



## Clinical trial results:

**An open, dose-escalation Phase I/II study to assess the safety, immunogenicity and clinical activity of recPRAME + AS15 Antigen-Specific Cancer Immunotherapeutic as first-line treatment of patients with PRAME-positive metastatic melanoma**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2009-016636-13   |
| Trial protocol           | DE FR CZ         |
| Global end of trial date | 19 December 2016 |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1              |
| This version publication date  | 04 January 2018 |
| First version publication date | 04 January 2018 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 113173 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01149343 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                                       |
|------------------------------|-------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals                                                                           |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330                                                      |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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:

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**Results analysis stage**

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|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 19 June 2017     |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 11 February 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 19 December 2016 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

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Main objective of the trial:

This open-label, Phase I/II study contains two consecutive segments: a dose-escalation Phase I segment and a Phase II segment assessing the clinical activity of the recPRAME + AS15 ASCI at the dose selected.

The co-primary objectives of the Phase I segment of the study were to document and characterize for each dose tested:

- The dose limiting toxicity;
- The anti-PRAME humoral immune response.

The co-primary objectives of the Phase II segment of the study were to characterize:

- The clinical activity of recPRAME + AS15 in terms of objective responses in the overall cohort;
- Any occurrence of dose-limiting toxicity.

Protection of trial subjects:

The patients were observed closely for at least 30 minutes following the administration of the study medication with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 02 July 2010 |
| Long term follow-up planned                               | Yes          |
| Long term follow-up rationale                             | Safety       |
| Long term follow-up duration                              | 1 Years      |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Czech Republic: 9      |
| Country: Number of subjects enrolled | Germany: 33            |
| Country: Number of subjects enrolled | France: 14             |
| Country: Number of subjects enrolled | Italy: 30              |
| Country: Number of subjects enrolled | Poland: 6              |
| Country: Number of subjects enrolled | Russian Federation: 14 |
| Worldwide total number of subjects   | 106                    |
| EEA total number of subjects         | 92                     |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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)                      | 55 |
| From 65 to 84 years                       | 50 |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

The 106 patients included in the total treated population were enrolled by 31 different study centers.

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

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

Blinding implementation details:

The study is an open-label clinical trial.

### Arms

|                              |                      |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes                  |
| Arm title                    | GSK2302025A Cohort 1 |

Arm description:

Male or female patients with histologically proven cutaneous melanoma received the investigational Low-Dose (LD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.

|                                        |                                                                              |
|----------------------------------------|------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                 |
| Investigational medicinal product name | Recombinant PRAME protein combined with the AS15 Adjuvant System GSK2302025A |
| Investigational medicinal product code |                                                                              |
| Other name                             |                                                                              |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                |
| Routes of administration               | Intramuscular use                                                            |

Dosage and administration details:

Patients received a total of 24 PRAME ASCI intramuscular administrations, into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection, according to the following schedule: Cycle 1: 6 PRAME ASCI administrations given at 2-week intervals (weeks 0, 2, 4, 6, 8, 10); Cycle 2: 6 PRAME ASCI administrations given at 3-week intervals (weeks 14, 17, 20, 23, 26, 29); Cycle 3: 4 PRAME ASCI administrations given at 6-week intervals (weeks 33, 39, 45, 51); Cycle 4: 4 PRAME ASCI administrations given at 3-month intervals followed by 4 PRAME ASCI administrations given at 6-month intervals.

|           |                      |
|-----------|----------------------|
| Arm title | GSK2302025A Cohort 2 |
|-----------|----------------------|

Arm description:

Male or female patients with histologically proven cutaneous melanoma received the investigational Middle-Dose (MD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                        |                                                                              |
|----------------------------------------|------------------------------------------------------------------------------|
| Investigational medicinal product name | Recombinant PRAME protein combined with the AS15 Adjuvant System GSK2302025A |
| Investigational medicinal product code |                                                                              |
| Other name                             |                                                                              |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                |
| Routes of administration               | Intramuscular use                                                            |

**Dosage and administration details:**

Patients received a total of 24 PRAME ASCI intramuscular administrations, into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection, according to the following schedule: Cycle 1: 6 PRAME ASCI administrations given at 2-week intervals (weeks 0, 2, 4, 6, 8, 10); Cycle 2: 6 PRAME ASCI administrations given at 3-week intervals (weeks 14, 17, 20, 23, 26, 29); Cycle 3: 4 PRAME ASCI administrations given at 6-week intervals (weeks 33, 39, 45, 51); Cycle 4: 4 PRAME ASCI administrations given at 3-month intervals followed by 4 PRAME ASCI administrations given at 6-month intervals.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | GSK2302025A Cohort 3 |
|------------------|----------------------|

**Arm description:**

Male or female patients with histologically proven cutaneous melanoma received the investigational High-Dose (HD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.

|                                        |                                                                              |
|----------------------------------------|------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                 |
| Investigational medicinal product name | Recombinant PRAME protein combined with the AS15 Adjuvant System GSK2302025A |
| Investigational medicinal product code |                                                                              |
| Other name                             |                                                                              |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                |
| Routes of administration               | Intramuscular use                                                            |

**Dosage and administration details:**

Patients received a total of 24 PRAME ASCI intramuscular administrations, into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection, according to the following schedule: Cycle 1: 6 PRAME ASCI administrations given at 2-week intervals (weeks 0, 2, 4, 6, 8, 10); Cycle 2: 6 PRAME ASCI administrations given at 3-week intervals (weeks 14, 17, 20, 23, 26, 29); Cycle 3: 4 PRAME ASCI administrations given at 6-week intervals (weeks 33, 39, 45, 51); Cycle 4: 4 PRAME ASCI administrations given at 3-month intervals followed by 4 PRAME ASCI administrations given at 6-month intervals.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | GSK2302025A Cohort 4 |
|------------------|----------------------|

**Arm description:**

In Phase 2 of the study subjects received the optimal investigational dose-level identified in Phase 1. Patients received a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic.

|                                        |                                                                              |
|----------------------------------------|------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                 |
| Investigational medicinal product name | Recombinant PRAME protein combined with the AS15 Adjuvant System GSK2302025A |
| Investigational medicinal product code |                                                                              |
| Other name                             |                                                                              |
| Pharmaceutical forms                   | Powder and solvent for solution for injection                                |
| Routes of administration               | Intramuscular use                                                            |

**Dosage and administration details:**

Patients received a total of 24 PRAME ASCI intramuscular administrations, into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection, according to the following schedule: Cycle 1: 6 PRAME ASCI administrations given at 2-week intervals (weeks 0, 2, 4, 6, 8, 10); Cycle 2: 6 PRAME ASCI administrations given at 3-week intervals (weeks 14, 17, 20, 23, 26, 29); Cycle 3: 4 PRAME ASCI administrations given at 6-week intervals (weeks 33, 39, 45, 51); Cycle 4: 4 PRAME ASCI administrations given at 3-month intervals followed by 4 PRAME ASCI administrations given at 6-month intervals.

| <b>Number of subjects in period 1</b> | GSK2302025A<br>Cohort 1 | GSK2302025A<br>Cohort 2 | GSK2302025A<br>Cohort 3 |
|---------------------------------------|-------------------------|-------------------------|-------------------------|
| Started                               | 20                      | 24                      | 22                      |
| Completed                             | 0                       | 0                       | 0                       |
| Not completed                         | 20                      | 24                      | 22                      |
| Adverse event, serious fatal          | 10                      | 13                      | 18                      |
| Consent withdrawn by subject          | 1                       | 1                       | 1                       |
| Recurrence / Progressive disease      | -                       | -                       | 1                       |
| Sponsor study termination             | -                       | -                       | -                       |
| Unspecified                           | 8                       | 10                      | 2                       |
| Lost to follow-up                     | 1                       | -                       | -                       |

| <b>Number of subjects in period 1</b> | GSK2302025A<br>Cohort 4 |
|---------------------------------------|-------------------------|
| Started                               | 40                      |
| Completed                             | 0                       |
| Not completed                         | 40                      |
| Adverse event, serious fatal          | 18                      |
| Consent withdrawn by subject          | 5                       |
| Recurrence / Progressive disease      | -                       |
| Sponsor study termination             | 2                       |
| Unspecified                           | 14                      |
| Lost to follow-up                     | 1                       |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 1 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                      |
| Male or female patients with histologically proven cutaneous melanoma received the investigational Low-Dose (LD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.    |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 2 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                      |
| Male or female patients with histologically proven cutaneous melanoma received the investigational Middle-Dose (MD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4. |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 3 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                      |
| Male or female patients with histologically proven cutaneous melanoma received the investigational High-Dose (HD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.   |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 4 |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                      |
| In Phase 2 of the study subjects received the optimal investigational dose-level identified in Phase 1. Patients received a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic.                                                                                                                                                                                                                                                                                                                                                                                            |                      |

| Reporting group values | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 |
|------------------------|----------------------|----------------------|----------------------|
| Number of subjects     | 20                   | 24                   | 22                   |
| Age categorical        |                      |                      |                      |
| Units: Subjects        |                      |                      |                      |

|                                       |        |        |        |
|---------------------------------------|--------|--------|--------|
| Age continuous                        |        |        |        |
| Units: years                          |        |        |        |
| arithmetic mean                       | 60.3   | 60.8   | 59.5   |
| standard deviation                    | ± 14.9 | ± 15.5 | ± 15.2 |
| Gender categorical                    |        |        |        |
| Units: Subjects                       |        |        |        |
| Female                                | 7      | 11     | 10     |
| Male                                  | 13     | 13     | 12     |
| Race/Ethnicity, Customized            |        |        |        |
| Units: Subjects                       |        |        |        |
| White - Caucasian / European Heritage | 20     | 23     | 21     |
| Other                                 | 0      | 1      | 1      |

| Reporting group values | GSK2302025A | Total |  |
|------------------------|-------------|-------|--|
|------------------------|-------------|-------|--|

Cohort 4

|                              |        |     |  |
|------------------------------|--------|-----|--|
| Number of subjects           | 40     | 106 |  |
| Age categorical              |        |     |  |
| Units: Subjects              |        |     |  |
| Age continuous               |        |     |  |
| Units: years                 |        |     |  |
| arithmetic mean              | 60.7   |     |  |
| standard deviation           | ± 18.1 | -   |  |
| Gender categorical           |        |     |  |
| Units: Subjects              |        |     |  |
| Female                       | 29     | 57  |  |
| Male                         | 11     | 49  |  |
| Race/Ethnicity, Customized   |        |     |  |
| Units: Subjects              |        |     |  |
| White - Caucasian / European | 40     | 104 |  |
| Heritage                     |        |     |  |
| Other                        | 0      | 2   |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 1 |
| Reporting group description:<br>Male or female patients with histologically proven cutaneous melanoma received the investigational Low-Dose (LD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.    |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 2 |
| Reporting group description:<br>Male or female patients with histologically proven cutaneous melanoma received the investigational Middle-Dose (MD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4. |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 3 |
| Reporting group description:<br>Male or female patients with histologically proven cutaneous melanoma received the investigational High-Dose (HD) adjuvanted GSK2302025A immunotherapeutic vaccine, intramuscularly into the deltoid or lateral region of the thigh, with alternation on right or left side at each succeeding injection. Subjects received a total of 24 administrations in 4 cycles: 6 administrations given at 2 weeks intervals in cycle 1, 6 administrations given at 3 weeks intervals in cycle 2, 4 administrations given at 6 weeks intervals in cycle 3 and 4 administrations given at 3 months interval in cycle 4.   |                      |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | GSK2302025A Cohort 4 |
| Reporting group description:<br>In Phase 2 of the study subjects received the optimal investigational dose-level identified in Phase 1. Patients received a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic.                                                                                                                                                                                                                                                                                                                                                                                            |                      |

### Primary: Number of patients with dose-limiting toxicity (Phase I)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Number of patients with dose-limiting toxicity (Phase I) <sup>[1][2]</sup> |
| End point description:<br>The dose-limiting toxicities (DLT) were defined as follows: •An Antigen-Specific Cancer Immunotherapeutic (ASCI) related or possibly ASCI related grade 3 or higher toxicity. Grade 3 myalgia, arthralgia, headache, fever, rigors/chills and fatigue (including lethargy, malaise and asthenia) persisting for 48 hours despite therapy. •An ASCI related or possibly ASCI related grade 2 or higher allergic reaction occurring within 24 hours following the ASCI administration. •An ASCI related or possibly ASCI related decrease in renal function, with a creatinine clearance lower than (<) 40 milliliters per minute (mL/min). •An ASCI-related or possibly ASCI-related symptomatic and confirmed adrenal insufficiency. The grading used was defined according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0: Grade 3 DLT = severe DLT. Related = DLT considered by investigator as possibly related to product administration. |                                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Primary                                                                    |
| End point timeframe:<br>During the study treatment (up to 4 years), for all patients                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                            |
| Notes:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                            |

[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.

Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[2] - 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: The results in this study were tabulated by age group and study period. Hence for each

related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 |  |
|-----------------------------|----------------------|----------------------|----------------------|--|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      |  |
| Number of subjects analysed | 20                   | 24                   | 22                   |  |
| Units: Days                 |                      |                      |                      |  |
| Patients with DLT           | 0                    | 1                    | 1                    |  |
| Patients with related DLT   | 0                    | 1                    | 1                    |  |
| Patients with severe DLT    | 0                    | 1                    | 1                    |  |
| Brain oedema                | 0                    | 1                    | 0                    |  |
| Microalbuminuria            | 0                    | 0                    | 1                    |  |
| Proteinuria                 | 0                    | 0                    | 1                    |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of patients with anti-PReferentially expressed Antigen of MELanoma (Anti-PRAME) humoral immune response (Phase I)

|                 |                                                                                                                                                |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percentage of patients with anti-PReferentially expressed Antigen of MELanoma (Anti-PRAME) humoral immune response (Phase I) <sup>[3][4]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

A seronegative/seropositive patient for anti-PRAME antibodies was a patient with antibody concentration lower (<)/ higher than or equal to (≥) cut-off level. Humoral immune response was defined as a) if baseline concentration < cut-off level: post treatment concentration ≥ cut-off level, or b) if baseline concentration ≥ cut-off level: post treatment concentration at least twice the baseline value. Cut-off values for seropositivity (by enzyme-linked immunosorbent assay [ELISA]) were 12 ELISA Units per milliliter (EL.U/mL).

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

End point timeframe:

After the administration of dose 4 at Week 8

Notes:

[3] - 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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[4] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                 | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 |  |
|----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type               | Reporting group      | Reporting group      | Reporting group      |  |
| Number of subjects analysed      | 13                   | 13                   | 17                   |  |
| Units: Percentage of patients    |                      |                      |                      |  |
| number (confidence interval 95%) |                      |                      |                      |  |
| Percentage of patients           | 100 (75.3 to 100)    | 100 (75.3 to 100)    | 100 (80.5 to 100)    |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of patients with best overall response to study treatment (Phase II)

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Number of patients with best overall response to study treatment (Phase II) <sup>[5]</sup> |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

The best overall response is the best response recorded from the start of the treatment until disease progression (taking as reference for progressive disease the smallest measurements recorded since the treatment started). In general the patient's best response assignment depended on the achievement of both measurement and confirmation criteria. The best overall response includes the complete response (CR) defined as disappearance of all targeted/non-targeted lesions and partial response (PR) defined as at least 30% decrease in the sum of longest diameter (LD) of target lesions taking as reference the baseline sum LD and persistence of one or more non-targeted lesion(s).

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

End point timeframe:

Up to study conclusion at year 4 + 1 month

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: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| CR                          | 0                    | 0                    | 0                    | 0                    |
| PR                          | 0                    | 0                    | 0                    | 4                    |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of patients with any unsolicited adverse events (AEs), by maximum grading

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Number of patients with any unsolicited adverse events (AEs), by maximum grading |
|-----------------|----------------------------------------------------------------------------------|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. The grading to be used by the investigators for the assessment of the severity of adverse events (AEs) was defined as

|                                                                               |           |
|-------------------------------------------------------------------------------|-----------|
| End point type                                                                | Secondary |
| End point timeframe:                                                          |           |
| During the study treatment period until 30 days after the last administration |           |

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| Grade 1                     | 9                    | 9                    | 8                    | 12                   |
| Grade 2                     | 6                    | 6                    | 10                   | 15                   |
| Grade 3                     | 4                    | 5                    | 3                    | 7                    |
| Grade 4                     | 1                    | 1                    | 0                    | 3                    |
| Grade 5                     | 0                    | 0                    | 0                    | 2                    |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of patients with Serious Adverse Events (SAEs), by maximum grading

|                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                              | Number of patients with Serious Adverse Events (SAEs), by maximum grading |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                       |                                                                           |
| Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. The grading to be used by the investigators for the assessment of the severity of adverse events (AEs) was defined as the Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0. |                                                                           |
| End point type                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                                                                 |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                         |                                                                           |
| During the study period - up to 4 years + 1 month post last study treatment administration                                                                                                                                                                                                                                                                                                                   |                                                                           |

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| Grade 1                     | 0                    | 0                    | 0                    | 0                    |
| Grade 2                     | 0                    | 0                    | 1                    | 0                    |
| Grade 3                     | 2                    | 2                    | 1                    | 0                    |
| Grade 4                     | 1                    | 1                    | 0                    | 3                    |
| Grade 5                     | 0                    | 0                    | 0                    | 2                    |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of patients with laboratory abnormalities versus baseline, by maximum grading

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Number of patients with laboratory abnormalities versus baseline, by maximum grading |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                      |
| Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTTP], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Unknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [ <a href="http://evs.nci.nih.gov/ftp1/CTCAE">http://evs.nci.nih.gov/ftp1/CTCAE</a> ]. This endpoint presents values for [APTTP] grading versus baseline parameter grading. |                                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Secondary                                                                            |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                      |
| During the study period - up to 4 years + 1 month post last study treatment administration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                      |

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| [APTTP], G0-GUnknown        | 0                    | 0                    | 0                    | 0                    |
| [APTTP], G1-GUnknown        | 0                    | 0                    | 0                    | 0                    |
| [APTTP], G2-GUnknown        | 0                    | 0                    | 0                    | 0                    |
| [APTTP], G3-GUnknown        | 0                    | 0                    | 0                    | 1                    |
| [APTTP], G4-GUnknown        | 0                    | 0                    | 0                    | 0                    |
| [APTTP], GUnknown-GUnknown  | 2                    | 0                    | 1                    | 0                    |
| [APTTP], G0-G0              | 13                   | 16                   | 18                   | 33                   |
| [APTTP], G1-G0              | 2                    | 3                    | 1                    | 3                    |
| [APTTP], G2-G0              | 0                    | 0                    | 1                    | 0                    |
| [APTTP], G3-G0              | 0                    | 1                    | 0                    | 1                    |
| [APTTP], G4-G0              | 0                    | 0                    | 0                    | 0                    |
| [APTTP], GUnknown-G0        | 2                    | 0                    | 1                    | 0                    |
| [APTTP], G0-G1              | 0                    | 1                    | 0                    | 1                    |
| [APTTP], G1-G1              | 0                    | 2                    | 0                    | 0                    |
| [APTTP], G2-G1              | 0                    | 0                    | 0                    | 1                    |
| [APTTP], G3-G1              | 0                    | 0                    | 0                    | 0                    |
| [APTTP], G4-G1              | 0                    | 0                    | 0                    | 0                    |
| [APTTP], GUnknown-G1        | 0                    | 1                    | 0                    | 0                    |

|                      |   |   |   |   |
|----------------------|---|---|---|---|
| [APTTP], G0-G2       | 0 | 0 | 0 | 0 |
| [APTTP], G1-G2       | 0 | 0 | 0 | 0 |
| [APTTP], G2-G2       | 1 | 0 | 0 | 0 |
| [APTTP], G3-G2       | 0 | 0 | 0 | 0 |
| [APTTP], G4-G2       | 0 | 0 | 0 | 0 |
| [APTTP], GUnknown-G2 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with laboratory abnormalities versus baseline, by maximum grading

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Number of patients with laboratory abnormalities versus baseline, by maximum grading |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTTP], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Unknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [ALT/I] and [APH/I] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| [ALT/I], G0-G0              | 11                   | 18                   | 16                   | 34                   |
| [ALT/I], G1-G0              | 4                    | 4                    | 5                    | 1                    |
| [ALT/I], G2-G0              | 0                    | 0                    | 0                    | 1                    |
| [ALT/I], G3-G0              | 0                    | 0                    | 0                    | 0                    |
| [ALT/I], G4-G0              | 0                    | 0                    | 0                    | 0                    |
| [ALT/I], GUnknown-G0        | 2                    | 0                    | 1                    | 0                    |
| [ALT/I], G0-G1              | 0                    | 2                    | 0                    | 1                    |
| [ALT/I], G1-G1              | 3                    | 0                    | 0                    | 3                    |
| [ALT/I], G2-G1              | 0                    | 0                    | 0                    | 0                    |
| [ALT/I], G3-G1              | 0                    | 0                    | 0                    | 0                    |
| [ALT/I], G4-G1              | 0                    | 0                    | 0                    | 0                    |
| [ALT/I], GUnknown-G1        | 0                    | 0                    | 0                    | 0                    |
| [APH/I], G0-G0              | 16                   | 20                   | 15                   | 33                   |
| [APH/I], G1-G0              | 1                    | 3                    | 5                    | 5                    |
| [APH/I], G2-G0              | 0                    | 0                    | 1                    | 1                    |

|                     |   |   |   |   |
|---------------------|---|---|---|---|
| [APH/I], G3-G0      | 0 | 0 | 0 | 0 |
| [APH/I], G4-G0      | 0 | 0 | 0 | 0 |
| [APH/I], GUknown-G0 | 2 | 0 | 1 | 0 |
| [APH/I], G0-G1      | 0 | 0 | 0 | 0 |
| [APH/I], G1-G1      | 0 | 0 | 0 | 1 |
| [APH/I], G2-G1      | 0 | 1 | 0 | 0 |
| [APH/I], G3-G1      | 0 | 0 | 0 | 0 |
| [APH/I], G4-G1      | 0 | 0 | 0 | 0 |
| [APH/I], GUknown-G1 | 0 | 0 | 0 | 0 |
| [APH/I], G0-G2      | 0 | 0 | 0 | 0 |
| [APH/I], G1-G2      | 0 | 0 | 0 | 0 |
| [APH/I], G2-G2      | 0 | 0 | 0 | 0 |
| [APH/I], G3-G2      | 1 | 0 | 0 | 0 |
| [APH/I], G4-G2      | 0 | 0 | 0 | 0 |
| [APH/I], GUknown-G2 | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with hematological and biochemical abnormalities versus baseline, by maximum grading

|                 |                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------|
| End point title | Number of patients with hematological and biochemical abnormalities versus baseline, by maximum grading |
|-----------------|---------------------------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTT], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Uknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [AN], [AST/I] and [CRE/I] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| [AN], G0-G0                 | 12                   | 10                   | 10                   | 21                   |
| [AN], G1-G0                 | 1                    | 6                    | 5                    | 12                   |
| [AN], G2-G0                 | 0                    | 0                    | 1                    | 3                    |
| [AN], G3-G0                 | 1                    | 0                    | 0                    | 0                    |
| [AN], G4-G0                 | 0                    | 0                    | 0                    | 0                    |
| [AN], GUknown-G0            | 1                    | 0                    | 1                    | 0                    |

|                      |    |    |    |    |
|----------------------|----|----|----|----|
| [AN], G0-G1          | 2  | 1  | 0  | 0  |
| [AN], G1-G1          | 2  | 5  | 5  | 4  |
| [AN], G2-G1          | 0  | 1  | 0  | 0  |
| [AN], G3-G1          | 0  | 1  | 0  | 0  |
| [AN], G4-G1          | 0  | 0  | 0  | 0  |
| [AN], GUnknown-G1    | 1  | 0  | 0  | 0  |
| [AST/I], G0-G0       | 13 | 18 | 17 | 36 |
| [AST/I], G1-G0       | 3  | 6  | 4  | 2  |
| [AST/I], G2-G0       | 0  | 0  | 0  | 0  |
| [AST/I], G3-G0       | 0  | 0  | 0  | 0  |
| [AST/I], G4-G0       | 0  | 0  | 0  | 0  |
| [AST/I], GUnknown-G0 | 1  | 0  | 1  | 0  |
| [AST/I], G0-G1       | 1  | 0  | 0  | 0  |
| [AST/I], G1-G1       | 1  | 0  | 0  | 2  |
| [AST/I], G2-G1       | 0  | 0  | 0  | 0  |
| [AST/I], G3-G1       | 0  | 0  | 0  | 0  |
| [AST/I], G4-G1       | 0  | 0  | 0  | 0  |
| [AST/I], GUnknown-G1 | 1  | 0  | 0  | 0  |
| [BB/I], G0-G0        | 16 | 21 | 19 | 38 |
| [BB/I], G1-G0        | 1  | 2  | 1  | 0  |
| [BB/I], G2-G0        | 1  | 0  | 0  | 0  |
| [BB/I], G3-G0        | 0  | 0  | 0  | 0  |
| [BB/I], G4-G0        | 0  | 0  | 0  | 0  |
| [BB/I], GUnknown-G0  | 2  | 0  | 1  | 0  |
| [BB/I], G0-G1        | 0  | 0  | 0  | 0  |
| [BB/I], G1-G1        | 0  | 1  | 1  | 1  |
| [BB/I], G2-G1        | 0  | 0  | 0  | 1  |
| [BB/I], G3-G1        | 0  | 0  | 0  | 0  |
| [BB/I], G4-G1        | 0  | 0  | 0  | 0  |
| [BB/I], GUnknown-G1  | 0  | 0  | 0  | 0  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with laboratory hematological and biochemical abnormalities versus baseline, by maximum grading

|                 |                                                                                                                    |
|-----------------|--------------------------------------------------------------------------------------------------------------------|
| End point title | Number of patients with laboratory hematological and biochemical abnormalities versus baseline, by maximum grading |
|-----------------|--------------------------------------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTT], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Unknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [CRE/I] and [GGT/I] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A<br>Cohort 1 | GSK2302025A<br>Cohort 2 | GSK2302025A<br>Cohort 3 | GSK2302025A<br>Cohort 4 |
|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type          | Reporting group         | Reporting group         | Reporting group         | Reporting group         |
| Number of subjects analysed | 20                      | 24                      | 22                      | 40                      |
| Units: Participants         |                         |                         |                         |                         |
| [CRE/I], G0-G0              | 20                      | 22                      | 20                      | 33                      |
| [CRE/I], G1-G0              | 0                       | 0                       | 1                       | 6                       |
| [CRE/I], G2-G0              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G3-G0              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G4-G0              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], GUnknown-G0        | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G0-G1              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G1-G1              | 0                       | 1                       | 1                       | 0                       |
| [CRE/I], G2-G1              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G3-G1              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G4-G1              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], GUnknown-G1        | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G0-G2              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G1-G2              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G2-G2              | 0                       | 1                       | 0                       | 1                       |
| [CRE/I], G3-G2              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], G4-G2              | 0                       | 0                       | 0                       | 0                       |
| [CRE/I], GUnknown-G2        | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G0-G0              | 10                      | 17                      | 14                      | 30                      |
| [GGT/I], G1-G0              | 1                       | 1                       | 1                       | 4                       |
| [GGT/I], G2-G0              | 2                       | 2                       | 1                       | 0                       |
| [GGT/I], G3-G0              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G4-G0              | 0                       | 0                       | 0                       | 1                       |
| [GGT/I], GUnknown-G0        | 1                       | 0                       | 1                       | 0                       |
| [GGT/I], G0-G1              | 2                       | 1                       | 1                       | 1                       |
| [GGT/I], G1-G1              | 0                       | 1                       | 1                       | 3                       |
| [GGT/I], G2-G1              | 1                       | 1                       | 0                       | 0                       |
| [GGT/I], G3-G1              | 0                       | 0                       | 1                       | 0                       |
| [GGT/I], G4-G1              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], GUnknown-G1        | 1                       | 0                       | 0                       | 0                       |
| [GGT/I], G0-G2              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G1-G2              | 0                       | 1                       | 0                       | 0                       |
| [GGT/I], G2-G2              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G3-G2              | 1                       | 0                       | 2                       | 0                       |
| [GGT/I], G4-G2              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], GUnknown-G2        | 1                       | 0                       | 0                       | 0                       |
| [GGT/I], G0-G3              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G1-G3              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G2-G3              | 0                       | 0                       | 0                       | 0                       |
| [GGT/I], G3-G3              | 0                       | 0                       | 0                       | 1                       |
| [GGT/I], G4-G3              | 0                       | 0                       | 0                       | 0                       |

|                      |   |   |   |   |
|----------------------|---|---|---|---|
| [GGT/I], GUnknown-G3 | 0 | 0 | 0 | 0 |
|----------------------|---|---|---|---|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with laboratory hematological and biochemical abnormalities versus baseline, by maximum grading

|                 |                                                                                                                    |
|-----------------|--------------------------------------------------------------------------------------------------------------------|
| End point title | Number of patients with laboratory hematological and biochemical abnormalities versus baseline, by maximum grading |
|-----------------|--------------------------------------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTT], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Uknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [Hgb/I] and [HYP] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| [Hgb/I], G0-G0              | 16                   | 24                   | 21                   | 37                   |
| [Hgb/I], G1-G0              | 0                    | 0                    | 0                    | 2                    |
| [Hgb/I], G2-G0              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G3-G0              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G4-G0              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], GUnknown-G0        | 2                    | 0                    | 1                    | 0                    |
| [Hgb/I], G0-G1              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G1-G1              | 1                    | 0                    | 0                    | 0                    |
| [Hgb/I], G2-G1              | 0                    | 0                    | 0                    | 1                    |
| [Hgb/I], G3-G1              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G4-G1              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], GUnknown-G1        | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G0-G2              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G1-G2              | 1                    | 0                    | 0                    | 0                    |
| [Hgb/I], G2-G2              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G3-G2              | 0                    | 0                    | 0                    | 0                    |
| [Hgb/I], G4-G2              | 0                    | 0                    | 0                    | 0                    |

|                      |    |    |    |    |
|----------------------|----|----|----|----|
| [Hgb/I], GUnknown-G2 | 0  | 0  | 0  | 0  |
| [HYP], G0-G0         | 13 | 17 | 18 | 30 |
| [HYP], G1-G0         | 2  | 5  | 2  | 5  |
| [HYP], G2-G0         | 0  | 1  | 0  | 1  |
| [HYP], G3-G0         | 0  | 0  | 0  | 0  |
| [HYP], G4-G0         | 0  | 0  | 0  | 0  |
| [HYP], GUnknown-G0   | 3  | 0  | 2  | 0  |
| [HYP], G0-G1         | 0  | 0  | 0  | 0  |
| [HYP], G1-G1         | 1  | 1  | 0  | 3  |
| [HYP], G2-G1         | 1  | 0  | 0  | 0  |
| [HYP], G3-G1         | 0  | 0  | 0  | 0  |
| [HYP], G4-G1         | 0  | 0  | 0  | 0  |
| [HYP], GUnknown-G1   | 0  | 0  | 0  | 0  |
| [HYP], G0-G3         | 0  | 0  | 0  | 1  |
| [HYP], G1-G3         | 0  | 0  | 0  | 0  |
| [HYP], G2-G3         | 0  | 0  | 0  | 0  |
| [HYP], G3-G3         | 0  | 0  | 0  | 0  |
| [HYP], G4-G3         | 0  | 0  | 0  | 0  |
| [HYP], GUnknown-G3   | 0  | 0  | 0  | 0  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with abnormal hematological and biochemical results versus baseline, by maximum grading

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Number of patients with abnormal hematological and biochemical results versus baseline, by maximum grading |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTT], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Unknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [LYMC/D] and [LYMC/I] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed | 20                   | 24                   | 22                   | 40                   |
| Units: Participants         |                      |                      |                      |                      |
| [LYMC/D], G0-G0             | 10                   | 14                   | 14                   | 28                   |
| [LYMC/D], G1-G0             | 3                    | 4                    | 3                    | 4                    |

|                       |    |    |    |    |
|-----------------------|----|----|----|----|
| [LYMC/D], G2-G0       | 1  | 1  | 0  | 0  |
| [LYMC/D], G3-G0       | 0  | 0  | 0  | 0  |
| [LYMC/D], G4-G0       | 0  | 0  | 0  | 0  |
| [LYMC/D], GUnknown-G0 | 0  | 0  | 1  | 0  |
| [LYMC/D], G0-G1       | 0  | 1  | 1  | 2  |
| [LYMC/D], G1-G1       | 3  | 3  | 2  | 5  |
| [LYMC/D], G2-G1       | 1  | 0  | 0  | 0  |
| [LYMC/D], G3-G1       | 0  | 0  | 0  | 0  |
| [LYMC/D], G4-G1       | 0  | 0  | 0  | 0  |
| [LYMC/D], GUnknown-G1 | 1  | 1  | 0  | 0  |
| [LYMC/D], G0-G2       | 0  | 0  | 0  | 0  |
| [LYMC/D], G1-G2       | 0  | 0  | 1  | 0  |
| [LYMC/D], G2-G2       | 0  | 0  | 0  | 1  |
| [LYMC/D], G3-G2       | 0  | 0  | 0  | 0  |
| [LYMC/D], G4-G2       | 0  | 0  | 0  | 0  |
| [LYMC/D], GUnknown-G2 | 0  | 0  | 0  | 0  |
| [LYMC/D], G0-G3       | 0  | 0  | 0  | 0  |
| [LYMC/D], G1-G3       | 0  | 0  | 0  | 0  |
| [LYMC/D], G2-G3       | 0  | 0  | 0  | 0  |
| [LYMC/D], G3-G3       | 0  | 0  | 0  | 0  |
| [LYMC/D], G4-G3       | 0  | 0  | 0  | 0  |
| [LYMC/D], GUnknown-G3 | 1  | 0  | 0  | 0  |
| [LYMC/I], G0-G0       | 16 | 23 | 21 | 40 |
| [LYMC/I], G1-G0       | 0  | 0  | 0  | 0  |
| [LYMC/I], G2-G0       | 2  | 0  | 0  | 0  |
| [LYMC/I], G3-G0       | 0  | 0  | 0  | 0  |
| [LYMC/I], G4-G0       | 0  | 0  | 0  | 0  |
| [LYMC/I], GUnknown-G0 | 2  | 1  | 1  | 0  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of patients with abnormal hematological and biochemical results versus baseline, by maximum grading

|                 |                                                                                                            |
|-----------------|------------------------------------------------------------------------------------------------------------|
| End point title | Number of patients with abnormal hematological and biochemical results versus baseline, by maximum grading |
|-----------------|------------------------------------------------------------------------------------------------------------|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: activated partial thromboplastin time prolonged [APTT], alanine aminotransferase increased [ALT/I], alkaline phosphatase increased [APH/I], anemia [AN], aspartate aminotransferase increased [AST/I], blood bilirubin increased [BB/I], creatinine increased [CRE/I], gamma glutamyltransferase increased [GGT/I], hemoglobin increased [Hgb/I], hypoalbuminemia [HYP], lymphocyte count decreased [LYMC/D], lymphocyte count increased [LYMC/I], neutrophil count decreased [NEUC/D], platelet count decreased [PLA/D], white blood cell decreased [WBC/D]. Parameter grades (G0,1,2,3,4,Unknown) were compared to baseline parameter grades (GUnknown,0,1,2,3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0 of May 28, 2009 [<http://evs.nci.nih.gov/ftp1/CTCAE>]. This endpoint presents values for [NEUC/D], [PLA/D] and [WBC/D] grading versus baseline parameter grading.

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

End point timeframe:

During the study period - up to 4 years + 1 month post last study treatment administration

| End point values            | GSK2302025A<br>Cohort 1 | GSK2302025A<br>Cohort 2 | GSK2302025A<br>Cohort 3 | GSK2302025A<br>Cohort 4 |
|-----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type          | Reporting group         | Reporting group         | Reporting group         | Reporting group         |
| Number of subjects analysed | 20                      | 24                      | 22                      | 40                      |
| Units: Participants         |                         |                         |                         |                         |
| [NEUC/D], G0-G0             | 17                      | 21                      | 21                      | 39                      |
| [NEUC/D], G1-G0             | 1                       | 2                       | 0                       | 0                       |
| [NEUC/D], G2-G0             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], G3-G0             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], G4-G0             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], GUnknown-G0       | 2                       | 1                       | 1                       | 0                       |
| [NEUC/D], G0-G1             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], G1-G1             | 0                       | 0                       | 0                       | 1                       |
| [NEUC/D], G2-G1             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], G3-G1             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], G4-G1             | 0                       | 0                       | 0                       | 0                       |
| [NEUC/D], GUnknown-G1       | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G0-G0              | 17                      | 24                      | 20                      | 38                      |
| [PLA/D], G1-G0              | 1                       | 0                       | 0                       | 2                       |
| [PLA/D], G2-G0              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G3-G0              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G4-G0              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], GUnknown-G0        | 2                       | 0                       | 1                       | 0                       |
| [PLA/D], G0-G1              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G1-G1              | 0                       | 0                       | 1                       | 0                       |
| [PLA/D], G2-G1              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G3-G1              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], G4-G1              | 0                       | 0                       | 0                       | 0                       |
| [PLA/D], GUnknown-G1        | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], G0-G0              | 14                      | 21                      | 19                      | 34                      |
| [WBC/D], G1-G0              | 2                       | 1                       | 1                       | 3                       |
| [WBC/D], G2-G0              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], G3-G0              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], G4-G0              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], GUnknown-G0        | 2                       | 0                       | 1                       | 0                       |
| [WBC/D], G0-G1              | 1                       | 0                       | 0                       | 2                       |
| [WBC/D], G1-G1              | 1                       | 2                       | 1                       | 1                       |
| [WBC/D], G2-G1              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], G3-G1              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], G4-G1              | 0                       | 0                       | 0                       | 0                       |
| [WBC/D], GUnknown-G1        | 0                       | 0                       | 0                       | 0                       |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of patients with anti-PRAME cellular (T-cell) response (Phase I)

|                 |                                                                                            |
|-----------------|--------------------------------------------------------------------------------------------|
| End point title | Percentage of patients with anti-PRAME cellular (T-cell) response (Phase I) <sup>[6]</sup> |
|-----------------|--------------------------------------------------------------------------------------------|

End point description:

Cellular response was defined as: Geometric Mean Response (GMR) above the 2.68 cut-off value and at least a four-fold increase of PRAME- specific Cluster of Differentiation (CD) 4/8 T cells. Considering that 2 studies failed to demonstrate clinical efficacy of recombinant protein based cancer vaccines, GSK decided in 2014 to stop the development and to stop recruitment in all the ongoing clinical studies. The decision was made to end the study (i.e., stopping patient enrollment, follow-ups, sample collection and analysis of samples for research purposes). Patients still on treatment at the time of the protocol amendment were offered to continue the administration of the study treatment until the last dose or until recurrence, whichever came first, or until the patient or the investigator decided to stop the study treatment. No further active protocol visit/contact was performed except for the concluding visit 30 days after the last treatment administration.

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

End point timeframe:

Up to Data Lock Point at Week 8

Notes:

[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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

| End point values                                  | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 |  |
|---------------------------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                                | Reporting group      | Reporting group      | Reporting group      |  |
| Number of subjects analysed                       | 8                    | 11                   | 14                   |  |
| Units: Percentage of patients                     |                      |                      |                      |  |
| number (confidence interval 95%)                  |                      |                      |                      |  |
| Patients with pre+post-administration results CD4 | 100 (63.1 to 100)    | 100 (71.5 to 100)    | 100 (76.8 to 100)    |  |
| Responders CD4                                    | 75.0 (34.9 to 96.8)  | 45.5 (16.7 to 76.6)  | 57.1 (28.9 to 82.3)  |  |
| Patients with pre+post-administration results CD8 | 100 (63.1 to 100)    | 100 (66.4 to 100)    | 100 (63.1 to 100)    |  |
| Responders CD8                                    | 0.0 (0.0 to 36.9)    | 0.0 (0.0 to 33.6)    | 0.0 (0.0 to 36.9)    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-PRAME humoral immune response (Phase I & II)

|                 |                                                                           |
|-----------------|---------------------------------------------------------------------------|
| End point title | Number of subjects with anti-PRAME humoral immune response (Phase I & II) |
|-----------------|---------------------------------------------------------------------------|

End point description:

A seropositive subject is a subject whose antibody concentrations are greater than or equal to the assay cut-off value of 12 EL/mL.

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

End point timeframe:

At Week 0, 4, 8, 10, 12, 29, 51, 75, 99 123, 147 and conclusion visit at 30 days post last treatment administration for each patient

| End point values             | GSK2302025A<br>Cohort 1 | GSK2302025A<br>Cohort 2 | GSK2302025A<br>Cohort 3 | GSK2302025A<br>Cohort 4 |
|------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Subject group type           | Reporting group         | Reporting group         | Reporting group         | Reporting group         |
| Number of subjects analysed  | 20                      | 24                      | 22                      | 40                      |
| Units: Participants          |                         |                         |                         |                         |
| anti-PRAME, week 0           | 0                       | 0                       | 0                       | 2                       |
| anti-PRAME, week 4           | 11                      | 14                      | 18                      | 33                      |
| anti-PRAME, week 8           | 14                      | 13                      | 21                      | 33                      |
| anti-PRAME, week 10          | 10                      | 12                      | 19                      | 33                      |
| anti-PRAME, week 12          | 9                       | 9                       | 16                      | 28                      |
| anti-PRAME, week 29          | 2                       | 4                       | 5                       | 13                      |
| anti-PRAME, week 51          | 1                       | 3                       | 3                       | 7                       |
| anti-PRAME, week 75          | 2                       | 2                       | 2                       | 1                       |
| anti-PRAME, week 99          | 2                       | 2                       | 2                       | 0                       |
| anti-PRAME, week 123         | 1                       | 1                       | 1                       | 0                       |
| anti-PRAME, week 147         | 1                       | 0                       | 0                       | 0                       |
| anti-PRAME, conclusion visit | 6                       | 12                      | 8                       | 23                      |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with best overall response, including Mixed Response (MxR) and Slow Progressive Disease (SPD) criteria (Phase I & II)

|                 |                                                                                                                                          |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with best overall response, including Mixed Response (MxR) and Slow Progressive Disease (SPD) criteria (Phase I & II) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Tumor response was assessed by the RECIST criteria, where SD for target lesions refers to neither enough shrinkage to qualify for CR nor sufficient increase to qualify for PD taking as references the smallest sum LD since the treatment started. For non-targeted lesions it refers to persistence of one or more non-target lesions. Progressive disease is related to a clear increase of diameters of lesions taking as references the smallest diameters recorded since the treatment started OR the appearance of one or more new lesions OR both of these. Mixed response is defined as at least 30% decrease in the longest diameter (LD) occurring in at least one target lesion recorded and measured at baseline. Such response occurring in otherwise SD or PD status of the LD of target lesions were classified as "SD with target lesion regression" or "PD with target lesion regression", respectively. New lesion(s) in otherwise PR status of the LD of target lesions were "PR with new lesion".

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

End point timeframe:

At 30 days after the last treatment administration for each patient

| End point values                      | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|---------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                    | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed           | 20                   | 24                   | 22                   | 40                   |
| Units: Participants                   |                      |                      |                      |                      |
| PR                                    | 0                    | 0                    | 0                    | 0                    |
| CR                                    | 0                    | 0                    | 0                    | 4                    |
| MxR: SD with target lesion regression | 0                    | 0                    | 0                    | 0                    |
| MxR: PD with target lesion regression | 2                    | 2                    | 2                    | 3                    |
| MxR: PR with new lesion               | 0                    | 0                    | 1                    | 0                    |
| SD/PR                                 | 0                    | 1                    | 1                    | 3                    |
| SD without mixed response             | 2                    | 0                    | 1                    | 1                    |
| PD with SPD criteria                  | 3                    | 5                    | 4                    | 19                   |
| PD without SPD/MxR                    | 4                    | 12                   | 8                    | 9                    |
| Non Evaluable                         | 2                    | 1                    | 0                    | 1                    |
| Missing Best overall response         | 7                    | 3                    | 5                    | 0                    |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The anti-Protein D humoral response (Phase I)

|                 |                                               |
|-----------------|-----------------------------------------------|
| End point title | The anti-Protein D humoral response (Phase I) |
|-----------------|-----------------------------------------------|

End point description:

Analysis of immunogenicity for anti-PD antibodies was not performed, following negative results to the NCT00480025 study which assessed another study product from same technology platform. For this study, the main analysis of the dose-escalation Phase I segment was performed according to protocol when all patients enrolled in the Phase I segment had received the first 4 treatment doses and had completed Week 8. The main analysis of the Phase II segment was performed according to protocol when all patients had either completed the treatment until the end of Cycle 3 or had been withdrawn from the study treatment, with the exception of anti-PD antibody responses and PRAME-specific cellular responses which were not yet performed. All samples that had been collected but not yet tested were not tested by default, except if a scientific rationale remained relevant.

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

End point timeframe:

At Week 0, 4, 8, 12, 29, 51, 75, 99, 123, 147, 30 days after the last treatment administration for each patient, with follow-up, 3, 6, 9 and 12 months after concluding visit

| End point values                         | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|------------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                       | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed              | 0 <sup>[7]</sup>     | 0 <sup>[8]</sup>     | 0 <sup>[9]</sup>     | 0 <sup>[10]</sup>    |
| Units: Titer                             |                      |                      |                      |                      |
| geometric mean (confidence interval 95%) |                      |                      |                      |                      |
| Titer                                    | ( to )               | ( to )               | ( to )               | ( to )               |

Notes:

[7] - Analysis of immunogenicity for anti-PD antibodies was not performed.

[8] - Analysis of immunogenicity for anti-PD antibodies was not performed.

[9] - Analysis of immunogenicity for anti-PD antibodies was not performed.

[10] - Analysis of immunogenicity for anti-PD antibodies was not performed.

## Statistical analyses

No statistical analyses for this end point

### Secondary: The anti-Cytosine Phosphate Guanosine oligodeoxynucleotide (CpG) humoral response (Phase I & II)

|                 |                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------|
| End point title | The anti-Cytosine Phosphate Guanosine oligodeoxynucleotide (CpG) humoral response (Phase I & II) |
|-----------------|--------------------------------------------------------------------------------------------------|

End point description:

Analysis of immunogenicity for anti-CpG antibodies was not performed, following negative results to the NCT00480025 study which assessed another study product from same technology platform. For this study, the main analysis of the dose-escalation Phase I segment was performed according to protocol when all patients enrolled in the Phase I segment had received the first 4 treatment doses and had completed Week 8. The main analysis of the Phase II segment was performed according to protocol when all patients had either completed the treatment until the end of Cycle 3 or had been withdrawn from the study treatment, with the exception of anti-CpG antibody responses and PRAME-specific cellular responses which were not yet performed. All samples that had been collected but not yet tested were not tested by default, except if a scientific rationale remained relevant.

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

End point timeframe:

At Week 0, 4, 8, 12, 29, 51, years 1.5, 2, 2.5, 3, 3.5, 4 years + 1 month, with follow-up, 3, 6, 9 and 12 months after concluding visit

| End point values                        | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|-----------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                      | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed             | 0 <sup>[11]</sup>    | 0 <sup>[12]</sup>    | 0 <sup>[13]</sup>    | 0 <sup>[14]</sup>    |
| Units: Specific T-cells/million T-cells |                      |                      |                      |                      |
| arithmetic mean (standard deviation)    |                      |                      |                      |                      |
| Specific T-cells/million T-cells        | ()                   | ()                   | ()                   | ()                   |

Notes:

[11] - Analysis of immunogenicity for anti-CpG antibodies was not performed.

[12] - Analysis of immunogenicity for anti-CpG antibodies was not performed.

[13] - Analysis of immunogenicity for anti-CpG antibodies was not performed.

[14] - Analysis of immunogenicity for anti-CpG antibodies was not performed.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to treatment failure, progression free survival, overall survival and duration of response (Phase I & II)

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Time to treatment failure, progression free survival, overall survival and duration of response (Phase I & II) |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

Time to treatment failure (TTF) was defined as the time from first administration of study product until the date of the last administration of the product, irrespective of the reason for study treatment

discontinuation. Progression-free survival (PFS) was defined as the time from first administration of study product until the date of either disease progression or death (for whatever reason), whichever comes first. Overall survival (OS) was defined as the time from first administration of study product until death. Duration of response (DR) was defined as the time from the first objective response (OR) or SD assessment until the first assessment of PD. The value "9999" is a placeholder as the 95% confidence interval lower limit was below the limit of detection.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to Month 54       |           |

| End point values                 | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type               | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed      | 20                   | 24                   | 22                   | 40                   |
| Units: Months                    |                      |                      |                      |                      |
| median (confidence interval 95%) |                      |                      |                      |                      |
| TTF                              | 2.3 (1.0 to 4.9)     | 2.3 (1.3 to 4.2)     | 3.0 (2.3 to 4.9)     | 4.6 (2.7 to 5.3)     |
| PFS                              | 2.7 (1.4 to 2.9)     | 2.7 (1.0 to 2.8)     | 2.8 (2.1 to 2.9)     | 2.8 (2.7 to 3.3)     |
| OS                               | 17.0 (8.1 to 9999)   | 11.5 (7.3 to 9999)   | 10.8 (8.4 to 25.5)   | 23.0 (15.5 to 9999)  |
| DR                               | 43.8 (19.0 to 48.6)  | 42.4 (23.7 to 45.9)  | 42.1 (40.1 to 46.0)  | 26.5 (22.8 to 28.0)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of response for patients with CR, PR and SD or SD/PR status (Phase II)

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Duration of response for patients with CR, PR and SD or SD/PR status (Phase II) |
|-----------------|---------------------------------------------------------------------------------|

End point description:

Following negative results to the NCT00480025 study which assessed another study product from same technology platform. For this study, the main analysis of the dose-escalation Phase I segment was performed according to protocol when all patients enrolled in the Phase I segment had received the first 4 treatment doses and had completed Week 8. The main analysis of the Phase II segment was performed according to protocol when all patients had either completed the treatment until the end of Cycle 3 or had been withdrawn from the study treatment, with the exception of anti-CpG/anti-PD antibody responses and PRAME-specific cellular responses which were not yet performed. All samples that had been collected but not yet tested were not tested by default, except if a scientific rationale remained relevant.

|                                                          |           |
|----------------------------------------------------------|-----------|
| End point type                                           | Secondary |
| End point timeframe:                                     |           |
| Up to data lock point LPLV for Main analysis in Phase II |           |

| End point values                 | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type               | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed      | 0 <sup>[15]</sup>    | 0 <sup>[16]</sup>    | 0 <sup>[17]</sup>    | 0 <sup>[18]</sup>    |
| Units: Months                    |                      |                      |                      |                      |
| median (confidence interval 95%) |                      |                      |                      |                      |
| Months                           | ( to )               | ( to )               | ( to )               | ( to )               |

Notes:

[15] - This analysis was not performed.

[16] - This analysis was not performed.

[17] - This analysis was not performed.

[18] - This analysis was not performed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with stable disease (SD), progressive disease (PD), mixed response (MR) (Phase I & II)

|                 |                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects with stable disease (SD), progressive disease (PD), mixed response (MR) (Phase I & II) |
|-----------------|-----------------------------------------------------------------------------------------------------------|

End point description:

Tumor response was assessed by the RECIST criteria, where SD for target lesions refers to neither enough shrinkage to qualify for CR nor sufficient increase to qualify for PD taking as references the smallest sum LD since the treatment started. For non-targeted lesions it refers to persistence of one or more non-target lesions. Progressive disease is related to a clear increase of diameters of lesions taking as references the smallest diameters recorded since the treatment started OR the appearance of one or more new lesions OR both of these.

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

End point timeframe:

At 30 days after the last treatment administration for each patient

| End point values                   | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 | GSK2302025A Cohort 4 |
|------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                 | Reporting group      | Reporting group      | Reporting group      | Reporting group      |
| Number of subjects analysed        | 20                   | 24                   | 22                   | 40                   |
| Units: Participants                |                      |                      |                      |                      |
| Complete response                  | 0                    | 0                    | 0                    | 0                    |
| Partial response                   | 0                    | 0                    | 0                    | 4                    |
| Stable disease                     | 2                    | 1                    | 1                    | 1                    |
| Stable Disease/Progressive disease | 0                    | 1                    | 1                    | 3                    |
| Progressive disease                | 9                    | 18                   | 15                   | 31                   |
| Non Evaluable                      | 2                    | 1                    | 0                    | 1                    |
| Missing Best overall response      | 7                    | 3                    | 5                    | 0                    |
| Disease control: Yes               | 2                    | 2                    | 2                    | 8                    |
| Disease control: No                | 18                   | 22                   | 20                   | 32                   |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From study start to Month 49.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GSK2302025A Cohort 1 |
|-----------------------|----------------------|

Reporting group description:

Subjects will receive investigational dose-level A (different from dose-levels B and C). Patients will receive a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic

|                       |                      |
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| Reporting group title | GSK2302025A Cohort 2 |
|-----------------------|----------------------|

Reporting group description:

Subjects will receive investigational dose-level B (different from dose-levels A and C). Patients will receive a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GSK2302025A Cohort 3 |
|-----------------------|----------------------|

Reporting group description:

Subjects will receive investigational dose-level C (different from dose-levels A and B). Patients will receive a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | GSK2302025A Cohort 4 |
|-----------------------|----------------------|

Reporting group description:

In Phase 2 of the study subjects will receive the optimal investigational dose-level identified in Phase 1. Patients will receive a treatment consisting of 24 injections of the experimental GSK2302025A immunotherapeutic

| Serious adverse events                                              | GSK2302025A Cohort 1 | GSK2302025A Cohort 2 | GSK2302025A Cohort 3 |
|---------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Total subjects affected by serious adverse events                   |                      |                      |                      |
| subjects affected / exposed                                         | 3 / 20 (15.00%)      | 3 / 24 (12.50%)      | 2 / 22 (9.09%)       |
| number of deaths (all causes)                                       | 0                    | 0                    | 0                    |
| number of deaths resulting from adverse events                      | 0                    | 0                    | 0                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                      |                      |                      |
| Renal neoplasm                                                      |                      |                      |                      |
| subjects affected / exposed                                         | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)       |
| occurrences causally related to treatment / all                     | 0 / 0                | 0 / 0                | 0 / 0                |
| deaths causally related to treatment / all                          | 0 / 0                | 0 / 0                | 0 / 0                |
| Vascular disorders                                                  |                      |                      |                      |
| Circulatory collapse                                                |                      |                      |                      |

|                                                      |                |                |                |
|------------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                                    |                |                |                |
| Atrial fibrillation                                  |                |                |                |
| subjects affected / exposed                          | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Nervous system disorders                             |                |                |                |
| Brain oedema                                         |                |                |                |
| subjects affected / exposed                          | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 0 / 22 (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          |
| Sciatica                                             |                |                |                |
| subjects affected / exposed                          | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| General disorders and administration site conditions |                |                |                |
| Fatigue                                              |                |                |                |
| subjects affected / exposed                          | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Pain                                                 |                |                |                |
| subjects affected / exposed                          | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Gastrointestinal disorders                           |                |                |                |
| Intestinal obstruction                               |                |                |                |
| subjects affected / exposed                          | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                              |                |                |                |
| Cholestasis                                          |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Chronic obstructive pulmonary disease           |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Skin ulcer                                      |                |                |                |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Renal and urinary disorders                     |                |                |                |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Bursitis                                        |                |                |                |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Osteoarthritis                                  |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 0 / 22 (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>Infections and infestations</b>              |                |                |                |
| Erysipelas                                      |                |                |                |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Infected skin ulcer                             |                |                |                |
| subjects affected / exposed                     | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (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          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Subcutaneous abscess                            |                |                |                |
| subjects affected / exposed                     | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 0 / 22 (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>Serious adverse events</b>                                       | GSK2302025A<br>Cohort 4 |  |  |
| Total subjects affected by serious adverse events                   |                         |  |  |
| subjects affected / exposed                                         | 5 / 40 (12.50%)         |  |  |
| number of deaths (all causes)                                       | 2                       |  |  |
| number of deaths resulting from adverse events                      | 0                       |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |  |  |
| Renal neoplasm                                                      |                         |  |  |
| subjects affected / exposed                                         | 1 / 40 (2.50%)          |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                   |  |  |
| deaths causally related to treatment / all                          | 0 / 0                   |  |  |
| Vascular disorders                                                  |                         |  |  |
| Circulatory collapse                                                |                         |  |  |

|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 1          |  |  |
| Cardiac disorders                                    |                |  |  |
| Atrial fibrillation                                  |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Nervous system disorders                             |                |  |  |
| Brain oedema                                         |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Sciatica                                             |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Fatigue                                              |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Pain                                                 |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Gastrointestinal disorders                           |                |  |  |
| Intestinal obstruction                               |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Hepatobiliary disorders                              |                |  |  |
| Cholestasis                                          |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Chronic obstructive pulmonary disease           |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Pneumothorax                                    |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pulmonary embolism                              |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Skin ulcer                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Haematuria                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Bursitis                                        |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Osteoarthritis                                  |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Infections and infestations</b>              |                |  |  |
| Erysipelas                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Infected skin ulcer</b>                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pneumonia</b>                                |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| <b>Subcutaneous abscess</b>                     |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                          | GSK2302025A<br>Cohort 1 | GSK2302025A<br>Cohort 2 | GSK2302025A<br>Cohort 3 |
|----------------------------------------------------------------------------|-------------------------|-------------------------|-------------------------|
| Total subjects affected by non-serious adverse events                      |                         |                         |                         |
| subjects affected / exposed                                                | 19 / 20 (95.00%)        | 21 / 24 (87.50%)        | 21 / 22 (95.45%)        |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |                         |                         |                         |
| Uterine leiomyoma                                                          |                         |                         |                         |
| subjects affected / exposed                                                | 0 / 20 (0.00%)          | 0 / 24 (0.00%)          | 0 / 22 (0.00%)          |
| occurrences (all)                                                          | 0                       | 0                       | 0                       |
| <b>Vascular disorders</b>                                                  |                         |                         |                         |
| Arteriosclerosis moenckeberg-type                                          |                         |                         |                         |
| subjects affected / exposed                                                | 1 / 20 (5.00%)          | 0 / 24 (0.00%)          | 0 / 22 (0.00%)          |
| occurrences (all)                                                          | 1                       | 0                       | 0                       |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| Haemorrhage                           |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Hot flush                             |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Hyperaemia                            |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Hypertension                          |                |                |                |
| subjects affected / exposed           | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 2 / 22 (9.09%) |
| occurrences (all)                     | 1              | 0              | 3              |
| Hypotension                           |                |                |                |
| subjects affected / exposed           | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                     | 1              | 0              | 1              |
| Lymphoedema                           |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Lymphostasis                          |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Peripheral arterial occlusive disease |                |                |                |
| subjects affected / exposed           | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Peripheral coldness                   |                |                |                |
| subjects affected / exposed           | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Thrombophlebitis                      |                |                |                |
| subjects affected / exposed           | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Surgical and medical procedures       |                |                |                |
| Catheter placement                    |                |                |                |
| subjects affected / exposed           | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |
| Tooth extraction                      |                |                |                |

|                                                      |                 |                 |                 |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 0               | 0               | 0               |
| General disorders and administration site conditions |                 |                 |                 |
| Administration site induration                       |                 |                 |                 |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                                    | 0               | 0               | 3               |
| Administration site pain                             |                 |                 |                 |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 1 / 22 (4.55%)  |
| occurrences (all)                                    | 0               | 2               | 2               |
| Asthenia                                             |                 |                 |                 |
| subjects affected / exposed                          | 2 / 20 (10.00%) | 0 / 24 (0.00%)  | 6 / 22 (27.27%) |
| occurrences (all)                                    | 2               | 0               | 21              |
| Axillary pain                                        |                 |                 |                 |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 0               | 1               | 0               |
| Chest discomfort                                     |                 |                 |                 |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 6               | 0               | 0               |
| Chills                                               |                 |                 |                 |
| subjects affected / exposed                          | 4 / 20 (20.00%) | 1 / 24 (4.17%)  | 4 / 22 (18.18%) |
| occurrences (all)                                    | 10              | 2               | 14              |
| Fatigue                                              |                 |                 |                 |
| subjects affected / exposed                          | 4 / 20 (20.00%) | 7 / 24 (29.17%) | 6 / 22 (27.27%) |
| occurrences (all)                                    | 10              | 36              | 10              |
| Feeling cold                                         |                 |                 |                 |
| subjects affected / exposed                          | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 2               | 0               | 0               |
| Feeling hot                                          |                 |                 |                 |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 0               | 0               | 0               |
| Gait disturbance                                     |                 |                 |                 |
| subjects affected / exposed                          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                    | 0               | 0               | 0               |
| Hyperplasia                                          |                 |                 |                 |

|                             |                 |                  |                  |
|-----------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)           | 1               | 0                | 0                |
| Hyperthermia                |                 |                  |                  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%)   | 1 / 22 (4.55%)   |
| occurrences (all)           | 1               | 0                | 1                |
| Inflammation                |                 |                  |                  |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)           | 1               | 0                | 0                |
| Influenza like illness      |                 |                  |                  |
| subjects affected / exposed | 4 / 20 (20.00%) | 6 / 24 (25.00%)  | 7 / 22 (31.82%)  |
| occurrences (all)           | 18              | 11               | 16               |
| Injection site discomfort   |                 |                  |                  |
| subjects affected / exposed | 0 / 20 (0.00%)  | 1 / 24 (4.17%)   | 0 / 22 (0.00%)   |
| occurrences (all)           | 0               | 1                | 0                |
| Injection site erythema     |                 |                  |                  |
| subjects affected / exposed | 3 / 20 (15.00%) | 7 / 24 (29.17%)  | 7 / 22 (31.82%)  |
| occurrences (all)           | 13              | 17               | 14               |
| Injection site induration   |                 |                  |                  |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%)   | 1 / 22 (4.55%)   |
| occurrences (all)           | 0               | 0                | 4                |
| Injection site inflammation |                 |                  |                  |
| subjects affected / exposed | 0 / 20 (0.00%)  | 1 / 24 (4.17%)   | 0 / 22 (0.00%)   |
| occurrences (all)           | 0               | 2                | 0                |
| Injection site oedema       |                 |                  |                  |
| subjects affected / exposed | 0 / 20 (0.00%)  | 1 / 24 (4.17%)   | 2 / 22 (9.09%)   |
| occurrences (all)           | 0               | 3                | 4                |
| Injection site pain         |                 |                  |                  |
| subjects affected / exposed | 9 / 20 (45.00%) | 10 / 24 (41.67%) | 12 / 22 (54.55%) |
| occurrences (all)           | 39              | 32               | 51               |
| Injection site pruritus     |                 |                  |                  |
| subjects affected / exposed | 2 / 20 (10.00%) | 2 / 24 (8.33%)   | 1 / 22 (4.55%)   |
| occurrences (all)           | 2               | 2                | 8                |
| Injection site reaction     |                 |                  |                  |
| subjects affected / exposed | 5 / 20 (25.00%) | 4 / 24 (16.67%)  | 2 / 22 (9.09%)   |
| occurrences (all)           | 6               | 8                | 5                |
| Injection site swelling     |                 |                  |                  |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 2 / 22 (9.09%)  |
| occurrences (all)                               | 0               | 4               | 4               |
| Malaise                                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%)  |
| occurrences (all)                               | 2               | 1               | 0               |
| Oedema                                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                               | 0               | 0               | 3               |
| Oedema peripheral                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 1 / 22 (4.55%)  |
| occurrences (all)                               | 0               | 1               | 1               |
| Pain                                            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 20 (10.00%) | 0 / 24 (0.00%)  | 3 / 22 (13.64%) |
| occurrences (all)                               | 2               | 0               | 4               |
| Pyrexia                                         |                 |                 |                 |
| subjects affected / exposed                     | 6 / 20 (30.00%) | 8 / 24 (33.33%) | 5 / 22 (22.73%) |
| occurrences (all)                               | 20              | 22              | 8               |
| Swelling                                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Xerosis                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                               | 0               | 0               | 1               |
| Immune system disorders                         |                 |                 |                 |
| Hypersensitivity                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Reproductive system and breast disorders        |                 |                 |                 |
| Metrorrhagia                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Uterine haemorrhage                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                               | 1               | 0               | 0               |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Cough                       |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 24 (8.33%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0              | 6              | 0              |
| Dyspnoea                    |                |                |                |
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 24 (8.33%) | 0 / 22 (0.00%) |
| occurrences (all)           | 2              | 2              | 0              |
| Haemoptysis                 |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Oropharyngeal pain          |                |                |                |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)           | 1              | 2              | 0              |
| Respiratory disorder        |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Psychiatric disorders       |                |                |                |
| Agitation                   |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Confusional state           |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)           | 0              | 0              | 1              |
| Depression                  |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)           | 0              | 0              | 1              |
| Dissociation                |                |                |                |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Insomnia                    |                |                |                |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 24 (4.17%) | 1 / 22 (4.55%) |
| occurrences (all)           | 0              | 1              | 1              |
| Mood altered                |                |                |                |

|                                                                                            |                     |                     |                     |
|--------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                           | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Investigations                                                                             |                     |                     |                     |
| Antinuclear antibody increased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)              | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Blood creatine phosphokinase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Blood glucose increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Blood lactic acid increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Blood urea increased<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Cortisol decreased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Cortisol increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Creatinine renal clearance decreased                                                       |                     |                     |                     |

|                                                                                                                           |                     |                     |                     |
|---------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                          | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Eosinophil count increased<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Haemoglobin decreased<br>subjects affected / exposed<br>occurrences (all)                                                 | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Liver function test<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>Traumatic haematoma<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Cardiac disorders<br>Nodal arrhythmia<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                                          | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                                           | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Nervous system disorders<br>Amnesia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>2 |
| Burning sensation<br>subjects affected / exposed<br>occurrences (all)                                                     | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Dizziness                                                                                                                 |                     |                     |                     |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed          | 2 / 20 (10.00%) | 0 / 24 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                    | 2               | 0               | 1               |
| Headache                             |                 |                 |                 |
| subjects affected / exposed          | 6 / 20 (30.00%) | 5 / 24 (20.83%) | 4 / 22 (18.18%) |
| occurrences (all)                    | 12              | 43              | 9               |
| Neuralgia                            |                 |                 |                 |
| subjects affected / exposed          | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                    | 1               | 0               | 1               |
| Paraesthesia                         |                 |                 |                 |
| subjects affected / exposed          | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0               |
| Parosmia                             |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Sciatica                             |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 1               | 0               |
| Seizure                              |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Sensory loss                         |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 1               | 0               |
| Somnolence                           |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Tremor                               |                 |                 |                 |
| subjects affected / exposed          | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 1               | 0               | 0               |
| Blood and lymphatic system disorders |                 |                 |                 |
| Anaemia                              |                 |                 |                 |
| subjects affected / exposed          | 0 / 20 (0.00%)  | 3 / 24 (12.50%) | 0 / 22 (0.00%)  |
| occurrences (all)                    | 0               | 3               | 0               |
| Leukopenia                           |                 |                 |                 |
| subjects affected / exposed          | 1 / 20 (5.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%)  |
| occurrences (all)                    | 1               | 1               | 0               |

|                                                                             |                     |                     |                     |
|-----------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)         | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Ear and labyrinth disorders                                                 |                     |                     |                     |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)         | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)                | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 20 (0.00%)<br>0 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Eye disorders                                                               |                     |                     |                     |
| Conjunctivitis allergic<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Eyelid oedema<br>subjects affected / exposed<br>occurrences (all)           | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Gastrointestinal disorders                                                  |                     |                     |                     |
| Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)    | 1 / 20 (5.00%)<br>1 | 1 / 24 (4.17%)<br>1 | 0 / 22 (0.00%)<br>0 |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)    | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Abdominal pain                                                              |                     |                     |                     |

|                                    |                 |                 |                |
|------------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed        | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                  | 1               | 0               | 4              |
| Abdominal pain upper               |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                  | 0               | 0               | 2              |
| Constipation                       |                 |                 |                |
| subjects affected / exposed        | 1 / 20 (5.00%)  | 2 / 24 (8.33%)  | 2 / 22 (9.09%) |
| occurrences (all)                  | 1               | 2               | 2              |
| Dental caries                      |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 0               | 0              |
| Diarrhoea                          |                 |                 |                |
| subjects affected / exposed        | 1 / 20 (5.00%)  | 1 / 24 (4.17%)  | 1 / 22 (4.55%) |
| occurrences (all)                  | 2               | 1               | 1              |
| Dry mouth                          |                 |                 |                |
| subjects affected / exposed        | 1 / 20 (5.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 1               | 0               | 0              |
| Dysphagia                          |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 2               | 0              |
| Flatulence                         |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 1               | 0              |
| Gastrointestinal motility disorder |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 0               | 0              |
| Nausea                             |                 |                 |                |
| subjects affected / exposed        | 5 / 20 (25.00%) | 4 / 24 (16.67%) | 2 / 22 (9.09%) |
| occurrences (all)                  | 5               | 8               | 2              |
| Odynophagia                        |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 0               | 0              |
| Oesophagitis                       |                 |                 |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 0               | 0              |
| Vomiting                           |                 |                 |                |

|                                                  |                      |                      |                     |
|--------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 2 / 20 (10.00%)<br>2 | 4 / 24 (16.67%)<br>8 | 0 / 22 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders           |                      |                      |                     |
| Acne                                             |                      |                      |                     |
| subjects affected / exposed                      | 1 / 20 (5.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Alopecia                                         |                      |                      |                     |
| subjects affected / exposed                      | 1 / 20 (5.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                   |
| Dermatitis atopic                                |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                   |
| Dry skin                                         |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                   |
| Erythema                                         |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 3 / 22 (13.64%)     |
| occurrences (all)                                | 0                    | 0                    | 4                   |
| Hyperhidrosis                                    |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                    | 0                    | 1                   |
| Intertrigo                                       |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                    | 0                    | 1                   |
| Papule                                           |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                   |
| Pruritus                                         |                      |                      |                     |
| subjects affected / exposed                      | 1 / 20 (5.00%)       | 0 / 24 (0.00%)       | 1 / 22 (4.55%)      |
| occurrences (all)                                | 1                    | 0                    | 2                   |
| Purpura senile                                   |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 0 / 24 (0.00%)       | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                    | 0                    | 0                   |
| Rash                                             |                      |                      |                     |
| subjects affected / exposed                      | 0 / 20 (0.00%)       | 1 / 24 (4.17%)       | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                    | 1                    | 1                   |

|                                                                      |                     |                     |                     |
|----------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Rash pruritic<br>subjects affected / exposed<br>occurrences (all)    | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Skin irritation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Skin lesion<br>subjects affected / exposed<br>occurrences (all)      | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Vitiligo<br>subjects affected / exposed<br>occurrences (all)         | 1 / 20 (5.00%)<br>1 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Renal and urinary disorders                                          |                     |                     |                     |
| Albuminuria<br>subjects affected / exposed<br>occurrences (all)      | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Hyperoxaluria<br>subjects affected / exposed<br>occurrences (all)    | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Microalbuminuria<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 2 / 22 (9.09%)<br>4 |
| Nocturia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)      | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Polyuria<br>subjects affected / exposed<br>occurrences (all)         | 0 / 20 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 | 0 / 22 (0.00%)<br>0 |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)      | 1 / 20 (5.00%)<br>1 | 1 / 24 (4.17%)<br>2 | 1 / 22 (4.55%)<br>2 |
| Renal colic                                                          |                     |                     |                     |

|                                                                                                                   |                      |                      |                     |
|-------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                                                  | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Renal impairment<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Endocrine disorders<br>Adrenal insufficiency<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1 |
| Glucocorticoid deficiency<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 1 / 20 (5.00%)<br>1  | 2 / 24 (8.33%)<br>24 | 1 / 22 (4.55%)<br>1 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 1 / 20 (5.00%)<br>2  | 0 / 24 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1 |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)                                                     | 2 / 20 (10.00%)<br>5 | 1 / 24 (4.17%)<br>2  | 0 / 22 (0.00%)<br>0 |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)                                                    | 1 / 20 (5.00%)<br>1  | 0 / 24 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1 |
| Hypercreatinaemia<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 20 (0.00%)<br>0  | 1 / 24 (4.17%)<br>1  | 0 / 22 (0.00%)<br>0 |
| Joint ankylosis<br>subjects affected / exposed<br>occurrences (all)                                               | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Joint swelling<br>subjects affected / exposed<br>occurrences (all)                                                | 0 / 20 (0.00%)<br>0  | 0 / 24 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0 |
| Limb discomfort                                                                                                   |                      |                      |                     |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 1              | 0              |
| Muscle spasms               |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)           | 0               | 0              | 1              |
| Musculoskeletal chest pain  |                 |                |                |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| Musculoskeletal pain        |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Myalgia                     |                 |                |                |
| subjects affected / exposed | 4 / 20 (20.00%) | 2 / 24 (8.33%) | 1 / 22 (4.55%) |
| occurrences (all)           | 5               | 5              | 1              |
| Pain in extremity           |                 |                |                |
| subjects affected / exposed | 1 / 20 (5.00%)  | 2 / 24 (8.33%) | 2 / 22 (9.09%) |
| occurrences (all)           | 1               | 13             | 3              |
| Infections and infestations |                 |                |                |
| Bacteriuria                 |                 |                |                |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| Bronchitis                  |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Bronchitis viral            |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Conjunctivitis              |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Cystitis                    |                 |                |                |
| subjects affected / exposed | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |
| Infection                   |                 |                |                |
| subjects affected / exposed | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |

|                                         |                 |                |                |
|-----------------------------------------|-----------------|----------------|----------------|
| Influenza                               |                 |                |                |
| subjects affected / exposed             | 2 / 20 (10.00%) | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 3               | 0              | 0              |
| Localised infection                     |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 0              | 0              |
| Oral herpes                             |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 0              | 0              |
| Periodontitis                           |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                       | 0               | 0              | 1              |
| Pharyngitis                             |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                       | 0               | 0              | 1              |
| Rash pustular                           |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 0              | 0              |
| Rhinitis                                |                 |                |                |
| subjects affected / exposed             | 1 / 20 (5.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 1               | 1              | 0              |
| Skin infection                          |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 1              | 0              |
| Tinea infection                         |                 |                |                |
| subjects affected / exposed             | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 1               | 0              | 0              |
| Upper respiratory tract infection       |                 |                |                |
| subjects affected / exposed             | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 1 / 22 (4.55%) |
| occurrences (all)                       | 1               | 0              | 1              |
| Urinary tract infection                 |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 1              | 0              |
| Viral upper respiratory tract infection |                 |                |                |
| subjects affected / exposed             | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                       | 0               | 3              | 0              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| Metabolism and nutrition disorders |                 |                |                |
| Decreased appetite                 |                 |                |                |
| subjects affected / exposed        | 2 / 20 (10.00%) | 2 / 24 (8.33%) | 1 / 22 (4.55%) |
| occurrences (all)                  | 3               | 8              | 1              |
| Dehydration                        |                 |                |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 1              | 0              |
| Hypercholesterolaemia              |                 |                |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 1              | 0              |
| Hyperuricaemia                     |                 |                |                |
| subjects affected / exposed        | 1 / 20 (5.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 1               | 0              | 0              |
| Hypoglycaemia                      |                 |                |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 1              | 0              |
| Hypokalaemia                       |                 |                |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 1 / 24 (4.17%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 1              | 0              |
| Type 2 diabetes mellitus           |                 |                |                |
| subjects affected / exposed        | 0 / 20 (0.00%)  | 0 / 24 (0.00%) | 0 / 22 (0.00%) |
| occurrences (all)                  | 0               | 0              | 0              |

|                                                                     |                         |  |  |
|---------------------------------------------------------------------|-------------------------|--|--|
| <b>Non-serious adverse events</b>                                   | GSK2302025A<br>Cohort 4 |  |  |
| Total subjects affected by non-serious adverse events               |                         |  |  |
| subjects affected / exposed                                         | 37 / 40 (92.50%)        |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |  |  |
| Uterine leiomyoma                                                   |                         |  |  |
| subjects affected / exposed                                         | 1 / 40 (2.50%)          |  |  |
| occurrences (all)                                                   | 1                       |  |  |
| Vascular disorders                                                  |                         |  |  |
| Arteriosclerosis moenckeberg-type                                   |                         |  |  |
| subjects affected / exposed                                         | 0 / 40 (0.00%)          |  |  |
| occurrences (all)                                                   | 0                       |  |  |
| Haemorrhage                                                         |                         |  |  |

|                                       |                |  |  |
|---------------------------------------|----------------|--|--|
| subjects affected / exposed           | 1 / 40 (2.50%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Hot flush                             |                |  |  |
| subjects affected / exposed           | 2 / 40 (5.00%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Hyperaemia                            |                |  |  |
| subjects affected / exposed           | 0 / 40 (0.00%) |  |  |
| occurrences (all)                     | 0              |  |  |
| Hypertension                          |                |  |  |
| subjects affected / exposed           | 2 / 40 (5.00%) |  |  |
| occurrences (all)                     | 2              |  |  |
| Hypotension                           |                |  |  |
| subjects affected / exposed           | 1 / 40 (2.50%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Lymphoedema                           |                |  |  |
| subjects affected / exposed           | 1 / 40 (2.50%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Lymphostasis                          |                |  |  |
| subjects affected / exposed           | 1 / 40 (2.50%) |  |  |
| occurrences (all)                     | 1              |  |  |
| Peripheral arterial occlusive disease |                |  |  |
| subjects affected / exposed           | 0 / 40 (0.00%) |  |  |
| occurrences (all)                     | 0              |  |  |
| Peripheral coldness                   |                |  |  |
| subjects affected / exposed           | 0 / 40 (0.00%) |  |  |
| occurrences (all)                     | 0              |  |  |
| Thrombophlebitis                      |                |  |  |
| subjects affected / exposed           | 0 / 40 (0.00%) |  |  |
| occurrences (all)                     | 0              |  |  |
| Surgical and medical procedures       |                |  |  |
| Catheter placement                    |                |  |  |
| subjects affected / exposed           | 0 / 40 (0.00%) |  |  |
| occurrences (all)                     | 0              |  |  |
| Tooth extraction                      |                |  |  |
| subjects affected / exposed           | 1 / 40 (2.50%) |  |  |
| occurrences (all)                     | 2              |  |  |

|                                                      |                  |  |  |
|------------------------------------------------------|------------------|--|--|
| General disorders and administration site conditions |                  |  |  |
| Administration site induration                       |                  |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                                    | 0                |  |  |
| Administration site pain                             |                  |  |  |
| subjects affected / exposed                          | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                                    | 4                |  |  |
| Asthenia                                             |                  |  |  |
| subjects affected / exposed                          | 13 / 40 (32.50%) |  |  |
| occurrences (all)                                    | 32               |  |  |
| Axillary pain                                        |                  |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                                    | 0                |  |  |
| Chest discomfort                                     |                  |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                                    | 0                |  |  |
| Chills                                               |                  |  |  |
| subjects affected / exposed                          | 8 / 40 (20.00%)  |  |  |
| occurrences (all)                                    | 14               |  |  |
| Fatigue                                              |                  |  |  |
| subjects affected / exposed                          | 7 / 40 (17.50%)  |  |  |
| occurrences (all)                                    | 12               |  |  |
| Feeling cold                                         |                  |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                                    | 0                |  |  |
| Feeling hot                                          |                  |  |  |
| subjects affected / exposed                          | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                                    | 1                |  |  |
| Gait disturbance                                     |                  |  |  |
| subjects affected / exposed                          | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                                    | 1                |  |  |
| Hyperplasia                                          |                  |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                                    | 0                |  |  |
| Hyperthermia                                         |                  |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Inflammation                |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Influenza like illness      |                  |  |  |
| subjects affected / exposed | 13 / 40 (32.50%) |  |  |
| occurrences (all)           | 29               |  |  |
| Injection site discomfort   |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Injection site erythema     |                  |  |  |
| subjects affected / exposed | 8 / 40 (20.00%)  |  |  |
| occurrences (all)           | 18               |  |  |
| Injection site induration   |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Injection site inflammation |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Injection site oedema       |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Injection site pain         |                  |  |  |
| subjects affected / exposed | 24 / 40 (60.00%) |  |  |
| occurrences (all)           | 90               |  |  |
| Injection site pruritus     |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Injection site reaction     |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Injection site swelling     |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Malaise                     |                  |  |  |

|                                                 |                  |  |  |
|-------------------------------------------------|------------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                               | 3                |  |  |
| Oedema                                          |                  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| Oedema peripheral                               |                  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| Pain                                            |                  |  |  |
| subjects affected / exposed                     | 8 / 40 (20.00%)  |  |  |
| occurrences (all)                               | 9                |  |  |
| Pyrexia                                         |                  |  |  |
| subjects affected / exposed                     | 22 / 40 (55.00%) |  |  |
| occurrences (all)                               | 86               |  |  |
| Swelling                                        |                  |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                               | 4                |  |  |
| Xerosis                                         |                  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| Immune system disorders                         |                  |  |  |
| Hypersensitivity                                |                  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Reproductive system and breast disorders        |                  |  |  |
| Metrorrhagia                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                               | 1                |  |  |
| Uterine haemorrhage                             |                  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                               | 0                |  |  |
| Respiratory, thoracic and mediastinal disorders |                  |  |  |
| Cough                                           |                  |  |  |
| subjects affected / exposed                     | 4 / 40 (10.00%)  |  |  |
| occurrences (all)                               | 4                |  |  |
| Dyspnoea                                        |                  |  |  |

|                                |                |  |  |
|--------------------------------|----------------|--|--|
| subjects affected / exposed    | 2 / 40 (5.00%) |  |  |
| occurrences (all)              | 2              |  |  |
| Haemoptysis                    |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Oropharyngeal pain             |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Respiratory disorder           |                |  |  |
| subjects affected / exposed    | 1 / 40 (2.50%) |  |  |
| occurrences (all)              | 1              |  |  |
| Psychiatric disorders          |                |  |  |
| Agitation                      |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Anxiety                        |                |  |  |
| subjects affected / exposed    | 1 / 40 (2.50%) |  |  |
| occurrences (all)              | 1              |  |  |
| Confusional state              |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Depression                     |                |  |  |
| subjects affected / exposed    | 1 / 40 (2.50%) |  |  |
| occurrences (all)              | 1              |  |  |
| Dissociation                   |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Insomnia                       |                |  |  |
| subjects affected / exposed    | 1 / 40 (2.50%) |  |  |
| occurrences (all)              | 1              |  |  |
| Mood altered                   |                |  |  |
| subjects affected / exposed    | 0 / 40 (0.00%) |  |  |
| occurrences (all)              | 0              |  |  |
| Investigations                 |                |  |  |
| Antinuclear antibody increased |                |  |  |

|                                        |                 |  |  |
|----------------------------------------|-----------------|--|--|
| subjects affected / exposed            | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood bilirubin increased              |                 |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Blood creatine phosphokinase increased |                 |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Blood glucose increased                |                 |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                      | 1               |  |  |
| Blood lactate dehydrogenase increased  |                 |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                      | 2               |  |  |
| Blood lactic acid increased            |                 |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood urea increased                   |                 |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Body temperature increased             |                 |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Cortisol decreased                     |                 |  |  |
| subjects affected / exposed            | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                      | 2               |  |  |
| Cortisol increased                     |                 |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                      | 0               |  |  |
| Creatinine renal clearance decreased   |                 |  |  |
| subjects affected / exposed            | 4 / 40 (10.00%) |  |  |
| occurrences (all)                      | 4               |  |  |
| Eosinophil count increased             |                 |  |  |

|                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                             |  |  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Haemoglobin decreased</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Liver function test</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                      | <p>0 / 40 (0.00%)</p> <p>0</p> <p>0 / 40 (0.00%)</p> <p>0</p> <p>1 / 40 (2.50%)</p> <p>1</p>                                |  |  |
| <p>Injury, poisoning and procedural complications</p> <p>Traumatic haematoma</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                                                                                                                                                                                                     | <p>1 / 40 (2.50%)</p> <p>1</p>                                                                                              |  |  |
| <p>Cardiac disorders</p> <p>Nodal arrhythmia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Palpitations</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sinus tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Tachycardia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 40 (0.00%)</p> <p>0</p> <p>1 / 40 (2.50%)</p> <p>1</p> <p>1 / 40 (2.50%)</p> <p>1</p> <p>1 / 40 (2.50%)</p> <p>1</p> |  |  |
| <p>Nervous system disorders</p> <p>Amnesia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Burning sensation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dizziness</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Headache</p>                                                                     | <p>0 / 40 (0.00%)</p> <p>0</p> <p>1 / 40 (2.50%)</p> <p>1</p> <p>2 / 40 (5.00%)</p> <p>2</p>                                |  |  |

|                                      |                 |  |  |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed          | 7 / 40 (17.50%) |  |  |
| occurrences (all)                    | 12              |  |  |
| Neuralgia                            |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Paraesthesia                         |                 |  |  |
| subjects affected / exposed          | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Parosmia                             |                 |  |  |
| subjects affected / exposed          | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Sciatica                             |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Seizure                              |                 |  |  |
| subjects affected / exposed          | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Sensory loss                         |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Somnolence                           |                 |  |  |
| subjects affected / exposed          | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Tremor                               |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Blood and lymphatic system disorders |                 |  |  |
| Anaemia                              |                 |  |  |
| subjects affected / exposed          | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                    | 1               |  |  |
| Leukopenia                           |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |
| Lymph node pain                      |                 |  |  |
| subjects affected / exposed          | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                    | 0               |  |  |

|                                                                             |                     |  |  |
|-----------------------------------------------------------------------------|---------------------|--|--|
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 40 (0.00%)<br>0 |  |  |
| Ear and labyrinth disorders                                                 |                     |  |  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)         | 0 / 40 (0.00%)<br>0 |  |  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                | 1 / 40 (2.50%)<br>1 |  |  |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)              | 1 / 40 (2.50%)<br>1 |  |  |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)                | 0 / 40 (0.00%)<br>0 |  |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 40 (0.00%)<br>0 |  |  |
| Eye disorders                                                               |                     |  |  |
| Conjunctivitis allergic<br>subjects affected / exposed<br>occurrences (all) | 1 / 40 (2.50%)<br>1 |  |  |
| Eyelid oedema<br>subjects affected / exposed<br>occurrences (all)           | 1 / 40 (2.50%)<br>1 |  |  |
| Gastrointestinal disorders                                                  |                     |  |  |
| Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)    | 0 / 40 (0.00%)<br>0 |  |  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all)    | 1 / 40 (2.50%)<br>1 |  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)          | 3 / 40 (7.50%)<br>3 |  |  |
| Abdominal pain upper                                                        |                     |  |  |

|                                        |                  |  |  |
|----------------------------------------|------------------|--|--|
| subjects affected / exposed            | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Constipation                           |                  |  |  |
| subjects affected / exposed            | 3 / 40 (7.50%)   |  |  |
| occurrences (all)                      | 3                |  |  |
| Dental caries                          |                  |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Diarrhoea                              |                  |  |  |
| subjects affected / exposed            | 5 / 40 (12.50%)  |  |  |
| occurrences (all)                      | 7                |  |  |
| Dry mouth                              |                  |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                      | 0                |  |  |
| Dysphagia                              |                  |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                      | 0                |  |  |
| Flatulence                             |                  |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%)   |  |  |
| occurrences (all)                      | 0                |  |  |
| Gastrointestinal motility disorder     |                  |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Nausea                                 |                  |  |  |
| subjects affected / exposed            | 11 / 40 (27.50%) |  |  |
| occurrences (all)                      | 14               |  |  |
| Odynophagia                            |                  |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Oesophagitis                           |                  |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                      | 1                |  |  |
| Vomiting                               |                  |  |  |
| subjects affected / exposed            | 5 / 40 (12.50%)  |  |  |
| occurrences (all)                      | 5                |  |  |
| Skin and subcutaneous tissue disorders |                  |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| Acne                        |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Alopecia                    |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Dermatitis atopic           |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 2              |  |  |
| Dry skin                    |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Erythema                    |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyperhidrosis               |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Intertrigo                  |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Papule                      |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pruritus                    |                |  |  |
| subjects affected / exposed | 2 / 40 (5.00%) |  |  |
| occurrences (all)           | 2              |  |  |
| Purpura senile              |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Rash                        |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Rash pruritic               |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| Skin irritation             |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Skin lesion                 |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Vitiligo                    |                |  |  |
| subjects affected / exposed | 2 / 40 (5.00%) |  |  |
| occurrences (all)           | 2              |  |  |
| Renal and urinary disorders |                |  |  |
| Albuminuria                 |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Hyperoxaluria               |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Microalbuminuria            |                |  |  |
| subjects affected / exposed | 2 / 40 (5.00%) |  |  |
| occurrences (all)           | 3              |  |  |
| Nocturia                    |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Pollakiuria                 |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Polyuria                    |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Proteinuria                 |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Renal colic                 |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Renal impairment            |                |  |  |

|                                                  |                     |  |  |
|--------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 40 (2.50%)<br>1 |  |  |
| Endocrine disorders                              |                     |  |  |
| Adrenal insufficiency                            |                     |  |  |
| subjects affected / exposed                      | 0 / 40 (0.00%)      |  |  |
| occurrences (all)                                | 0                   |  |  |
| Glucocorticoid deficiency                        |                     |  |  |
| subjects affected / exposed                      | 2 / 40 (5.00%)      |  |  |
| occurrences (all)                                | 2                   |  |  |
| Musculoskeletal and connective tissue disorders  |                     |  |  |
| Arthralgia                                       |                     |  |  |
| subjects affected / exposed                      | 6 / 40 (15.00%)     |  |  |
| occurrences (all)                                | 7                   |  |  |
| Back pain                                        |                     |  |  |
| subjects affected / exposed                      | 2 / 40 (5.00%)      |  |  |
| occurrences (all)                                | 2                   |  |  |
| Bone pain                                        |                     |  |  |
| subjects affected / exposed                      | 0 / 40 (0.00%)      |  |  |
| occurrences (all)                                | 0                   |  |  |
| Groin pain                                       |                     |  |  |
| subjects affected / exposed                      | 1 / 40 (2.50%)      |  |  |
| occurrences (all)                                | 1                   |  |  |
| Hypercreatinaemia                                |                     |  |  |
| subjects affected / exposed                      | 0 / 40 (0.00%)      |  |  |
| occurrences (all)                                | 0                   |  |  |
| Joint ankylosis                                  |                     |  |  |
| subjects affected / exposed                      | 1 / 40 (2.50%)      |  |  |
| occurrences (all)                                | 1                   |  |  |
| Joint swelling                                   |                     |  |  |
| subjects affected / exposed                      | 1 / 40 (2.50%)      |  |  |
| occurrences (all)                                | 1                   |  |  |
| Limb discomfort                                  |                     |  |  |
| subjects affected / exposed                      | 0 / 40 (0.00%)      |  |  |
| occurrences (all)                                | 0                   |  |  |
| Muscle spasms                                    |                     |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 4 / 40 (10.00%) |  |  |
| occurrences (all)           | 6               |  |  |
| Musculoskeletal chest pain  |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Musculoskeletal pain        |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Myalgia                     |                 |  |  |
| subjects affected / exposed | 5 / 40 (12.50%) |  |  |
| occurrences (all)           | 5               |  |  |
| Pain in extremity           |                 |  |  |
| subjects affected / exposed | 8 / 40 (20.00%) |  |  |
| occurrences (all)           | 9               |  |  |
| Infections and infestations |                 |  |  |
| Bacteriuria                 |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Bronchitis                  |                 |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)  |  |  |
| occurrences (all)           | 3               |  |  |
| Bronchitis viral            |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Conjunctivitis              |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Cystitis                    |                 |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Infection                   |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Influenza                   |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |

|                                         |                 |  |  |
|-----------------------------------------|-----------------|--|--|
| Localised infection                     |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Oral herpes                             |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Periodontitis                           |                 |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Pharyngitis                             |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Rash pustular                           |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Rhinitis                                |                 |  |  |
| subjects affected / exposed             | 4 / 40 (10.00%) |  |  |
| occurrences (all)                       | 4               |  |  |
| Skin infection                          |                 |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Tinea infection                         |                 |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                       | 0               |  |  |
| Upper respiratory tract infection       |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Urinary tract infection                 |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Viral upper respiratory tract infection |                 |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                       | 1               |  |  |
| Metabolism and nutrition disorders      |                 |  |  |
| Decreased appetite                      |                 |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 2              |  |  |
| Dehydration                 |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypercholesterolaemia       |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hyperuricaemia              |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypoglycaemia               |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Hypokalaemia                |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |
| Type 2 diabetes mellitus    |                |  |  |
| subjects affected / exposed | 1 / 40 (2.50%) |  |  |
| occurrences (all)           | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|                                                                                                                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| As a consequence of the decision to stop the study, not all data are available for a full final analysis as originally planned. Analyses are merely descriptive and the results are presented as an abridged study report. |
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Notes: