plasma (Method reference number: [redacted]		
Method description	Total mAb was captured in human plasma using [redacted] and detected through [redacted] conjugated to an HRP reporter tag.		
Materials used for calibration curve and concentration	Belantamab mafodotin; 200 (anchor), 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL		
Validated assay range	500 to 10 000 ng/mL		
Material used for QCs and concentration	Belantamab mafodotin; 500, 1500, 3500, 8000, 10 000 ng/mL		
Minimum required dilutions	33.3-fold in assay buffer		
Source and lot of reagents (LBA)	Belantamab mafodotin, GSK, Lot no.: [redacted] ([redacted]) and [redacted] ([redacted]) Recombinant [redacted], BioRad, Lot no.: 10 and 15 HRP-labeled [redacted], Molecular probes, Lot no.: 1708571 and 2031436		
Regression model and weighting	Four parameter - weighted 1/x		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	7	2019N396866_02, Table 3
	Cumulative accuracy (%bias) from LLOQ to ULOQ	–0.8% to +1.0%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤2.84%	
QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	–4.40% to –3.03%	2019N396866_02, Table 7
	Inter-batch %CV	≤6.73%	
	TE	≤11.1%	
Selectivity and matrix effect	The selectivity of the method in normal human plasma and in plasma from multiple myeloma patients was established by analyzing 10 individual donor lots of plasma for each plasma type unspiked or spiked at 500 ng/mL (LLOQ) Belantamab mafodotin. The accuracy in 10/10 normal plasma and 9/10 multiple myeloma plasma lots spiked at LLOQ met the acceptance criteria. Unspiked samples were all measured less than LLOQ.		2019N396866_02, Table 14 and 15

Interference and specificity	The ability of the method to tolerate sBCMA in human plasma was evaluated by spiking sBCMA at 25 to 1000 ng/mL into human plasma containing 1500 (LQC) and 8000 (HQC) ng/mL belantamab mafodotin. The precision and accuracy under the conditions tested was <20% at sBCMA concentrations up to 100 ng/mL. The precision and accuracy of belantamab mafodotin samples containing up to 500 ng/mL sBCMA was <20% following dilution of 2-fold. The precision and accuracy of belantamab mafodotin samples containing up to 1000 ng/mL sBCMA was <20% following dilution of 5- to 10-fold. These data indicate that the method can accurately quantitate total mAb in the presence of up to 100 ng/mL sBCMA, up to 500 ng/mL sBCMA following 2-fold dilution or up to 1000 ng/mL sBCMA following 5- to 10-fold dilution. Sample dilutions and concentrations of sBCMA were reviewed prior to assessing the acceptability of the total mAb concentrations.	2019N396866_02, Table 11 to 13
Hemolysis effect	Ten lots of hemolyzed human plasma were spiked with 500 ng/mL belantamab mafodotin. Hemolyzed plasma did not meet the acceptance criteria. Hence, hemolyzed samples were not analyzed and marked as 'Not Reportable'.	2019N396866_02, Table 16 to 18
Lipemic effect	Five lots of lipemic plasma were spiked with 500 ng/mL belantamab mafodotin. The accuracy under the conditions tested was <20%.	2019N396866_02, Table19
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 1 000 000 ng/mL belantamab mafodotin from 8- to 8192-fold. All replicates of the 1 000 000 ng/mL belantamab mafodotin sample diluted 8- to 64-fold were greater than ULOQ and samples diluted 2048- to 8192-fold were less than LLOQ. The precision and accuracy of all the 128- to 1024-fold diluted samples was <20%. Dilution linearity was considered acceptable, and no hook effect was observed at or below 1 000 000 ng/mL belantamab mafodotin in human plasma.	2019N396866_02, Table 20
Bench-top/process stability	The stability of total mAb at 1500 and 3500 ng/mL was assessed in human whole blood stored on ice for 2 hours or at ambient temperature for 4 hours, prior to processing to plasma. All samples were within 20% of similarly spiked samples in which the blood was processed to plasma immediately. The stability of total mAb in human plasma stored at ambient temperature for 18 hours was assessed at 1500 and 8000 ng/mL. The precision and accuracy for the stored samples was <20%.	2019N396866_02, Table 21 and 25
Freeze-thaw stability	The stability of total mAb in human plasma after 8 freeze-thaw cycles from –80°C to room temperature was assessed at 1500 and 8000 ng/mL. The precision and accuracy under the conditions tested was <20%.	2019N396866_02, Table 22
Long-term storage	The stability of total mAb in human plasma stored at –20°C for 734 days and at –80°C for 1144 days was assessed at 1500 and 8000 ng/mL. The precision and accuracy under the conditions tested was <20%.	2019N396866_02, Table 23, Table 24, F.6, F.7, G.5, and G.6
Parallelism	Five samples at near Cmax from DREAMM-2 were diluted at 4 different dilution factors. Eighty percent or more of the samples tested had results within 30% of each other.	2018N390896_01, Appendix E
Carry over	Not applicable	
Method Performance in DREAMM-2 Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples. Report Number 2018N390896		
Assay passing rate	125/141 analytical runs met the predefined acceptance criteria.	2018N390896_2, Table 1 and Table 26

Standard curve performance	For sample analysis runs from 17 December 2018 to 17 July 2019 (until interim bioanalytical report 2018N390896_01): Cumulative bias range: –1.2% to +0.6% Cumulative precision: ≤5.5%CV For sample analysis runs from 15 August 2019 to 25 March 2022 (additional runs reported in 2018N390896_02): Cumulative bias range: –1.73% to +1.00% Cumulative precision: ≤2.96%CV	2018N390896_2, Table 10 and Table 35
QC performance	For sample analysis runs from 17 December 2018 to 17 July 2019 (until interim bioanalytical report 2018N390896_01): Cumulative bias range: –4.6% to –0.4% Cumulative precision: ≤11.3%CV TE: not reported For sample analysis runs from 15 August 2019 to 25 March 2022 (additional runs reported in 2018N390896_02): Cumulative bias range: –5.38% to –0.667% Cumulative precision: ≤9.31%CV TE: not reported	2018N390896_2, Table 12 and Table 37
Method reproducibility	ISR was performed in 12.2% of study samples analyzed using this method and 87.1% of samples met the pre-specified criteria.	2018N390896_2, Section 4.4
Study sample analysis/stability	Calibration standards were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt. QC samples were stored frozen at –80°C.	
Method Performance in DREAMM-3 **Interim Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207495. Report Number 2022N524971_00**		
Assay passing rate	108 out of 119 analytical runs met the predefined acceptance criteria	2022N524971_00, Table 1
Standard curve performance	Cumulative bias range: –0.600% to 0.00% Cumulative precision: ≤3.04%CV	2022N524971_00, Table 10
QC performance	Cumulative bias range: –5.38% to –1.75% Cumulative precision: ≤9.29 %CV TE: not reported	2022N524971_00, Table 12
Method reproducibility	ISR was performed in 7.6% of study samples analyzed using this method and 78.8% of samples met the pre-specified criteria.	2022N524971_00, Table 14
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-6 **Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207497. Report Number 2023N536470_00**		
Assay passing rate	116 out of 119 analytical runs met the predefined acceptance criteria	2023N536470_00, Table 1
Standard curve performance	Cumulative bias range: –0.800% to +1.00% Cumulative precision: ≤3.57%CV	2023N536470_00, Table 12
QC performance	Cumulative bias range: –4.75% to +6.00% Cumulative precision: ≤13.2%CV	2023N536470_00, Table 15
Method reproducibility	ISR was performed in 7.9% of study samples analyzed using this method and 90% of samples met the pre-specified criteria.	2023N536470_00, Table 18
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-7 **Interim Bioanalytical Report: Determination of GSK2857916 (Total mAb) and GSK2857916 (Conjugated Drug [ADC]) in Human K2EDTA Plasma Samples from Protocol 207503. Report Number: 2023N539579_01**		
Assay passing rate	154 out of 168 analytical runs met the predefined acceptance criteria	2023N539579_01, Table 1

Standard curve performance	Cumulative bias range: –0.400% to +0.200% Cumulative precision: ≤3.35%CV	2023N539579_01, Table 10
QC performance	Cumulative bias range: –6.00% to +1.88% Cumulative precision: ≤53.5%CV TE: not reported	2023N539579_01, Table 12
Method reproducibility	ISR was performed in 7.1% of study samples analyzed using this method and 76.5% of samples met the pre-specified criteria.	2023N539579_01, Table 14
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-11 **Final Bioanalytical Report: Determination of GSK2857916 in Human K2EDTA Plasma Samples from Protocol 207504. Report Number** 2023N533324_00		
Assay passing rate	10 out of 10 analytical runs met the predefined acceptance criteria	2023N533324_00, Table 1
Standard curve performance	Cumulative bias range: –1.20% to +1.00% Cumulative precision: ≤2.99%CV	2023N533324_00, Table 9
QC performance	Cumulative bias range: –5.75% to –1.00% Cumulative precision: ≤8.99%CV	2023N533324_00, Table 12
Method reproducibility	ISR was performed in 52.1% of study samples analyzed using this method and 98.0% of samples met the pre-specified criteria.	2023N533324_00, Table 15
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt.	
Method Performance in DREAMM-12 **Interim Bioanalytical Report: Determination of GSK2857916 (Total mAb) and GSK2857916 (Conjugated Drug [ADC]) in Human K2EDTA Plasma Samples from Protocol 209626. Report Number** 2023N536270_00		
Assay passing rate	21 out of 21 analytical runs met the predefined acceptance criteria	2023N536270_00, Table 1
Standard curve performance	Cumulative bias range: –1.40% to +1.00% Cumulative precision: ≤2.89%CV	2023N536270_00, Table 10
QC performance	Cumulative bias range: –6.88% to –2.00% Cumulative precision: ≤13.0%CV	2023N536270_00, Table 12
Method reproducibility	ISR was performed in 11% of study samples analyzed using this method and 88.1% of samples met the pre-specified criteria.	2023N536270_00, Table 14
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –80°C) and used within established stability. All study samples were stored frozen at –80°C on receipt.	

表 2.7.1.4.31 血漿中総 mAb 分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2015N243565 The Validation of a method for the monoclonal antibody of GSK2857916 from 200 to 10 000 ng/mL in human plasma using chemiluminescent Immunoassay (Method reference number: [redacted]) Report number 2019N396866_02 Validation and cross-validation of a chemiluminescent immunoassay for the quantitation of GSK2857916 (total antibody) in human K2EDTA plasma (Method reference number: [redacted])	
Changes in method	None	
New validated assay range if any	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	A selection of samples from DREAMM-1 were grouped together to create 20 different pools across the concentration ranges of the assays. The calculated concentrations of 15 out of 20 pooled samples were within ±30% of the mean, showing that the 2 assays return results that are within acceptable equivalence.	2015N243565, Table 18 and 2019N396866_01, Appendix D, Table 5

表 2.7.1.4.32 血漿中総 mAb 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments and hyperlink	Report number 2021N468428_00 and 2021N468428_01 Validation of an ELISA assay for measuring GSK2857916 (total antibody) in human plasma (K2EDTA) (Method reference number#: [redacted])		
Method description	Total mAb was captured in human plasma using [redacted] and detected through [redacted] conjugated to an HRP reporter tag.		
Materials used for calibration curve and concentration	Belantamab mafodotin; 200 (anchor), 500, 750, 1000, 1750, 2500, 5000, 10 000 ng/mL		
Validated assay range	500 to 10 000 ng/mL		
Material used for QCs and concentration	Belantamab mafodotin; 500 (LLOQ), 1500 (LQC), 3500 (MQC), 8000 (HQC), 10 000 ng/mL (ULOQ)		
Minimum required dilutions	33-fold in assay buffer		
Source and lot of reagents (LBA)	Belantamab mafodotin, GSK, Lot no.: [redacted], [redacted], and [redacted], BioRad, Lot no.: 39 [redacted], Thermo Fisher, Lot no.: 1917176		
Regression model and weighting	Four parameter - weighted 1/Y		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	7	2021N468428_00, Table 1
	Cumulative accuracy (%bias) from LLOQ to ULOQ	–1.3% to +2.3%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤1.9%	
QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	–9.5% to +2.0%	2021N468428_00, Table 3
	Inter-batch %CV	≤7.6%	
	TE	≤17.1%	
Selectivity and matrix effect	The selectivity of the method in normal human plasma was established by analyzing 10 lots of normal human plasma (gender balanced) as blank matrix as well as spiked with belantamab mafodotin at LLOQ and ULOQ. 10 out of 10 (100%) spiked samples met precision and accuracy criteria at LLOQ and ULOQ, and all 10 unspiked samples were less than LLOQ. The data indicated there were no matrix effects in normal human plasma.		2021N468428_00, Table 6
Interference and specificity	The ability of the method to tolerate soluble BCMA in human plasma was evaluated by spiking BCMA at concentrations from 25 to 4000 ng/mL into human plasma as blank and containing belantamab mafodotin at LLOQ and ULOQ levels. A total of 2 lots of BCMA were tested, Lot# LC13NO1907 from Sino Biological and Lot# E10295-B1 from GSK. For Lot# LC13NO1907, no interference was observed at the LLOQ level with up to 500 ng/mL of soluble BCMA, no interference was observed at the ULOQ level with up to 2000 ng/mL of soluble BCMA. For Lot# E10295-B1, no interference was observed at the LLOQ and ULOQ levels with up to 2000 ng/mL of soluble BCMA.		2021N468428_00, Table 9

Hemolysis effect	Five lots of hemolyzed matrix were prepared by spiking whole blood matrix into individual normal plasma matrix to get the desired percentage of hemolysis. The resultant 5 lots of hemolyzed human plasma were tested blank and spiked with belantamab mafodotin at LLOQ and ULOQ. At 2% Hemolyzed) level, 0 out of 5 spiked samples met criteria at the LLOQ, 4 out of 5 spiked samples met criteria at the ULOQ, and 0 out of 5 unspiked samples generated a result less than the LLOQ. At 0.5% hemolyzed level, 5 out of 5 (100%) spiked samples met acceptance criteria at the LLOQ, 4 out of 5 (80%) spiked samples met criteria at the ULOQ, and all 5 unspiked samples generated a result less than the LLOQ. The data indicates there were no matrix effects in 0.5% hemolyzed human plasma.	2021N468428_00, Table 7-2
Lipemic effect	Five lots of lipemic plasma were tested blank and spiked with belantamab mafodotin at LLOQ and ULOQ. Five out of 5 (100%) unspiked samples generated a result less than the LLOQ, 4 out of 5 (80%) spiked samples met acceptance criteria at the LLOQ, and 5 out of 5 (100%) spiked samples met criteria at the ULOQ. The data indicates there were no matrix effects in Lipemic Human Plasma.	2021N468428_00, Table 7-1
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 500 000 ng/mL belantamab mafodotin from 10- to 2500-fold. All replicates of the 500 000 ng/mL belantamab mafodotin sample undiluted and diluted by 10-fold were tested greater than ULOQ, and samples diluted by 2500-fold were tested less than LLOQ. The precision and accuracy of all the 50- to 1000-fold diluted samples met the predefined acceptance criteria. Dilution linearity was considered acceptable, and no hook effect was observed at or below 500 000 ng/mL belantamab mafodotin in human plasma.	2021N468428_00, Table 8 and Figure 2
Ambient temperature stability	The stability of belantamab mafodotin in human plasma stored at ambient temperature for up to 45 hours 58 minutes was established at the LQC and the HQC of the assay.	2021N468428_00, Table 12
Refrigerator stability	The stability of belantamab mafodotin in human plasma stored at 2°C to 8°C for 71 hours 54 minutes was established at the LQC and the HQC of the assay.	2021N468428_00, Table 13
Freeze-thaw stability	The stability of belantamab mafodotin in human plasma after 6 freeze-thaw cycles from –60°C to –80°C to room temperature and from –10°C to –30°C to room temperature was established at the LQC and the HQC of the assay.	2021N468428_00, Table 11
Long-term storage	The stability of belantamab mafodotin in human plasma stored at –10°C to –30°C for 502 days and at –60°C to –80°C for 776 days was established at the LQC and the HQC of the assay.	2021N468428_00, Table 14 and 2021N468428_01, Table 6-9
Whole blood stability	The stability of belantamab mafodotin in human blood was established for 2 hours at ambient temperature and on wet ice at the LQC and the HQC of the assay.	2021N468428_01, Table 4
Parallelism	Not applicable	
Carry over	Not applicable	

Method Performance in DREAMM-3 **Interim Bioanalytical Report: Determination of GSK2857916 (Total antibody) in Human Plasma Samples from Clinical Study 207495. Report Number 2022N524955_00**		
Assay passing rate	13 out of 13 analytical runs met the predefined acceptance criteria. (including ISR)	2022N524955_00, Table 1
Standard curve performance	Cumulative bias range: –0.7% to +1.7% Cumulative precision: ≤2.8%CV	2022N524955_00, Table 2
QC performance	Cumulative bias range: –5.4% to –1.8% Cumulative precision: ≤7.8%CV TE: not reported	2022N524955_00, Table 4
Method reproducibility	ISR was performed in 11.0% of study samples analyzed using this method and 100% of samples met the pre-specified criteria.	2022N524955_00, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All study samples were stored frozen at –60°C to –80°C on receipt.	
Method Performance in DREAMM-7 **Interim Bioanalytical Report: Determination of GSK2857916 (Total antibody) in Human Plasma Samples Using ELISA From Clinical Study 207503. Report Number 2023N539561_00**		
Assay passing rate	18 out of 19 analytical runs met the predefined acceptance criteria. (including ISR)	2023N539561_00, Table 1
Standard curve performance	Cumulative bias range: –1.2 to +1.1% Cumulative precision: ≤3.7%CV	2023N539561_00, Table 2
QC performance	Cumulative bias range: –1.1 to +6.6% Cumulative precision: ≤35.1%CV TE: not reported	2023N539561_00, Table 4
Method reproducibility	ISR was performed in 8.3% of study samples analyzed using this method and 100% of samples met the pre-specified criteria. ISR testing is ongoing, and updated ISR results will be presented in the final bioanalytical report.	2023N539561_00, Table 8
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All study samples were stored frozen at –60°C to –80°C on receipt.	

表 2.7.1.4.33 血漿中総 mAb 分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2021N468428_00 Validation of an ELISA assay for measuring GSK2857916 (total antibody) in human plasma (K2EDTA)	
Changes in method	None	
New validated assay range if any	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	A selection of samples from DREAMM-1 were grouped together to create 20 different pools across the concentration ranges of the assays. The calculated concentrations of all 20 pooled samples were within ±30% of the mean, showing that the 2 assays return results that are within acceptable equivalence.	2021N468428_00, Table 10

ヒト血漿中 cys-mcMMAF 分析法

表 2.7.1.4.34 血漿中 cys-mcMMAF 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments and hyperlink	Report number 2019N411691_03 The full validation of a method for the determination of cys-mcMMAF in human plasma (range 50 to 10 000 pg/mL) using protein precipitation and UHPLC-MS/MS (Method reference number: [redacted])		
Method description	Cys-mcMMAF was extracted from 50 µL human plasma by protein precipitation using [$^{15}N^{13}C_3D_3$]-cys-mcMMAF as an internal standard. Extracts were analyzed by UHPLC-MS/MS using an electrospray interface and multiple reaction monitoring.		
Materials used for calibration curve and concentration	Cys-mcMMAF; 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL		
Validated assay range	50 to 10 000 pg/mL		
Material used for QCs and concentration	Cys-mcMMAF; 50, 150, 500, 8000, 10 000 pg/mL		
Minimum required dilutions	Not applicable		
Source and lot of reagents (LBA)	Not applicable		
Regression model and weighting	Linear - weighted $1/x^2$		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2019N411691_03, Table 2
	Cumulative accuracy (%bias) from LLOQ to ULOQ	–2.4% to +2.3%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤5.1%	
QCs performance during accuracy and precision	Cumulative accuracy (%bias) in 5 QCs	+1.0% to +3.2%	2019N411691_03, Table 3
	Inter-batch %CV	≤3.5%	
	TE	Not applicable	
QCs performance during accuracy and precision in the presence of belantamab mafodotin	Cumulative accuracy (%bias) in 3 QCs In the presence of 25 µg/mL belantamab mafodotin In the presence of 75 µg/mL belantamab mafodotin In the presence of 150 µg/mL belantamab mafodotin	–2.0% to +4.1% –1.3% to +8.4% 0.0% to +5.9%	2019N411691_03, Table 24 to Table 26
	Inter-batch %CV in 3 QCs In the presence of 25 µg/mL belantamab mafodotin In the presence of 75 µg/mL belantamab mafodotin In the presence of 150 µg/mL belantamab mafodotin	 ≤4.5% ≤3.2% ≤2.7%	2019N411691_03, Table 24 to Table 26
	TE	Not applicable	
Selectivity and matrix effect	The selectivity of the method in control plasma was established by analyzing 12 individual donor lots of plasma. The precision and accuracy in 11/12 lots spiked at 150 and 8000 pg/mL was <15%.		2019N411691_03, Table 5 and Table 6

Interference and specificity	Interference of lenalidomide/dexamethasone (1800/1800 ng/mL) and bortezomib/dexamethasone (450/900 ng/mL) was assessed by spiking into blank plasma. The observed response was ≤20% of the LLOQ.	2019N411691_03, Section 4, Section 4.1.3
Hemolysis effect	Six replicates of 2% hemolyzed plasma were spiked with 150 pg/mL cys-mcMMAF. The precision and accuracy under the conditions tested was <15%.	2019N411691_03, Table 22
Lipemic effect	Six replicates of lipemic plasma were spiked with 150 pg/mL cys-mcMMAF. The precision and accuracy under the conditions tested was <15%.	2019N411691_03, Table 23
Dilution linearity and hook effect	Not assessed as dilutions were not expected during sample analysis	
Bench-top/process stability	The stability of cys-mcMMAF at 150 and 8000 pg/mL was assessed in human whole blood in the presence of nominally 150 µg/mL belantamab mafodotin. Samples were stored on wet ice for 2 hours, prior to processing to plasma. All samples were within 15% of similarly spiked samples in which the blood was processed to plasma immediately. The stability of cys-mcMMAF was assessed in human plasma in the presence and absence of nominally 150 µg/mL belantamab mafodotin. The cys-mcMMAF concentrations tested were 150 and 8000 pg/mL in the absence of belantamab mafodotin and 211 and 1066 pg/mL in the presence of belantamab mafodotin. Samples were stored on wet ice for 7 hours (which included 2 freeze-thaw cycles from –70°C to wet ice). The precision and accuracy for the stored samples in the presence and absence of belantamab mafodotin was <15%. The stability of cys-mcMMAF was assessed in extracted samples in the presence and absence of nominally 150 µg/mL belantamab mafodotin. The cys-mcMMAF concentrations tested were 50, 150, 500, 8000 and 10 000 pg/mL in the absence of belantamab mafodotin and 211 and 1066 pg/mL in the presence of belantamab mafodotin. Samples were stored at nominally +20°C for up to 3 days. The precision and accuracy for the extracted samples in the presence and absence of belantamab mafodotin was <15%.	2019N411691_03, Table 7, Table 8, Table 19, Table 20, Table 21
Freeze-thaw stability	The stability of cys-mcMMAF in human plasma after 8 freeze-thaw cycles from –20°C and –70°C to wet ice was assessed at 150 and 8000 pg/mL. The stability of cys-mcMMAF in human plasma in the presence of nominally 150 µg/mL belantamab mafodotin after 6 freeze-thaw cycles from –20°C to wet ice and after 8 freeze-thaw cycles from –70°C to wet ice was assessed at 211 and 1066 pg/mL. The precision and accuracy under the conditions tested was <15%.	2019N411691_03, Table 11 to Table 18
Long-term storage	The stability of cys-mcMMAF in human plasma stored at –20°C and –70°C for 407 days was assessed at 150 and 8000 pg/mL. The stability of cys-mcMMAF in human plasma in the presence of nominally 150 µg/mL belantamab mafodotin stored at –20°C was assessed for 229 days at ≥500 pg/mL cys-mcMMAF and for 84 days at 150 pg/mL cys-mcMMAF. The stability of cys-mcMMAF in human plasma in the presence of nominally 150 µg/mL belantamab mafodotin stored at –70°C was assessed for 367 days at nominal 200 pg/mL cys-mcMMAF and for 407 days at ≥1000 pg/mL cys-mcMMAF. Stability was assessed at –20°C at 150 pg/mL cys-mcMMAF for 217 days in the presence of 20, 40, and 60 µg/mL belantamab mafodotin and for 175 days in the presence of 80 µg/mL belantamab mafodotin. Stability was assessed at –20°C at 500 and 1000 pg/mL cys-mcMMAF for 217 days in the presence of 20, 40, 60, and 80 µg/mL belantamab mafodotin. Stability was assessed at –70°C at 150, 500 and 1000 pg/mL cys-mcMMAF for 566 days in presence of 20, 40, 60, and 80 µg/mL belantamab mafodotin. The precision and accuracy under the conditions tested was <15%.	2019N411691_03, Table 34 and Table 49 and Table 56 and 57, Table 64 to 70
Parallelism	Not applicable	
Carry over	Carry over was assessed on a per run basis and the impact was assessed	

Recovery	≥81.1%	2019N411691_03, Table 4
Method Performance in DREAMM-2 Within-Study Analytical Performance Data for the Determination of cys-mcMMAF in Human Plasma. Report Number 2022N505659_00		
Assay passing rate	26/30 analytical runs met the predefined acceptance criteria	2022N505659_00, Table 1
Standard curve performance	Cumulative bias range: –1.1% to +0.7% Cumulative precision: ≤5.9%CV	2022N505659_00, Table 3
QC performance	Cumulative bias range: –2.2% to –0.2% Cumulative precision: ≤6.6%CV TE: not applicable	2022N505659_00, Table 5
Method reproducibility	ISR was performed in 7.4% of study samples and >66.7% of samples met the pre-specified criteria.	2022N505659_00, Section 6.4.2
Study sample analysis/stability	Each batch of experimental samples was run against calibration standards freshly prepared or frozen within established stability. All study samples were stored frozen at –20°C or –70°C along with QC samples.	
Method Performance in DREAMM-6 Within-Study Analytical Performance Data for the Determination of cys-mcMMAF in Human Plasma. Report Number 2023N530064_00		
Assay passing rate	24/28 analytical runs met the predefined acceptance criteria	2023N530064_00, Table 1
Standard curve performance	Cumulative bias range: –1.9% to +4.0% Cumulative precision: ≤7.0%CV	2023N530064_00, Table 2 and Table 3
QC performance	Cumulative bias range: –3.3% to +3.0% Cumulative precision: ≤12.2%CV	2023N530064_00, Table 4 and Table 5
Method reproducibility	ISR was performed in 7.8% of study samples and >66.7% of samples met the pre-specified criteria.	2023N530064_00, Section 6.5
Study sample analysis/stability	Each batch of experimental samples was run against calibration standards freshly prepared or frozen within established stability. All study samples were stored frozen at –70°C along with QC samples.	

表 2.7.1.4.35 血漿中 cys-mcMMAF 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments and hyperlink	2022N519749_00, 2022N519749_01, and 2022N519749_02 Validation of an LC-MS/MS method for the quantitative bioanalysis of cys-mcMMAF in human plasma (Method reference number: [redacted])		
Method description	Cys-mcMMAF was extracted from 50 µL human plasma by protein precipitation using [$^{15}N^{13}C_3D_3$]-cys-mcMMAF or [D8]- cys-mcMMAF as an internal standard. Extracts were analyzed by UHPLC-MS/MS using an electrospray interface and multiple reaction monitoring.		
Materials used for calibration curve and concentration	Cys-mcMMAF; 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL		
Validated assay range	50 to 10 000 pg/mL		
Material used for QCs and concentration	Cys-mcMMAF; LLOQ-QC, 50.0 pg/mL; LQC, 150 pg/mL; MQC, 750 pg/mL; HQC, 7500 pg/mL		
Minimum required dilutions	Not applicable		
Regression model and weighting	Linear - weighted $1/x^2$		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2022N519749_00, Table 3
	Inter-batch accuracy (%bias) from LLOQ to ULOQ	–1.4% to +2.0%	
	Inter-batch precision (%CV) from LLOQ to ULOQ	≤7.8%	
QCs performance during accuracy and precision	Inter-batch accuracy (%bias) in 4 QCs	0.0% to +3.8%	2022N519749_00, Table 4
	Inter-batch %CV	≤8.5%	
Dilution integrity	Dilution integrity was demonstrated at 10-fold dilution.		2022N519749_00, Table 6
Selectivity	The selectivity of the method in normal human plasma was established by analyzing 6 individual donor lots of plasma as blank and spiked at the LLOQ level. The chromatographic regions of the analyte and the internal standard in 6 out of 6 lots of blank human plasma were free from significant interference. The %CV (precision) and %bias (accuracy) in all 6 lots spiked at LLOQ met the acceptance criteria.		2022N519749_00, Table 7
Matrix effect	To evaluate matrix effect, extracts of blank matrix from 6 different lots of human plasma were spiked with a standard solution containing the analyte and the internal standard each at concentrations equivalent to the LQC and HQC levels. No significant matrix effect for the analyte or the internal standard was observed in human plasma.		2022N519749_00, Table 11

Interference and specificity	Interference of co-administered medications was evaluated. Bortezomib, lenalidomide, pomalidomide, and dexamethasone were spiked at 500, 1000, 200, and 1000 ng/mL, respectively, in blank matrix and in matrix spiked with the analyte at LLOQ and HQC levels. The results showed that there was no impact on the quantification of cys-mcMMAF in the presence of bortezomib, lenalidomide, pomalidomide, and dexamethasone. Specificity of the internal standard, [$^{15}N^{13}C_3D_3$]-cys-mcMMAF, was demonstrated in blank matrix in the presence of up to 300 µg/mL of belantamab mafodotin as well as in the presence of co-administered medications (bortezomib, lenalidomide, pomalidomide, and dexamethasone spiked at 500, 1000, 200, and 1000 ng/mL, respectively).	2022N519749_00, Table 8 - 10
Hemolysis effect	The effect of hemolysis was assessed by spiking hemolyzed human whole blood at a final concentration of 2% into an LLOQ sample. The outcome indicated that hemolysis did not affect assay performance.	2022N519749_00, Table 13
Lipemic effect	Lipemic effect was assessed at LLOQ in lipemic plasma. The outcome indicated that there were no matrix effects in Lipemic Human Plasma.	2022N519749_00, Table 14
Dilution linearity and hook effect	Not assessed as dilutions were not expected during sample analysis	
Injection carry over	Carry over was tested by injecting at least 1 matrix blank sample immediately following the highest calibration standard. The chromatographic regions of the analyte and the internal standard in the matrix blank sample were free from significant interference, indicating no injection carry over was observed.	2022N519749_00, Figure 9
Recovery	The overall recovery of cys-mcMMAF and [$^{15}N^{13}C_3D_3$]-cys-mcMMAF was 93.9% and 111.1%, respectively, which was adequate to obtain precise and accurate determinations in the method-specified assay range.	2022N519749_00, Table 12
Working solution stability	The working standard solution of cys-mcMMAF was stable for at least 131 days following storage at –70°C.	2022N519749_00, Table 16
Whole blood stability	Analyte stability in human whole blood was demonstrated for 2 hours at room temperature or on wet ice, and for 2 hours on wet ice in the presence of up to 300 µg/mL of belantamab mafodotin.	2022N519749_00, Table 17
Processed sample stability	Processed samples at LQC and HQC levels were demonstrated to be stable at 4ºC for 72 hours. They were also shown to be stable for 48 hours at 4ºC in the presence of up to 300 µg/mL belantamab mafodotin and be stable for 72 hours at 4ºC in the presence of bortezomib, lenalidomide, pomalidomide and dexamethasone at 500, 1000, 200, 1000 ng/mL, respectively.	2022N519749_00, Table 20, 21, and 22

Bench-top stability	Benchtop stability of cys-mcMMAF in human plasma was assessed at LQC and HQC. The analyte was shown to be stable for at least 21 hours on wet ice, for at least 13 hours on wet ice in the presence of up to 300 µg/mL belantamab mafodotin, and for at least 13 hours on wet ice in the presence of bortezomib, lenalidomide, pomalidomide and dexamethasone at 500, 1000, 200, 1000 ng/mL, respectively.	2022N519749_00, Table 23, 24, 25, and 26
Freeze-thaw stability	The freeze/thaw stability of cys-mcMMAF in human plasma was established under these conditions: 1). Four freeze-thaw cycles for working standard solution from –70°C to wet ice. 2). Four freeze-thaw cycles for LQC and HQC from –70°C to wet ice. 3). Four freeze-thaw cycles for LQC and HQC from –70°C to wet ice in the presence of up to 300 µg/mL belantamab mafodotin. 4). Four freeze-thaw cycles for LQC and HQC from –70°C to wet ice in the presence of bortezomib, lenalidomide, pomalidomide and dexamethasone at 500, 1000, 200, 1000 ng/mL, respectively.	2022N519749_00, Table 27, 28, 29, and 30
Long-term storage	The long-term stability of cys-mcMMAF in human plasma was demonstrated for: 1) 795 days at –70ºC in the presence of up to 150 µg/mL belantamab mafodotin. 2) 470 days at –70°C in the presence of bortezomib, lenalidomide, pomalidomide and dexamethasone at 500, 1000, 200, 1000 ng/mL, respectively.	2022N519749_00, Table 31, 32, and 33; 2022N519749_01, Tables 3 and 4;2022N519749_02, Table 3
Parallelism	Not applicable	
Method Performance in DREAMM-3 **Interim Bioanalytical Report: Quantification of Cys-mcMMAF in Human Plasma Using LC-MS/MS for Clinical Study 207495. Report Number** 2022N525492_00		
Assay passing rate	35 out of 41 analytical runs met the predefined acceptance criteria	2022N525492_00, Table 1
Standard curve performance	Cumulative bias range: –2.0% to +0.2% Cumulative precision: ≤8.3%CV	2022N525492_00, Table 3
QC performance	Cumulative bias range: +4.7% to +6.7% Cumulative precision: ≤6.6%CV TE: not applicable	2022N525492_00, Table 4
Method reproducibility	ISR was performed in 4.8% of study samples and 75% of samples met the pre-specified criteria. ISR is ongoing and the updated ISR results will be presented in the final bioanalytical report.	2022N525492_00, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	
Method Performance in DREAMM-7 **Interim Bioanalytical Report: Quantification of Cys-mcMMAF in Human Plasma Using LC-MS/MS for Clinical Study 207503. Report Number** 2023N538470_01		
Assay passing rate	52 out 63 of analytical runs met the predefined acceptance criteria (including ISR)	2023N538470_01, Table 1
Standard curve performance	Cumulative bias range: –1.0% to 0.0% Cumulative precision: ≤7.2%CV	2023N538470_01, Table 3
QC performance	Cumulative bias range: +2.1% to +4.7% Cumulative precision: ≤22.7%CV TE: not applicable	2023N538470_01, Table 4

Method reproducibility	ISR was performed in 4.0% of study samples and 69.2% of samples met the pre-specified criteria. ISR is ongoing and the updated ISR results will be presented in the final bioanalytical report.	2023N538470_01, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	
Method Performance in DREAMM-8 **Interim Bioanalytical Report: Quantification of cys-mcMMAF in Human Plasma K2EDTA Using LC-MS/MS for Clinical Study 207499. Report Number: 2024N550649_01**		
Assay passing rate	36 out of 48 analytical runs met the predefined acceptance criteria	2024N550649_01, Table 1
Standard curve performance	Cumulative bias range: –0.8% to 1.5% Cumulative precision: ≤7.6%CV	2024N550649_01, Table 3
QC performance	Cumulative bias range: –4.0% to 2.7 % Cumulative precision: ≤7.5%CV	2024N550649_01, Table 4
Method reproducibility	ISR was performed in 8.6% of study samples and 82.7% of samples met the pre-specified criteria. ISR is ongoing and the updated ISR results will be presented in the final bioanalytical report.	2024N550649_01, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	
Method Performance in DREAMM-11 **Final Bioanalytical Report: Quantification of Cys-mcMMAF in Human Plasma Using LC-MS/MS for Clinical Study 207504. Report Number 2023N535795_00**		
Assay passing rate	8 out 10 of analytical runs met the predefined acceptance criteria (including ISR)	2023N535795_00, Table 1
Standard curve performance	Cumulative bias range: –1.0% to +1.0% Cumulative precision: ≤7.1%CV	2023N535795_00, Table 3
QC performance	Cumulative bias range: –4.0% to –0.1% Cumulative precision: ≤9.1%CV TE: not applicable	2023N535795_00, Table 4
Method reproducibility	ISR was performed in 16.7% of study samples and 78.6% of samples met the pre-specified criteria.	2023N535795_00, Table 6
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	
Method Performance in DREAMM-12 **Interim Bioanalytical Report: Quantification of Cys-mcMMAF in Human Plasma Using LC-MS/MS for Clinical Study 209626. Report Number 2023N535698_00**		
Assay passing rate	11 out 12 of analytical runs met the predefined acceptance criteria (including ISR)	2023N535698_00, Table 1
Standard curve performance	Cumulative bias range: –2.5% to +3.0% Cumulative precision: ≤8.7%CV	2023N535698_00, Table 3
QC performance	Cumulative bias range: +0.7% to +4.3% Cumulative precision: ≤6.9%CV TE: not applicable	2023N535698_00, Table 4
Method reproducibility	ISR was performed in 11% of study samples and 76.2% of samples met the pre-specified criteria.	2023N535698_00, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	
Method Performance in DREAMM-14 **Interim Bioanalytical Report: Quantification of Cys-mcMMAF in Human K2 EDTA Plasma Using LC-MS/MS for Clinical Study 209628. Report Number 2023N536676_00**		
Assay passing rate	19 out of 26 analytical runs met the predefined acceptance criteria (including ISR)	2023N536676_00, Table 1
Standard curve performance	Cumulative bias range: –1.4% to +1.0% Cumulative precision: ≤7.7%CV	2023N536676_00, Table 3

QC performance	Cumulative bias range: –0.7% to +2.8% Cumulative precision: ≤10.2%CV TE: not applicable	2023N536676_00, Table 4
Method reproducibility	ISR was performed in 9.9% of study samples and 71% of samples met the pre-specified criteria. ISR is ongoing and the updated ISR results will be presented in the final bioanalytical report.	2023N536676_00, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	

表 2.7.1.4.36 血漿中 cys-mcMMAF 分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2022N519749_00 Validation of an LC-MS/MS method for the quantitative bioanalysis of cys-mcMMAF in human plasma (Method reference number: [redacted])	
Changes in method	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	Nineteen different pools across the concentration ranges of the assay were prepared at GSK. The samples were re-analyzed using the method under validation at [redacted] Fifteen out of 19 (78.9%) of the calculated concentrations met the acceptance criteria, confirming the acceptability of using this method between [redacted] and GSK for cys-mcMMAF in human plasma.	2022N519749_00, Table 34

表 2.7.1.4.37 血漿中 cys-mcMMAF 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments and hyperlink	2020N448658_00 and 2020N448658_01 Validation of a method for the determination of cys-mcMMAF in human plasma by LC/MS/MS detection (Method reference number: [redacted])		
Method description	Cys-mcMMAF was extracted from 50 µL human plasma by protein precipitation using [$^{15}N^{13}C_3D_3$]-cys-mcMMAF as an internal standard. Extracts were analyzed by UHPLC-MS/MS using an electrospray interface and multiple reaction monitoring.		
Materials used for calibration curve and concentration	Cys-mcMMAF; 50.0, 100, 250, 500, 1600, 5000, 9000, 10 000 pg/mL		
Validated assay range	50.0 to 10 000 pg/mL		
Material used for QCs and concentration	Cys-mcMMAF; LLOQ-QC, 50.0 pg/mL; LQC, 150 pg/mL; MQC, 1500 pg/mL; HQC, 8000 pg/mL.		
Minimum required dilutions	Not applicable		
Regression model and weighting	Linear - weighted $1/x^2$		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2020N448658_00, Table 7.2
	Inter-batch accuracy (%bias) from LLOQ to ULOQ	–4.3% to +3.0%	
	Inter-batch precision (%CV) from LLOQ to ULOQ	≤6.0%	
QCs performance during accuracy and precision	Inter-batch accuracy (%bias) in 4 QCs	–2.0% to +5.3%	2020N448658_00, Table 7.6
	Inter-batch %CV	≤10.2%	
Matrix selectivity and matrix effect	The matrix selectivity of the method in normal human plasma was established by analyzing 6 individual donor lots of plasma as blank and spiked at LLOQ. All 6 individual matrices tested demonstrated lack of significant interference in the chromatographic regions of the analyte and internal standard. The %CV (precision) and %bias (accuracy) in all 6 lots spiked at LLOQ met the acceptance criteria.		2020N448658_00, Table 7.11, Figure 8.8 and 8.13
Interference and specificity	Specificity of the method in the presence of belantamab mafodotin was assessed by analyzing LQC and HQC spiked with up to 300 µg/mL belantamab mafodotin. The spiked QCs were analyzed in replicates of 6 on all 3 precision and accuracy runs. The outcome met the acceptance criteria, indicating that belantamab mafodotin up to 300 µg/mL does not interfere with the assay. Interference of co-administered medications was evaluated. Bortezomib, lenalidomide, pomalidomide, nirogacestat, and dexamethasone were spiked at 500, 1200, 400, 1600, and 1200 ng/mL, respectively, in blank matrix and in matrix spiked with the analyte at LQC and HQC level. The results showed that there was no impact on the quantification of cys-mcMMAF in the presence of bortezomib, lenalidomide, pomalidomide, nirogacestat, and dexamethasone.		2020N448658_00, Table 7.10, 2020N448658_01, Table 8.5 and 8.6

Hemolysis effect	LQC and HQC samples were prepared in blank plasma containing 2% lysed whole blood. The %CV (precision) and %bias (accuracy) under the condition tested met the acceptance criteria, indicating that hemolysis did not affect assay performance.	2020N448658_00, Table 7.14
Lipemic effect	Low QC and High QC samples were prepared in matrix with a natural high lipid content ≥300 mg/dL triglyceride level. The %CV (precision) and %bias (accuracy) under the condition tested met the acceptance criteria, indicating that there were no matrix effects in lipemic human plasma.	2020N448658_00, Table 7.15
Dilution linearity and hook effect	Not assessed as dilutions were not expected during sample analysis	
Working solution stability	The primary solution (1.00 mg/mL cys-mcMMAF prepared in acetonitrile: methanol: water: BSA: formic acid [30:30:40:0.1:1]) was shown to be stable at –10 to –30°C for 377 days and be stable at room temperature for 21 hours.	2020N448658_00, Table 7.16 and Table 7.17
Whole blood stability	The stability of cys-mcMMAF in human whole blood was demonstrated for 1 hour at room temperature in the presence of 150 µg/mL of belantamab mafodotin, and for 2 hours on wet ice in the presence of 300 µg/mL of belantamab mafodotin.	2020N448658_00, Table 7.28
Processed sample stability	Processed samples at LQC and HQC levels were demonstrated to be stable at room temperature for 142 hours.	2020N448658_00, Table 7.27
Bench-top stability	Benchtop stability of cys-mcMMAF in human plasma was assessed at LQC and HQC. The analyte was shown to be stable for 21 hours on wet ice by itself or in the presence of 300 µg/mL belantamab mafodotin.	2020N448658_00, Tables 7.18 and 7.19
Freeze-thaw stability	The freeze/thaw stability of cys-mcMMAF in human plasma with or without 300 µg/mL belantamab mafodotin was established at LQC and HQC for 5 freeze-thaw cycles from –60°C to –80°C to wet ice and from –10°C to –30°C to wet ice.	2020N448658_00, Tables 7.20 and 7.21
Long-term storage	The long-term stability of cys-mcMMAF in human plasma was established at LQC and HQC for: 714 days following storage at –60°C to –80°C; 467 days in the presence of 300 µg/mL belantamab mafodotin following storage at –60°C to –80°C; 87 days with or without 300 µg/mL belantamab mafodotin following storage at –10°C to –30°C.	2020N448658_00, Table 7.22 - 7.26, 2020N448658_01, Table 8.10
Parallelism	Not applicable	
Injection carry over	No carry over was observed	2020N448658_00, Figure 8.7
Recovery	The overall recovery of cys-mcMMAF and [$^{15}N^{13}C_3D_3$]-cys-mcMMAF was 120.9% and 129.2%, respectively, which was adequate to obtain precise and accurate determinations in the method-specified assay range.	2020N448658_00, Table 7.13
Method Performance in DREAMM-3 Interim Bioanalytical Report: Determination of Cys-mcMMAF in Human Plasma by LC-MS/MS to Support Clinical Study 207495. Report Number 2022N502523_00		
Assay passing rate	3 out of 3 analytical runs met the predefined acceptance criteria (including ISR)	2022N502523_00, Table 9.1
Standard curve performance	Cumulative bias range: –1.6% to +2.5% Cumulative precision: ≤6.4%CV	2022N502523_00, Table 9.3

QC performance	Cumulative bias range: –2.0% to +2.7% Cumulative precision: ≤5.5%CV TE: not applicable	2022N502523_00, Table 9.5
Method reproducibility	ISR was performed in 3.9% of study samples and 91.7% of samples met the pre-specified criteria. ISR testing is ongoing, and updated ISR results will be presented in the final bioanalytical report.	2022N502523_00, Table 9.6
Study sample analysis/stability	Calibration standards were freshly prepared for each analytical run. All study samples were stored frozen at –60°C to –80°C along with QC samples.	
Method Performance in DREAMM-7 Interim Bioanalytical Report: Determination of Cys-mcMMAF in Human Plasma by LC-MS/MS for Study 207503. Report Number 2022N514277_00		
Assay passing rate	4 out of 4 analytical runs met the predefined acceptance criteria (including ISR)	2022N514277_00, Table 9.1
Standard curve performance	Cumulative bias range: –1.8% to +1.8% Cumulative precision: ≤8.2%CV	2022N514277_00, Table 9.3
QC performance	Cumulative bias range: –2.7% to –0.1% Cumulative precision: ≤9.9%CV TE: not applicable	2022N514277_00, Table 9.5
Method reproducibility	ISR was performed in 10.8% of study samples and 89.7% of samples met the pre-specified criteria.	2022N514277_00, Table 9.6
Study sample analysis/stability	Calibration standards were freshly prepared for each analytical run. All study samples were stored frozen at –60°C to –80°C along with QC samples.	
Method Performance in DREAMM-8 Interim Bioanalytical Report: Determination of Cys-mcMMAF in Human Plasma by LC-MS/MS for Study 207499. Report Number 2024N550524_00		
Assay passing rate	2 out 3 of analytical runs met the predefined acceptance criteria (including ISR)	2024N550524_00, Table 9.1
Standard curve performance	Cumulative bias range: –6.3% to 10.0% Cumulative precision: ≤13.2%CV	2024N550524_00, Table 9.3
QC performance	Cumulative bias range: –8.7% to 0.0% Cumulative precision: ≤12.9%CV TE: not applicable	2024N550524_00, Table 9.5
Method reproducibility	ISR was performed in 4.5% of study samples and 100% of samples met the pre–specified criteria. Study is ongoing, and more ISR will be conducted as needed and reported in the final bioanalytical report.	2024N550524_00, Table 9.7
Study sample analysis/stability	Calibration standards were freshly prepared for each analytical run. All study samples were stored frozen at –60°C to –80°C along with QC samples.	

表 2.7.1.4.38 血漿中 cys-mcMMAF 分析法の変更とクロスバリデーション結果の要約

（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2020N448658_00 Validation of a method for the determination of cys-mcMMAF in human plasma by LC/MS/MS detection (Method reference number: [redacted])	
Changes in method	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	Nineteen different pools across the concentration ranges of the assay were prepared at GSK. The samples were re-analyzed using the method under validation at [redacted]. All 19 (100%) calculated concentrations met the acceptance criteria, confirming the acceptability of using this method between [redacted] and GSK for cys-mcMMAF in human plasma.	2020N448658_00, Table 10.1

ヒト尿中 cys-mcMMAF 分析法

表 2.7.1.4.39 尿中 cys-mcMMAF 分析法性能の要約

Bioanalytical method validation report name, amendments and hyperlink	2023N535702_00 Validation of an LC-MS/MS method for the quantification of cys-mcMMAF in human urine (Method reference number: [redacted])		
Method description	Cys-mcMMAF was extracted from 75 µL human urine by protein precipitation using [$^{15}N^{13}C_3D_3$]-cys-mcMMAF or [D8]-cys-mcMMAF as an internal standard. Extracts were analyzed using Turbo Ion spray LC-MS/MS.		
Materials used for calibration curve and concentration	Cys-mcMMAF; 50, 100, 200, 500, 1000, 5000, 8000, 10 000 pg/mL		
Validated assay range	50 to 10 000 pg/mL		
Material used for QCs and concentration	Cys-mcMMAF; LLOQ-QC, 50.0 pg/mL; LQC, 150 pg/mL; MQC, 750 pg/mL; HQC, 7500 pg/mL		
Minimum required dilutions	Not applicable		
Regression model and weighting	Linear - weighted $1/x^2$		
Validation parameters	Method validation summary		Source location
Calibration curve performance in validation	Number of standard calibrators from LLOQ to ULOQ	8	2023N535702_00, Table 3
	Inter-batch accuracy (%bias) from LLOQ to ULOQ	–3.9% to +3.4%	
	Inter-batch precision (%CV) from LLOQ to ULOQ	≤7.5%	
QCs performance during accuracy and precision	Inter-batch accuracy (%bias) in 4 QCs	–3.3% to +13.6%	2023N535702_00, Table 4
	Inter-batch %CV	≤11.3%	
Selectivity	The selectivity of the method was assessed in 6 individual lots of human urine as blank and spiked at the LLOQ level. The chromatographic regions of the analyte and the internal standard in all 6 lots of blank human urine were free from significant interference. The precision and accuracy also met the acceptance criteria at LLOQ. The results demonstrated acceptable selectivity for cys-mcMMAF in human urine.		2023N535702_00, Table 6 and Figure 7
Dilution integrity	Dilution integrity was demonstrated at 10-fold dilution.		2023N535702_00, Table 5
Injection carry over	Carry over was tested by injecting at least 1 matrix blank sample immediately following the highest calibration standard. The chromatographic regions of the analyte and the internal standard in the matrix blank sample were free from significant interference, indicating no injection carry over was observed.		2023N535702_00, Figure 8
Recovery	The overall recovery of cys-mcMMAF and [$^{15}N^{13}C_3D_3$]-cys-mcMMAF was 107.9% and 122.5%, respectively, which was adequate to obtain precise and accurate determinations in the method-specified assay range.		2023N535702_00, Table 7
Working solution stability	The working standard solution of cys-mcMMAF was shown to be stable for at least 8 days following storage at –20°C.		2023N535702_00, Table 10
Processed sample stability	Processed samples at LQC and HQC levels were demonstrated to be stable at 4ºC for 87 hours.		2023N535702_00, Table 11

Bench-top stability	Benchtop stability of cys-mcMMAF in human urine was assessed at LQC and HQC. The analyte was shown to be stable for at least 24 hours at ambient temperature and 18 hours on wet ice.	2023N535702_00, Table 12
Freeze-thaw stability	The freeze/thaw stability of cys-mcMMAF in human urine was assessed at LQC and HQC. The analyte was shown to be stable after 4 freeze-thaw cycles from –80°C to wet ice and from –20°C to wet ice.	2023N535702_00, Table 13
Long-term storage	The long-term stability of cys-mcMMAF in human urine was assessed at LQC and HQC. The analyte was shown to be stable for 579 days at –80ºC and 31 days at –20°C.	2023N535702_00, Table 14
Parallelism	Not applicable	
Method Performance in DREAMM-12 Interim Bioanalytical Report: Quantification of Cys-mcMMAF in Human Urine Using LC-MS/MS for Clinical Study 209626. Report Number 2023N535699_00		
Assay passing rate	9 out 9 of analytical runs met the predefined acceptance criteria (including ISR)	2023N535699_00, Table 1
Standard curve performance	Cumulative bias range: –3.5% to +1.9% Cumulative precision: ≤8.4%CV	2023N535699_00, Table 3
QC performance	Cumulative bias range: –12.0% to –0.9% Cumulative precision: ≤7.2%CV	2023N535699_00, Table 4
Method reproducibility	ISR was performed in 9.4% of study samples and 90.9% of samples met the pre-specified criteria. ISR is ongoing and the updated ISR results will be presented in the final bioanalytical report.	2023N535699_00, Table 7
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –70°C) and used within established stability. All study samples were stored frozen at –70°C on receipt.	

ヒト涙液中 cys-mcMMAF 分析法

表 2.7.1.4.40 涙液中 cys-mcMMAF 分析法性能の要約

Bioanalytical method validation report name, amendments, and hyperlink	2020N458494 and 2021N485434_00 The validation of a qualitative assay for the determination of the presence/absence of cys-mcMMAF (qualitative analysis) in human tears using LC-MS/MS. (Method reference number: [redacted])
Method description	Cys-mcMMAF was extracted from 20 µL of artificial or human tears by protein precipitation using acidified acetonitrile containing an isotopically labeled internal standard ([$^{2}H_3$ ^{15}N $^{13}C_3$]-cys-mcMMAF followed by dry down and solid phase extraction. Extracts were analysed by LC-MS/MS.
Materials used for calibration curve and concentration	Cys-mcMMAF, LOD calibrators at 1.25, 2.5, and 5 pg/mL
Validated assay range	LOD calibrator levels 1.25, 2.5 and 5 pg/mL
Material used for QCs and concentration	Cys-mcMMAF
Minimum required dilutions	NA
Source and lot of reagents (LBA)	NA
Regression model and weighting	Linear $1/x^2$
Validation parameters	NA
Calibration curve performance during accuracy and precision	NA
Selectivity and matrix effect	Assessed in 6 individual sources
Interference and specificity	Assessed in 6 individual sources
Hemolysis effect	NA
Lipemic effect	NA
Dilution linearity and hook effect	NA
Parallelism	NA

ヒト血清中遊離 BCMA 分析法

表 2.7.1.4.41 血清中遊離 BCMA 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report number 2018N393390_00, 2018N393390_01, 2018N393390_02, 2018N393390_03, and 2018N393390_04 Validation of an electrochemiluminescence-based method for the quantification of free BCMA in human serum (Method reference number: [redacted])		
Method description	Free BCMA was captured in human serum using [redacted] and detected using a different biotinylated [redacted] and sulfoTAG-labeled streptavidin.		
Materials used for calibration curve and concentration	BCMA; 0.980 (anchor), 1.95, 3.91, 7.81, 15.63, 31.25, 62.5, 125, 250, 500, 1000 ng/mL		
Validated assay range	1.95 to 1000 ng/mL		
Material used for QCs and concentration	BCMA; 1.95, 6, 50, 750, 1000 ng/mL		
Minimum required dilutions	1:20		
Source and lot of reagents (LBA)	Glycosylated [redacted], GSK, Lot no.: GRITS48017 and N38580-51-P1 GSK2857914, GSK, Lot no.: 122370432 Biotinylated [redacted], R&D Systems, Lot no.:FQV0717091, GSK, Lot no.: ELX11877-C1 SulfoTAG-labeled streptavidin, MSD, Lot no.: W0017855S		
Regression model and weighting	Four parameter - $1/y^2$ weighting		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	10	2018N393390_00, Table 2
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–1.0% to +2.7%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤4.1%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 5 QCs	–3.5% to +0.3%	2018N393390_00, Table 3
	Inter-batch %CV	≤18.3%	
	TE	≤18.6%	
Selectivity and matrix effect	The selectivity of the method in normal human serum and serum from participants with multiple myeloma was established by spiking BCMA at 1.95 and 750 ng/mL into 10 lots of each type of serum. The bias compared to the measured endogenous level of BCMA met the acceptance criteria in 10/10 normal human serum lots and 9/10 multiple myeloma serum lots.		2018N393390_00, Table 5 and Table 6
Interference and specificity	Interference from belantamab mafodotin to the assay was assessed by spiking belantamab mafodotin at 1, 10, and 100 µg/mL into BCMA depleted human serum containing huBCMA at 1000, 500, 250, 125, 62.5, 31.25, 15.63, 7.81, 3.91, 1.95, and 0.98 ng/mL. Only samples at 1000 ng/mL and 500 ng/mL huBCMA in the presence of 1 µg/mL belantamab mafodotin met the target acceptance criteria. Belantamab mafodotin at 1, 10 and 100 µg/mL significantly reduced the free BCMA concentration recovery at other levels. The results indicate that the presence of belantamab mafodotin significantly interferes with the quantification of free huBCMA in human serum.		2018N393390_00, Table 8

Hemolysis effect	Free BCMA was spiked into 2% hemolyzed serum at concentrations from 0.980 to 1000 ng/mL. The bias compared to non-hemolyzed serum met the acceptance criteria, demonstrating that quantification of huBCMA is not affected by hemolysis	2018N393390_00, Table 9
Lipemic effect	Free BCMA was spiked into lipemic serum (containing approximately 300 to 500 mg/dL triglycerides) at concentrations from 0.980 to 1000 ng/mL. The bias under the conditions tested met the acceptance criteria, demonstrating that quantification of huBCMA is not affected by lipemia. criteria	2018N393390_00, Table 10
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 1600 ng/mL free sBCMA from 2- to 1024-fold. All replicates of the undiluted 1600 ng/mL free sBCMA sample were greater than ULOQ and samples diluted 1024-fold were less than LLOQ. The precision and accuracy of all the 2- to 512-fold diluted samples met the acceptance criteria. Therefore, dilution linearity was considered acceptable, and no hook effect was observed at 1600 ng/mL free sBCMA in human serum.	2018N393390_00, Table 7
Bench-top/process stability	The stability of free sBCMA in human serum stored at ambient temperature and at 4°C for 25 hours was established at LQC (5.92 ng/mL) and HQC (750 ng/mL).	2018N393390_00, Table 11
Freeze-thaw stability	The stability of free sBCMA in human serum after 6 freeze-thaw cycles from –70°C to room temperature was established at LQC (5.92 ng/mL) and HQC (750 ng/mL).	2018N393390_00, Table 11
Long-term storage	For endogenous free sBCMA (LQC, established nominal concentration of 5.92 ng/mL), the long-term stability of free sBCMA in human serum was established for up to 1333 days at –70°C and up to 136 days at –20°C. For spiked free sBCMA at the HQC level of 750 ng/mL, the long-term stability of free sBCMA in human serum was established for up to 1196 days at –70°C and up to 136 days at –20°C.	2018N393390_00, Table 11; 2018N393390_01, Table 4; and 2018N393390_03, Table 4
Parallelism	Parallelism was evaluated by serial diluting 5 participant predose samples with levels >200 ng/mL for at least 3 dilutions in BCMA depleted serum prior to dilution to the MRD in the serum cytokine assay diluent 2 prior to the assay. Parallelism was acceptable as all 5 samples showed precision of ≤5% up to the maximum tested dilutions of 1:16.	2018N393390_02,Table 4
Carry over	Not applicable	
Method Performance in DREAMM-2 Bioanalytical Report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 205678 using an Electrochemiluminescence-Based Method. Report Number 2022N511202_00.		
Assay passing rate	76/95 analytical runs met the predefined acceptance criteria	2022N511202_00, Table 1
Standard curve performance	Cumulative bias range: –2.2% to +3.6% Cumulative precision: ≤4.6%CV	2022N511202_00, Table 2
QC performance	Cumulative bias range: –13.2% to +9.5% Cumulative precision: 10.9%CV TE: not provided	2022N511202_00, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	Calibration standards were freshly prepared for each analytical run. All study samples were stored frozen at –70°C along with QC samples.	
Method Performance in DREAMM-3 Interim Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 207495 Using a Validated Electrochemiluminescence-Based Method. Report Number 2022N523127_00		
Assay passing rate	80 out of 99 analytical runs met the predefined acceptance criteria	2022N523127_00, Table 1

Standard curve performance	Cumulative bias range: –8.2% to +7.0% Cumulative precision: ≤7.8%CV	2022N523127_00, Table 2
QC performance	Cumulative bias range: –2.3% to +6.5% Cumulative precision: ≤7.5%CV	2022N523127_00, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	
Method Performance in DREAMM-6 **Interim Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 207497 Using an Electrochemiluminescence-Based Method.** **Report Number** 2023N530039_00		
Assay passing rate	77 out of 99 analytical runs met the predefined acceptance criteria	2023N530039_00, Table 1
Standard curve performance	Cumulative bias range: –2.9% to +5.2% Cumulative precision: ≤4.6%CV	2023N530039_00, Table 2
QC performance	Cumulative bias range: –15.9% to +7.2% Cumulative precision: ≤12.2%CV	2023N530039_00, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	
Method Performance in DREAMM-7 **Interim Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 207503 Using a Validated Electrochemiluminescence-Based Method. Report Number** 2023N546327_01		
Assay passing rate	255 out of 283 analytical runs met the predefined acceptance criteria	2023N546327_01, Table 1
Standard curve performance	Cumulative bias range: –7.1% to +7.0% Cumulative precision: ≤8.8%CV	2023N546327_01, Table 2
QC performance	Cumulative bias range: –4.4% to +6.7% Cumulative precision: ≤7.2%CV	2023N546327_01, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	
Method Performance in DREAMM-8 **Interim Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 207499 Using a Validated Electrochemiluminescence-Based Method. Report Number** 2024N550098_01		
Assay passing rate	133 out of 136 analytical runs met the predefined acceptance criteria	2024N550098_01, Table 1
Standard curve performance	Cumulative bias range: –5.2% to +6.3% Cumulative precision: ≤6.5%CV	2024N550098_01, Table 2
QC performance	Cumulative bias range: –4.5% to +4.6% Cumulative precision: ≤6.6%CV	2024N550098_01, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	
Method Performance in DREAMM-11 **Final Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 207504 Using a Validated Electrochemiluminescence-Based Method. Report Number** 2023N533364_00		
Assay passing rate	9 out of 9 analytical runs met the predefined acceptance criteria	2023N533364_00, Table 1
Standard curve performance	Cumulative bias range: –4.2% to +7.6% Cumulative precision: ≤5.2%CV	2023N533364_00, Table 2
QC performance	Cumulative bias range: –16.9% to +4.5% Cumulative precision: ≤14.6%CV	2023N533364_00, Table 3

Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	
Method Performance in DREAMM-12 **Interim Bioanalytical report: Quantification of Free BCMA in Human Serum Samples from Sponsor Clinical Study 209626 Using a Validated Electrochemiluminescence-Based Method. Report Number** 2023N532337_00		
Assay passing rate	16 out 22 of analytical runs met the predefined acceptance criteria	2023N532337_00, Table 1
Standard curve performance	Cumulative bias range: –8.2% to +7.0% Cumulative precision: ≤6.7%CV	2023N532337_00, Table 2
QC performance	Cumulative bias range: –4.1% to +6.0% Cumulative precision: ≤7.0%CV	2023N532337_00, Table 3
Method reproducibility	ISR was not performed	
Study sample analysis/stability	All study samples were stored frozen at –70°C and analyzed within the established long-term stability.	

表 2.7.1.4.42 血清中遊離 BCMA 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments and hyperlink	Report number 2021N468639_00, 2021N468639_01 and 2021N468639_02 Fit-for-purpose validation of a method for the determination of free BCMA in human serum using the meso scale discovery (MSD) platform (Method reference number: [redacted])		
Method description	Free BCMA was captured in human serum using an [redacted] and detected using a different biotinylated [redacted] and SulfoTAG-labeled streptavidin.		
Materials used for calibration curve and concentration	BCMA; 0.98 (anchor), 1.95, 3.91, 7.81, 15.6, 31.3, 62.5, 125, 250, 500, 1000 (anchor) ng/mL		
Validated assay range	1.76 to 953 ng/mL		
Material used for QCs and concentration	BCMA; 1.95, 6, 50, 750, 1000 ng/mL 1.76 (LLOQ), 6.09 (LQC), 50.4 (MQC), 747 (HQC), 953 (ULOQ) ng/mL		
Minimum required dilutions	1:20		
Source and lot of reagents (LBA)	Glycosylated [redacted], GSK, Lot no.: E10295-B1 and N38580-51-P1 [redacted], GSK, Lot no.: HB4V and 122370432 Biotinylated [redacted], R&D Systems, Lot no.: FQV0717091 and ELX11877-C1 BCMA Depleted Human Serum, GSK, Lot no.: AU-28-AUG-2020-000057 and AU-11-SEP-2020-002633 SulfoTAG-labeled streptavidin, MSD, Lot no.: W0018728S, W0018126S, and W0020408S		
Regression model and weighting	Four parameter - $1/y^2$ weighting		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	10	2021N468639_00, Table 1
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–1.3% to +3.0%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤4.5%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 5 QCs	–0.2% to +4.0%	2021N468639_00, Table 3
	Inter-batch %CV	≤10.9%	
	TE	≤14.5%	
Selectivity and matrix effect	The selectivity of the method was assessed in ten lots of normal human serum. Samples with varying endogenous BCMA levels were tested unspiked (blank) and spiked at approximate LQC and ULOQ concentrations with reference huBCMA. Ten out of 10 (100%) spiked samples met criteria at LQC and ULOQ.		2021N468639_00, Table 7
Interference and specificity	To assess potential interference from belantamab mafodotin in the assay, the calibration standards were spiked with 1, 10 and 100 µg/mL of belantamab mafodotin. At 1 µg/mL belantamab mafodotin, no interference was observed at 500 to 1000 ng/mL of free BCMA. At 10 and 100 µg/mL belantamab mafodotin, interference was observed through the assay standard curve concentration range (0.98 to 1000 ng/mL).		2021N468639_00, Table 11

Hemolysis effect	Five lots of serum matrix with the lowest endogenous BCMA level were selected. Hemolyzed matrix lots were prepared by spiking whole blood matrix into each of those 5 serum lots to get the desired percentage of hemolysis at 2% and 10% respectively. The 5 lots of hemolyzed matrix were tested unspiked (blank) and spiked at approximate LQC and ULOQ concentrations with reference huBCMA. Among the 2% hemolyzed lots, 5 out of 5 (100%) spiked samples met criteria at each level. Among the 10% hemolyzed lots, 4 out of 5 (80%) spiked samples met criteria at each level. The data indicated there were no matrix effects at 10% hemolyzed sample.	2021N468639_00, Table 8 and 9
Lipemic effect	Five lots of lipemic serum matrix (approximately 300 mg/dL of triglycerides) were tested unspiked (blank) and spiked at approximately LQC and ULOQ concentrations with reference huBCMA. Five out of 5 (100%) spiked samples met criteria at each level, indicating there is no lipemic effects.	2021N468639_00, Table 8
Dilution linearity and hook effect	Dilution linearity and hook effect were evaluated by diluting a sample containing 80 000 ng/mL free BCMA from 89- to 82051-fold. All replicates of the undiluted 80 000 ng/mL free BCMA sample were greater than ULOQ, and samples diluted 82051-fold were less than LLOQ. The %CV (precision) and %bias (accuracy) of all the 89– to 4 1026–fold diluted samples were <20%. Dilution linearity was considered acceptable, and no hook effect was observed.	2021N468639_00, Table 10
Bench-top stability	Benchtop stability of free sBCMA at ambient room temperature was assessed at LQC, MQC, and HQC. The analyte was shown to be stable for at least 24 hours 5 minutes in normal human serum and in BCMA depleted human serum.	2021N468639_00, Table 14 and 15
Refrigerator stability	Refrigerator stability of free sBCMA was assessed at LQC, MQC, and HQC. The analyte was shown to be stable for at least 72 hours 7 minutes in normal human serum at 2°C to 8°C and for at least 72 hours 6 minutes in BCMA depleted human serum at 2°C to 8°C.	2021N468639_00, Table 16 and 17
Freeze-thaw stability	The stability of free sBCMA in normal human serum and in BCMA depleted human serum was established after 6 freeze/thaw cycles from –60°C to –80°C to room temperature and from –10°C to –30°C to room temperature at LQC, MQC, and HQC.	2021N468639_00, Table 12 and 13
Long-term storage	The long-term stability of free sBCMA was established at LQC, MQC, and HQC under these conditions: 1) 741 days in normal human serum following storage at –60°C to –80°C. 2) 185 days in normal human serum following storage at –10°C to –30°C. 3) 740 days in BCMA depleted human serum following storage at –60°C to –80°C. 4) 496 days in BCMA depleted human serum following storage at –10°C to –30°C.	2021N468639_00, Table 18 to 21 and 2021N468639_01, Table 4 to Table 7
Parallelism	Not applicable	
Carry over	Not applicable	
Method Performance in DREAMM-3 Interim Bioanalytical Report: Determination of Free BCMA in Human Serum Samples from Clinical Study 207495. Report Number 2022N525047_00		
Assay passing rate	11 out of 11 analytical runs met the predefined acceptance criteria	2022N525047_00, Table 1
Standard curve performance	Cumulative bias range: –6.5% to +14.1% Cumulative precision: ≤5.0%CV	2022N525047_00, Table 2

QC performance	Cumulative bias range: –6.1% to +7.4% Cumulative precision: ≤7.2%CV TE: %CV	2022N525047_00, Table 4
Method reproducibility	ISR was not performed	
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C upon receipt.	
Method Performance in DREAMM–7 Interim Bioanalytical Report: Determination of Free BCMA in Human Serum Samples Using ECL From Clinical Study 207503. Report Number 2023N544471_00		
Assay passing rate	40 out of 45 analytical runs met the predefined acceptance criteria	2023N544471_00, Table 1
Standard curve performance	Cumulative bias range: –6.4% to +10.0% Cumulative precision: ≤6.1%CV	2023N544471_00, Table 2
QC performance	Cumulative bias range: –13.3% to +7.4% Cumulative precision: ≤7.3%CV TE: %CV	2023N544471_00, Table 4
Method reproducibility	ISR was not performed	
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C upon receipt.	
Method performance in DREAMM-8 Interim Bioanalytical Report: Determination of Free BCMA in Human Serum Samples Using ECL From Clinical Study 207499. Report number 2024N549481_00		
Assay passing rate	5 out of 5 analytical runs met the predefined acceptance criteria	2024N549481_00, Table 1
Standard curve performance	Cumulative bias range –8.0 to +14.4% Cumulative precision: ≤6.6%CV	2024N549481_00, Table 2
QC performance	Cumulative bias range: –13.4 to +7.9% Cumulative precision: ≤6.7%CV TE: %CV	2024N549481_00, Table 4
Method reproducibility	ISR was not performed	
Study sample analysis/stability	Calibration standards and QC samples were stored frozen (nominal –60°C to –80°C) and used within established stability. All clinical study samples were stored frozen at –60°C to –80°C upon receipt.	

表 2.7.1.4.43 血清中遊離 BCMA 分析法の変更とクロスバリデーション結果の要約（[redacted]）

Bioanalytical method validation report name and hyperlink	Report number 2021N468639_00 and 2021N468639_02 Fit-for-purpose validation of a method for the determination of free BCMA in human serum using the meso scale discovery (MSD) platform (Method reference number: [redacted])	
Changes in method	None	
Validation parameters	Cross-validation performance	Source location
Cross-validation	Fifteen cross-validation samples (all post-baseline) across the concentration range of the assay were prepared using the incurred study samples from DREAMM-2. The samples were re-analyzed at [redacted] and [redacted]. Only 1 out of 15 of the calculated concentrations were within ±30% of the mean, not meeting the acceptance criteria. A second round of cross-validation was performed among [redacted], [redacted] and GSK. QCs and 34 cross-validation samples were tested 3 times by each of the 3 labs. The 34 cross-validation samples were prepared using the incurred study samples from DREAMM-2, and each of the 34 sample pools consisted of some post-baseline samples. The outcome did not meet acceptance criteria between any 2 labs. An investigation was conducted and suggested that the free sBCMA assay should yield consistent results for baseline samples between labs. A third round of cross-validation was therefore performed using only baseline samples among [redacted], [redacted], and GSK. In this round, QCs and 30 baseline cross-validation samples were tested 3 times by each of the 3 labs. All 30 samples met the acceptance criteria between [redacted] and [redacted], and 28 out of 30 samples met the acceptance criteria between [redacted] and GSK.	2021N468639_00, Table 22 and 2021N468639_02, Table 7 to 10

表 2.7.1.4.44 血清中遊離 BCMA 分析法性能の要約（[redacted]）

Bioanalytical method validation report name, amendments, and hyperlink	Report Number 2023N527200_00 Supplemental validation of a method for the determination of free BCMA in human serum by electrochemiluminescent immunoassay (Method Reference [redacted])		
Method description	Free BCMA was captured in human serum using [redacted] and detected using a different biotinylated [redacted] and SulfoTAG labeled streptavidin.		
Materials used for calibration curve and concentration	BCMA; 0.98 (anchor), 1.95, 3.91, 7.81, 15.6, 31.3, 62.5, 125, 250, 500, 1000 ng/mL		
Validated assay range	1.95 to 1000 ng/mL		
Material used for QCs and concentration	BCMA; 6, 50, 750 ng/mL		
Minimum required dilutions	1:20		
Source and lot of reagents (LBA)	Glycosylated [redacted], GSK, Lot no.: N38580-51-P1, ELN114071-1 GSK2857914, GSK Lot no.: 172405900 Biotinylated [redacted], R&D Systems, Lot no.: ELX11877-C1, ELX14427-A1, ELX16362-A1 SulfoTAG labeled streptavidin, MSD, Lot no.: W0020889S, W0021245S		
Regression model and weighting	Four parameter - $1/y^2$ weighting		
Validation parameters	Method validation summary		Source location
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	10	2023N527200, Table 2-3
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–4.00% to +7.00%	
	Cumulative precision (%CV) from LLOQ to ULOQ	≤6.18%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 3 QCs	–2.60% to +8.67%	2023N527200, Table 5
	Inter-batch %CV	≤28.21%	
Selectivity and matrix effect	Not reassessed		See Table 3.4.2.1
Interference and specificity	Not reassessed		See Table 3.4.2.1
Hemolysis effect	Not reassessed		See Table 3.4.2.1
Lipemic effect	Not reassessed		See Table 3.4.2.1
Dilution linearity and hook effect	Not reassessed		See Table 3.4.2.1
Bench-top stability	Not reassessed		See Table 3.4.2.1
Refrigerator stability	Not reassessed		See Table 3.4.2.1
Freeze-thaw stability	Not reassessed		See Table 3.4.2.1
Long-term storage	Not reassessed		See Table 3.4.2.1
Parallelism	Not applicable		
Carry over	Not applicable		

Method performance in DREAMM-14 Interim Bioanalytical report: Report number 2023N539208_00		
Assay passing rate	40/51 analytical runs met the predefined acceptance criteria	2023N539208_00, Table 1
Standard curve performance	Cumulative bias range: –4.30% to +6.80% Cumulative precision: ≤4.92%CV	2023N539208_00, Table 2 and Table 3
QC performance	Cumulative bias range: –1.10% to +27.20% Cumulative precision: ≤32.6%CV	2023N539208_00, Table 5
Method reproducibility	Not assessed	NA
Study sample analysis/stability	Each batch of experimental samples was run against calibration standards freshly prepared or frozen within established stability. All study samples were stored frozen at –70°C along with QC samples.	

表 2.7.1.4.45 血清中遊離 BCMA 分析法の変更とクロスバリデーション結果の要約

（[redacted]）

Bioanalytical method validation report name	Report Number 2023N527200_00 Supplemental Validation of a Method for the Determination of Free BCMA in Human Serum by Electrochemiluminescent Immunoassay; (Appendix 7. 2023N539213_00 Statistical Report – Baseline Free sBCMA Cross Validation) (Method Reference [redacted])	
Validation parameters	Cross-validation performance of baseline samples	
Cross-validation	To assess bioanalytical cross validation, 30 pooled clinical baseline (pre-treatment) samples were measured in 3 separate instances by each of 3 labs – [redacted], [redacted], and GSK. Incurred free sBCMA baseline samples (Screening or Cycle 1 Day 1, Predose) had been selected from clinical study 205678 (DREAMM-2) and pooled by category or free sBCMA concentration. Each run by each lab corresponded to a separate individual plate for testing samples. Both [redacted] and GSK met a minimum level of evidence for agreement with [redacted], as the 67% limits of agreement in each case were within the unofficial ±1.3-fold thresholds. For [redacted] a small but uniform offset in results was detected ([redacted] results were on average slightly lower than [redacted]'s); but due to the modest size and consistency of this difference across runs, a conversion was not deemed necessary to support agreement. However, for GSK, Deming regression and data visualization pointed to larger and more inconsistent differences across runs between the 2 labs. Thus, converting GSK's results did very little to improve the evidence of agreement with [redacted]'s, as this conversion was determined by the average relationship of results.	

ヒト血漿中ボルテゾミブ分析法

表 2.7.1.4.46 血漿中ボルテゾミブ分析法性能の要約

Bioanalytical method validation report name, amendments and hyperlink	Quantitation of bortezomib in human plasma using UPLC with MS/MS detection 2019N413318		
Method description	Protein precipitation with evaporation followed by analysis by UPLC-MS/MS		
Materials used for calibration curve and concentration	Bortezomib, 0.1, 0.2, 0.4, 1.5, 6.0, 25.0, 80.0, 100.0 ng/mL		
Validated assay range	0.1 to 100 ng/mL		
Material used for QCs and concentration	Bortezomib, 0.1, 0.3, 40.0 and 75.0 ng/mL		
Minimum required dilutions	NA		
Source and lot of reagents (LBA)	NA		
Regression model and weighting	Linear 1/x		
Validation parameters	Method validation summary	Source location	
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2019N413318
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–0.977% to 1.1%	Table 3
	Cumulative precision (%CV) from LLOQ to ULOQ	1.69% to 4.43%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 4 QCs	–0.535 to 12.6%	Table 5
	Inter-batch %CV	<12.8%	
Selectivity and matrix effect	Bortezomib Specificity Matrix Effect	Tables 18A and 18B Tables 19A and 19B	
Interference and specificity	Interference check for dexamethasone at 500 ng/mL in QCs prepared at 0.3 and 75 ng/mL of bortezomib	Table 21	
Hemolysis effect	2% fully lysed whole blood in QCs prepared at 0.3 and 75 ng/mL bortezomib	Table 16	
Lipemic effect	Tested in plasma with a triglyceride level of >300 mg/dL in QCs prepared of 0.3 and 75 ng/mL bortezomib	Table 17	
Dilution linearity and hook effect	NA	NA	
Bench–top/process stability	27.33 hours in an ice bath	Table 10	
Freeze–thaw stability	5 cycles from –25°C and –80°C to ice bath	Table 9A and 9B	
Long–term storage	19 days at –25°C and 1032 days at –80°C	2019N413318 Table 12A and 2023N546218 Table 5 to 6	
Parallelism	NA	NA	
Carry over	<13.6%	Table 22	

Method Performance in DREAMM–6 Bioanalytical Report: Quantification of Bortezomib in Human Plasma Samples from Sponsor Clinical Study 207497 Using HPLC with MS/MS Detection. Report Number 2018N389799_00		
Assay passing rate	13 out of 15 analytical runs met the predefined acceptance criteria. (including ISR)	Tables 4A and 4B
Standard curve performance (method AKOJ)	Cumulative bias range: –6.28% to 2.25% Cumulative precision: <5.69%	Table 5A
Standard curve performance (method AKOJ2)	Cumulative bias range: –2.88% to 2.20% Cumulative precision: <6.44%	Table 5B
QC performance (method AKOJ)	Cumulative bias range: –2.05% to 2.85% Cumulative precision: <7.77%	Table 6A
QC performance (method AKOJ2)	Cumulative bias range: 3.52% to 5.39% Cumulative precision:<7.27%	Table 6B
Method reproducibility	ISR was performed, 9.9% of samples were re-analyzed with a 97.9% pass rate	Table 9
Study sample analysis/stability	Samples analyzed with 1010 days and long-term stability demonstrated for 1032 days at –80°C.	

表 2.7.1.4.47 血漿中ボルテゾミブ分析法の変更の要約

Bioanalytical method validation report name and hyperlink	Additional validation data for the quantitation of bortezomib in human plasma via UPLC with MS/MS detection 2023N546218
Changes in method	Frozen stability extended and interference checks with dexamethasone (1250 ng/mL and SGD-1362 (10 000 pg/mL)

ヒト血漿中レナリドミド分析法

表 2.7.1.4.48 血漿中レナリドミド分析法性能の要約

Bioanalytical method validation report name, amendments and hyperlink	Validation of a UHPLC method using MS/MS detection and automated extraction for the determination of lenalidomide (2.5 to 1000 ng/mL) in human EDTA K2 plasma 2023N533133_00		
Method description	Liquid/liquid extraction with UPLC-MS/MS		
Materials used for calibration curve and concentration	Lenalidomide; 2.5, 5.0, 50.0, 100.0, 200.0, 400.0, 800.0, and 1000.0 ng/mL		
Validated assay range	2.5 to 1000 ng/mL		
Material used for QCs and concentration	Lenalidomide, 2.5, 7.5, 500 and 750 ng/mL		
Minimum required dilutions	NA		
Source and lot of reagents (LBA)	NA		
Regression model and weighting	Linear $1/x^2$		
Validation parameters	Method validation summary	Source location	
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2023N533133_00
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–1.46% to 0.86%	Table 3A
	Cumulative precision (%CV) from LLOQ to ULOQ	1.24% to 2.69%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 5 QCs	–2.31% to 0.69%	Table 4A
	Inter–batch %CV	2.19% to 5.01%	
Selectivity and matrix effect	6 individual matrix batches tested	Table 13A and 14A	
Interference and specificity	Interference check with commonly used drugs	Tables 12A	
Hemolysis effect	5% Hemolysis check	Table 11A, 13A and 14A	
Lipemic effect	Fortified with 100 mg of triglycerides check	Table 11A, 13A and 14A	
Dilution linearity and hook effect	NA		
Bench–top/process stability	3 hours and 26 minutes at room temperature	Table 20A	
Freeze–thaw stability	4 cycles at –20°C and –80°C	Table 18 and 19	
Long–term storage	4 days at –20°C and 516 days at –80°C	Table 22A and 23.3A	
Parallelism	NA		
Carry over	<20% of the LLOQ sample for the analyte <5% of the LLOQ sample for the internal standard	Table 15A Table 16A	

Method Performance in DREAMM-6 Bioanalytical Report: Quantification of Lenalidomide in Human Plasma Samples from Sponsor Clinical Study 207497 Using a Liquid/Liquid extraction method with a UPLC-MS/MS Method. Report Number 2018N393429		
Assay passing rate	12 out 13 analytical runs met the predefined acceptance criteria (Including ISR)	Table 1
Standard curve performance	Cumulative bias range: –1.60 to 1.00% Cumulative precision: 2.21 to 6.40%	Table 6
QC performance	Cumulative bias range: –0.40 to 2.27% Cumulative precision: 3.40 to 9.35%	Table 7
Method reproducibility	ISR was performed, 17.2% of samples were re-analyzed with a pass rate of 96.43%	Table 8
Study sample analysis/stability	Samples were analyzed within 253 days, 516 days frozen stability at –80°C was validated	

ヒト血漿中ポマリドミド分析法

表 2.7.1.4.49 血漿中ポマリドミド分析法性能の要約

Bioanalytical method validation report name, amendments and hyperlink	Validation of a UPLC-MS/MS method with automated extraction for the determination of pomalidomide in human plasma (range 0.5 to 200 ng/mL). interference validation of bortezomib, cys-mcMMAF and dexamethasone on an LC-MS/MS for the determination of pomalidomide (0.5 to 200 ng/mL) in human plasma. 2023N527155_00 and 2023N527169_00		
Method description	Human plasma samples were extracted using an automated liquid-liquid method prior to analysis by UPLC-MS/MS		
Materials used for calibration curve and concentration	Pomalidomide; 0.5, 1.0, 4.0, 20.0, 40.0, 80.0, 160.0 and 200.0 ng/mL		
Validated assay range	0.5 to 200 ng/mL		
Material used for QCs and concentration	Pomalidomide; 0.5, 1.5, 100.0 and 150.0 ng/mL		
Minimum required dilutions	NA		
Source and lot of reagents (LBA)	NA		
Regression model and weighting	Linear $1/x^2$		
Validation parameters	Method validation summary	Source location	
Calibration curve performance during accuracy and precision	Number of standard calibrators from LLOQ to ULOQ	8	2023N527155_00
	Cumulative accuracy (%RE) from LLOQ to ULOQ	–1.69% to 1.71%	Table 3A
	Cumulative precision (%CV) from LLOQ to ULOQ	1.19% to 3.60%	
QCs performance during accuracy and precision	Cumulative accuracy (%RE) in 5 QCs	–5.79% to –1.49%	Table 4A
	Inter-batch %CV	2.48% to 7.59%	Table 4A
Selectivity and matrix effect	Tested at 2 QC levels	Tables 13A and 14A	
Interference and specificity	Interference checked with commonly used drugs. Interference checked with bortezomib, cys-mcMMAF and dexamethasone	Table 12A Report 2023N527169	
Hemolysis effect	Tested	Table 11A	
Lipemic effect	Tested	Table 11A	
Dilution linearity	20 fold dilution	Table 9A	
Bench-top/process stability	2 hours and 2 mins at room temperature and 24 hours and 25 min at +4°C	Tables 20A and 21A	
Freeze-thaw stability	4 cycles from –20°C and –80°C to room temperature	Tables 18A and 19A	
Long-term storage	10 days at –20°C and 525 days at –80°C	Tables 22A and 23.2A	
Parallelism	NA		
Carry over	<20% for analyte and <5% for internal standard	Tables 15A and 16A	

Method performance in DREAMM-8 **Bioanalytical Report: Quantification of Pomalidomide in Human Plasma Samples from Sponsor Clinical Study 207499 Using an Electrochemiluminescence-Based Method. Report Number 2023N532441_00**		
Assay passing rate	5 out of 6 analytical runs met the predefined acceptance criteria including ISR runs	Table 1
Standard curve performance	Cumulative bias range: –1.75% to 2.00% Cumulative precision: 3.02% to 7.53%	Table 7
QC performance	Cumulative bias range: 0.00% to 2.67% Cumulative precision: 2.85% to 9.94% TE:	Table 8
Method reproducibility	ISR was performed, 10.4% of study samples were reanalyzed with a pass rate of 96.7%	Table 5
Study sample analysis/stability	Samples were analyzed within 486 Days, Stability generated for 525 days at –80°C	

2.7.1.4.4. Cys-mcMMAF の分析法別 PK パラメータ

表 2.7.1.4.50 ベランタマブ　マホドチンを投与した時のサイクル 1 における cys-mcMMAF の分析法別 PK パラメータ（DREAMM-1 試験、パート 1）

Parameter	Assay Method	Treatment Group								
		0.12 mg/kg (N=4)	0.24 mg/kg (N=4)	0.48 mg/kg (N=4)	0.96 mg/kg (N=3)	1.92 mg/kg (N=4)	2.50 mg/kg (N=8)	3.40 mg/kg (N=3)	4.60 mg/kg (N=6)	Total (N=38)
AUC(0-tlast) (pg·h/mL)	[redacted]	1157[1]	1624 (41)	14682[3] (92)	20787 (209)	72608[3] (18)	ND	119177 (36)	181148 (94)	ND
	[redacted]	ND	1335[3] (26)	3350[3] (19)	9231 (181)	50472[3] (17)	ND	76529 (26)	121340 (94)	ND
tlast (days)	[redacted]	2.05[1]	1.01 (0.99, 1.03)	7.00[3] (1.08, 7.28)	6.98 (0.95, 7.02)	9.95[3] (6.94, 12.95)	ND	6.96 (6.93, 13.85)	7.63 (1.00, 13.95)	ND
	[redacted]	ND	1.03[3] (0.99, 1.03)	1.03[3] (1.00, 1.08)	1.00 (0.92, 7.02)	9.96[3] (6.94, 12.95)	ND	6.93 (6.90, 6.96)	7.63 (1.00, 12.98)	ND
C-EOI (pg/mL)	[redacted]	ND	ND	83.7[3] (2)	106 (30)	285[3] (62)	381 (43)	378 (28)	918 (95)	ND
	[redacted]	ND	ND	62.0[3] (1)	76.9 (28)	198[3] (59)	263 (43)	260 (28)	625 (94)	ND
Cmax (pg/mL)	[redacted]	51.5[1]	91.5 (32)	261[3] (16)	488 (39)	1054[3] (19)	ND	1200 (35)	2544 (87)	ND
	[redacted]	ND	75.9[3] (19)	181[3] (15)	334 (38)	715[3] (19)	ND	813 (35)	1719 (87)	ND
tmax (h)	[redacted]	49.13[1]	23.88 (9.00, 24.63)	24.73[3] (24.00, 25.83)	9.05 (8.78, 22.83)	8.75[3] (7.75, 24.00)	ND	23.70 (23.17, 24.97)	24.04 (7.83, 25.00)	24.00[5] (7.75, 49.13)
	[redacted]	ND	23.73[3] (9.00, 24.63)	24.73[3] (24.00, 25.83)	9.05[3] (8.78, 22.83)	8.75[3] (7.75, 24.00)	ND	23.70 (23.17, 24.97)	24.04 (7.83, 25.00)	23.73[7] (7.75, 25.83)
Ctrough (pg/mL)	[redacted]	ND	ND	ND	ND	ND	ND	ND	ND	ND
	[redacted]	ND	ND	ND	ND	ND	ND	ND	ND	ND

Source: 5.3.3.2, DREAMM-1 CPSR Table 4.0080; 5.3.3.2, DREAMM-1 Cys-mcMMAF Supplement Pharmacokinetic Report Table 9.0080
For Treatment Groups 0.03 mg/kg and 0.06 mg/kg, all cys-mcMMAF concentrations were below the limit of quantification (<50 pg/mL).
Data presented as geometric mean, (%CVb), except tmax and tlast, presented as median, (minimum, maximum). N is in column heading unless footnoted.
1: n=1; 2: n=2; 3: n=3; 4: n=32; 5: n=23; 6: n=31; 7: n=21