

**Clinical trial results:****A Phase II, Open Label, Randomized, Two-Arm Study to Investigate the Efficacy and Safety of Two Doses of the Antibody Drug Conjugate GSK2857916 in Participants with Multiple Myeloma Who Had 3 or More Prior Lines of Treatment, Are Refractory to a Proteasome Inhibitor and an Immunomodulatory Agent and Have Failed an Anti-CD38 Antibody (DREAMM 2)****Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-004810-25 |
| Trial protocol           | GB DE ES IT    |
| Global end of trial date |                |

**Results information**

|                                |  |
|--------------------------------|--|
| Result version number          | v3   |
| This version publication date  | 01 January 2024  |
| First version publication date | 26 April 2020  |
| Version creation reason        | <ul style="list-style-type: none"><li>• New data added to full data set</li></ul> NIH comments addressal |

**Trial information****Trial identification**

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 205678 |
|-----------------------|--------|

**Additional study identifiers**

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN)   | - |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 GreatWest Road, Brentford, Middlesex, United Kingdom, TW8 9GS                |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com |

Notes:

**Paediatric regulatory details**

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Interim      |
| Date of interim/final analysis                       | 04 May 2022  |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 21 June 2019 |
| Global end of trial reached?                         | No           |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of 2 doses of GSK2857916 in participants with relapsed/refractory multiple myeloma

Protection of trial subjects:

In order to minimize corneal events associated with GSK2857916 prophylactic preservative-free artificial tears should be administered in each eye at least 4 to 8 times daily beginning on Cycle 1 Day 1 until the end of treatment. In the event of ocular symptoms (e.g., dry eyes), the use of artificial tears may be increased up to every 2 hours as needed.

While not yet clinically demonstrated, it is theoretically possible that the application of a cooling eye mask during GSK2857916 administration, and in the first few hours after infusion may subsequently decrease ocular side effects. On the day of infusion at the discretion of the participant and the investigator, the following may be considered:

- Beginning with the start of each GSK2857916 infusion, participants may apply cooling eye masks to their eyes for approximately 1 hour or as much as tolerated.
- Participants may continue using the cooling eye mask beyond the first hour for up to 4 hours. Further use beyond 4 hours is at the participant's discretion.

Participants should receive full supportive care during the study, including transfusions of blood products, growth factors, and treatment with antibiotics, anti-emetics, antidiarrheal, and analgesics, as appropriate. Concomitant therapy with bisphosphonates is allowed. Participants may receive local irradiation for pain or stability control.

Background therapy: -

Evidence for comparator: -

|   |                             |
|---|-----------------------------|
| Actual start date of recruitment                          | 18 June 2018                |
| Long term follow-up planned                               | Yes                         |
| Long term follow-up rationale                             | Safety, Scientific research |
| Long term follow-up duration                              | 5 Years                     |
| Independent data monitoring committee (IDMC) involvement? | Yes                         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 5       |
| Country: Number of subjects enrolled | Canada: 12         |
| Country: Number of subjects enrolled | France: 26         |
| Country: Number of subjects enrolled | Germany: 16        |
| Country: Number of subjects enrolled | Italy: 7           |
| Country: Number of subjects enrolled | Spain: 17          |
| Country: Number of subjects enrolled | United Kingdom: 12 |
| Country: Number of subjects enrolled | United States: 126 |

|                                    |     |
|------------------------------------|-----|
| Worldwide total number of subjects | 221 |
| EEA total number of subjects       | 66  |

Notes:

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**Subjects enrolled per age group**

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 91  |
| From 65 to 84 years                       | 127 |
| 85 years and over                         | 3   |

## Subject disposition

### Recruitment

Recruitment details:

This was an open-label, randomized, multicenter study to evaluate the efficacy and safety of belantamab mafodotin monotherapy at a dose of 2.5 milligram per kilogram (mg/kg) or 3.4 mg/kg, given intravenously (IV) in participants with relapsed/refractory multiple myeloma (RRMM).

### Pre-assignment

Screening details:

A total of 221 participants were enrolled. The results presented based on data cut-off date of 04 May 2022. Those participants still benefiting from study drug in opinion of treating physician continued to receive study drug in Post Analysis Continued Treatment phase their data will be reported after they stop receiving treatment per protocol.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |                                      |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes                                  |
| <b>Arm title</b>             | GSK2857916 2.5 mg/kg (Frozen liquid) |

Arm description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 2.5 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 39 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | GSK2857916  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate and solvent for concentrate for solution for infusion |
| Routes of administration               | Intravenous use   |

Dosage and administration details:

GSK2857916 frozen liquid was available as 30 milligrams per vial solution in single-use vial. It was diluted with 0.9 percent saline to the appropriate concentration for the dose (2.5 milligram per kilogram [mg/kg]). Participants were administered GSK2857916 via intravenous route

|                  |                                      |
|------------------|--------------------------------------|
| <b>Arm title</b> | GSK2857916 3.4 mg/kg (Frozen liquid) |
|------------------|--------------------------------------|

Arm description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 3.4 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 32 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | GSK2857916  |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Concentrate and solvent for concentrate for solution for infusion |
| Routes of administration               | Intravenous use   |

Dosage and administration details:

GSK2857916 frozen liquid was available as 30 milligrams per vial solution in single-use vial. It was diluted with 0.9 percent saline to the appropriate concentration for the dose (3.4 mg/kg). Participants were administered GSK2857916 via intravenous route.

|                  |                                    |
|------------------|------------------------------------|
| <b>Arm title</b> | GSK2857916 3.4 mg/kg (Lyophilized) |
|------------------|------------------------------------|

Arm description:

Participants were administered lyophilized powder (100 mg/vial in a single use vial) at a dose of 3.4 mg/kg GSK2857916 given IV for a maximum of up to 35 cycles (1 cycle= 21 days). Lyophilized powder was reconstituted using water for injection.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | GSK2857916                        |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Powder for solution for injection |
| Routes of administration               | Intravenous use                   |

Dosage and administration details:

GSK2857916 lyophilized powder was available as 100 milligrams per vial in single-use vial for reconstitution. It was reconstituted using water for injection and diluted with 0.9 percent saline to the appropriate concentration for the dose (3.4 mg/kg). Participants were administered GSK2857916 via intravenous route.

| <b>Number of subjects in period 1</b> | GSK2857916 2.5 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Lyophilized) |
|---------------------------------------|--------------------------------------|--------------------------------------|------------------------------------|
| Started                               | 97                                   | 99                                   | 25                                 |
| Received Study Treatment              | 95                                   | 99                                   | 24                                 |
| Completed                             | 0                                    | 0                                    | 0                                  |
| Not completed                         | 97                                   | 99                                   | 25                                 |
| Consent withdrawn by subject          | 8                                    | 2                                    | 2                                  |
| Physician decision                    | 2                                    | 4                                    | -                                  |
| other reasons                         | 14                                   | 10                                   | 5                                  |
| Death                                 | 70                                   | 80                                   | 16                                 |
| ongoing at the time of analysis       | 1                                    | 2                                    | -                                  |
| Lost to follow-up                     | 2                                    | 1                                    | 2                                  |

## Baseline characteristics

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | GSK2857916 2.5 mg/kg (Frozen liquid) |
|-----------------------|--------------------------------------|

Reporting group description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 2.5 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 39 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | GSK2857916 3.4 mg/kg (Frozen liquid) |
|-----------------------|--------------------------------------|

Reporting group description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 3.4 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 32 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | GSK2857916 3.4 mg/kg (Lyophilized) |
|-----------------------|------------------------------------|

Reporting group description:

Participants were administered lyophilized powder (100 mg/vial in a single use vial) at a dose of 3.4 mg/kg GSK2857916 given IV for a maximum of up to 35 cycles (1 cycle= 21 days). Lyophilized powder was reconstituted using water for injection.

| Reporting group values   | GSK2857916 2.5 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Lyophilized) |
|--|--------------------------------------|--------------------------------------|------------------------------------|
| Number of subjects   | 97                                   | 99                                   | 25                                 |
| Age categorical  |                                      |                                      |                                    |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |                                      |                                      |                                    |
| Units: Participants  |                                      |                                      |                                    |
| Total Participants   | 97                                   | 99                                   | 25                                 |
| Age Continuous   |                                      |                                      |                                    |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |                                      |                                      |                                    |
| Units: years   |                                      |                                      |                                    |
| arithmetic mean  | 64.1                                 | 66.0                                 | 67.2                               |
| standard deviation   | ± 10.01                              | ± 9.09                               | ± 10.78                            |
| Sex: Female, Male  |                                      |                                      |                                    |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |                                      |                                      |                                    |
| Units: Participants  |                                      |                                      |                                    |
| Female   | 46                                   | 43                                   | 11                                 |
| Male   | 51                                   | 56                                   | 14                                 |
| Race/Ethnicity, Customized   |                                      |                                      |                                    |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |                                      |                                      |                                    |
| Units: Subjects  |                                      |                                      |                                    |
| Black or African American  | 16                                   | 11                                   | 3                                  |
| Asian - Central/South Asian Heritage   | 1                                    | 0                                    | 0                                  |
| Asian - East Asian Heritage  | 1                                    | 0                                    | 0                                  |
| Asian - South East Asian Heritage  | 0                                    | 1                                    | 1                                  |
| White - Arabic/North African Heritage  | 4                                    | 2                                    | 0                                  |
| White - White/Caucasian/European Heritage  | 72                                   | 83                                   | 21                                 |
| Mixed Asian Race   | 0                                    | 1                                    | 0                                  |

|                  |   |   |   |
|------------------|---|---|---|
| Mixed White Race | 0 | 1 | 0 |
| Unknown          | 1 | 0 | 0 |
| Missing          | 2 | 0 | 0 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>  | Total |  |  |
| Number of subjects   | 221   |  |  |
| Age categorical  |       |  |  |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |       |  |  |
| Units: Participants  |       |  |  |
| Total Participants   | 221   |  |  |
| Age Continuous   |       |  |  |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |       |  |  |
| Units: years   |       |  |  |
| arithmetic mean  |       |  |  |
| standard deviation   | -     |  |  |
| Sex: Female, Male  |       |  |  |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |       |  |  |
| Units: Participants  |       |  |  |
| Female   | 100   |  |  |
| Male   | 121   |  |  |
| Race/Ethnicity, Customized   |       |  |  |
| Baseline characteristics were presented for all randomized participants including 3 randomized participants who never received treatment (2-withdrawal by physician decision and 1-death). |       |  |  |
| Units: Subjects  |       |  |  |
| Black or African American  | 30    |  |  |
| Asian - Central/South Asian Heritage   | 1     |  |  |
| Asian - East Asian Heritage  | 1     |  |  |
| Asian - South East Asian Heritage  | 2     |  |  |
| White - Arabic/North African Heritage  | 6     |  |  |
| White - White/Caucasian/European Heritage  | 176   |  |  |
| Mixed Asian Race   | 1     |  |  |
| Mixed White Race   | 1     |  |  |
| Unknown  | 1     |  |  |
| Missing  | 2     |  |  |

## End points

### End points reporting groups

|   |                                      |
|---|--------------------------------------|
| Reporting group title   | GSK2857916 2.5 mg/kg (Frozen liquid) |
| Reporting group description:<br>Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 2.5 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 39 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline. |                                      |
| Reporting group title   | GSK2857916 3.4 mg/kg (Frozen liquid) |
| Reporting group description:<br>Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 3.4 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 32 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline. |                                      |
| Reporting group title   | GSK2857916 3.4 mg/kg (Lyophilized)   |
| Reporting group description:<br>Participants were administered lyophilized powder (100 mg/vial in a single use vial) at a dose of 3.4 mg/kg GSK2857916 given IV for a maximum of up to 35 cycles (1 cycle= 21 days). Lyophilized powder was reconstituted using water for injection.                    |                                      |

### Primary: Overall response rate (ORR) by Independent Review Committee (IRC) (Full Analysis Population)

|  |   |
|--|---|
| End point title  | Overall response rate (ORR) by Independent Review Committee (IRC) (Full Analysis Population) <sup>[1]</sup> |
| End point description:<br>ORR was determined according to the 2016 international myeloma working group (IMWG) response criteria by IRC. ORR was calculated as the percentage of participants with a confirmed partial response (PR) or better (that is [i.e.], PR, very good partial response [VGPR], complete response [CR] and stringent complete response [sCR]). Confidence intervals were based on the exact method. Full Analysis Population comprised of all randomized participants (any participant who received a treatment randomization number was considered as randomized) whether or not randomized treatment was administered. This population was based on the treatment the participant was randomized to. |   |
| End point type   | Primary   |
| End point timeframe:<br>Up to 48 weeks   |   |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: There are no statistical data to report.   |   |

| End point values                   | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|------------------------------------|--|--|--|--|
| Subject group type                 | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed        | 97 <sup>[2]</sup>                          | 99 <sup>[3]</sup>                          | 25 <sup>[4]</sup>                        |  |
| Units: Percentage of Participants  |  |  |  |  |
| number (confidence interval 97.5%) | 31 (20.8 to<br>42.6)                       | 34 (23.9 to<br>46.0)                       | 48 (25.5 to<br>71.1)                     |  |

Notes:

[2] - Full Analysis Population

[3] - Full Analysis Population

[4] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

### Primary: Overall response rate by Independent Review Committee (Efficacy Population)

|                 |   |
|-----------------|---|
| End point title | Overall response rate by Independent Review Committee (Efficacy Population) <sup>[5][6]</sup> |
|-----------------|---|

End point description:

ORR was determined according to the 2016 IMWG response criteria by IRC. ORR was calculated as the percentage of participants with a confirmed PR or better (i.e., PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Efficacy Population comprised of first 130 intent-to-treat participants whether or not randomized treatment (frozen solution) was administered. Intent-to-treat Population comprised of all randomized participants whether or not randomized treatment was administered. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 48 weeks

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

| End point values                  | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 64 <sup>[7]</sup>                          | 66 <sup>[8]</sup>                          |  |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 30 (18.9 to 42.4)                          | 30 (19.6 to 42.9)                          |  |  |

Notes:

[7] - Efficacy Population

[8] - Efficacy Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall response rate by investigator assessment (IA) (Full Analysis Population)

|                 |  |
|-----------------|--|
| End point title | Overall response rate by investigator assessment (IA) (Full Analysis Population) |
|-----------------|--|

End point description:

ORR was determined by the investigator according to the 2016 IMWG response criteria. ORR was calculated as the percentage of participants with a confirmed PR or better (i.e., PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed       | 97 <sup>[9]</sup>                          | 99 <sup>[10]</sup>                         | 25 <sup>[11]</sup>                       |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 33 (23.8 to<br>43.3)                       | 32 (23.3 to<br>42.5)                       | 52 (31.3 to<br>72.2)                     |  |

Notes:

[9] - Full Analysis Population

[10] - Full Analysis Population

[11] - Full Analysis Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical benefit rate by investigator assessment (Efficacy Population)

|                 |  |
|-----------------|--|
| End point title | Clinical benefit rate by investigator assessment (Efficacy Population) <sup>[12]</sup> |
|-----------------|--|

End point description:

CBR was determined by the investigator according to the 2016 IMWG response criteria. CBR was calculated as the percentage of participants with a confirmed MR or better (i.e., MR, PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 64 <sup>[13]</sup>                         | 66 <sup>[14]</sup>                         |  |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 34 (22.9 to<br>47.3)                       | 35 (23.5 to<br>47.6)                       |  |  |

Notes:

[13] - Efficacy Population.

[14] - Efficacy Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall response rate by investigator assessment (Efficacy Population)

|                 |  |
|-----------------|--|
| End point title | Overall response rate by investigator assessment (Efficacy Population) <sup>[15]</sup> |
|-----------------|--|

End point description:

ORR was determined by the investigator according to the 2016 IMWG response criteria. ORR was calculated as the percentage of participants with a confirmed PR or better (i.e., PR, VGPR, CR and sCR).

Confidence intervals were based on the exact method. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

| End point values                  | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 64 <sup>[16]</sup>                         | 66 <sup>[17]</sup>                         |  |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 33 (21.6 to<br>45.7)                       | 26 (15.8 to<br>38.0)                       |  |  |

Notes:

[16] - Efficacy Population.

[17] - Efficacy Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clinical benefit rate (CBR) by investigator assessment (Full Analysis Population)

|                 |   |
|-----------------|---|
| End point title | Clinical benefit rate (CBR) by investigator assessment (Full Analysis Population) |
|-----------------|---|

End point description:

CBR was determined by the investigator according to the 2016 IMWG response criteria. CBR was calculated as the percentage of participants with a confirmed minimal response (MR) or better (i.e., MR, PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

| End point values                  | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed       | 97 <sup>[18]</sup>                         | 99 <sup>[19]</sup>                         | 25 <sup>[20]</sup>                       |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 35 (25.6 to<br>45.4)                       | 38 (28.8 to<br>48.7)                       | 60 (38.7 to<br>78.9)                     |  |

Notes:

[18] - Full Analysis Population

[19] - Full Analysis Population

[20] - Full Analysis Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of response (DoR) by investigator assessment (Full Analysis Population)

|                 |  |
|-----------------|--|
| End point title | Duration of response (DoR) by investigator assessment (Full Analysis Population) |
|-----------------|--|

End point description:

DoR is defined as the time from first documented evidence of PR or better until the earliest date of documented disease progression (PD) per IMWG response criteria; or death due to PD among participants who achieved an overall response, i.e., confirmed PR or better. DOR based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of DOR are presented. Only responders (confirmed PR or better) by investigator assessment were included in this analysis.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 32 <sup>[21]</sup>                         | 32 <sup>[22]</sup>                         | 13 <sup>[23]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 12.4 (4.2 to 21.4)                         | 12.6 (5.6 to 22.8)                         | 5.3 (2.8 to 9.0)                         |  |

Notes:

[21] - Full Analysis Population.

[22] - Full Analysis Population.

[23] - Full Analysis Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical benefit rate by Independent Review Committee (Efficacy Population)

|                 |   |
|-----------------|---|
| End point title | Clinical benefit rate by Independent Review Committee (Efficacy Population) <sup>[24]</sup> |
|-----------------|---|

End point description:

CBR was determined according to the 2016 IMWG response criteria by IRC. CBR was calculated as the percentage of participants with a confirmed MR or better (i.e., MR, PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 64 <sup>[25]</sup>                         | 66 <sup>[26]</sup>                         |  |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 34 (22.9 to<br>47.3)                       | 38 (26.2 to<br>50.7)                       |  |  |

Notes:

[25] - Efficacy Population.

[26] - Efficacy Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical benefit rate by Independent Review Committee (Full Analysis Population)

|                 |  |
|-----------------|--|
| End point title | Clinical benefit rate by Independent Review Committee (Full Analysis Population) |
|-----------------|--|

End point description:

CBR was determined according to the 2016 IMWG response criteria by IRC. CBR was calculated as the percentage of participants with a confirmed MR or better (i.e., MR, PR, VGPR, CR and sCR). Confidence intervals were based on the exact method. Percentage values are rounded off.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

|                                   |  |  |  |  |
|-----------------------------------|--|--|--|--|
| <b>End point values</b>           | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed       | 97 <sup>[27]</sup>                         | 99 <sup>[28]</sup>                         | 25 <sup>[29]</sup>                       |  |
| Units: Percentage of Participants |  |  |  |  |
| number (confidence interval 95%)  | 36 (26.6 to<br>46.5)                       | 40 (30.7 to<br>50.7)                       | 56 (34.9 to<br>75.6)                     |  |

Notes:

[27] - Full Analysis Population

[28] - Full Analysis Population

[29] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of response by Independent Review Committee (Full Analysis Population)

|                 |   |
|-----------------|---|
| End point title | Duration of response by Independent Review Committee (Full Analysis Population) |
|-----------------|---|

End point description:

DoR is defined as the time from first documented evidence of PR or better until the earliest date of documented PD per IMWG response criteria; or death due to PD among participants who achieved an overall response, i.e., confirmed PR or better. DOR based on responses assessed by IRC is presented. Median and inter-quartile range (first quartile and third quartile) of DOR are presented. Only responders

(confirmed PR or better) by Independent Review committee were included in this analysis.88888 indicates <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 31 <sup>[30]</sup>                         | 35 <sup>[31]</sup>                         | 13 <sup>[32]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 12.5 (4.2 to 19.4)                         | 6.2 (4.2 to 88888)                         | 9.0 (3.4 to 10.4)                        |  |

Notes:

[30] - Full Analysis Population.

[31] - Full Analysis Population.

[32] - Full Analysis Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of response by investigator assessment (Efficacy Population)

|                 |   |
|-----------------|---|
| End point title | Duration of response by investigator assessment (Efficacy Population) <sup>[33]</sup> |
|-----------------|---|

End point description:

DoR is defined as the time from first documented evidence of PR or better until the earliest date of documented PD per IMWG response criteria; or death due to PD among participants who achieved an overall response, i.e., confirmed PR or better. DOR based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of DOR are presented. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Only responders (confirmed PR or better) by investigator assessment were included in this analysis. 88888 indicates <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
| Subject group type                    | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed           | 21 <sup>[34]</sup>                         | 17 <sup>[35]</sup>                         |  |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 6.9 (4.2 to 20.8)                          | 15.9 (12.6 to 88888)                       |  |  |

Notes:

[34] - Efficacy Population.

[35] - Efficacy Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of response by Independent Review Committee (Efficacy Population)

|                 |  |
|-----------------|--|
| End point title | Duration of response by Independent Review Committee (Efficacy Population) <sup>[36]</sup> |
|-----------------|--|

End point description:

DoR is defined as the time from first documented evidence of PR or better until the earliest date of documented PD per IMWG response criteria; or death due to PD among participants who achieved an overall response, i.e., confirmed PR or better. DOR based on responses assessed by IRC is presented. Median and inter-quartile range (first quartile and third quartile) of DOR are presented. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Only responders (confirmed PR or better) by Independent Review Committee were included in this analysis. 88888 indicates <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed           | 20 <sup>[37]</sup>                         | 20 <sup>[38]</sup>                         |  |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 11.0 (4.0 to 19.4)                         | 15.9 (4.2 to 88888)                        |  |  |

Notes:

[37] - Efficacy Population.

[38] - Efficacy Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to response by investigator assessment (Full Analysis Population)

|                 |  |
|-----------------|--|
| End point title | Time to response by investigator assessment (Full Analysis Population) |
|-----------------|--|

End point description:

Time to response is defined as the time between the date of randomization and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better). Time to response based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of time to response are presented. Only responders

(confirmed PR or better) by investigator assessment were included in this analysis

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 32 <sup>[39]</sup>                         | 32 <sup>[40]</sup>                         | 13 <sup>[41]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.5 (0.8 to 2.5)                           | 1.5 (0.9 to 3.0)                           | 0.9 (0.8 to 1.0)                         |  |

Notes:

[39] - Full Analysis Population.

[40] - Full Analysis Population.

[41] - Full Analysis Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to response by investigator assessment (Efficacy Population)

|                 |   |
|-----------------|---|
| End point title | Time to response by investigator assessment (Efficacy Population) <sup>[42]</sup> |
|-----------------|---|

End point description:

Time to response is defined as the time between the date of randomization and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better). Time to response based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of time to response are presented. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Only responders (confirmed PR or better) by investigator assessment were included in this analysis.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
| Subject group type                    | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed           | 21 <sup>[43]</sup>                         | 17 <sup>[44]</sup>                         |  |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.4 (0.8 to 2.8)                           | 1.5 (1.4 to 2.8)                           |  |  |

Notes:

[43] - Efficacy Population

[44] - Efficacy Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to response by Independent Review Committee (Efficacy Population)

|                 |  |
|-----------------|--|
| End point title | Time to response by Independent Review Committee (Efficacy Population) <sup>[45]</sup> |
|-----------------|--|

End point description:

Time to response is defined as the time between the date of randomization and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better). Time to response based on responses assessed by IRC is presented. Median and inter-quartile range (first quartile and third quartile) of time to response are presented. Data is not presented for 'GSK2857916 3.4 mg/kg (Lyophilized)' arm as it is not included in Efficacy Population. Only responders (confirmed PR or better) by Independent Review Committee were included in this analysis

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed           | 20 <sup>[46]</sup>                         | 20 <sup>[47]</sup>                         |  |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.5 (0.8 to 2.5)                           | 1.4 (1.1 to 1.9)                           |  |  |

Notes:

[46] - Efficacy Population.

[47] - Efficacy Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression free survival by investigator assessment

|                 |  |
|-----------------|--|
| End point title | Progression free survival by investigator assessment |
|-----------------|--|

End point description:

Progression free survival is defined as the time from randomization until the earliest date of documented PD per IMWG, or death due to any cause. Progressive Disease is defined as at least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. Progression free survival based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of progression free survival are presented.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 97 <sup>[48]</sup>                         | 99 <sup>[49]</sup>                         | 25 <sup>[50]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 2.2 (0.8 to 7.7)                           | 3.2 (1.0 to 9.8)                           | 3.6 (1.5 to 8.7)                         |  |

Notes:

[48] - Full Analysis Population

[49] - Full Analysis Population

[50] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to response by Independent Review Committee (Full Analysis Population)

|                 |   |
|-----------------|---|
| End point title | Time to response by Independent Review Committee (Full Analysis Population) |
|-----------------|---|

End point description:

Time to response is defined as the time between the date of randomization and the first documented evidence of response (PR or better), among participants who achieve a response (i.e., confirmed PR or better). Time to response based on responses assessed by IRC is presented. Median and inter-quartile range (first quartile and third quartile) of time to response are presented. Only responders (confirmed PR or better) by Independent Review Committee were included in this analysis

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

|                                       |  |  |  |  |
|---------------------------------------|--|--|--|--|
| <b>End point values</b>               | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 31 <sup>[51]</sup>                         | 35 <sup>[52]</sup>                         | 13 <sup>[53]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 1.5 (0.8 to 2.2)                           | 1.4 (0.8 to 2.8)                           | 0.9 (0.8 to 2.3)                         |  |

Notes:

[51] - Full Analysis Population.

[52] - Full Analysis Population.

[53] - Full Analysis Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression free survival by Independent Review Committee

|                 |   |
|-----------------|---|
| End point title | Progression free survival by Independent Review Committee |
|-----------------|---|

End point description:

Progression free survival is defined as the time from randomization until the earliest date of documented PD per IMWG, or death due to any cause. Progressive Disease is defined as at least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. Progression free survival based on responses assessed by IRC is presented. Median and inter-quartile range (first

quartile and third quartile) of progression free survival are presented.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 97 <sup>[54]</sup>                         | 99 <sup>[55]</sup>                         | 25 <sup>[56]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 2.8 (0.9 to 9.7)                           | 3.9 (0.8 to 9.0)                           | 5.7 (2.2 to 9.7)                         |  |

Notes:

[54] - Full Analysis Population

[55] - Full Analysis Population

[56] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to progression by investigator assessment

|  |  |
|--|--|
| End point title  | Time to progression by investigator assessment |
| End point description:   |  |
| Time to progression is defined as the time from randomization until the earliest date of documented PD per IMWG, or death due to PD. Time to Progression based on responses assessed by investigator is presented. Median and inter-quartile range (first quartile and third quartile) of time to progression are presented. |  |
| End point type   | Secondary                                      |
| End point timeframe:   |  |
| Up to 186 weeks  |  |

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 97 <sup>[57]</sup>                         | 99 <sup>[58]</sup>                         | 25 <sup>[59]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 2.2 (0.8 to 7.7)                           | 3.9 (1.0 to 11.9)                          | 3.6 (1.5 to 9.7)                         |  |

Notes:

[57] - Full Analysis Population

[58] - Full Analysis Population

[59] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to progression by Independent Review Committee

|                 |   |
|-----------------|---|
| End point title | Time to progression by Independent Review Committee |
|-----------------|---|

End point description:

Time to progression is defined as the time from randomization until the earliest date of documented PD per IMWG, or death due to PD. Time to Progression based on responses assessed by IRC is presented. Median and inter-quartile range (first quartile and third quartile) of time to progression are presented.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 97 <sup>[60]</sup>                         | 99 <sup>[61]</sup>                         | 25 <sup>[62]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 2.9 (0.9 to 9.7)                           | 4.9 (0.8 to 11.1)                          | 5.7 (2.2 to 9.7)                         |  |

Notes:

[60] - Full Analysis Population

[61] - Full Analysis Population

[62] - Full Analysis Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with change from Baseline in hematology parameters with respect to the normal range

|                 |  |
|-----------------|--|
| End point title | Number of participants with change from Baseline in hematology parameters with respect to the normal range |
|-----------------|--|

End point description:

Blood samples were collected for assessment of basophils, eosinophils, hematocrit, mean corpuscular hemoglobin (MCH), MCH concentration (MCHC), MC volume (MCV), monocyte, erythrocytes, reticulocytes. Baseline is latest pre-dose assessment (Day 1) with non-missing value, including unscheduled visits. If values were unchanged (eg. high to high) or whose value became normal, were recorded in change to normal/NC category. Participants were counted twice if participant had both decreased to low/increased to high during post-Baseline (PB). Data for worst case PB is presented. Full Safety Population (FSP) comprised of all participants who received at least 1 dose of study drug (frozen liquid or lyophilized powder). 3 out of 221 participants did not receive any study treatment were excluded from FSP. All participants in study were included in analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Up to 186 weeks

| <b>End point values</b>                              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|--|--|--|--|--|
| Subject group type                                   | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                          | 95 <sup>[63]</sup>                         | 99 <sup>[64]</sup>                         | 24 <sup>[65]</sup>                       |  |
| Units: Participants                                  |  |  |  |  |
| Basophils, decrease to low, n=94,96,23               | 2  | 7  | 0  |  |
| Basophils, change to normal or NC,<br>n=94,96,23     | 87   | 85   | 19                                       |  |
| Basophils, increase to high, n=94,96,23              | 5  | 5  | 4  |  |
| Eosinophils, decrease to low,<br>n=95,97,23          | 14   | 13   | 0  |  |
| Eosinophils, change to normal or NC,<br>n=95,97,23   | 71   | 78   | 16                                       |  |
| Eosinophils, increase to high,<br>n=95,97,23         | 10   | 8  | 7  |  |
| Hematocrit, decrease to low,<br>n=95,97,24           | 10   | 3  | 1  |  |
| Hematocrit, change to normal or NC,<br>n=95,97,24    | 84   | 94   | 23                                       |  |
| Hematocrit, increase to high,<br>n=95,97,24          | 3  | 0  | 0  |  |
| MCH, decrease to low, n=95,95,21                     | 14   | 17   | 5  |  |
| MCH, change to normal or NC,<br>n=95,95,21           | 79   | 68   | 14                                       |  |
| MCH, increase to high, n=95,95,21                    | 2  | 12   | 2  |  |
| MCHC, decrease to low, n=94,96,21                    | 20   | 28   | 6  |  |
| MCHC, change to normal or NC,<br>n=94,96,21          | 70   | 66   | 14                                       |  |
| MCHC, increase to high, n=94,96,21                   | 5  | 2  | 1  |  |
| MCV, decrease to low, n=95,97,24                     | 12   | 15   | 4  |  |
| MCV, change to normal or NC,<br>n=95,97,24           | 77   | 73   | 18                                       |  |
| MCV, increase to high, n=95,97,24                    | 7  | 10   | 3  |  |
| Monocytes, decrease to low,<br>n=95,97,24            | 6  | 10   | 1  |  |
| Monocytes, change to normal or NC,<br>n=95,97,24     | 62   | 50   | 12                                       |  |
| Monocytes, increase to high,<br>n=95,97,24           | 28   | 45   | 12                                       |  |
| Erythrocytes, decrease to low,<br>n=95,97,24         | 4  | 1  | 0  |  |
| Erythrocytes, change to normal or NC,<br>n=95,97,24  | 91   | 95   | 21                                       |  |
| Erythrocytes, increase to high,<br>n=95,97,24        | 2  | 1  | 3  |  |
| Reticulocytes, decrease to low,<br>n=73,65,19        | 11   | 15   | 7  |  |
| Reticulocytes, change to normal or NC,<br>n=73,65,19 | 49   | 33   | 3  |  |
| Reticulocytes, increase to high,<br>n=73,65,19       | 16   | 21   | 10                                       |  |

Notes:

[63] - Full Safety Population.

[64] - Full Safety Population.

[65] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall survival

|  |                  |
|--|------------------|
| End point title  | Overall survival |
| End point description:<br>Overall survival is defined as the time from randomization until death due to any cause. Overall survival was analyzed using the Kaplan-Meier method by dose level. Median and inter-quartile range (first quartile and third quartile) of overall survival are presented. 88888 indicates <75% of participants experienced the event within the treatment arm. Hence, third-quartile could not be derived |                  |
| End point type   | Secondary        |
| End point timeframe:<br>Up to 186 weeks  |                  |

| End point values                      | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed           | 97 <sup>[66]</sup>                         | 99 <sup>[67]</sup>                         | 25 <sup>[68]</sup>                       |  |
| Units: Months                         |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 15.3 (4.8 to 36.4)                         | 14.0 (6.2 to 26.6)                         | 24.5 (7.7 to 88888)                      |  |

Notes:

[66] - Full Analysis Population

[67] - Full Analysis Population

[68] - Full Analysis Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with grade change from Baseline in hematology parameters

|   |   |
|---|---|
| End point title   | Number of participants with grade change from Baseline in hematology parameters |
| End point description:<br>Blood samples were collected for the analysis of following hematology parameters: hemoglobin (Hb), lymphocyte count (Lymph), neutrophil count (Neutro), platelet count (PC), and leukocyte count (leuko). The laboratory parameters were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.03. Grade 1: mild; Grade 2: moderate; Grade 3: severe or medically significant; Grade 4: life-threatening consequences. Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. An increase is defined as an increase in CTCAE grade relative to Baseline grade. Data for worst-case post Baseline is presented. Only those participants with increase to grade 3 and increase to grade 4 have been presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Baseline (Day 1) and Up to 186 weeks  |   |

| <b>End point values</b>                           | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                       | 95 <sup>[69]</sup>                         | 97 <sup>[70]</sup>                         | 24 <sup>[71]</sup>                       |  |
| Units: Participants                               |  |  |  |  |
| Hb, Hb increased, increase to Grade 3             | 0  | 0  | 0  |  |
| Hb, Hb increased, increase to Grade 4             | 0  | 0  | 0  |  |
| Hb, Anemia, increase to Grade 3                   | 19   | 30   | 5  |  |
| Hb, Anemia, increase to Grade 4                   | 0  | 0  | 0  |  |
| Lymph, Lymph count increased, increase to Grade 3 | 0  | 0  | 0  |  |
| Lymph, Lymph count increased, increase to Grade 4 | 0  | 0  | 0  |  |
| Lymph, Lymph count decreased, increase to Grade 3 | 16   | 24   | 6  |  |
| Lymph, Lymph count decreased, increase to Grade 4 | 5  | 5  | 2  |  |
| Neutro, increase to Grade 3                       | 4  | 10   | 2  |  |
| Neutro, increase to Grade 4                       | 6  | 3  | 1  |  |
| PC, increase to Grade 3                           | 9  | 11   | 1  |  |
| PC, increase to Grade 4                           | 13   | 25   | 2  |  |
| Leuko, Leukocytosis, increase to Grade 3          | 0  | 0  | 0  |  |
| Leuko, Leukocytosis, increase to Grade 4          | 0  | 0  | 0  |  |
| Leuko, Leuko decreased, increase to Grade 3       | 5  | 9  | 2  |  |
| Leuko, Leuko decreased, increase to Grade 4       | 3  | 3  | 0  |  |

Notes:

[69] - Full Safety Population.

[70] - Full Safety Population.

[71] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with change from Baseline in clinical chemistry parameters with respect to the normal range

|                 |  |
|-----------------|--|
| End point title | Number of participants with change from Baseline in clinical chemistry parameters with respect to the normal range |
|-----------------|--|

End point description:

Blood samples were collected for analysis of bicarbonate, direct bilirubin(D.Bil), calcium, chloride, lactate dehydrogenase(LDH), total protein,Urea enzymatic colorimetry.Baseline is latest pre-dose assessment(Day 1) with a non-missing value, including unscheduled visits. If values were unchanged (example: high to high), or whose value became normal, were recorded in the change to normal or NC category. Participants were counted twice if the participant had both decreased to low and increased to high during post Baseline. 3 out of 221participants did not receive any study treatment, were excluded from FSP.All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Up to 186 weeks

| <b>End point values</b>                                | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|--|--|--|--|--|
| Subject group type                                     | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                            | 95 <sup>[72]</sup>                         | 99 <sup>[73]</sup>                         | 24 <sup>[74]</sup>                       |  |
| Units: Participants                                    |  |  |  |  |
| Bicarbonate, decrease to low,<br>n=90,93,24            | 12   | 22   | 4  |  |
| Bicarbonate, change to normal or NC,<br>n=90,93,24     | 67   | 59   | 16                                       |  |
| Bicarbonate, increase to high,<br>n=90,93,24           | 12   | 16   | 4  |  |
| D.Bil, decrease to low, n=70,72,21                     | 0  | 2  | 0  |  |
| D.Bil, change to normal or NC,<br>n=70,72,21           | 60   | 60   | 20                                       |  |
| D.Bil, increase to high, n=70,72,21                    | 10   | 10   | 1  |  |
| Calcium, decrease to low, n=95,98,24                   | 26   | 28   | 8  |  |
| Calcium, change to normal or NC,<br>n=95,98,24         | 49   | 48   | 9  |  |
| Calcium, increase to high, n=95,98,24                  | 29   | 27   | 9  |  |
| Chloride, decrease to low, n=94,97,24                  | 17   | 14   | 2  |  |
| Chloride, change to normal or NC,<br>n=94,97,24        | 63   | 63   | 20                                       |  |
| Chloride, increase to high, n=94,97,24                 | 14   | 24   | 2  |  |
| LDH, decrease to low, n=92,98,23                       | 1  | 1  | 0  |  |
| LDH, change to normal or NC,<br>n=92,98,23             | 46   | 51   | 12                                       |  |
| LDH, increase to high, n=92,98,23                      | 45   | 47   | 11                                       |  |
| Protein, decrease to low, n=94,98,24                   | 32   | 32   | 8  |  |
| Protein, change to normal or NC,<br>n=94,98,24         | 49   | 58   | 14                                       |  |
| Protein, increase to high, n=94,98,24                  | 17   | 11   | 2  |  |
| Ureaenzymaticcolorimetrydecrease<br>tolow, n=90,93,24  | 10   | 13   | 0  |  |
| Ureaenzymaticcolorimetrychangenormal<br>/NCn=90,93,24  | 66   | 56   | 16                                       |  |
| Ureaenzymaticcolorimetryincreasetohigh<br>, n=90,93,24 | 15   | 26   | 8  |  |

Notes:

[72] - Full Safety Population.

[73] - Full Safety Population.

[74] - Full Safety Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with grade change from Baseline in clinical chemistry parameters

|                 |   |
|-----------------|---|
| End point title | Number of participants with grade change from Baseline in clinical chemistry parameters |
|-----------------|---|

End point description:

Bloodsamples collected analysis of glucose(GI),albumin,alkaline phosphatase (ALP),alanine

aminotransferase(ALT), aspartate aminotransferase(AST), total bilirubin(T.Bil), creatinine kinase (CK), creatinine, gamma glutamyl transferase (GGT), potassium (Pot), magnesium (Mg), sodium (Sod), phosphate (Ph)urate & estimated glomerular filtration rate (eGFR). Grading was as per NCI-CTCAE version 4.03. Grade1: mild; Grade2: moderate; Grade3: severe or medically significant; Grade4: life-threatening consequences. Baseline is latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. An increase is defined as increase in CTCAE grade relative to Baseline grade. 3 out of 221 participants did not receive any study treatment, were excluded from FSP. All participants in study were included in analysis (95, 99 and 24 Participants), but only those participants with data available at specified data points were analyzed (represented by n=X in the category titles).

|                                      |           |
|--------------------------------------|-----------|
| End point type                       | Secondary |
| End point timeframe:                 |           |
| Baseline (Day 1) and Up to 186 weeks |           |

| End point values                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|--|--|--|--|--|
| Subject group type                           | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                  | 95 <sup>[75]</sup>                         | 99 <sup>[76]</sup>                         | 24 <sup>[77]</sup>                       |  |
| Units: Participants                          |  |  |  |  |
| GI, Hyper, increase to Grade 3, n=94,95,24   | 3  | 5  | 0  |  |
| GI, Hyper, increase to Grade 4, n=94,95,24   | 0  | 0  | 0  |  |
| GI, Hypo, increase to Grade 3, n=94,95,24    | 0  | 0  | 0  |  |
| GI, Hypo, increase to Grade 4, n=94,95,24    | 0  | 0  | 0  |  |
| Albumin, increase to Grade 3, n=94,98,24     | 4  | 7  | 1  |  |
| Albumin, increase to Grade 4, n=94,98,24     | 0  | 0  | 0  |  |
| ALP, increase to Grade 3, n=93,97,24         | 1  | 0  | 0  |  |
| ALP, increase to Grade 4, n=93,97,24         | 0  | 0  | 0  |  |
| ALT, increase to Grade 3, n=93,97,24         | 0  | 0  | 0  |  |
| ALT, increase to Grade 4, n=93,97,24         | 0  | 0  | 0  |  |
| AST, increase to Grade 3, n=93,96,24         | 3  | 7  | 0  |  |
| AST, increase to Grade 4, n=93,96,24         | 0  | 0  | 0  |  |
| T.Bil, increase to Grade 3, n=92,97,23       | 0  | 0  | 0  |  |
| T.Bil, increase to Grade 4, n=92,97,23       | 0  | 0  | 0  |  |
| CK, increase to Grade 3, n= 87,91,24         | 1  | 0  | 1  |  |
| CK, increase to Grade 4, n= 87,91,24         | 2  | 0  | 0  |  |
| Creatinine, increase to Grade 3, n= 95,97,24 | 4  | 3  | 0  |  |
| Creatinine, increase to Grade 4, n= 95,97,24 | 1  | 0  | 0  |  |
| GGT, increase to Grade 3, n= 91,95,24        | 5  | 11   | 1  |  |
| GGT, increase to Grade 4, n= 91,95,24        | 1  | 1  | 0  |  |
| Pot, Hyper, increase to Grade 3, n= 95,97,24 | 0  | 1  | 0  |  |
| Pot, Hyper, increase to Grade 4, n= 95,97,24 | 0  | 0  | 0  |  |
| Pot, Hypo, increase to Grade 3, n= 95,97,24  | 0  | 4  | 1  |  |
| Pot, Hypo, increase to Grade 4, n= 95,97,24  | 2  | 0  | 0  |  |

|  |   |    |   |  |
|--|---|----|---|--|
| Mg, Hyper, increase to Grade 3, n= 91,96,24  | 3 | 1  | 0 |  |
| Mg, Hyper, increase to Grade 4, n= 91,96,24  | 0 | 0  | 0 |  |
| Mg, Hypo, increase to Grade 3, n= 91,96,24   | 0 | 0  | 0 |  |
| Mg, Hypo, increase to Grade 4, n= 91,96,24   | 0 | 0  | 0 |  |
| Phosphate, increase to Grade 3, n= 90,93,24  | 4 | 8  | 2 |  |
| Phosphate, increase to Grade 4, n= 90,93,24  | 0 | 0  | 0 |  |
| Sod, Hyper, increase to Grade 3, n= 95,97,24 | 0 | 0  | 0 |  |
| Sod, Hyper, increase to Grade 4, n= 95,97,24 | 0 | 0  | 0 |  |
| Sod, Hypo, increase to Grade 3, n= 95,97,24  | 2 | 6  | 1 |  |
| Sod, Hypo, increase to Grade 4, n= 95,97,24  | 0 | 0  | 0 |  |
| Urate, increase to Grade 3, n= 93,96,24      | 0 | 0  | 0 |  |
| Urate, increase to Grade 4, n= 93,96,24      | 3 | 5  | 1 |  |
| eGFR, increase to Grade 3, n= 84,85,23       | 8 | 11 | 0 |  |
| eGFR, increase to Grade 4, n= 84,85,23       | 3 | 1  | 0 |  |

Notes:

[75] - Full Safety Population.

[76] - Full Safety Population.

[77] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with abnormal findings during physical examination

|                 |   |
|-----------------|---|
| End point title | Number of participants with abnormal findings during physical examination |
|-----------------|---|

End point description:

Physical examination included assessment of the head, eyes, ears, nose, throat, skin, thyroid, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes, and extremities. This analysis was planned, but data was not collected and captured in the database.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

| End point values            | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 0 <sup>[78]</sup>                          | 0 <sup>[79]</sup>                          | 0 <sup>[80]</sup>                        |  |
| Units: Participants         |  |  |  |  |

Notes:

[78] - Full Safety Population.

[79] - Full Safety Population.

[80] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with change from Baseline in pulse rate

|                 |  |
|-----------------|--|
| End point title | Number of participants with change from Baseline in pulse rate |
|-----------------|--|

End point description:

Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Number of participants with worst case change from Baseline in pulse rate is presented. Data is categorized as: pulse rate 'decrease to <60 beats per minute [bpm]', 'increase to >100 bpm' and 'change to normal or no change'. If values were unchanged (example: increase to >100 bpm to increase to >100 bpm), or whose value became normal, were recorded in the 'change to normal or no change' category. Participants were counted twice if the participant had both 'decreased to <60 bpm' and 'increased to >100 bpm' during post Baseline. Data for worst-case post Baseline is presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Up to 186 weeks

| End point values              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed   | 95 <sup>[81]</sup>                         | 99 <sup>[82]</sup>                         | 24 <sup>[83]</sup>                       |  |
| Units: Participants           |  |  |  |  |
| Decrease to <60               | 14   | 17   | 6  |  |
| Change to normal or no change | 57   | 55   | 15                                       |  |
| Increase to >100              | 25   | 28   | 3  |  |

Notes:

[81] - Full Safety Population.

[82] - Full Safety Population.

[83] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with change from Baseline in body temperature

|                 |  |
|-----------------|--|
| End point title | Number of participants with change from Baseline in body temperature |
|-----------------|--|

End point description:

Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Number of participants with worst case change from Baseline in body temperature are presented. Data is categorized as: body temperature 'decrease to <=35 degrees celsius', 'increase to >=38 degrees celsius' and 'change to normal or no change'. If values were unchanged (example: increase to >=38 to increase to >=38 degrees celsius), or whose value became normal, were recorded

in the 'change to normal or no change' category. Participants were counted twice if the participant had both 'decreased to  $\leq 35$ ' and 'increased to  $\geq 38$  degrees celsius' during post Baseline. Data for worst-case post Baseline is presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

|                                      |           |
|--------------------------------------|-----------|
| End point type                       | Secondary |
| End point timeframe:                 |           |
| Baseline (Day 1) and Up to 186 weeks |           |

| End point values              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed   | 95 <sup>[84]</sup>                         | 98 <sup>[85]</sup>                         | 24 <sup>[86]</sup>                       |  |
| Units: Participants           |  |  |  |  |
| Decrease to $\leq 35$         | 1  | 3  | 0  |  |
| Change to normal or no change | 86   | 85   | 21                                       |  |
| Increase to $\geq 38$         | 8  | 10   | 3  |  |

Notes:

[84] - Full Safety Population.

[85] - Full Safety Population.

[86] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with serious adverse events (SAEs), common ( $\geq 5\%$ ) non-serious adverse events and adverse events of special interest (AESI)

|                 |   |
|-----------------|---|
| End point title | Number of Participants with serious adverse events (SAEs), common ( $\geq 5\%$ ) non-serious adverse events and adverse events of special interest (AESI) |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE defined as any untoward medical occurrence that; results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is congenital anomaly/birth defect, other situations judged by physician, is associated with liver injury and impaired liver function. Adverse events which were not Serious were considered as non-serious adverse events. Number of participants who had SAEs and common ( $\geq 5\%$ ) nonSAEs are presented. Number of participants with AESI (keratopathy, dry eye events, blurred vision, thrombocytopenia, infusion-related reactions, corneal events and neutropenia) are presented. 3 out of 221 participants did not receive any study treatment and thus were excluded from the Full Safety Population.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 186 weeks      |           |

| <b>End point values</b>     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 95 <sup>[87]</sup>                         | 99 <sup>[88]</sup>                         | 24 <sup>[89]</sup>                       |  |
| Units: Participants         |  |  |  |  |
| Common non-SAE              | 93   | 96   | 24                                       |  |
| SAE                         | 43   | 53   | 15                                       |  |
| Keratopathy                 | 67   | 74   | 23                                       |  |
| Dry eye events              | 17   | 25   | 6  |  |
| Blurred vision              | 24   | 36   | 10                                       |  |
| Thrombocytopenia            | 36   | 56   | 10                                       |  |
| Infusion-related reactions  | 20   | 16   | 4  |  |
| Corneal events              | 68   | 76   | 23                                       |  |
| Neutropenia                 | 14   | 28   | 2  |  |

Notes:

[87] - Full Safety Population

[88] - Full Safety Population

[89] - Full Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with grade change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP)

|                 |  |
|-----------------|--|
| End point title | Number of participants with grade change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) |
|-----------------|--|

End point description:

SBP and DBP were graded using NCI CTCAE version 4.03. For SBP: Grade 0: <120 millimeter mercury (mmHg); Grade 1: 120-139 mmHg; Grade 2: 140-159 mmHg; Grade 3:  $\geq$ 160 mmHg. For DBP: Grade 0: <80 mmHg; Grade 1: 80-89 mmHg; Grade 2: 90-99 mmHg; Grade 3:  $\geq$ 100 mmHg. Baseline was defined as the latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. An increase is defined as an increase in CTCAE grade relative to Baseline grade. Data for worst-case post Baseline is presented. Only those participants with increase to grade 2 and increase to grade 3 have been presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Up to 186 weeks

| <b>End point values</b>     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 95 <sup>[90]</sup>                         | 99 <sup>[91]</sup>                         | 24 <sup>[92]</sup>                       |  |
| Units: Participants         |  |  |  |  |
| SBP, increase to Grade 2    | 29   | 41   | 4  |  |
| SBP, increase to Grade 3    | 14   | 22   | 8  |  |
| DBP, increase to Grade 2    | 18   | 16   | 2  |  |
| DBP, increase to Grade 3    | 9  | 8  | 1  |  |

Notes:

[90] - Full Safety Population.

[91] - Full Safety Population.

[92] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with change from Baseline in best corrected visual acuity (BCVA) test scores

|  |   |
|--|---|
| End point title  | Number of participants with change from Baseline in best corrected visual acuity (BCVA) test scores |
| End point description:<br>Baseline was defined as latest pre-dose assessment (Day 1) with non-missing value, including unscheduled visits. BCVA score was assessed individually for each eye. BCVA test scores were categorized as no change/improved vision, possible worsened vision & definite worsened vision. No change/improved vision was defined as change from Baseline $<0.12$ Logarithm of the Minimum Angle of Resolution (logMAR) score; a possible worsened vision was defined as change from Baseline $\geq 0.12$ to $<0.3$ logMAR score; a definite worsened vision was defined as a change from Baseline $\geq 0.3$ logMAR score. Data for worst-case change from Baseline is presented. 3 out of 221 participants did not receive any study treatment & thus, were excluded from Full Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline (Day 1) and Up to 186 weeks   |   |

| End point values                                    | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 88 <sup>[93]</sup>                         | 94 <sup>[94]</sup>                         | 24 <sup>[95]</sup>                       |  |
| Units: Participants                                 |  |  |  |  |
| Left eye, no change/improved vision,<br>n=88,94,24  | 35   | 45   | 4  |  |
| Left eye, possible worsened vision,<br>n=88,94,24   | 11   | 15   | 4  |  |
| Left eye, definite worsened vision,<br>n=88,94,24   | 42   | 34   | 16                                       |  |
| Right eye, no change/improved vision,<br>n=87,93,23 | 32   | 38   | 5  |  |
| Right eye, possible worsened vision,<br>n=87,93,23  | 21   | 13   | 6  |  |
| Right eye, definite worsened vision,<br>n=87,93,23  | 34   | 42   | 12                                       |  |

Notes:

[93] - Full Safety Population.

[94] - Full Safety Population.

[95] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with intraocular pressure (IOP) $\geq$ 22 mmHg anytime post-Baseline

|                 |   |
|-----------------|---|
| End point title | Number of participants with intraocular pressure (IOP) $\geq$ 22 mmHg anytime post-Baseline |
|-----------------|---|

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. IOP was assessed individually for each eye. Number of participants with IOP  $\geq$ 22 mmHg anytime post-Baseline are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

| End point values            | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 88 <sup>[96]</sup>                         | 93 <sup>[97]</sup>                         | 24 <sup>[98]</sup>                       |  |
| Units: Participants         |  |  |  |  |
| Right eye, n=88,93,23       | 17   | 16   | 8  |  |
| Left eye, n=88,92,24        | 14   | 15   | 7  |  |

Notes:

[96] - Full Safety Population

[97] - Full Safety Population

[98] - Full Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with shift in extraocular muscle movement from yes (Baseline) to no (worst post-Baseline)

|                 |  |
|-----------------|--|
| End point title | Number of participants with shift in extraocular muscle movement from yes (Baseline) to no (worst post-Baseline) |
|-----------------|--|

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Extraocular muscle movement was assessed individually for each eye. Number of participants with shift in extraocular muscle movement from yes (Baseline) to no (worst post-Baseline) are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Up to 186 weeks

| <b>End point values</b>     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 95 <sup>[99]</sup>                         | 93 <sup>[100]</sup>                        | 23 <sup>[101]</sup>                      |  |
| Units: Participants         |  |  |  |  |
| Right eye, n=95,93,23       | 0  | 4  | 0  |  |
| Left eye, n=93,92,22        | 0  | 2  | 0  |  |

Notes:

[99] - Full Safety Population.

[100] - Full Safety Population.

[101] - Full Safety Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with shift in pupillary examination findings from normal (Baseline) to abnormal (worst post-Baseline)

|                 |  |
|-----------------|--|
| End point title | Number of participants with shift in pupillary examination findings from normal (Baseline) to abnormal (worst post-Baseline) |
|-----------------|--|

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Number of participants with shift in pupillary examination findings from normal (Baseline) to abnormal (worst post-Baseline) are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Up to 186 weeks

| <b>End point values</b>     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 91 <sup>[102]</sup>                        | 90 <sup>[103]</sup>                        | 23 <sup>[104]</sup>                      |  |
| Units: Participants         | 4  | 12   | 3  |  |

Notes:

[102] - Full Safety Population.

[103] - Full Safety Population.

[104] - Full Safety Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with shift in corneal epithelium findings from normal (Baseline) to abnormal (worst post-Baseline) for corneal epithelium (CE) and corneal stroma (CS)

|                 |   |
|-----------------|---|
| End point title | Number of participants with shift in corneal epithelium findings from normal (Baseline) to abnormal (worst post-Baseline) for corneal epithelium (CE) and corneal stroma (CS) |
|-----------------|---|

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Corneal epithelium findings for CE and CS were assessed individually for each eye. Number of participants with shift in corneal epithelium findings from normal (Baseline) to abnormal (worst post-Baseline) for CE and CS are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type Secondary

End point timeframe:

Baseline and Up to 186 weeks

| End point values            | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 92 <sup>[105]</sup>                        | 94 <sup>[106]</sup>                        | 24 <sup>[107]</sup>                      |  |
| Units: Participants         |  |  |  |  |
| CE, Right eye, n=53,54,17   | 39   | 40   | 16                                       |  |
| CE, Left eye, n=55,55,15    | 39   | 44   | 14                                       |  |
| CS, Right eye, n=92,94,24   | 5  | 7  | 3  |  |
| CS, Left eye, n=92,89,23    | 8  | 5  | 3  |  |

Notes:

[105] - Full Safety Population.

[106] - Full Safety Population.

[107] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with shift in corneal epithelium findings from no (Baseline) to yes (worst post-Baseline)

End point title Number of participants with shift in corneal epithelium findings from no (Baseline) to yes (worst post-Baseline)

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Corneal epithelium findings like active edema, active opacity, corneal neovascularization (CN), corneal ulcer, epithelial microcystic edema (EME) and subepithelial were performed using a slit lamp. Number of participants with shift in corneal epithelium findings from no (Baseline) to yes (worst post-Baseline) are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

End point type Secondary

End point timeframe:

Baseline and Up to 186 weeks

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[108]</sup>                        | 99 <sup>[109]</sup>                        | 24 <sup>[110]</sup>                      |  |
| Units: Participants                                 |  |  |  |  |
| Active edema, Right eye, n=94,99,24                 | 3  | 5  | 1  |  |
| Active edema, Left eye, n=95,99,24                  | 4  | 4  | 1  |  |
| Active opacity, Right eye, n=93,97,24               | 3  | 3  | 3  |  |
| Active opacity, Left eye, n=94,95,24                | 4  | 4  | 3  |  |
| Corneal Neovascularization, Right eye, n=93,99,24   | 1  | 1  | 1  |  |
| Corneal Neovascularization, Left eye, n=93,99,23    | 1  | 0  | 1  |  |
| Corneal ulcer, Right eye, n=61,60,22                | 1  | 1  | 0  |  |
| Corneal ulcer, Left eye, n=63,61,20                 | 1  | 2  | 0  |  |
| Epithelial Microcystic Edema, Right eye, n=95,99,24 | 15   | 24   | 9  |  |
| Epithelial Microcystic Edema, Left eye, n=95,99,23  | 16   | 25   | 8  |  |
| Subepithelial haze, Right eye, n=95,98,24           | 18   | 28   | 8  |  |
| Subepithelial haze, Left eye, n=95,97,23            | 18   | 29   | 6  |  |

Notes:

[108] - Full Safety Population.

[109] - Full Safety Population.

[110] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the concentration-time curve from time zero extrapolated to infinite time (AUC[0-infinity]) of GSK2857916 following IV dose in participants with RRMM

|                 |  |
|-----------------|--|
| End point title | Area under the concentration-time curve from time zero extrapolated to infinite time (AUC[0-infinity]) of GSK2857916 following IV dose in participants with RRMM |
|-----------------|--|

End point description:

Blood samples were collected at designated timepoints. Pharmacokinetic (PK) parameters of GSK2857916 were calculated using non-compartmental methods. Full Pharmacokinetic (PK) Population comprised of all participants in the Full Safety Population who had at least 1 non-missing PK assessment. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, end of infusion (EOI), 2 hours and 24 hours post start of infusion (SOI) on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[111]</sup>                        | 99 <sup>[112]</sup>                        | 24 <sup>[113]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=26,18,18                                 | 5644 (± 39.6)                              | 6495 (± 54.3)                              | 6962 (± 51.4)                            |  |
| Cycle 3, n=19,21,9                                  | 7848 (± 42.7)                              | 9199 (± 45.1)                              | 9694 (± 49.9)                            |  |

Notes:

[111] - Full PK Population

[112] - Full PK Population

[113] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with shift in tear break-up time from >10 seconds (Baseline) to ≤5 seconds (worst post-Baseline)

|                 |   |
|-----------------|---|
| End point title | Number of participants with shift in tear break-up time from >10 seconds (Baseline) to ≤5 seconds (worst post-Baseline) |
|-----------------|---|

End point description:

Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Number of participants with shift in tear break-up time from >10 seconds (Baseline) to ≤5 seconds (worst post-Baseline) are presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and Up to 186 weeks

| <b>End point values</b>     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 34 <sup>[114]</sup>                        | 31 <sup>[115]</sup>                        | 2 <sup>[116]</sup>                       |  |
| Units: Participants         |  |  |  |  |
| Left eye, n=34,30,2         | 14   | 12   | 2  |  |
| Right eye, n=30,31,2        | 11   | 12   | 1  |  |

Notes:

[114] - Full Safety Population.

[115] - Full Safety Population.

[116] - Full Safety Population.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the concentration-time curve over the dosing interval (AUC

**[0-tau]) of GSK2857916 following IV dose in participants With RRMM**

|                 |   |
|-----------------|---|
| End point title | Area under the concentration-time curve over the dosing interval (AUC[0-tau]) of GSK2857916 following IV dose in participants With RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| End point values                                    | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[117]</sup>                        | 99 <sup>[118]</sup>                        | 24 <sup>[119]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=30,20,22                                 | 4666 (± 45.7)                              | 5678 (± 40.1)                              | 5946 (± 37.2)                            |  |
| Cycle 3, n=26,24,11                                 | 6399 (± 31.6)                              | 6941 (± 34.2)                              | 7593 (± 34.5)                            |  |

## Notes:

[117] - Full PK Population

[118] - Full PK Population

[119] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Area under the concentration-time curve from zero to time of last quantifiable concentration (AUC[0-tlast]) of GSK2857916 following IV dose in participants with RRMM**

|                 |   |
|-----------------|---|
| End point title | Area under the concentration-time curve from zero to time of last quantifiable concentration (AUC[0-tlast]) of GSK2857916 following IV dose in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[120]</sup>                        | 99 <sup>[121]</sup>                        | 24 <sup>[122]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=32,21,22                                 | 4607 (± 54.4)                              | 5567 (± 51.0)                              | 6293 (± 45.7)                            |  |
| Cycle 3, n=28,28,11                                 | 6033 (± 44.7)                              | 6084 (± 73.8)                              | 8388 (± 46.1)                            |  |

Notes:

[120] - Full PK Population

[121] - Full PK Population

[122] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum observed concentration (C<sub>max</sub>) of GSK2857916 following IV dose in participants with RRMM

|                 |  |
|-----------------|--|
| End point title | Maximum observed concentration (C <sub>max</sub> ) of GSK2857916 following IV dose in participants with RRMM |
|-----------------|--|

End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[123]</sup>                        | 99 <sup>[124]</sup>                        | 24 <sup>[125]</sup>                      |  |
| Units: Microgram per milliliter                     |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=32,21,22                                 | 42.51 (± 26.3)                             | 52.03 (± 19.8)                             | 51.32 (± 18.3)                           |  |
| Cycle 3, n=29,28,11                                 | 42.35 (± 25.6)                             | 45.5 (± 25.3)                              | 48.06 (± 17.1)                           |  |

Notes:

[123] - Full PK Population

[124] - Full PK Population

[125] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to reach maximum observed concentration (T<sub>max</sub>) of GSK2857916

**following IV dose in participants with RRMM**

|                 |   |
|-----------------|---|
| End point title | Time to reach maximum observed concentration (Tmax) of GSK2857916 following IV dose in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| End point values              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed   | 95 <sup>[126]</sup>                        | 99 <sup>[127]</sup>                        | 24 <sup>[128]</sup>                      |  |
| Units: Hours                  |  |  |  |  |
| median (full range (min-max)) |  |  |  |  |
| Cycle 1, n=32,21,22           | 0.780 (0.42 to 2.50)                       | 0.700 (0.43 to 2.15)                       | 0.750 (0.48 to 2.88)                     |  |
| Cycle 3, n=29,28,11           | 0.580 (0.47 to 2.03)                       | 0.715 (0.42 to 2.90)                       | 0.870 (0.50 to 2.02)                     |  |

## Notes:

[126] - Full PK Population

[127] - Full PK Population

[128] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Terminal half-life (t<sub>1/2</sub>) of GSK2857916 following IV dose in participants with RRMM**

|                 |  |
|-----------------|--|
| End point title | Terminal half-life (t <sub>1/2</sub> ) of GSK2857916 following IV dose in participants with RRMM |
|-----------------|--|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[129]</sup>                        | 99 <sup>[130]</sup>                        | 24 <sup>[131]</sup>                      |  |
| Units: Hours  |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=29,19,22                                 | 164.4 (± 46.2)                             | 165.8 (± 55.0)                             | 196.2 (± 40.9)                           |  |
| Cycle 3, n=26,23,11                                 | 193.7 (± 48.4)                             | 214.4 (± 45.9)                             | 279.5 (± 40.3)                           |  |

Notes:

[129] - Full PK Population

[130] - Full PK Population

[131] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: AUC(0-infinity) of GSK2857916 total antibody following IV dose in participants with RRMM

|                 |  |
|-----------------|--|
| End point title | AUC(0-infinity) of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|--|

End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[132]</sup>                        | 99 <sup>[133]</sup>                        | 24 <sup>[134]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=16,10,9                                  | 10268 (± 65.8)                             | 10209 (± 64.9)                             | 10170 (± 75.0)                           |  |
| Cycle 3, n=10,11,3                                  | 20526 (± 45.1)                             | 18637 (± 69.4)                             | 22782 (± 161.1)                          |  |

Notes:

[132] - Full PK Population.

[133] - Full PK Population.

[134] - Full PK Population.

### Statistical analyses

No statistical analyses for this end point

**Secondary: AUC(0-tlast) of GSK2857916 total antibody following IV dose in participants with RRMM**

|                 |   |
|-----------------|---|
| End point title | AUC(0-tlast) of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| End point values                                    | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[135]</sup>                        | 99 <sup>[136]</sup>                        | 24 <sup>[137]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=30,19,20                                 | 7417 (± 58.5)                              | 9628 (± 52.8)                              | 9017 (± 55.4)                            |  |
| Cycle 3, n=27,26,11                                 | 10725 (± 59.4)                             | 11295 (± 80.0)                             | 17715 (± 61.0)                           |  |

## Notes:

[135] - Full PK Population

[136] - Full PK Population

[137] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: AUC(0-tau) of GSK2857916 total antibody following IV dose in participants with RRMM**

|                 |   |
|-----------------|---|
| End point title | AUC(0-tau) of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[138]</sup>                        | 99 <sup>[139]</sup>                        | 24 <sup>[140]</sup>                      |  |
| Units: Hours*microgram per milliliter               |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=29,18,19                                 | 7305 (± 41.9)                              | 9566 (± 42.2)                              | 9029 (± 40.2)                            |  |
| Cycle 3, n=23,24,11                                 | 11243 (± 34.6)                             | 11646 (± 38.0)                             | 15311 (± 43.9)                           |  |

Notes:

[138] - Full PK Population

[139] - Full PK Population

[140] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cmax of GSK2857916 total antibody following IV dose in participants with RRMM

|                 |   |
|-----------------|---|
| End point title | Cmax of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|---|

End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[141]</sup>                        | 99 <sup>[142]</sup>                        | 24 <sup>[143]</sup>                      |  |
| Units: Microgram per milliliter                     |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=30,19,20                                 | 48.94 (± 30.0)                             | 61.06 (± 26.9)                             | 60.08 (± 18.3)                           |  |
| Cycle 3, n=29,28,11                                 | 49.34 (± 32.9)                             | 55.60 (± 26.5)                             | 65.07 (± 17.4)                           |  |

Notes:

[141] - Full PK Population

[142] - Full PK Population

[143] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Tmax of GSK2857916 total antibody following IV dose in participants

**with RRMM**

|                 |   |
|-----------------|---|
| End point title | Tmax of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| End point values              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed   | 95 <sup>[144]</sup>                        | 99 <sup>[145]</sup>                        | 24 <sup>[146]</sup>                      |  |
| Units: Hours                  |  |  |  |  |
| median (full range (min-max)) |  |  |  |  |
| Cycle 1, n=30,19,20           | 1.750 (0.42 to 2.50)                       | 1.870 (0.50 to 24.50)                      | 0.650 (0.48 to 2.17)                     |  |
| Cycle 3, n=29,28,11           | 0.830 (0.47 to 46.05)                      | 1.150 (0.42 to 2.90)                       | 1.750 (0.50 to 2.02)                     |  |

## Notes:

[144] - Full PK Population

[145] - Full PK Population

[146] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: AUC(0-infinity) of Cysteine-maleimidocaproyl monomethyl auristatin F (Cys-mcMMAF) following IV dose of GSK2857916 in participants with RRMM**

|                 |   |
|-----------------|---|
| End point title | AUC(0-infinity) of Cysteine-maleimidocaproyl monomethyl auristatin F (Cys-mcMMAF) following IV dose of GSK2857916 in participants with RRMM |
|-----------------|---|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 66666 indicates Cys-mcMMAF was not detectable throughout the elimination phase; therefore, AUC(0-infinity) could not be estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[147]</sup>                        | 99 <sup>[148]</sup>                        | 24 <sup>[149]</sup>                      |  |
| Units: Hours*nanogram per milliliter                |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=27,20,19                                 | 66666 (± 66666)                            | 66666 (± 66666)                            | 66666 (± 66666)                          |  |
| Cycle 3, n=26,29,11                                 | 66666 (± 66666)                            | 66666 (± 66666)                            | 66666 (± 66666)                          |  |

Notes:

[147] - Full PK Population

[148] - Full PK Population

[149] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: t1/2 of GSK2857916 total antibody following IV dose in participants with RRMM

|                 |   |
|-----------------|---|
| End point title | t1/2 of GSK2857916 total antibody following IV dose in participants with RRMM |
|-----------------|---|

End point description:

Blood samples were collected at designated timepoints. PK parameters of GSK2857916 total antibody were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[150]</sup>                        | 99 <sup>[151]</sup>                        | 24 <sup>[152]</sup>                      |  |
| Units: Hours  |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=29,17,19                                 | 241.8 (± 49.3)                             | 250.8 (± 70.3)                             | 299.8 (± 61.0)                           |  |
| Cycle 3, n=23,23,11                                 | 352.4 (± 52.6)                             | 372.0 (± 49.6)                             | 557.3 (± 91.7)                           |  |

Notes:

[150] - Full PK Population

[151] - Full PK Population

[152] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

**Secondary: AUC(0-tau) of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM**

|                 |  |
|-----------------|--|
| End point title | AUC(0-tau) of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM |
|-----------------|--|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). 66666 indicates Cys-mcMMAF was not detectable throughout the dosing interval; therefore, AUC(0-tau) could not be estimated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| End point values                                    | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[153]</sup>                        | 99 <sup>[154]</sup>                        | 24 <sup>[155]</sup>                      |  |
| Units: Hours*nanogram per milliliter                |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=27,20,19                                 | 66666 (±<br>66666)                         | 66666 (±<br>66666)                         | 66666 (±<br>66666)                       |  |
| Cycle 3, n=26,29,11                                 | 66666 (±<br>66666)                         | 66666 (±<br>66666)                         | 66666 (±<br>66666)                       |  |

## Notes:

[153] - Full PK Population

[154] - Full PK Population

[155] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: AUC(0-tlast) of Cysteine-maleimidocaproyl monomethyl auristatin F (Cys-mcMMAF) following IV dose of GSK2857916 in participants with RRMM**

|                 |  |
|-----------------|--|
| End point title | AUC(0-tlast) of Cysteine-maleimidocaproyl monomethyl auristatin F (Cys-mcMMAF) following IV dose of GSK2857916 in participants with RRMM |
|-----------------|--|

## End point description:

Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[156]</sup>                        | 99 <sup>[157]</sup>                        | 24 <sup>[158]</sup>                      |  |
| Units: Hours*nanogram per milliliter                |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=27,20,19                                 | 79.26 (± 61.0)                             | 113.57 (± 58.3)                            | 100.35 (± 51.8)                          |  |
| Cycle 3, n=26,29,11                                 | 70.84 (± 46.9)                             | 74.04 (± 73.0)                             | 69.83 (± 36.6)                           |  |

Notes:

[156] - Full PK Population

[157] - Full PK Population

[158] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cmax of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM

|                 |  |
|-----------------|--|
| End point title | Cmax of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM |
|-----------------|--|

End point description:

Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)

| <b>End point values</b>                             | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[159]</sup>                        | 99 <sup>[160]</sup>                        | 24 <sup>[161]</sup>                      |  |
| Units: Nanogram per milliliter                      |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=27,20,19                                 | 0.903 (± 63.9)                             | 1.148 (± 64.7)                             | 1.017 (± 61.4)                           |  |
| Cycle 3, n=26,29,11                                 | 0.660 (± 52.3)                             | 0.749 (± 66.2)                             | 0.656 (± 47.6)                           |  |

Notes:

[159] - Full PK Population

[160] - Full PK Population

[161] - Full PK Population

### Statistical analyses

No statistical analyses for this end point

**Secondary: t1/2 of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM**

|                        |  |
|------------------------|--|
| End point title        | t1/2 of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM   |
| End point description: | Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods.                  |
| End point type         | Secondary  |
| End point timeframe:   | Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days) |

| End point values                                    | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed                         | 95 <sup>[162]</sup>                        | 99 <sup>[163]</sup>                        | 24 <sup>[164]</sup>                      |  |
| Units: Hours  |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Cycle 1, n=27,20,19                                 | 66666 (±<br>66666)                         | 66666 (±<br>66666)                         | 66666 (±<br>66666)                       |  |
| Cycle 3, n=26,29,11                                 | 66666 (±<br>66666)                         | 66666 (±<br>66666)                         | 66666 (±<br>66666)                       |  |

Notes:

[162] - Full PK Population

[163] - Full PK Population

[164] - Full PK Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Tmax of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM**

|                        |   |
|------------------------|---|
| End point title        | Tmax of Cys-mcMMAF following IV dose of GSK2857916 in participants with RRMM  |
| End point description: | Blood samples were collected at designated timepoints. PK parameters of Cys-mcMMAF were calculated using non-compartmental methods. All the participants in the study were included in the analysis (95, 99 and 24 Participants), but only those participants with data available at the specified data points were analyzed (represented by n=X in the category titles). |
| End point type         | Secondary   |
| End point timeframe:   | Cycle 1 and Cycle 3: Pre-dose, EOI, 2 hours and 24 hours post SOI on Day 1, anytime on Day 4, and anytime on Day 8 to Day 15 (each cycle of 21 days)  |

| <b>End point values</b>       | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed   | 95 <sup>[165]</sup>                        | 99 <sup>[166]</sup>                        | 24 <sup>[167]</sup>                      |  |
| Units: Hours                  |  |  |  |  |
| median (full range (min-max)) |  |  |  |  |
| Cycle 1, n=27,20,19           | 22.830 (1.92<br>to 65.63)                  | 23.835 (17.38<br>to 72.65)                 | 24.080 (0.97<br>to 69.47)                |  |
| Cycle 3, n=26,29,11           | 23.235 (0.58<br>to 46.08)                  | 22.570 (0.55<br>to 70.98)                  | 22.780 (0.50<br>to 71.93)                |  |

Notes:

[165] - Full PK Population

[166] - Full PK Population

[167] - Full PK Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers of anti-drug antibodies against GSK2857916

|                 |  |
|-----------------|--|
| End point title | Titers of anti-drug antibodies against GSK2857916 <sup>[168]</sup> |
|-----------------|--|

End point description:

Serum samples were collected for the determination of ADA using a validated ECL immunoassay. The assay involved screening, confirmation and titration steps. If serum samples contained ADA, they were further analyzed for the specificity of antibodies by a confirmation assay. Confirmed positive samples were titrated to obtain the titers of antibodies. Titers of anti-drug antibodies against GSK2857916 is presented. No participant was found with positive results for ADA test in arm GSK2857916 3.4 mg/kg (Lyophilized). Hence, titer values was not presented for the arm. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to 186 weeks

Notes:

[168] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

| <b>End point values</b>              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) |  |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed          | 4 <sup>[169]</sup>                         | 2 <sup>[170]</sup>                         |  |  |
| Units: Titers                        |  |  |  |  |
| arithmetic mean (standard deviation) | 125.0 (±<br>50.00)                         | 100.0 (± 0.00)                             |  |  |

Notes:

[169] - Full Safety Population.

[170] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

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**Secondary: Number of participants with at least one confirmed positive post-Baseline anti-drug antibody (ADA) result**

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|                 |   |
|-----------------|---|
| End point title | Number of participants with at least one confirmed positive post-Baseline anti-drug antibody (ADA) result |
|-----------------|---|

---

## End point description:

Serum samples were collected for the determination of anti-GSK2857916 antibodies (ADA) using a validated electrochemiluminescent (ECL) immunoassay. The assay involved screening, confirmation and titration steps. If serum samples tested positive in the screening assay, they were considered 'potentially positive' and were further analyzed for the specificity using the confirmation assay. Samples that confirmed positive in the confirmation assay were reported as 'positive'. Confirmed positive ADA samples were further characterized in the titration assay to quasi-quantitate the amount of ADA in the sample. Additionally, confirmed positive ADA samples were also tested in a validated neutralizing antibody assay to determine the potential neutralizing activity of the ADA. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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## End point timeframe:

Up to 186 weeks

---

| End point values            | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed | 89 <sup>[171]</sup>                        | 92 <sup>[172]</sup>                        | 24 <sup>[173]</sup>                      |  |
| Units: Participants         | 2  | 0  | 0  |  |

## Notes:

[171] - Full Safety Population.

[172] - Full Safety Population.

[173] - Full Safety Population.

**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Number of participants with symptomatic AEs measured by patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE)**

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|                 |   |
|-----------------|---|
| End point title | Number of participants with symptomatic AEs measured by patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE) |
|-----------------|---|

---

## End point description:

The PRO-CTCAE is a patient-reported outcome measure developed to evaluate symptomatic toxicity in participants on cancer clinical trials. It included symptomatic toxicities drawn from the CTCAE like blurred vision, chills, constipation, decreased appetite, fatigue, general pain, heart palpitations, mouth/throat sores, nausea, nosebleed, shortness of breath, vomiting and watery eyes. Items were scored individually on a 0 to 4 scale for severity, frequency and interference. Number of participants with symptomatic AEs (those who had a maximum post-Baseline rating greater than 0, example; 1, 2, 3, or 4) measured by PRO-CTCAE are presented. Full Safety Population.

---

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

---

## End point timeframe:

Up to 186 weeks

---

| <b>End point values</b>          | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed      | 84 <sup>[174]</sup>                        | 92 <sup>[175]</sup>                        | 22 <sup>[176]</sup>                      |  |
| Units: Participants              |  |  |  |  |
| Blurred Vision , n= 84,92,22     | 59   | 67   | 19                                       |  |
| Chills, n=43,42,13               | 39   | 36   | 12                                       |  |
| Constipation,n=84,92, 22         | 42   | 47   | 17                                       |  |
| Decreased Appetite, n=84,92, 22  | 60   | 65   | 16                                       |  |
| Fatigue, n=84,92, 22             | 81   | 87   | 21                                       |  |
| General Pain, n= 79, 80, 20      | 78   | 80   | 19                                       |  |
| Heart Palpitations,n=37, 37, 14  | 35   | 33   | 14                                       |  |
| Mouth/Throat Sores,n=84,92, 22   | 28   | 25   | 8  |  |
| Nausea,n=48, 52, 11              | 47   | 50   | 11                                       |  |
| Nosebleed,n=23, 33, 6            | 22   | 33   | 6  |  |
| Shortness Of Breath, n=84,92, 22 | 60   | 58   | 17                                       |  |
| Vomiting,n=21, 28, 6             | 20   | 28   | 5  |  |
| Watery Eyes,n=84,92, 22          | 50   | 59   | 19                                       |  |

Notes:

[174] - Full Safety Population.

[175] - Full Safety Population.

[176] - Full Safety Population.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Worst change from Baseline in National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) overall composite score

|                 |  |
|-----------------|--|
| End point title | Worst change from Baseline in National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) overall composite score |
|-----------------|--|

End point description:

The NEI-VFQ-25 consisted of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question to assess the impact of ocular toxicity on visual function. Items were coded to a 0 to 100 scale and averaged to calculate domains. Domain scores ranged from 0 to 100; higher scores are better. Therefore, increase in score means improvement. Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Data for worst-case post Baseline is presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and up to Week 186

|                                      |  |  |  |  |
|--------------------------------------|--|--|--|--|
| <b>End point values</b>              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                   | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed          | 83 <sup>[177]</sup>                        | 92 <sup>[178]</sup>                        | 22 <sup>[179]</sup>                      |  |
| Units: Scores on a scale             |  |  |  |  |
| arithmetic mean (standard deviation) | -20.0 (±<br>22.60)                         | -19.6 (±<br>21.66)                         | -23.1 (±<br>23.82)                       |  |

Notes:

[177] - Full Safety Population

[178] - Full Safety Population

[179] - Full Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Worst change from Baseline in Ocular Surface Disease Index (OSDI) total score

|                 |   |
|-----------------|---|
| End point title | Worst change from Baseline in Ocular Surface Disease Index (OSDI) total score |
|-----------------|---|

End point description:

The OSDI is a 12-item questionnaire designed to assess both the frequency of dry eye symptoms and their impact on vision-related functioning. The total OSDI score was calculated as (sum of scores for all questions answered\*100) divided by (total number of questions answered\*4). Domain scores ranged from 0 to 100; lower scores are better. Therefore, decrease in score from Baseline means improvement. Baseline was defined as latest pre-dose assessment (Day 1) with a non-missing value, including unscheduled visits. Change from Baseline was calculated by subtracting Baseline value from the post-dose visit value. Data for worst-case post Baseline is presented. 3 participants out of 221 participants did not receive any study treatment and thus, were excluded from the Full Safety Population. Only those participants with data available at the specified data points were analyzed.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and up to Week 186

|                                      |  |  |  |  |
|--------------------------------------|--|--|--|--|
| <b>End point values</b>              | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
| Subject group type                   | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed          | 83 <sup>[180]</sup>                        | 92 <sup>[181]</sup>                        | 22 <sup>[182]</sup>                      |  |
| Units: Scores on a scale             |  |  |  |  |
| arithmetic mean (standard deviation) | 26.9 (± 29.61)                             | 28.2 (± 28.49)                             | 35.0 (± 29.02)                           |  |

Notes:

[180] - Full Safety Population

[181] - Full Safety Population

[182] - Full Safety Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core module (EORTC QLQ-C30) score

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30-item Core module (EORTC QLQ-C30) score |
|-----------------|--|

End point description:

The EORTC QLQ-C30(physicalfunctioning [PF],rolefunctioning [RF],cognitivefunctioning [CF],emotionalfunctioning [EF]&socialfunctioning [SF]),(fatigue,pain,nausea/vomiting [N/V]),global health status (GHS)/Quality-of-Life (QoL) scale,(constipation,diarrhoea,insomnia,dyspnoea,appetite loss [AL],financial difficulties [FD]).Response options:1 to 4.Scores were averaged & transformed to 0 to 100,high score for functional scales GHS/QoLbetter functioning ability or healthrelated quality-of-life(HRQoL),whereas high score for symptom scales/single items-significant symptomatology.Baseline was latest predose assessment with non-missing value,including unscheduled visits.Change from Baseline was post-dose visit minus Baseline value.Only those participants who were measured analyzed(i.e.contributed data reported in the table)were included in the Overall Number of Participants Analyzed field.99999 indicates data is not available.77777 indicates SD could not be calculated for single participant

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 07, Week 13, Week 19, Week 25, Week 31, Week 37, Week 43, Week 61, Week 79, Week 97, Week 115, Week 133, Week 151, Week 169, and Week 186

| End point values                     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed          | 97 <sup>[183]</sup>                        | 99 <sup>[184]</sup>                        | 25 <sup>[185]</sup>                      |  |
| Units: Scores on a scale             |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| GHS/QoL,Week 07,n=48,47,17           | -0.7 (± 20.47)                             | -4.1 (± 18.54)                             | 1.5 (± 23.80)                            |  |
| GHS/QoL,Week 13,n=29,29,16           | -3.2 (± 18.42)                             | 6.0 (± 16.50)                              | 1.0 (± 14.23)                            |  |
| GHS/QoL,Week 19,n=19,27,10           | -2.2 (± 13.84)                             | 3.7 (± 20.19)                              | 0 (± 12.42)                              |  |
| GHS/QoL,Week 25,n=20,23,7            | -4.6 (± 16.10)                             | -2.5 (± 20.94)                             | 7.1 (± 8.91)                             |  |
| GHS/QoL,Week 31,n=15,18,7            | -2.2 (± 14.59)                             | 5.1 (± 20.44)                              | 2.4 (± 14.20)                            |  |
| GHS/QoL,Week 37,n=15,13,5            | -1.7 (± 14.50)                             | 1.9 (± 21.29)                              | 11.7 (± 4.56)                            |  |
| GHS/QoL,Week 43,n=15,14,4            | -4.4 (± 14.04)                             | 10.7 (± 15.82)                             | 12.5 (± 10.76)                           |  |
| GHS/QoL,Week 61,n=11,11,3            | -3.8 (± 17.23)                             | -5.3 (± 13.58)                             | 0.0 (± 0.00)                             |  |
| GHS/QoL,Week 79,n=3,2,1              | 2.8 (± 24.06)                              | 16.7 (± 23.57)                             | 16.7 (± 77777)                           |  |
| GHS/QoL,Week 97,n=4,5,3              | 8.3 (± 11.79)                              | 1.7 (± 25.28)                              | 8.3 (± 0.00)                             |  |
| GHS/QoL,Week 115,n=2,6,3             | -4.2 (± 17.68)                             | 1.4 (± 22.00)                              | 2.8 (± 4.81)                             |  |
| GHS/QoL,Week 133,n=2,1,2             | -4.2 (± 17.68)                             | 33.3 (± 77777)                             | -8.3 (± 11.79)                           |  |
| GHS/QoL,Week 151,n=0,2,0             | 99999 (± 99999)                            | 8.3 (± 35.36)                              | 99999 (± 99999)                          |  |
| GHS/QoL,Week 169,n=0,1,0             | 99999 (± 99999)                            | 33.3 (± 77777)                             | 99999 (± 99999)                          |  |
| GHS/QoL,Week 186n=41,46,17           | -8.1 (± 19.50)                             | -11.6 (± 22.46)                            | -3.9 (± 15.34)                           |  |
| PF,,Week 07,n=48,47,17               | 4.4 (± 15.70)                              | -1.0 (± 21.93)                             | -5.5 (± 24.18)                           |  |
| PF,Week 13, n=29,29,16               | 0.7 (± 14.62)                              | 4.1 (± 11.19)                              | -12.5 (± 23.84)                          |  |
| PF,,Week 19,n=19,27,10               | 0.4 (± 13.78)                              | 6.2 (± 24.87)                              | -4.0 (± 14.81)                           |  |
| PF,Week 25, n=20,23,7                | 1.3 (± 12.16)                              | 5.5 (± 25.08)                              | -1.0 (± 14.62)                           |  |
| PF,Week 31,n=15,18,7                 | -2.7 (± 8.66)                              | 9.3 (± 22.88)                              | 4.8 (± 10.69)                            |  |
| PF, Week 37,n=15,13, 5               | 4.0 (± 11.76)                              | 15.4 (± 25.15)                             | 10.7 (± 18.62)                           |  |
| PF, Week 43,n=15,14, 4               | 3.1 (± 11.23)                              | 14.8 (± 26.04)                             | 6.7 (± 27.22)                            |  |
| PF, Week 61,n=11,11, 3               | 4.2 (± 12.39)                              | 9.7 (± 22.18)                              | 15.6 (± 3.85)                            |  |

|                         |                 |                 |                 |
|-------------------------|-----------------|-----------------|-----------------|
| PF, Week 79,n=3,2, 2    | 2.2 (± 3.85)    | 10.0 (± 4.71)   | 10.0 (± 4.71)   |
| PF, Week 97,n=4,5, 3    | 0.0 (± 9.43)    | 0.0 (± 9.43)    | -2.2 (± 23.41)  |
| PF, Week 115,n=2,6, 3   | 3.3 (± 4.71)    | 4.4 (± 13.11)   | 4.4 (± 10.18)   |
| PF, Week 133,n=2,1, 2   | 3.3 (± 4.71)    | 13.3 (± 77777)  | -6.7 (± 18.86)  |
| PF, Week 151,n=0,2,0    | 99999 (± 99999) | 0.0 (± 18.86)   | 99999 (± 99999) |
| PF, Week 169, n=0,1,0   | 4.7 (± 20.98)   | 13.3 (± 77777)  | -1.0 (± 20.81)  |
| PF, Week 186,n=41,46,17 | -0.8 (± 21.20)  | -6.2 (± 21.29)  | -13.3 (± 24.38) |
| RF,Week 07,n=48,47,17   | 0.3 (± 33.24)   | -6.0 (± 35.68)  | -7.8 (± 25.08)  |
| RF,Week 13,n=29,29,16   | 2.3 (± 33.55)   | -0.6 (± 32.88)  | -6.3 (± 30.96)  |
| RF,Week 19,n=19,27,10   | -4.4 (± 31.35)  | 1.9 (± 36.50)   | -5.0 (± 23.64)  |
| RF,Week 25,n=20,23,7    | 2.5 (± 32.57)   | 0.0 (± 32.57)   | 11.9 (± 32.93)  |
| RF,Week 31,n=15,18,7    | 8.9 (± 24.29)   | 3.7 (± 34.09)   | 7.1 (± 21.21)   |
| RF,Week 37,n=15,13,5    | 8.9 (± 29.46)   | 3.8 (± 39.76)   | 20.0 (± 27.39)  |
| RF,Week 43,n=15,14,4    | 8.9 (± 30.12)   | 11.9 (± 32.31)  | 8.3 (± 21.52)   |
| RF,Week 61,n=11,11,3    | 12.1 (± 36.58)  | -3.0 (± 29.64)  | 16.7 (± 16.67)  |
| RF,Week 79,n=3,2,2      | 5.6 (± 34.69)   | 8.3 (± 11.79)   | 8.3 (± 35.36)   |
| RF,Week 97,n=4,5,3      | -4.2 (± 43.83)  | -6.7 (± 19.00)  | 5.6 (± 34.69)   |
| RF,Week 115,n=2,6,3     | 0.0 (± 47.14)   | -5.6 (± 17.21)  | 16.7 (± 44.10)  |
| RF,Week 133,n=2,1,2     | 8.3 (± 35.36)   | 16.7 (± 77777)  | 25.0 (± 11.79)  |
| RF,Week 151,n=0,2,0     | 99999 (± 99999) | -16.7 (± 23.57) | 99999 (± 99999) |
| RF,Week 169,n=0,1,0     | -7.7 (± 23.78)  | 0.0 (± 77777)   | -1.4 (± 24.97)  |
| RF,Week 186,n=41,46,17  | -0.4 (± 30.84)  | -8.3 (± 33.66)  | -16.7 (± 30.62) |
| EF,Week 07,n=48,47,17   | 1.4 (± 18.86)   | 1.4 (± 27.10)   | -4.4 (± 21.27)  |
| EF,Week 13,n=29,29,16   | -2.0 (± 23.00)  | -0.0 (± 25.00)  | -9.4 (± 23.35)  |
| EF,Week 19,n=19,27,10   | 0.4 (± 19.93)   | 3.1 (± 20.30)   | -1.7 (± 21.08)  |
| EF,Week 25, n=20, 23, 7 | -4.6 (± 21.20)  | 4.0 (± 20.39)   | -2.4 (± 14.20)  |
| EF,Week 37, n=15,13, 5  | 1.7 (± 13.44)   | 9.6 (± 23.29)   | 13.3 (± 16.24)  |
| EF,Week 43, n=15,14, 4  | 0.0 (± 18.90)   | 8.3 (± 27.74)   | 4.2 (± 4.81)    |
| EF,Week 61, n=11,11, 3  | 6.8 (± 12.81)   | -5.3 (± 16.36)  | 19.4 (± 12.73)  |
| EF,Week 79, n=3,2,2     | 2.8 (± 4.81)    | 8.3 (± 11.79)   | 16.7 (± 23.57)  |
| EF,Week 97, n=4,5,3     | 2.1 (± 10.49)   | 1.7 (± 25.95)   | 8.3 (± 16.67)   |
| EF,Week 115, n=2,6,3    | 0.0 (± 23.57)   | -2.8 (± 11.39)  | 11.1 (± 12.73)  |
| EF,Week 133, n=2,1,2    | -4.2 (± 29.46)  | 16.7 (± 77777)  | 8.3 (± 23.57)   |
| EF,Week 169, n=0,1,0    | 99999 (± 99999) | 16.7 (± 77777)  | 99999 (± 99999) |
| EF,Week 186, n=41,46,17 | -6.7 (± 24.45)  | -6.2 (± 21.04)  | -10.8 (± 17.37) |
| CF,Week 07,n=48,47,17   | 4.5 (± 20.55)   | -2.1 (± 21.03)  | -1.0 (± 20.81)  |
| CF,Week 13,n=29,29,16   | 2.3 (± 23.45)   | -1.1 (± 15.39)  | -15.6 (± 27.53) |
| CF,Week 19,n=19,27,10   | -1.8 (± 26.58)  | -0.6 (± 22.87)  | -6.7 (± 21.08)  |
| CF,Week 25, n=20, 23, 7 | -1.7 (± 27.52)  | 1.4 (± 21.27)   | -11.9 (± 18.54) |
| CF,Week 31, n=15,18, 7  | 6.7 (± 23.40)   | -3.7 (± 19.43)  | -4.8 (± 12.60)  |
| CF,Week 37, n=15,13, 5  | 3.3 (± 22.00)   | 3.8 (± 13.87)   | 3.3 (± 13.94)   |
| CF,Week 43, n=15,14, 4  | 2.2 (± 24.29)   | 1.2 (± 10.26)   | -4.2 (± 8.33)   |
| CF,Week 61, n=11,11, 3  | 10.6 (± 27.15)  | -1.5 (± 15.73)  | 5.6 (± 9.62)    |
| CF,Week 79, n=3,2,2     | 11.1 (± 19.25)  | -25.0 (± 35.36) | 8.3 (± 11.79)   |
| CF,Week 97, n=4,5,3     | -4.2 (± 25.00)  | -16.7 (± 33.33) | 0.0 (± 16.67)   |

|                              |                 |                 |                 |
|------------------------------|-----------------|-----------------|-----------------|
| CF,Week 115, n=2,6,3         | 0.0 (± 23.57)   | -0.0 (± 18.26)  | 11.1 (± 9.62)   |
| CF,Week 133, n=2,1,2         | -8.3 (± 35.36)  | 0.0 (± 77777)   | 8.3 (± 11.79)   |
| CF,Week 151, n=0,2,0         | 99999 (± 99999) | -16.7 (± 23.57) | 99999 (± 99999) |
| CF,Week 169, n=0,1,0         | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| CF,Week 186, n=41,46,17      | -3.3 (± 25.88)  | -11.2 (± 26.07) | -9.8 (± 13.25)  |
| SF,Week 07,n=48,47,17        | 3.8 (± 29.02)   | 1.1 (± 32.49)   | -1.0 (± 33.58)  |
| SF,Week 13,n=29,29,16        | -4.0 (± 28.75)  | 1.7 (± 28.64)   | -7.3 (± 31.01)  |
| SF,Week 19,n=19,27,10        | -6.1 (± 28.44)  | 5.6 (± 28.50)   | -6.7 (± 28.54)  |
| SF,Week 25, n=20, 23, 7      | -6.7 (± 26.71)  | 13.8 (± 22.84)  | 2.4 (± 32.53)   |
| SF,Week 31, n=15,18, 7       | 2.2 (± 16.51)   | 15.7 (± 31.56)  | 2.4 (± 24.40)   |
| SF,Week 37, n=15,13, 5       | 2.2 (± 21.70)   | 16.7 (± 29.66)  | 20.0 (± 21.73)  |
| SF,Week 43, n=15,14, 4       | -1.1 (± 17.21)  | 20.2 (± 30.08)  | 16.7 (± 23.57)  |
| SF,Week 61, n=11,11, 3       | 7.6 (± 32.80)   | -1.5 (± 17.41)  | 33.3 (± 16.67)  |
| SF,Week 79, n=3,2,2          | 5.6 (± 19.25)   | 8.3 (± 35.36)   | 25.0 (± 35.36)  |
| SF,Week 97, n=4,5,3          | -4.2 (± 43.83)  | 16.7 (± 20.41)  | 33.3 (± 16.67)  |
| SF,Week 115, n=2,6,3         | 16.7 (± 23.57)  | 2.8 (± 24.53)   | 27.8 (± 25.46)  |
| SF,Week 133, n=2,1,2         | 16.7 (± 23.57)  | 33.3 (± 77777)  | 41.7 (± 11.79)  |
| SF,Week 151, n=0,2,0         | 99999 (± 99999) | 16.7 (± 23.57)  | 99999 (± 99999) |
| SF,Week 169, n=0,1,0         | 99999 (± 99999) | 33.3 (± 77777)  | 99999 (± 99999) |
| SF,Week 186, n=41,46,17      | -4.1 (± 26.56)  | -10.1 (± 25.93) | -8.8 (± 31.80)  |
| Fatigue,Week 07,n=48,47,17   | -3.7 (± 21.90)  | -0.5 (± 23.74)  | -5.2 (± 20.83)  |
| Fatigue,Week 13,n=29,29,16   | -7.7 (± 23.78)  | -7.7 (± 19.27)  | -1.4 (± 24.97)  |
| Fatigue,Week 19,n=19,27,10   | -0.6 (± 22.67)  | -2.9 (± 22.77)  | -11.1 (± 15.71) |
| Fatigue,Week 25, n=20, 23, 7 | 3.3 (± 23.67)   | -2.4 (± 21.70)  | -11.1 (± 16.97) |
| Fatigue,Week 31, n=15,18, 7  | -0.7 (± 21.61)  | -11.7 (± 22.05) | -12.7 (± 18.62) |
| Fatigue,Week 37, n=15,13, 5  | -9.6 (± 18.24)  | -13.7 (± 24.07) | -20.0 (± 14.49) |
| Fatigue,Week 43, n=15,14, 4  | -12.6 (± 17.25) | -10.3 (± 32.16) | -22.2 (± 12.83) |
| Fatigue,Week 61, n=11,11, 3  | -12.1 (± 24.07) | 3.0 (± 22.82)   | -11.1 (± 0.00)  |
| Fatigue,Week 79, n=3,2,2     | -22.2 (± 11.11) | -16.7 (± 7.86)  | 5.6 (± 23.57)   |
| Fatigue,Week 97, n=4,5,3     | -5.6 (± 26.45)  | 6.7 (± 20.18)   | -25.9 (± 23.13) |
| Fatigue,Week 115, n=2,6,3    | -16.7 (± 23.57) | -3.7 (± 15.18)  | -18.5 (± 23.13) |
| Fatigue,Week 133, n=2,1,2    | -5.6 (± 39.28)  | -22.2 (± 77777) | -22.2 (± 15.71) |
| Fatigue,Week 151, n=0,2,0    | 99999 (± 99999) | 16.7 (± 23.57)  | 99999 (± 99999) |
| Fatigue,Week 169, n=0,1,0    | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| Fatigue,Week 186, n=41,46,17 | -1.6 (± 23.12)  | 4.1 (± 23.35)   | 6.5 (± 22.93)   |
| N/V,Week 07,n=46,46,17       | 2.4 (± 14.17)   | 4.3 (± 17.88)   | 2.0 (± 14.29)   |
| N/V,Week 13,n=29,29,16       | 2.3 (± 13.16)   | 1.1 (± 9.89)    | 7.3 (± 25.80)   |
| N/V,Week 19,n=19,27,10       | -1.8 (± 15.61)  | -1.2 (± 15.96)  | 1.7 (± 5.27)    |
| N/V,Week 25,n=20,23,7        | 5.0 (± 12.21)   | -0.7 (± 12.79)  | -4.8 (± 12.60)  |
| N/V,Week 31,n=15,18,7        | -3.3 (± 6.90)   | 1.9 (± 7.86)    | -2.4 (± 15.00)  |

|                              |                 |                 |                 |
|------------------------------|-----------------|-----------------|-----------------|
| N/V,Week 37,n=15,13, 5       | -6.7 (± 16.43)  | 2.6 (± 11.48)   | 0.0 (± 0.00)    |
| N/V,Week 43,n=15,14,4        | -7.8 (± 15.26)  | 1.2 (± 7.91)    | -8.3 (± 16.67)  |
| N/V,Week 61, n=11,11,3       | -4.5 (± 10.78)  | 4.5 (± 7.78)    | 0.0 (± 16.67)   |
| N/V,Week 79, n=3,2,2         | 0.0 (± 0.00)    | 0.0 (± 0.00)    | 0.0 (± 0.00)    |
| N/V,Week 97, n=4,5,3         | 0.0 (± 0.00)    | 0.0 (± 0.00)    | -11.1 (± 19.25) |
| N/V,Week 115, n=2,6,3        | 0.0 (± 0.00)    | 0.0 (± 0.00)    | -16.7 (± 16.67) |
| N/V,Week 133, n=2,1,2        | 0.0 (± 0.00)    | 0.0 (± 77777)   | -25.0 (± 11.79) |
| N/V, Week 151, n=0,2,0       | 99999 (± 99999) | 0.0 (± 0.00)    | 99999 (± 99999) |
| N/V, Week 169, n=0,1,0       | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| N/V, Week 186, n=41,46,17    | 5.7 (± 24.04)   | 3.3 (± 18.47)   | 1.0 (± 21.63)   |
| Pain,Week 07,n=48,47,17      | -3.1 (± 28.69)  | -1.1 (± 28.32)  | 8.8 (± 28.33)   |
| Pain,Week 13,n=29,28,16      | -4.0 (± 26.97)  | -2.3 (± 25.48)  | 5.2 (± 27.02)   |
| Pain,Week 19,n=19,27,10      | 4.4 (± 19.12)   | -8.6 (± 31.14)  | 1.7 (± 30.88)   |
| Pain,Week 25,n=20,23,7       | 2.5 (± 18.16)   | -1.4 (± 24.57)  | -0.0 (± 28.87)  |
| Pain,Week 31,n=15,18,7       | 4.4 (± 19.38)   | -0.9 (± 23.90)  | 2.4 (± 35.26)   |
| Pain,Week 37,n=15,13,5       | -2.2 (± 21.70)  | -10.3 (± 24.09) | -3.3 (± 24.72)  |
| Pain,Week 43,n=15,14,4       | -2.2 (± 15.26)  | -8.3 (± 24.24)  | 4.2 (± 36.96)   |
| Pain,Week 61,n=11,11,3       | -10.6 (± 18.67) | -0.0 (± 21.08)  | -5.6 (± 34.69)  |
| Pain,Week 79,n=3,2,2         | -16.7 (± 16.67) | 0.0 (± 23.57)   | 8.3 (± 58.93)   |
| Pain,Week 97,n=4,5,3         | -4.2 (± 20.97)  | 26.7 (± 22.36)  | -0.0 (± 44.10)  |
| Pain,Week 115,n=2,6, 3       | 0.0 (± 0.00)    | 8.3 (± 27.39)   | 5.6 (± 53.58)   |
| Pain,Week 133,n=2,1, 2       | 0.0 (± 0.00)    | 16.7 (± 77777)  | 16.7 (± 70.71)  |
| Pain,Week 151,n=0,2, 0       | 99999 (± 99999) | 33.3 (± 23.57)  | 99999 (± 99999) |
| Pain,Week 169,n=0,1, 0       | 99999 (± 99999) | 16.7 (± 77777)  | 99999 (± 99999) |
| Pain,Week 186,n=41,46, 17    | 1.6 (± 27.59)   | 1.4 (± 25.29)   | 16.7 (± 31.73)  |
| Dyspnoea,Week 07,n=48,47,17  | -2.1 (± 22.18)  | 2.1 (± 14.59)   | -7.8 (± 18.74)  |
| Dyspnoea,Week 13,n=29,29,16  | -1.1 (± 18.86)  | 1.1 (± 22.68)   | 2.1 (± 30.96)   |
| Dyspnoea,Week 19,n=19,27,10  | -5.3 (± 20.07)  | 3.7 (± 25.04)   | -16.7 (± 28.33) |
| Dyspnoea,Week 25,n=20,23,7   | -1.7 (± 20.16)  | 4.3 (± 18.27)   | 0.0 (± 27.22)   |
| Dyspnoea,Week 31,n=15, 18, 7 | -6.7 (± 18.69)  | 0.0 (± 16.17)   | -9.5 (± 16.27)  |
| Dyspnoea,Week 37,n=15, 13, 5 | -8.9 (± 19.79)  | 12.8 (± 16.88)  | -26.7 (± 27.89) |
| Dyspnoea,Week 43,n=15, 14, 4 | -6.7 (± 22.54)  | 2.4 (± 15.82)   | -25.0 (± 31.91) |
| Dyspnoea,Week 61,n=11,11,3   | 0.0 (± 21.08)   | 3.0 (± 17.98)   | -33.3 (± 33.33) |
| Dyspnoea,Week 79,n=3, 2,2    | 0.0 (± 0.00)    | 0.0 (± 0.00)    | -33.3 (± 47.14) |
| Dyspnoea,Week 97,n=4, 5,3    | 16.7 (± 19.25)  | 0.0 (± 23.57)   | -22.2 (± 38.49) |
| Dyspnoea,Week 115,n=2, 6,3   | 0.0 (± 0.00)    | 5.6 (± 13.61)   | -33.3 (± 33.33) |
| Dyspnoea,Week 133,n=2,1,2    | 0.0 (± 0.00)    | 0.0 (± 77777)   | -16.7 (± 23.57) |
| Dyspnoea,Week 151,n=0,2,0    | 99999 (± 99999) | 0.0 (± 0.00)    | 99999 (± 99999) |

|                                 |                 |                 |                 |
|---------------------------------|-----------------|-----------------|-----------------|
| Dyspnoea,Week 169,n=0,1,0       | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| Dyspnoea,Week 186,n=41, 46,17   | 0.0 (± 19.72)   | 12.3 (± 24.70)  | -9.8 (± 25.72)  |
| Insomnia,Week 07,n=48, 47, 17   | -6.2 (± 29.70)  | -2.8 (± 26.77)  | -0.0 (± 23.57)  |
| Insomnia,Week 13,n=29,29,16     | 0.0 (± 26.73)   | -1.1 (± 25.95)  | -0.0 (± 34.43)  |
| Insomnia,Week 19,n=19,27,10     | -8.8 (± 24.45)  | -4.9 (± 28.80)  | -13.3 (± 35.83) |
| Insomnia,Week 25,n=20,23,7      | -5.0 (± 32.94)  | -7.2 (± 22.38)  | 0.0 (± 33.33)   |
| Insomnia,Week 31,n=15,18,7      | -17.8 (± 27.79) | -9.3 (± 33.93)  | 4.8 (± 40.50)   |
| Insomnia,Week 37,n=15,13,5      | -15.6 (± 33.01) | -10.3 (± 16.01) | -13.3 (± 38.01) |
| Insomnia,Week 43,n=15,14,4      | -15.6 (± 30.52) | -4.8 (± 22.10)  | -0.0 (± 47.14)  |
| Insomnia,Week 61,n=11,11,3      | -9.1 (± 15.57)  | -9.1 (± 21.56)  | -11.1 (± 19.25) |
| Insomnia,Week 79,n=3,2,2        | 0.0 (± 33.33)   | 16.7 (± 23.57)  | -33.3 (± 47.14) |
| Insomnia,Week 97,n=4,5,3        | -25.0 (± 31.91) | -6.7 (± 14.91)  | -44.4 (± 38.49) |
| Insomnia,Week 115,n=2,6,3       | -33.3 (± 47.14) | 5.6 (± 25.09)   | -33.3 (± 33.33) |
| Insomnia,Week 133,n=2,1,2       | -16.7 (± 70.71) | 0.0 (± 77777)   | -66.7 (± 0.00)  |
| Insomnia,Week 151,n=0,2,0       | 99999 (± 99999) | 0.0 (± 0.00)    | 99999 (± 99999) |
| Insomnia,Week 169,n=0,1,0       | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| Insomnia,Week 186,n=41,46,17    | 2.4 (± 33.66)   | -2.9 (± 32.07)  | 2.0 (± 29.98)   |
| AL,Week 07,n=48,47,17           | 4.9 (± 24.78)   | 2.1 (± 29.00)   | 2.0 (± 27.56)   |
| AL,Week 13,n=29,29,16           | 8.0 (± 29.08)   | -2.3 (± 25.09)  | 12.5 (± 26.87)  |
| AL,Week 19,n=19,27,10           | 0.0 (± 24.85)   | -0.0 (± 38.12)  | -3.3 (± 10.54)  |
| AL,Week 25,n=20, 23, 7          | 6.7 (± 31.72)   | -5.8 (± 21.68)  | -9.5 (± 16.27)  |
| AL,Week 31,n=15,18, 7           | -8.9 (± 15.26)  | 0.0 (± 19.80)   | -4.8 (± 23.00)  |
| AL,Week 37,n=15,13,5            | -4.4 (± 17.21)  | -5.1 (± 22.96)  | -20.0 (± 18.26) |
| AL,Week 43,n=15,14,4            | -4.4 (± 17.21)  | -9.5 (± 24.21)  | -25.0 (± 16.67) |
| AL,Week 61,n=11,11,3            | -6.1 (± 20.10)  | 0.0 (± 36.51)   | 11.1 (± 19.25)  |
| AL,Week 79,n=3,2,2              | -33.3 (± 0.00)  | 16.7 (± 23.57)  | 16.7 (± 23.57)  |
| AL,Week 97,n=4,5,3              | -8.3 (± 16.67)  | 13.3 (± 18.26)  | 0.0 (± 33.33)   |
| AL,Week 115,n=2,6,3             | 0.0 (± 0.00)    | 0.0 (± 21.08)   | 0.0 (± 33.33)   |
| AL,Week 133,n=2,1,2             | 0.0 (± 0.00)    | 0.0 (± 77777)   | -16.7 (± 23.57) |
| AL,Week 151,n=0,2,0             | 99999 (± 99999) | 33.3 (± 47.14)  | 99999 (± 99999) |
| AL,Week 169,n=0,1,0             | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| AL,Week 186,n=41,46,17          | 5.7 (± 24.61)   | -0.0 (± 32.96)  | 2.0 (± 21.96)   |
| Constipation,Week 07,n=48,47,17 | 1.4 (± 22.76)   | -2.1 (± 17.59)  | -7.8 (± 25.08)  |
| Constipation,Week 13,n=29,29,16 | 0.0 (± 25.20)   | -5.7 (± 17.97)  | 8.3 (± 31.03)   |
| Constipation,Week 19,n=19,27,10 | -7.0 (± 21.02)  | 1.2 (± 17.25)   | -3.3 (± 18.92)  |
| Constipation,Week 25,n=20,23,7  | -3.3 (± 14.91)  | -1.4 (± 18.74)  | -14.3 (± 32.53) |
| Constipation,Week 31,n=15,18,7  | -4.4 (± 11.73)  | -3.7 (± 15.71)  | -19.0 (± 26.23) |
| Constipation,Week 37,n=15,13,5  | 2.2 (± 23.46)   | -5.1 (± 22.96)  | -20.0 (± 38.01) |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Constipation,Week 43,n=15,14,4   | -4.4 (± 17.21)  | -2.4 (± 20.52)  | -16.7 (± 43.03) |
| Constipation,Week 61,n=11,11,3   | 0.0 (± 14.91)   | -9.1 (± 30.15)  | -11.1 (± 38.49) |
| Constipation,Week 79,n=3,2,2     | 0.0 (± 0.00)    | 0.0 (± 0.00)    | 0.0 (± 47.14)   |
| Constipation,Week 97,n=4,5,3     | 0.0 (± 0.00)    | 0.0 (± 0.00)    | -22.2 (± 50.92) |
| Constipation,Week 115,n=2,6,3    | 0.0 (± 0.00)    | -5.6 (± 13.61)  | -22.2 (± 50.92) |
| Constipation,Week 133,n=2,1,2    | 0.0 (± 0.00)    | 0.0 (± 77777)   | -50.0 (± 23.57) |
| Constipation,Week 151,n=0,2,0    | 99999 (± 99999) | 0.0 (± 0.00)    | 99999 (± 99999) |
| Constipation,Week 169,n=0,1,0    | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| Constipation,Week 186,n=41,46,17 | 5.7 (± 20.95)   | 3.6 (± 20.16)   | 3.9 (± 33.09)   |
| Diarrhoea,Week 07,n=48,47,17     | -2.8 (± 26.48)  | -0.0 (± 28.66)  | -2.0 (± 24.92)  |
| Diarrhoea,Week 13,n=29,29,16     | 0.0 (± 25.20)   | -6.9 (± 18.64)  | 4.2 (± 31.91)   |
| Diarrhoea,Week 19,n=19,27,10     | 1.8 (± 26.00)   | -2.5 (± 24.33)  | -3.3 (± 18.92)  |
| Diarrhoea,Week 25,n=20,23,7      | 3.3 (± 28.41)   | -7.2 (± 33.27)  | -19.0 (± 17.82) |
| Diarrhoea,Week 31,n=15,18,7      | -2.2 (± 23.46)  | -3.7 (± 34.09)  | -4.8 (± 29.99)  |
| Diarrhoea,Week 37,n=15,13,5      | -2.2 (± 23.46)  | 2.6 (± 28.74)   | -20.0 (± 18.26) |
| Diarrhoea,Week 43,n=15,14,4      | -4.4 (± 21.33)  | 14.3 (± 28.39)  | -16.7 (± 19.25) |
| Diarrhoea,Week 61,n=11,11,3      | 0.0 (± 21.08)   | 15.2 (± 31.14)  | 0.0 (± 33.33)   |
| Diarrhoea,Week 79,n=3,2,2        | 0.0 (± 0.00)    | 0.0 (± 0.00)    | 0.0 (± 47.14)   |
| Diarrhoea,Week 97,n=4,5,3        | -8.3 (± 16.67)  | 0.0 (± 0.00)    | -22.2 (± 19.25) |
| Diarrhoea,Week 115,n=2,6,3       | 0.0 (± 0.00)    | 0.0 (± 0.00)    | -22.2 (± 19.25) |
| Diarrhoea,Week 133,n=2,1,2       | 0.0 (± 0.00)    | 0.0 (± 77777)   | -33.3 (± 0.00)  |
| Diarrhoea,Week 151,n=0,2,0       | 99999 (± 99999) | 0.0 (± 0.00)    | 99999 (± 99999) |
| Diarrhoea,Week 169,n=0,1,0       | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| Diarrhoea,Week 186,n=41,46,17    | -0.8 (± 21.72)  | -5.1 (± 28.08)  | 0.0 (± 35.36)   |
| FD,Week 07,n=48,47,17            | -4.9 (± 25.72)  | 2.8 (± 24.90)   | 0.0 (± 16.67)   |
| FD,Week 13,n=29,29,16            | -4.6 (± 23.10)  | 4.6 (± 19.36)   | 10.4 (± 20.07)  |
| FD,Week 19,n=19,27,10            | -7.0 (± 21.02)  | 3.7 (± 26.69)   | 10.0 (± 22.50)  |
| FD,Week 25,n=20,23,7             | -3.3 (± 26.27)  | -1.4 (± 15.82)  | 0.0 (± 19.25)   |
| FD,Week 31,n=15,18,7             | -6.7 (± 22.54)  | -1.9 (± 17.98)  | 4.8 (± 23.00)   |
| FD,Week 37,n=15,13,5             | -2.2 (± 23.46)  | -2.6 (± 16.45)  | 6.7 (± 14.91)   |
| FD,Week 43,n=15,14,4             | -6.7 (± 18.69)  | 0.0 (± 22.65)   | 8.3 (± 31.91)   |
| FD,Week 61,n=11,11,3             | -12.1 (± 37.34) | 6.1 (± 29.13)   | 11.1 (± 19.25)  |
| FD,Week 79,n=3,2,1               | 0.0 (± 0.00)    | -16.7 (± 23.57) | 0.0 (± 77777)   |
| FD,Week 97,n=4,5,3               | -25.0 (± 31.91) | 0.0 (± 23.57)   | -11.1 (± 19.25) |
| FD,Week 115,n=2,6,3              | 0.0 (± 0.00)    | 22.2 (± 50.18)  | -11.1 (± 19.25) |
| FD,Week 133,n=2,1,2              | -50.0 (± 23.57) | -33.3 (± 77777) | -16.7 (± 23.57) |
| FD,Week 151,n=0,2,0              | 99999 (± 99999) | -33.3 (± 0.00)  | 99999 (± 99999) |
| FD,Week 169,n=0,1,0              | 99999 (± 99999) | -33.3 (± 77777) | 99999 (± 99999) |

|                        |                |                |               |
|------------------------|----------------|----------------|---------------|
| FD,Week 186,n=41,46,17 | -1.6 (± 24.67) | 12.3 (± 25.68) | 5.9 (± 21.20) |
|------------------------|----------------|----------------|---------------|

Notes:

[183] - Full Analysis Population

[184] - Full Analysis Population

[185] - Full Analysis Population

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in EORTC QLQ 20-item multiple myeloma module (MY20) score

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in EORTC QLQ 20-item multiple myeloma module (MY20) score |
|-----------------|--|

End point description:

The EORTC QLQ-MY20 is supplement to QLQ-C30 instrument used in participants with multiple myeloma. The module comprised 20 questions that addressed four myeloma-specific HRQoL domains: disease symptoms (DS), side effects of treatment (SET), future perspective (FP), body image (BI). Responses are 1 to 4. Scores were averaged & scales were transformed to 0 to 100 scale. A high score for disease symptoms & side effects of treatment represented high level of symptomatology or problems, whereas high score for future perspective & body image represented better outcomes. Baseline was latest pre-dose assessment (Day 1) with non-missing value, including unscheduled visits. Change from Baseline was subtracting Baseline value from post-dose visit value. 99999 indicates data is not available. 77777 indicates SD could not be calculated for single participant. Only those participants who were measured analyzed (i.e., contributed data reported in the table) were included in the Overall Number of Participants Analyzed field.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline (Day 1) and Week 07, Week 13, Week 19, Week 25, Week 31, Week 37, Week 43, Week 61, Week 79, Week 97, Week 115, Week 133, Week 151, Week 169, and Week 186

| End point values                     | GSK2857916<br>2.5 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Frozen liquid) | GSK2857916<br>3.4 mg/kg<br>(Lyophilized) |  |
|--------------------------------------|--|--|--|--|
| Subject group type                   | Reporting group                            | Reporting group                            | Reporting group                          |  |
| Number of subjects analysed          | 97 <sup>[186]</sup>                        | 99 <sup>[187]</sup>                        | 25 <sup>[188]</sup>                      |  |
| Units: Scores on a scale             |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| FP, Week 07, n=47,45,16              | 2.8 (± 25.11)                              | 4.2 (± 29.99)                              | 8.3 (± 24.51)                            |  |
| FP, Week 13, n=28,28,15              | -2.0 (± 24.39)                             | 8.3 (± 22.55)                              | -2.2 (± 27.28)                           |  |
| FP, Week 19, n=18,25,10              | 3.7 (± 22.87)                              | 10.7 (± 20.91)                             | 3.3 (± 27.24)                            |  |
| FP, Week 25, n=19,23,7               | 2.3 (± 27.11)                              | 13.5 (± 29.39)                             | 4.8 (± 31.98)                            |  |
| FP, Week 31, n=14,18,7               | 7.1 (± 18.80)                              | 19.1 (± 24.93)                             | 7.9 (± 27.00)                            |  |
| FP, Week 37, n=14,13,5               | 6.3 (± 17.28)                              | 29.1 (± 22.47)                             | 11.1 (± 31.43)                           |  |
| FP, Week 43, n=15,13,4               | 8.1 (± 21.19)                              | 29.9 (± 26.98)                             | 8.3 (± 5.56)                             |  |
| FP, Week 61, n=11,11,3               | 10.1 (± 18.89)                             | 4.0 (± 20.65)                              | 25.9 (± 54.81)                           |  |
| FP, Week 79, n=3,2,2                 | -7.4 (± 6.42)                              | 33.3 (± 31.43)                             | 38.9 (± 39.28)                           |  |
| FP, Week 97, n=4,5,3                 | 5.6 (± 14.34)                              | 17.8 (± 39.75)                             | 22.2 (± 40.06)                           |  |
| FP, Week 115, n=2,6,3                | 11.1 (± 15.71)                             | 16.7 (± 25.09)                             | 33.3 (± 58.79)                           |  |
| FP, Week 133, n=2,1,2                | 27.8 (± 7.86)                              | 55.6 (± 77777)                             | 38.9 (± 55.00)                           |  |
| FP, Week 151, n=0,2,0                | 99999 (± 99999)                            | 44.4 (± 15.71)                             | 99999 (± 99999)                          |  |

|                         |                 |                 |                 |
|-------------------------|-----------------|-----------------|-----------------|
| FP,Week 169,n=0,1,0     | 99999 (± 99999) | 55.6 (± 77777)  | 99999 (± 99999) |
| FP,Week 186,n=39,46,16  | -9.4 (± 19.34)  | -7.7 (± 26.69)  | 3.5 (± 24.59)   |
| BI,Week 07,n=47,45,16   | 2.8 (± 22.87)   | 9.6 (± 28.09)   | 4.2 (± 43.67)   |
| BI,Week 13,n=28,28,15   | 6.0 (± 25.75)   | 6.0 (± 35.20)   | -4.4 (± 37.52)  |
| BI,Week 19,n=18,25,10   | 5.6 (± 23.57)   | 8.0 (± 25.96)   | -3.3 (± 42.89)  |
| BI,Week 25,n=19,23,7    | 7.0 (± 23.78)   | 15.9 (± 31.57)  | 9.5 (± 53.45)   |
| BI,Week 31,n=14,18,7    | 2.4 (± 20.52)   | 14.8 (± 30.73)  | 9.5 (± 56.81)   |
| BI,Week 37,n=14,13,5    | 9.5 (± 27.51)   | 25.6 (± 30.89)  | 26.7 (± 54.77)  |
| BI,Week 43,n=15,13,4    | 4.4 (± 24.77)   | 28.2 (± 38.12)  | 8.3 (± 16.67)   |
| BI,Week 61,n=11,11,3    | 6.1 (± 25.03)   | 12.1 (± 26.97)  | 33.3 (± 57.74)  |
| BI,Week 79,n=3,2,2      | 0.0 (± 0.00)    | 0.0 (± 0.00)    | 33.3 (± 94.28)  |
| BI,Week 97,n=4,5,3      | 8.3 (± 31.91)   | 6.7 (± 27.89)   | 44.4 (± 69.39)  |
| BI,Week 115,n=2,6,3     | -16.7 (± 70.71) | 5.6 (± 25.09)   | 55.6 (± 50.92)  |
| BI,Week 133,n=2,1,2     | 16.7 (± 23.57)  | 0.0 (± 77777)   | 83.3 (± 23.57)  |
| BI,Week 151,n=0,2,0     | 99999 (± 99999) | 16.7 (± 23.57)  | 99999 (± 99999) |
| BI,Week 169,n=0,1,0     | 99999 (± 99999) | 0.0 (± 77777)   | 99999 (± 99999) |
| BI,Week 186,n=39,46,16  | -4.3 (± 30.76)  | -0.7 (± 35.48)  | 10.4 (± 41.67)  |
| DS,Week 07,n=47,45,16   | -1.8 (± 19.73)  | -1.0 (± 17.78)  | -2.8 (± 12.17)  |
| DS,Week 13,n=28,28,15   | -1.0 (± 16.22)  | -3.2 (± 22.95)  | 1.1 (± 25.65)   |
| DS,Week 19,n=18,25,10   | 0.9 (± 14.91)   | -6.4 (± 17.98)  | -1.7 (± 20.63)  |
| DS,Week 25,n=19,23,7    | -0.0 (± 16.25)  | -3.6 (± 17.78)  | -1.6 (± 25.20)  |
| DS,Week 31,n=14,18,7    | -3.6 (± 10.59)  | -10.5 (± 19.23) | -4.8 (± 23.88)  |
| DS,Week 37,n=14,13,5    | -6.0 (± 12.22)  | -9.8 (± 22.92)  | -14.4 (± 16.01) |
| DS,Week 43,n=15,13,4    | -5.9 (± 12.51)  | -14.5 (± 24.06) | -8.3 (± 26.64)  |
| DS,Week 61,n=11,11,3    | -11.6 (± 12.29) | -7.6 (± 10.02)  | -11.1 (± 16.67) |
| DS,Week 79,n=3,2,2      | -16.7 (± 11.11) | -2.8 (± 3.93)   | -2.8 (± 27.50)  |
| DS,Week 97,n=4,5,3      | -12.5 (± 15.30) | -3.3 (± 15.52)  | -7.4 (± 25.05)  |
| DS,Week 115,n=2,6,3     | -19.4 (± 3.93)  | -7.4 (± 10.92)  | -10.0 (± 16.59) |
| DS,Week 133,n=2,1,2     | -13.9 (± 11.79) | -5.6 (± 77777)  | 8.3 (± 51.07)   |
| DS,Week 151,n=0,2,0     | 99999 (± 99999) | 5.6 (± 15.71)   | 99999 (± 99999) |
| DS,Week 169,n=0,1,0     | 99999 (± 99999) | -5.6 (± 77777)  | 99999 (± 99999) |
| DS,Week 186, n=39,46,16 | -0.6 (± 17.28)  | 2.5 (± 18.36)   | 4.9 (± 24.50)   |
| SET,Week 07,n=47,45,16  | 1.5 (± 9.21)    | 0.4 (± 13.33)   | 0.2 (± 15.49)   |
| SET,Week 13,n=28,28,15  | 2.0 (± 10.44)   | -1.7 (± 11.96)  | 6.8 (± 23.69)   |
| SET,Week 19,n=18,25,10  | 0.0 (± 10.40)   | -1.2 (± 10.87)  | 0.9 (± 9.04)    |
| SET,Week 25,n=19,23,7   | 3.4 (± 8.41)    | 0.1 (± 13.10)   | 0.4 (± 6.45)    |
| SET,Week 31,n=14,18,7   | 2.0 (± 6.07)    | -2.9 (± 13.87)  | 5.5 (± 11.12)   |
| SET,Week 37,n=14,13,5   | 2.2 (± 6.91)    | -6.0 (± 17.82)  | -1.8 (± 4.04)   |
| SET,Week 43,n=15,13,4   | 1.0 (± 8.81)    | -5.6 (± 19.05)  | -4.9 (± 5.76)   |
| SET,Week 61,n=11,11,3   | -2.1 (± 12.32)  | 1.9 (± 12.82)   | 2.0 (± 9.84)    |
| SET,Week 79,n=3,2,2     | 5.9 (± 11.40)   | 9.1 (± 12.83)   | -1.3 (± 4.45)   |
| SET,Week 97,n=4,5,3     | -0.2 (± 5.42)   | 5.0 (± 13.80)   | -4.7 (± 3.44)   |

|                         |                 |                 |                 |  |
|-------------------------|-----------------|-----------------|-----------------|--|
| SET,Week 115,n=2,6,3    | 5.7 (± 13.36)   | 0.7 (± 7.21)    | -1.0 (± 7.09)   |  |
| SET,Week 133,n=2,1,2    | 5.7 (± 13.36)   | -7.4 (± 77777)  | -8.1 (± 5.24)   |  |
| SET,Week 151,n=0,2,0    | 99999 (± 99999) | 0.0 (± 15.71)   | 99999 (± 99999) |  |
| SET,Week 169,n=0,1,0    | 99999 (± 99999) | -11.1 (± 77777) | 99999 (± 99999) |  |
| SET,Week 186,n=39,46,16 | 4.0 (± 10.98)   | 4.0 (± 12.61)   | 3.7 (± 10.75)   |  |

Notes:

[186] - Full Analysis Population.

[187] - Full Analysis Population.

[188] - Full Analysis Population.

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality, Serious adverse events (SAEs) and ( $\geq 5\%$ ) non-serious AEs (Non SAEs) were collected from the start of study treatment until maximum of 186 weeks

Adverse event reporting additional description:

SAEs & non-SAEs reported for FSP (who received atleast 1 dose of frozen liquid or lyophilized powder). 3 out of 221 participants did not receive drug & SAEs & non-SAEs were not reported. Deaths is reported for FSP(221)[all randomized whether or not randomized treatment was given]. The results presented are based on data cut-off date 04 May 2022

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | GSK2857916 2.5 mg/kg (Frozen liquid) |
|-----------------------|--------------------------------------|

Reporting group description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 2.5 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 39 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

|                       |                                    |
|-----------------------|------------------------------------|
| Reporting group title | GSK2857916 3.4 mg/kg (Lyophilized) |
|-----------------------|------------------------------------|

Reporting group description:

Participants were administered lyophilized powder (100 mg/vial in a single use vial) at a dose of 3.4 mg/kg GSK2857916 given IV for a maximum of up to 35 cycles (1 cycle= 21 days). Lyophilized powder was reconstituted using water for injection.

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | GSK2857916 3.4 mg/kg (Frozen liquid) |
|-----------------------|--------------------------------------|

Reporting group description:

Participants were administered frozen liquid (30 mg/vial solution in a single use vial) at a dose of 3.4 mg/kg GSK2857916 as IV solution once every three weeks for a maximum of up to 32 cycles (1 cycle= 21 days). Frozen liquid was diluted with 0.9 percent saline.

| <b>Serious adverse events</b>                                       | GSK2857916 2.5 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Lyophilized) | GSK2857916 3.4 mg/kg (Frozen liquid) |
|---|--------------------------------------|------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events                   |                                      |                                    |                                      |
| subjects affected / exposed   | 43 / 95 (45.26%)                     | 15 / 24 (62.50%)                   | 53 / 99 (53.54%)                     |
| number of deaths (all causes)                                       | 70                                   | 16                                 | 80                                   |
| number of deaths resulting from adverse events                      |                                      |                                    |                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                      |                                    |                                      |
| Acute myeloid leukaemia   |                                      |                                    |                                      |
| subjects affected / exposed   | 0 / 95 (0.00%)                       | 0 / 24 (0.00%)                     | 1 / 99 (1.01%)                       |
| occurrences causally related to treatment / all                     | 0 / 0                                | 0 / 0                              | 0 / 1                                |
| deaths causally related to treatment / all                          | 0 / 0                                | 0 / 0                              | 0 / 1                                |
| Basal cell carcinoma  |                                      |                                    |                                      |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                                 | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Prostate cancer</b>                                      |                |                |                |
| subjects affected / exposed                                 | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metastases to meninges</b>                               |                |                |                |
| subjects affected / exposed                                 | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Squamous cell carcinoma</b>                              |                |                |                |
| subjects affected / exposed                                 | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Vascular disorders</b>                                   |                |                |                |
| <b>Haematoma</b>  |                |                |                |
| subjects affected / exposed                                 | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all             | 0 / 0          | 1 / 1          | 0 / 1          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Aortic stenosis</b>                                      |                |                |                |
| subjects affected / exposed                                 | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypertension</b>   |                |                |                |
| subjects affected / exposed                                 | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>General disorders and administration site conditions</b> |                |                |                |
| <b>Pyrexia</b>  |                |                |                |
| subjects affected / exposed                                 | 7 / 95 (7.37%) | 0 / 24 (0.00%) | 5 / 99 (5.05%) |
| occurrences causally related to treatment / all             | 2 / 8          | 0 / 0          | 5 / 7          |
| deaths causally related to treatment / all                  | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| General physical health deterioration           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Chest pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fatigue   |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza like illness                          |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Immune system disorders                         |                |                |                |
| Haemophagocytic lymphohistiocytosis             |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Pleural effusion                                |                |                |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 1 / 24 (4.17%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Epistaxis                                       |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Cough</b>                                    |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Dyspnoea</b>                                 |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Respiratory failure</b>                      |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypoxia</b>                                  |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| <b>Chronic obstructive pulmonary disease</b>    |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Psychiatric disorders</b>                    |                |                |                |
| <b>Delirium</b>                                 |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Confusional state</b>                        |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Investigations</b>                           |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Blood lactate dehydrogenase increased           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Aspartate aminotransferase increased            |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Alanine aminotransferase increased              |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Electrocardiogram T wave inversion              |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Infusion related reaction                       |                |                |                |
| subjects affected / exposed                     | 3 / 95 (3.16%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 4 / 4          | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal compression fracture                     |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clavicle fracture                               |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fracture  |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Humerus fracture                                |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Upper limb fracture                             |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tibia fracture                                  |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Subdural haematoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Road traffic accident                           |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Cardiac arrest                                  |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| Atrial fibrillation                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Mitral valve disease</b>                     |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Pericarditis</b>                             |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Pericardial effusion</b>                     |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Tachycardia</b>                              |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Cardiac failure</b>                          |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| <b>Cardiac failure acute</b>                    |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Cardiac failure congestive</b>               |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Ventricular tachycardia</b>                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                         | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all     | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Nervous system disorders</b>                     |                |                |                |
| <b>Cerebral haemorrhage</b>                         |                |                |                |
| subjects affected / exposed                         | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 3 / 99 (3.03%) |
| occurrences causally related to treatment / all     | 0 / 0          | 0 / 0          | 1 / 3          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 1 / 3          |
| <b>Cognitive disorder</b>                           |                |                |                |
| subjects affected / exposed                         | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all     | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Headache</b>                                     |                |                |                |
| subjects affected / exposed                         | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Lethargy</b>                                     |                |                |                |
| subjects affected / exposed                         | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all     | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Posterior reversible encephalopathy syndrome</b> |                |                |                |
| subjects affected / exposed                         | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Seizure</b>                                      |                |                |                |
| subjects affected / exposed                         | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Spinal cord compression</b>                      |                |                |                |
| subjects affected / exposed                         | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Blood and lymphatic system disorders</b>         |                |                |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Thrombocytopenia                                |                |                 |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 3 / 24 (12.50%) | 3 / 99 (3.03%) |
| occurrences causally related to treatment / all | 2 / 2          | 2 / 3           | 3 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Hyperviscosity syndrome                         |                |                 |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%)  | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Febrile neutropenia                             |                |                 |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%)  | 3 / 99 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Anaemia   |                |                 |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%)  | 3 / 99 (3.03%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pancytopenia                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%)  | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Eye disorders                                   |                |                 |                |
| Keratopathy                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%)  | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Ulcerative keratitis                            |                |                 |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%)  | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Gastrointestinal disorders                      |                |                 |                |
| Gastrointestinal haemorrhage                    |                |                 |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%)  | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0           | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ascites   |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Colitis   |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Constipation                                    |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastric fibrosis                                |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haematochezia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Large intestinal obstruction                    |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Large intestinal haemorrhage                    |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Pancreatitis</b>                             |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Intestinal haemorrhage</b>                   |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hepatobiliary disorders</b>                  |                |                |                |
| <b>Bile duct stone</b>                          |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Cholestasis</b>                              |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Renal and urinary disorders</b>              |                |                |                |
| <b>Acute kidney injury</b>                      |                |                |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Renal failure</b>                            |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Renal impairment</b>                         |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Urinary retention</b>                        |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                            | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Musculoskeletal and connective tissue disorders</b> |                |                |                |
| <b>Back pain</b>                                       |                |                |                |
| subjects affected / exposed                            | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Pathological fracture</b>                           |                |                |                |
| subjects affected / exposed                            | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Osteolysis</b>                                      |                |                |                |
| subjects affected / exposed                            | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Muscular weakness</b>                               |                |                |                |
| subjects affected / exposed                            | 1 / 95 (1.05%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Bone pain</b>                                       |                |                |                |
| subjects affected / exposed                            | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Arthritis</b>                                       |                |                |                |
| subjects affected / exposed                            | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Haematoma muscle</b>                                |                |                |                |
| subjects affected / exposed                            | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Lumbar spinal stenosis</b>                          |                |                |                |

|   |                |                |                  |
|---|----------------|----------------|------------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%)   |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Pain in extremity                               |                |                |                  |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%)   |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Osteonecrosis of jaw                            |                |                |                  |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 1 / 24 (4.17%) | 0 / 99 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Spinal osteoarthritis                           |                |                |                  |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%)   |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Infections and infestations                     |                |                |                  |
| Sepsis  |                |                |                  |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%) | 2 / 99 (2.02%)   |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 2 / 2            |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0            |
| Pneumonia                                       |                |                |                  |
| subjects affected / exposed                     | 7 / 95 (7.37%) | 1 / 24 (4.17%) | 14 / 99 (14.14%) |
| occurrences causally related to treatment / all | 2 / 8          | 0 / 1          | 6 / 16           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 2            |
| Escherichia urinary tract infection             |                |                |                  |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 2 / 99 (2.02%)   |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Cellulitis                                      |                |                |                  |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 2 / 99 (2.02%)   |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0            |
| Influenza                                       |                |                |                  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Pneumonia influenzal</b>                     |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Vascular device infection</b>                |                |                |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Upper respiratory tract infection</b>        |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 2 / 99 (2.02%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Staphylococcal sepsis</b>                    |                |                |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Brain abscess</b>                            |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Device related infection</b>                 |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Enterocolitis infectious</b>                 |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Escherichia bacteraemia</b>                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Escherichia sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes simplex pneumonia                        |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lower respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia respiratory syncytial viral           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia legionella                            |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Otitis media                                    |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nocardiosis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sinusitis                                       |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral infection                                 |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Staphylococcal infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Staphylococcal bacteraemia                      |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device related sepsis                           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Epiglottitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis viral                           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective keratitis                             |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 95 (0.00%) | 0 / 24 (0.00%) | 1 / 99 (1.01%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Metabolism and nutrition disorders</b>       |                |                |                |
| <b>Hypercalcaemia</b>                           |                |                |                |
| subjects affected / exposed                     | 4 / 95 (4.21%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Dehydration</b>                              |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 2 / 24 (8.33%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hyponatraemia</b>                            |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypokalaemia</b>                             |                |                |                |
| subjects affected / exposed                     | 2 / 95 (2.11%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hyperglycaemia</b>                           |                |                |                |
| subjects affected / exposed                     | 0 / 95 (0.00%) | 1 / 24 (4.17%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypophosphataemia</b>                        |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypomagnesaemia</b>                          |                |                |                |
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hypocalcaemia</b>                            |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 95 (1.05%) | 0 / 24 (0.00%) | 0 / 99 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | GSK2857916 2.5 mg/kg (Frozen liquid) | GSK2857916 3.4 mg/kg (Lyophilized) | GSK2857916 3.4 mg/kg (Frozen liquid) |
|---|--------------------------------------|------------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events |                                      |                                    |                                      |
| subjects affected / exposed                           | 93 / 95 (97.89%)                     | 24 / 24 (100.00%)                  | 96 / 99 (96.97%)                     |
| Vascular disorders                                    |                                      |                                    |                                      |
| Hypertension  |                                      |                                    |                                      |
| subjects affected / exposed                           | 9 / 95 (9.47%)                       | 2 / 24 (8.33%)                     | 10 / 99 (10.10%)                     |
| occurrences (all)                                     | 10                                   | 6                                  | 11                                   |
| General disorders and administration site conditions  |                                      |                                    |                                      |
| Fatigue   |                                      |                                    |                                      |
| subjects affected / exposed                           | 15 / 95 (15.79%)                     | 12 / 24 (50.00%)                   | 28 / 99 (28.28%)                     |
| occurrences (all)                                     | 19                                   | 13                                 | 37                                   |
| Pyrexia   |                                      |                                    |                                      |
| subjects affected / exposed                           | 18 / 95 (18.95%)                     | 4 / 24 (16.67%)                    | 22 / 99 (22.22%)                     |
| occurrences (all)                                     | 21                                   | 6                                  | 29                                   |
| Asthenia  |                                      |                                    |                                      |
| subjects affected / exposed                           | 3 / 95 (3.16%)                       | 2 / 24 (8.33%)                     | 11 / 99 (11.11%)                     |
| occurrences (all)                                     | 3                                    | 2                                  | 11                                   |
| Chills  |                                      |                                    |                                      |
| subjects affected / exposed                           | 8 / 95 (8.42%)                       | 2 / 24 (8.33%)                     | 4 / 99 (4.04%)                       |
| occurrences (all)                                     | 8                                    | 2                                  | 4                                    |
| Oedema peripheral                                     |                                      |                                    |                                      |
| subjects affected / exposed                           | 5 / 95 (5.26%)                       | 3 / 24 (12.50%)                    | 4 / 99 (4.04%)                       |
| occurrences (all)                                     | 5                                    | 5                                  | 10                                   |
| Pain  |                                      |                                    |                                      |
| subjects affected / exposed                           | 5 / 95 (5.26%)                       | 0 / 24 (0.00%)                     | 4 / 99 (4.04%)                       |
| occurrences (all)                                     | 5                                    | 0                                  | 4                                    |
| Chest pain  |                                      |                                    |                                      |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 2 / 95 (2.11%)<br>2 | 3 / 24 (12.50%)<br>3 | 2 / 99 (2.02%)<br>2 |
| Respiratory, thoracic and mediastinal disorders  |                     |                      |                     |
| Epistaxis  |                     |                      |                     |
| subjects affected / exposed                      | 9 / 95 (9.47%)      | 1 / 24 (4.17%)       | 17 / 99 (17.17%)    |
| occurrences (all)                                | 11                  | 1                    | 21                  |
| Cough  |                     |                      |                     |
| subjects affected / exposed                      | 10 / 95 (10.53%)    | 3 / 24 (12.50%)      | 19 / 99 (19.19%)    |
| occurrences (all)                                | 11                  | 4                    | 20                  |
| Dyspnoea   |                     |                      |                     |
| subjects affected / exposed                      | 8 / 95 (8.42%)      | 3 / 24 (12.50%)      | 6 / 99 (6.06%)      |
| occurrences (all)                                | 8                   | 3                    | 7                   |
| Oropharyngeal pain                               |                     |                      |                     |
| subjects affected / exposed                      | 1 / 95 (1.05%)      | 1 / 24 (4.17%)       | 5 / 99 (5.05%)      |
| occurrences (all)                                | 1                   | 1                    | 5                   |
| Psychiatric disorders                            |                     |                      |                     |
| Insomnia   |                     |                      |                     |
| subjects affected / exposed                      | 6 / 95 (6.32%)      | 2 / 24 (8.33%)       | 1 / 99 (1.01%)      |
| occurrences (all)                                | 6                   | 2                    | 1                   |
| Depression                                       |                     |                      |                     |
| subjects affected / exposed                      | 5 / 95 (5.26%)      | 0 / 24 (0.00%)       | 2 / 99 (2.02%)      |
| occurrences (all)                                | 5                   | 0                    | 3                   |
| Confusional state                                |                     |                      |                     |
| subjects affected / exposed                      | 0 / 95 (0.00%)      | 1 / 24 (4.17%)       | 5 / 99 (5.05%)      |
| occurrences (all)                                | 0                   | 1                    | 6                   |
| Investigations                                   |                     |                      |                     |
| Aspartate aminotransferase increased             |                     |                      |                     |
| subjects affected / exposed                      | 21 / 95 (22.11%)    | 6 / 24 (25.00%)      | 24 / 99 (24.24%)    |
| occurrences (all)                                | 26                  | 8                    | 30                  |
| Blood creatinine increased                       |                     |                      |                     |
| subjects affected / exposed                      | 10 / 95 (10.53%)    | 2 / 24 (8.33%)       | 11 / 99 (11.11%)    |
| occurrences (all)                                | 11                  | 2                    | 14                  |
| Gamma-glutamyltransferase increased              |                     |                      |                     |
| subjects affected / exposed                      | 10 / 95 (10.53%)    | 2 / 24 (8.33%)       | 14 / 99 (14.14%)    |
| occurrences (all)                                | 10                  | 2                    | 14                  |

|  |                        |                      |                        |
|--|------------------------|----------------------|------------------------|
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)               | 13 / 95 (13.68%)<br>15 | 2 / 24 (8.33%)<br>3  | 10 / 99 (10.10%)<br>13 |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)     | 9 / 95 (9.47%)<br>10   | 1 / 24 (4.17%)<br>1  | 11 / 99 (11.11%)<br>11 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)                 | 15 / 95 (15.79%)<br>18 | 3 / 24 (12.50%)<br>3 | 11 / 99 (11.11%)<br>26 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)               | 7 / 95 (7.37%)<br>10   | 2 / 24 (8.33%)<br>2  | 11 / 99 (11.11%)<br>13 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)         | 7 / 95 (7.37%)<br>8    | 0 / 24 (0.00%)<br>0  | 9 / 99 (9.09%)<br>11   |
| Intraocular pressure increased<br>subjects affected / exposed<br>occurrences (all)           | 6 / 95 (6.32%)<br>10   | 5 / 24 (20.83%)<br>6 | 8 / 99 (8.08%)<br>8    |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)    | 4 / 95 (4.21%)<br>5    | 4 / 24 (16.67%)<br>4 | 7 / 99 (7.07%)<br>8    |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                         | 8 / 95 (8.42%)<br>8    | 1 / 24 (4.17%)<br>1  | 2 / 99 (2.02%)<br>2    |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)       | 6 / 95 (6.32%)<br>6    | 0 / 24 (0.00%)<br>0  | 4 / 99 (4.04%)<br>5    |
| Urine albumin/creatinine ratio increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 95 (2.11%)<br>2    | 0 / 24 (0.00%)<br>0  | 8 / 99 (8.08%)<br>8    |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)             | 3 / 95 (3.16%)<br>3    | 1 / 24 (4.17%)<br>1  | 5 / 99 (5.05%)<br>5    |
| Blood creatine phosphokinase increased   |                        |                      |                        |

|   |                        |                       |                        |
|---|------------------------|-----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                              | 5 / 95 (5.26%)<br>13   | 0 / 24 (0.00%)<br>0   | 3 / 99 (3.03%)<br>3    |
| Bacterial test positive<br>subjects affected / exposed<br>occurrences (all)   | 0 / 95 (0.00%)<br>0    | 2 / 24 (8.33%)<br>2   | 0 / 99 (0.00%)<br>0    |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 95 (1.05%)<br>1    | 2 / 24 (8.33%)<br>2   | 1 / 99 (1.01%)<br>2    |
| <b>Injury, poisoning and procedural complications</b>                         |                        |                       |                        |
| Infusion related reaction<br>subjects affected / exposed<br>occurrences (all) | 15 / 95 (15.79%)<br>16 | 2 / 24 (8.33%)<br>2   | 9 / 99 (9.09%)<br>10   |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 95 (0.00%)<br>0    | 2 / 24 (8.33%)<br>2   | 8 / 99 (8.08%)<br>8    |
| Rib fracture<br>subjects affected / exposed<br>occurrences (all)              | 1 / 95 (1.05%)<br>1    | 2 / 24 (8.33%)<br>2   | 2 / 99 (2.02%)<br>2    |
| Fall<br>subjects affected / exposed<br>occurrences (all)                      | 3 / 95 (3.16%)<br>4    | 2 / 24 (8.33%)<br>2   | 0 / 99 (0.00%)<br>0    |
| <b>Nervous system disorders</b>   |                        |                       |                        |
| Headache<br>subjects affected / exposed<br>occurrences (all)                  | 11 / 95 (11.58%)<br>12 | 5 / 24 (20.83%)<br>6  | 17 / 99 (17.17%)<br>22 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 95 (1.05%)<br>1    | 1 / 24 (4.17%)<br>1   | 7 / 99 (7.07%)<br>8    |
| <b>Blood and lymphatic system disorders</b>                                   |                        |                       |                        |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                   | 25 / 95 (26.32%)<br>28 | 8 / 24 (33.33%)<br>14 | 36 / 99 (36.36%)<br>49 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)          | 22 / 95 (23.16%)<br>34 | 8 / 24 (33.33%)<br>12 | 44 / 99 (44.44%)<br>73 |
| Neutropenia   |                        |                       |                        |

|   |                         |                         |                         |
|---|-------------------------|-------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)                          | 7 / 95 (7.37%)<br>17    | 1 / 24 (4.17%)<br>4     | 18 / 99 (18.18%)<br>27  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)            | 9 / 95 (9.47%)<br>9     | 0 / 24 (0.00%)<br>0     | 7 / 99 (7.07%)<br>8     |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)           | 6 / 95 (6.32%)<br>6     | 1 / 24 (4.17%)<br>1     | 5 / 99 (5.05%)<br>5     |
| Eye disorders   |                         |                         |                         |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)        | 22 / 95 (23.16%)<br>37  | 8 / 24 (33.33%)<br>13   | 30 / 99 (30.30%)<br>50  |
| Keratopathy<br>subjects affected / exposed<br>occurrences (all)           | 67 / 95 (70.53%)<br>267 | 23 / 24 (95.83%)<br>100 | 74 / 99 (74.75%)<br>320 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)               | 14 / 95 (14.74%)<br>18  | 5 / 24 (20.83%)<br>10   | 19 / 99 (19.19%)<br>21  |
| Photophobia<br>subjects affected / exposed<br>occurrences (all)           | 7 / 95 (7.37%)<br>12    | 3 / 24 (12.50%)<br>3    | 9 / 99 (9.09%)<br>16    |
| Diplopia<br>subjects affected / exposed<br>occurrences (all)              | 2 / 95 (2.11%)<br>3     | 2 / 24 (8.33%)<br>2     | 4 / 99 (4.04%)<br>5     |
| Eye pruritus<br>subjects affected / exposed<br>occurrences (all)          | 2 / 95 (2.11%)<br>2     | 1 / 24 (4.17%)<br>1     | 5 / 99 (5.05%)<br>10    |
| Blepharitis<br>subjects affected / exposed<br>occurrences (all)           | 2 / 95 (2.11%)<br>3     | 0 / 24 (0.00%)<br>0     | 6 / 99 (6.06%)<br>6     |
| Visual acuity reduced<br>subjects affected / exposed<br>occurrences (all) | 5 / 95 (5.26%)<br>8     | 3 / 24 (12.50%)<br>3    | 5 / 99 (5.05%)<br>5     |
| Gastrointestinal disorders  |                         |                         |                         |
| Nausea  |                         |                         |                         |

|  |                        |                      |                        |
|--|------------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 24 / 95 (25.26%)<br>29 | 2 / 24 (8.33%)<br>3  | 32 / 99 (32.32%)<br>40 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 12 / 95 (12.63%)<br>13 | 4 / 24 (16.67%)<br>5 | 9 / 99 (9.09%)<br>9    |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 8 / 95 (8.42%)<br>11   | 0 / 24 (0.00%)<br>0  | 21 / 99 (21.21%)<br>23 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 11 / 95 (11.58%)<br>14 | 4 / 24 (16.67%)<br>4 | 15 / 99 (15.15%)<br>15 |
| Skin and subcutaneous tissue disorders<br>Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)      | 3 / 95 (3.16%)<br>3    | 2 / 24 (8.33%)<br>2  | 2 / 99 (2.02%)<br>2    |
| Renal and urinary disorders<br>Proteinuria<br>subjects affected / exposed<br>occurrences (all)                   | 5 / 95 (5.26%)<br>11   | 3 / 24 (12.50%)<br>3 | 3 / 99 (3.03%)<br>21   |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)   | 2 / 95 (2.11%)<br>8    | 2 / 24 (8.33%)<br>2  | 1 / 99 (1.01%)<br>1    |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 12 / 95 (12.63%)<br>13 | 6 / 24 (25.00%)<br>6 | 12 / 99 (12.12%)<br>12 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)   | 19 / 95 (20.00%)<br>24 | 4 / 24 (16.67%)<br>6 | 16 / 99 (16.16%)<br>19 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)  | 8 / 95 (8.42%)<br>8    | 1 / 24 (4.17%)<br>1  | 12 / 99 (12.12%)<br>16 |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)  | 4 / 95 (4.21%)<br>5    | 0 / 24 (0.00%)<br>0  | 9 / 99 (9.09%)<br>10   |
| Musculoskeletal chest pain   |                        |                      |                        |

|   |                        |                      |                        |
|---|------------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 7 / 95 (7.37%)<br>7    | 1 / 24 (4.17%)<br>1  | 7 / 99 (7.07%)<br>9    |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 95 (2.11%)<br>2    | 2 / 24 (8.33%)<br>2  | 4 / 99 (4.04%)<br>5    |
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 95 (2.11%)<br>2    | 0 / 24 (0.00%)<br>0  | 6 / 99 (6.06%)<br>6    |
| <b>Infections and infestations</b>  |                        |                      |                        |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 10 / 95 (10.53%)<br>12 | 4 / 24 (16.67%)<br>4 | 20 / 99 (20.20%)<br>24 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 6 / 95 (6.32%)<br>7    | 1 / 24 (4.17%)<br>1  | 9 / 99 (9.09%)<br>16   |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                        | 6 / 95 (6.32%)<br>6    | 0 / 24 (0.00%)<br>0  | 2 / 99 (2.02%)<br>2    |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 95 (1.05%)<br>1    | 0 / 24 (0.00%)<br>0  | 5 / 99 (5.05%)<br>6    |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 95 (2.11%)<br>2    | 2 / 24 (8.33%)<br>2  | 5 / 99 (5.05%)<br>5    |
| <b>Metabolism and nutrition disorders</b>   |                        |                      |                        |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 12 / 95 (12.63%)<br>16 | 5 / 24 (20.83%)<br>5 | 19 / 99 (19.19%)<br>21 |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 5 / 95 (5.26%)<br>5    | 3 / 24 (12.50%)<br>7 | 12 / 99 (12.12%)<br>13 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 10 / 95 (10.53%)<br>11 | 4 / 24 (16.67%)<br>5 | 15 / 99 (15.15%)<br>17 |
| Hyponatraemia   |                        |                      |                        |

|   |                      |                      |                        |
|---|----------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                      | 5 / 95 (5.26%)<br>6  | 4 / 24 (16.67%)<br>4 | 12 / 99 (12.12%)<br>14 |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)    | 9 / 95 (9.47%)<br>23 | 1 / 24 (4.17%)<br>1  | 7 / 99 (7.07%)<br>7    |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)  | 4 / 95 (4.21%)<br>4  | 1 / 24 (4.17%)<br>1  | 8 / 99 (8.08%)<br>12   |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all) | 7 / 95 (7.37%)<br>10 | 3 / 24 (12.50%)<br>3 | 8 / 99 (8.08%)<br>11   |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)   | 5 / 95 (5.26%)<br>7  | 1 / 24 (4.17%)<br>1  | 6 / 99 (6.06%)<br>8    |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)     | 4 / 95 (4.21%)<br>4  | 2 / 24 (8.33%)<br>2  | 3 / 99 (3.03%)<br>3    |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)    | 5 / 95 (5.26%)<br>9  | 3 / 24 (12.50%)<br>4 | 7 / 99 (7.07%)<br>11   |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 02 April 2018     | Amendment 01: Addressed regulatory agency advice. The original single-arm design with 1 dose level (3.4 milligram per kilogram [mg/kg] GSK2857916 once every 3 weeks [Q3W]) was amended to an open label, randomized, 2-arm study with 2 dose levels by including the 2.5 mg/kg Q3W dose. In addition, a new exploratory cohort of 25 participants, who will receive a lyophilized configuration of GSK2857916, was added to gain clinical experience with the lyophilized configuration. To accommodate these main changes, the overall sample size and related analytical methods were changed.   |
| 04 September 2018 | Amendment 02: Addressed feedback from regulatory agencies, ethics committee/institutional review board, and investigators. The updates included the addition of Exclusion Criteria defining the use of high dose steroids, clarification of specific timeframe from last treatment required for systemic anti-myeloma therapy, and increase of corrected QT interval Fridericia criteria. Additional pharmacokinetic sampling timepoints were added to capture the maximum observed concentration of the free cytotoxic drug (cysteine-maleimidocaproyl monomethyl auristatin F [cys-mcMMAF]) and to better define the kinetics of cys-mcMMAF and the elimination phase of antibody drug conjugate and cys-mcMMAF. Soluble B-cell maturation antigen (BCMA) collection timepoints were also added to capture the effect of GSK2857916 administration on soluble BCMA concentrations over time as a marker of pharmacodynamic effect. The dose modifications guidelines for GSK2857916 related Corneal Events clarified dose adjustments for GlaxoSmithKline Scale Grade 2 events. |
| 17 December 2018  | Amendment 03: Addressed over-enrolment in the frozen liquid solution portion of the study. Due to the over-enrolment, the primary analysis will be based on all randomized participants (anticipated approximately 200) enrolled into the frozen liquid solution arms. In addition, a sensitivity analysis based on the first 130 participants will be performed to account for the original design.  |
| 21 October 2019   | Amendment 04: Updated schedule of activities to include the footnotes. Updated risk assessment, modified dose justification, modified treatments administered, updated dose reductions for toxicity, modified corneal supportive care guidelines and schedule of activities, updated guidance on prohibited medications, updated requirements for efficacy assessments, modified timeframes for contraception usage in males and females, modified monocular prophylaxis and treatment, updated immunogenicity, updated timeframe of minimal residual disease testing, updated GlaxoSmithKline corneal event severity scale and mitigation strategy for treatment related corneal events.   |
| 08 October 2020   | Amendment 05: The protocol has been amended to provide updates based on analyses of data from the DREAMM-1, DREAMM-2 and the exposure Corrected QT interval. The updates include the removal of ECG collection, unless clinically indicated, and updated contraception timeframe. The dose modification guidelines for belantamab mafodotin related corneal events was updated to align with the approved label and an appendix on Home Healthcare and Telemedicine Approaches was introduced as a result of the COVID-19 pandemic to ensure sites and participants had alternate approaches to assist participants to continue receiving care while maintaining protocol adherence.  |
| 19 November 2021  | Amendment 06: The protocol has been amended to provide updates including the addition of the end of study definition and continued access to study intervention after the end of the study section (Post Analysis Continued Treatment [PACT])   |

Notes:

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported