



## Clinical trial results:

**A phase II/III, randomised, observer-blind, placebo-controlled, multicentre, clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster GSK1437173A candidate vaccine when administered intramuscularly on a 0 and 1 to 2 months schedule to adults 18 years of age with solid tumours receiving chemotherapy.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-002966-11 |
| Trial protocol           | ES GB CZ       |
| Global end of trial date | 20 May 2016    |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2  |
| This version publication date  | 04 June 2017  |
| First version publication date | 02 July 2016  |
| Version creation reason        | • New data added to full data set<br>Addition of LSLV results |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 116427 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01798056 |
| 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

|  |               |
|--|---------------|
| Analysis stage                                       | Interim       |
| Date of interim/final analysis                       | 23 April 2016 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 18 June 2015  |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 20 May 2016   |
| Was the trial ended prematurely?                     | No            |

Notes:

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## General information about the trial

Main objective of the trial:

- To evaluate anti-gE humoral immune responses at Month 2, following a two-dose administration of the GSK1437173A vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).

Criteria to be used:

The objective is met if the lower limit of the 95% confidence interval (CI) of the Geometric Mean (GM) ratio (GSK1437173A PreChemo Group over Placebo PreChemo Group) in anti-gE ELISA antibody concentrations is greater than 3.

-To evaluate the safety and reactogenicity following administration of the GSK1437173A vaccine as compared to placebo up to 30 days post last vaccination in subjects with solid tumours receiving chemotherapy.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 05 March 2013 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Spain: 170             |
| Country: Number of subjects enrolled | United Kingdom: 30     |
| Country: Number of subjects enrolled | Czech Republic: 5      |
| Country: Number of subjects enrolled | France: 20             |
| Country: Number of subjects enrolled | Korea, Republic of: 35 |
| Country: Number of subjects enrolled | Canada: 6              |
| Worldwide total number of subjects   | 266                    |
| EEA total number of subjects         | 225                    |

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)                      | 192 |
| From 65 to 84 years                       | 72  |
| 85 years and over                         | 2   |

## Subject disposition

### Recruitment

Recruitment details: -

### 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.

### Pre-assignment period milestones

|                              |     |
|------------------------------|-----|
| Number of subjects started   | 266 |
| Number of subjects completed | 232 |

### Pre-assignment subject non-completion reasons

|                            |                             |
|----------------------------|-----------------------------|
| Reason: Number of subjects | No vaccination received: 34 |
|----------------------------|-----------------------------|

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall Period (overall period) |
| Is this the baseline period? | Yes                             |
| Allocation method            | Randomised - controlled         |
| Blinding used                | Double blind <sup>[1]</sup>     |
| Roles blinded                | Subject, Carer, Assessor        |

Blinding implementation details:

Observer-blind for study vaccine but not for time of vaccination relative to chemotherapy.

### Arms

|                              |                   |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes               |
| <b>Arm title</b>             | GSK1437173A Group |

Arm description:

Subjects received the first dose of GSK 1437173A at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of GSK 1437173A vaccine was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | GSK 1437173A                                    |
| Investigational medicinal product code |   |
| Other name                             | HZ/su vaccine                                   |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection |
| Routes of administration               | Intramuscular use                               |

Dosage and administration details:

The vaccine was administered intramuscularly into the deltoid muscle of the non-dominant arm.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Placebo Group |
|------------------|---------------|

Arm description:

Subjects received the first dose of placebo at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of placebo was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|  |   |
|--|---|
| Arm type                               | Placebo                                       |
| Investigational medicinal product name | Placebo                                       |
| Investigational medicinal product code |   |
| Other name                             | Saline solution                               |
| Pharmaceutical forms                   | Powder and solvent for solution for injection |
| Routes of administration               | Intramuscular use                             |

Dosage and administration details:

The placebo was administered intramuscularly into the deltoid muscle of the non-dominant arm.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: This was an Observer-blind for study vaccine but not for time of vaccination relative to chemotherapy.

| <b>Number of subjects in period 1<sup>[2]</sup></b> | <b>GSK1437173A Group</b> | <b>Placebo Group</b> |
|---|--------------------------|----------------------|
| Started   | 117                      | 115                  |
| Completed   | 90                       | 90                   |
| Not completed                                       | 27                       | 25                   |
| Consent withdrawn by subject                        | 12                       | 9                    |
| Migrated/moved from study area                      | 1                        | 1                    |
| Unspecified   | -                        | 2                    |
| Lost to follow-up                                   | 1                        | 1                    |
| Serious Adverse Event                               | 13                       | 12                   |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

## Baseline characteristics

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | GSK1437173A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects received the first dose of GSK 1437173A at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of GSK 1437173A vaccine was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

Subjects received the first dose of placebo at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of placebo was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

| Reporting group values                             | GSK1437173A Group | Placebo Group | Total |
|--|-------------------|---------------|-------|
| Number of subjects                                 | 117               | 115           | 232   |
| Age categorical<br>Units: Subjects                 |                   |               |       |
| In utero   |                   |               | 0     |
| Preterm newborn infants (gestational age < 37 wks) |                   |               | 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)                               |                   |               | 0     |
| From 65-84 years                                   |                   |               | 0     |
| 85 years and over                                  |                   |               | 0     |
| Age continuous<br>Units: years                     |                   |               |       |
| arithmetic mean                                    | 57.1              | 58.5          |       |
| standard deviation                                 | ± 10.8            | ± 11.7        | -     |
| Gender categorical<br>Units: Subjects              |                   |               |       |
| Female   | 70                | 69            | 139   |
| Male   | 47                | 46            | 93    |

## End points

### End points reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | GSK1437173A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects received the first dose of GSK 1437173A at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of GSK 1437173A vaccine was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

Subjects received the first dose of placebo at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of placebo was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|                            |                      |
|----------------------------|----------------------|
| Subject analysis set title | GSK1437173A-PreChemo |
|----------------------------|----------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects receiving the adjuvanted GSK1437173A vaccine, with the first vaccination at least 10 days (up to 1 month) before the start of a chemotherapy cycle.

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | Placebo-PreChemo |
|----------------------------|------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects receiving saline placebo, with the first vaccination at least 10 days (up to 1 month) before the start of a chemotherapy cycle.

### Primary: Adjusted geometric means (GMCs) of GSK1437173A over placebo for anti-glycoprotein E (gE) antibody ELISA concentrations in PreChemo Groups only

|                 |  |
|-----------------|--|
| End point title | Adjusted geometric means (GMCs) of GSK1437173A over placebo for anti-glycoprotein E (gE) antibody ELISA concentrations in PreChemo Groups only |
|-----------------|--|

End point description:

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

End point timeframe:

At Month 2

| End point values                         | GSK1437173A-PreChemo               | Placebo-PreChemo               |  |  |
|--|------------------------------------|--------------------------------|--|--|
| Subject group type                       | Subject analysis set               | Subject analysis set           |  |  |
| Number of subjects analysed              | 65                                 | 76                             |  |  |
| Units: EL.U/mL                           |                                    |                                |  |  |
| geometric mean (confidence interval 95%) |                                    |                                |  |  |
| Adjusted GMC of antibody titers          | 24501.57<br>(19051.99 to 31509.94) | 1056.77<br>(990.37 to 1127.62) |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Adjusted GMC ratio                      |
| Statistical analysis description:<br>The analysis evaluated the anti-gE humoral immune responses at Month 2, following a two-dose administration of the GSK1437173A vaccine, as compared to placebo in subjects with solid tumours receiving chemotherapy (PreChemo Groups only).<br>Criteria used:<br>The objective is met if the lower limit of the 95% confidence interval (CI) of the Geometric Mean (GM) ratio (GSK1437173A PreChemo group over Placebo PreChemo group) in anti-gE ELISA antibody concentrations is greater than 3. |   |
| Comparison groups  | GSK1437173A-PreChemo v Placebo-PreChemo |
| Number of subjects included in analysis  | 141                                     |
| Analysis specification   | Pre-specified                           |
| Analysis type  | non-inferiority <sup>[1]</sup>          |
| P-value  | < 0.0001                                |
| Method   | Adjusted GMC ratio                      |
| Parameter estimate   | Ratio                                   |
| Point estimate   | 23.2                                    |
| Confidence interval  |   |
| level  | 95 %                                    |
| sides  | 2-sided                                 |
| lower limit  | 17.9                                    |
| upper limit  | 30                                      |

Notes:

[1] - Difference of means between vaccines and placebo were calculated together with 2-sided confidence intervals and back-transformed to the original units to provide GMCs and GM ratios.

## Primary: Anti-gE antibody concentrations

|  |  |
|--|--|
| End point title  | Anti-gE antibody concentrations <sup>[2]</sup> |
| End point description:<br>Antibody concentrations are presented as geometric mean concentrations (GMCs), expressed in milliinternational units per milliliter (mIU/mL). The reference seropositivity cut-off value was equal to or above ( $\geq$ ) 97 mIU/mL. |  |
| End point type   | Primary  |
| End point timeframe:<br>At Month 2   |  |

Notes:

[2] - 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                         | GSK1437173A Group               | Placebo Group            |  |  |
|--|---------------------------------|--------------------------|--|--|
| Subject group type                       | Reporting group                 | Reporting group          |  |  |
| Number of subjects analysed              | 87                              | 98                       |  |  |
| Units: mIU/mL                            |                                 |                          |  |  |
| geometric mean (confidence interval 95%) |                                 |                          |  |  |
| Anti-gE                                  | 18291.7<br>(14432.1 to 23183.5) | 1060.5 (873.9 to 1287.1) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of days with solicited local symptoms

|                 |   |
|-----------------|---|
| End point title | Number of days with solicited local symptoms <sup>[3]</sup> |
|-----------------|---|

End point description:

The number of days with solicited local symptoms during the solicited post-vaccination period.

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

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

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.

| End point values                      | GSK1437173A Group | Placebo Group   |  |  |
|---------------------------------------|-------------------|-----------------|--|--|
| Subject group type                    | Reporting group   | Reporting group |  |  |
| Number of subjects analysed           | 117               | 115             |  |  |
| Units: Days                           |                   |                 |  |  |
| median (inter-quartile range (Q1-Q3)) |                   |                 |  |  |
| Pain, post-Dose 1                     | 2 (2 to 4)        | 2 (1 to 3)      |  |  |
| Pain, post-Dose 2                     | 2 (1 to 3.5)      | 1 (1 to 2)      |  |  |
| Redness, post-Dose 1                  | 3 (2 to 5)        | 0 (0 to 0)      |  |  |
| Redness, post-Dose 2                  | 4 (2 to 5)        | 0 (0 to 0)      |  |  |
| Swelling, post-Dose 1                 | 4 (2 to 5)        | 7 (7 to 7)      |  |  |
| Swelling, post-Dose 2                 | 3.5 (2 to 5.5)    | 0 (0 to 0)      |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of subjects with any, Grade 3 and related solicited general symptoms

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any, Grade 3 and related solicited general symptoms <sup>[4]</sup> |
|-----------------|--|

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), headache, myalgia, shivering and fever [defined as temperature equal to or above ( $\geq$ ) 37.5 degrees Celsius ( $^{\circ}$ C) for oral, axillary or tympanic route]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever  $> 39.0^{\circ}$ C. Related = symptom assessed by the investigator as causally related to the vaccination.

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

End point timeframe:

During the 7-day (Days 0-6) post-vaccination period following each dose and across doses

Notes:

[4] - 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                             | GSK1437173A Group | Placebo Group   |  |  |
|--|-------------------|-----------------|--|--|
| Subject group type                           | Reporting group   | Reporting group |  |  |
| Number of subjects analysed                  | 112               | 110             |  |  |
| Units: Subjects                              |                   |                 |  |  |
| Any Fatigue, Dose 1 (N=112;110)              | 56                | 44              |  |  |
| Grade 3 Fatigue, Dose 1 (N=112;110)          | 10                | 3               |  |  |
| Related Fatigue, Dose 1 (N=112;110)          | 15                | 10              |  |  |
| Any Gastrointestinal, Dose 1 (N=112;110)     | 32                | 21              |  |  |
| Grade 3 Gastrointestinal, Dose 1 (N=112;110) | 2                 | 5               |  |  |
| Related Gastrointestinal, Dose 1 (N=112;110) | 9                 | 2               |  |  |
| Any Headache, Dose 1 (N=112;110)             | 28                | 24              |  |  |
| Grade 3 Headache, Dose 1 (N=112;110)         | 3                 | 1               |  |  |
| Related Headache, Dose 1 (N=112;110)         | 10                | 4               |  |  |
| Any Myalgia, Dose 1 (N=112;110)              | 50                | 17              |  |  |
| Grade 3 Myalgia, Dose 1 (N=112;110)          | 8                 | 3               |  |  |
| Related Myalgia, Dose 1 (N=112;110)          | 25                | 3               |  |  |
| Any Shivering, Dose 1 (N=112;110)            | 27                | 13              |  |  |
| Grade 3 Shivering, Dose 1 (N=112;110)        | 5                 | 2               |  |  |
| Related Shivering, Dose 1 (N=112;110)        | 12                | 4               |  |  |
| Any Fever, Dose 1 (N=112;110)                | 13                | 4               |  |  |
| Grade 3 Fever, Dose 1 (N=112;110)            | 0                 | 0               |  |  |
| Related Fever, Dose 1 (N=112;110)            | 11                | 1               |  |  |
| Any Fatigue, Dose 2 (N=97;104)               | 57                | 57              |  |  |
| Grade 3 Fatigue, Dose 2 (N=97;104)           | 9                 | 6               |  |  |
| Related Fatigue, Dose 2 (N=97;104)           | 6                 | 8               |  |  |
| Any Gastrointestinal, Dose 2 (N=97;104)      | 41                | 39              |  |  |
| Grade 3 Gastrointestinal, Dose 2 (N=97;104)  | 5                 | 3               |  |  |
| Related Gastrointestinal, Dose 2 (N=97;104)  | 6                 | 2               |  |  |
| Any Headache, Dose 2 (N=97;104)              | 29                | 25              |  |  |
| Grade 3 Headache, Dose 2 (N=97;104)          | 3                 | 2               |  |  |
| Related Headache, Dose 2 (N=97;104)          | 7                 | 2               |  |  |
| Any Myalgia, Dose 2 (N=97;104)               | 32                | 23              |  |  |
| Grade 3 Myalgia, Dose 2 (N=97;104)           | 4                 | 1               |  |  |

|  |    |    |  |  |
|--|----|----|--|--|
| Related Myalgia, Dose 2 (N=97;104)                 | 13 | 4  |  |  |
| Any Shivering, Dose 2 (N=97;104)                   | 20 | 17 |  |  |
| Grade 3 Shivering, Dose 2 (N=97;104)               | 3  | 1  |  |  |
| Related Shivering, Dose 2 (N=97;104)               | 6  | 4  |  |  |
| Any Fever, Dose 2 (N=97;104)                       | 8  | 1  |  |  |
| Grade 3 Fever, Dose 2 (N=97;104)                   | 0  | 0  |  |  |
| Related Fever, Dose 2 (N=97;104)                   | 4  | 0  |  |  |
| Any Fatigue, Across doses (N=112;110)              | 78 | 68 |  |  |
| Grade 3 Fatigue, Across doses (N=112;110)          | 16 | 8  |  |  |
| Related Fatigue, Across doses (N=112;110)          | 19 | 14 |  |  |
| Any Gastrointestinal, Across doses (N=112;110)     | 51 | 49 |  |  |
| Grade 3 Gastrointestinal, Across doses (N=112;110) | 6  | 7  |  |  |
| Related Gastrointestinal, Across doses (N=112;110) | 11 | 3  |  |  |
| Any Headache, Across doses (N=112;110)             | 43 | 40 |  |  |
| Grade 3 Headache, Across doses (N=112;110)         | 6  | 3  |  |  |
| Related Headache, Across doses (N=112;110)         | 16 | 6  |  |  |
| Any Myalgia, Across doses (N=112;110)              | 60 | 31 |  |  |
| Grade 3 Myalgia, Across doses (N=112;110)          | 12 | 4  |  |  |
| Related Myalgia, Across doses (N=112;110)          | 30 | 5  |  |  |
| Any Shivering, Across doses (N=112;110)            | 39 | 25 |  |  |
| Grade 3 Shivering, Across doses (N=112;110)        | 6  | 3  |  |  |
| Related Shivering, Across doses (N=112;110)        | 16 | 5  |  |  |
| Any Fever, Across doses (N=112;110)                | 20 | 5  |  |  |
| Grade 3 Fever, Across doses (N=112;110)            | 0  | 0  |  |  |
| Related Fever, Across doses (N=112;110)            | 14 | 1  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of days with solicited general symptoms

|  |   |
|--|---|
| End point title  | Number of days with solicited general symptoms <sup>[5]</sup> |
| End point description:   |   |
| The number of days with solicited general symptoms during the solicited post-vaccination period. |   |
| End point type   | Primary   |
| End point timeframe:   |   |
| During the 7-day (Days 0-6) post-vaccination period following each dose and across doses         |   |

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                       | GSK1437173A Group | Placebo Group   |  |  |
|--|-------------------|-----------------|--|--|
| Subject group type                     | Reporting group   | Reporting group |  |  |
| Number of subjects analysed            | 117               | 115             |  |  |
| Units: Days                            |                   |                 |  |  |
| median (inter-quartile range (Q1-Q3))  |                   |                 |  |  |
| Fatigue, post-Dose 1                   | 3 (1.5 to 6)      | 5 (2 to 6)      |  |  |
| Fatigue, post-Dose 2                   | 5 (2 to 7)        | 5 (3 to 7)      |  |  |
| Gastrointestinal symptoms, post-Dose 1 | 2.5 (1.5 to 4)    | 4 (2 to 6)      |  |  |
| Gastrointestinal symptoms, post-Dose 2 | 4 (3 to 7)        | 3 (2 to 7)      |  |  |
| Headache, post-Dose 1                  | 2 (1 to 3.5)      | 2 (1.5 to 4.5)  |  |  |
| Headache, post-Dose 2                  | 2 (2 to 6)        | 2 (1 to 5)      |  |  |
| Myalgia, post-Dose 1                   | 2.5 (1 to 4)      | 2 (2 to 6)      |  |  |
| Myalgia, post-Dose 2                   | 3 (2 to 5.5)      | 5 (3 to 7)      |  |  |
| Shivering, post-Dose 1                 | 2 (1 to 3)        | 2 (1 to 2)      |  |  |
| Shivering, post-Dose 2                 | 3 (1 to 6)        | 2 (1 to 4)      |  |  |
| Fever, post-Dose 1                     | 1 (1 to 2)        | 1 (1 to 3)      |  |  |
| Fever, post-Dose 2                     | 1.5 (1 to 2.5)    | 1 (1 to 1)      |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with anti-gE antibody concentrations above the cut-off value as determined by ELISA

|                 |  |
|-----------------|--|
| End point title | Number of subjects with anti-gE antibody concentrations above the cut-off value as determined by ELISA |
|-----------------|--|

End point description:

Cut-off values assessed were greater than or equal to ( $\geq$ ) 97 mIU/mL in the sera of subjects seronegative before vaccination.

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

End point timeframe:

At Month 2

| End point values            | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 87                | 98              |  |  |
| Units: Subjects             |                   |                 |  |  |
| Anti-gE                     | 87                | 97              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine response for anti-gE antibody

|                 |   |
|-----------------|---|
| End point title | Number of subjects with vaccine response for anti-gE antibody |
|-----------------|---|

End point description:

Vaccine response for anti-gE antibody ELISA concentrations was defined as:

- For initially seronegative subjects, antibody concentration at post-vaccination  $\geq 4$  fold the cut-off for Anti-gE (4x97 mIU/ml);
- For initially seropositive subjects, antibody concentration at post-vaccination  $\geq 4$  fold the pre-vaccination antibody concentration.

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

End point timeframe:

At Months 1, 2, 6 and 13

| End point values                       | GSK1437173A Group | Placebo Group   |  |  |
|--|-------------------|-----------------|--|--|
| Subject group type                     | Reporting group   | Reporting group |  |  |
| Number of subjects analysed            | 87                | 94              |  |  |
| Units: Subjects                        |                   |                 |  |  |
| Vaccine responders, Month 1 (N=85;93)  | 73                | 0               |  |  |
| Vaccine responders, Month 2 (N=87;94)  | 75                | 0               |  |  |
| Vaccine responders, Month 6 (N=42;42)  | 31                | 1               |  |  |
| Vaccine responders, Month 13 (N=68;69) | 35                | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Frequency of gE-specific CD4+ T-cells expressing at least two activation markers

|                 |  |
|-----------------|--|
| End point title | Frequency of gE-specific CD4+ T-cells expressing at least two activation markers |
|-----------------|--|

End point description:

Descriptive statistics were tabulated for CD4[2+] cells, which are gE-specific CD4+ T-cells with at least two activation markers ([2+]), expressed from the activation markers interferon-gamma (IFN- $\gamma$ ), interleukin-2 (IL-2), tumour necrosis factor-alpha (TNF- $\alpha$ ) and cluster of differentiation 40-ligand (CD40-L), as determined by intracellular cytokine staining (ICS) method.

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

End point timeframe:  
At Months 0, 1, 2 and 13

| End point values                       | GSK1437173A-<br>PreChemo | Placebo-<br>PreChemo |  |  |
|--|--------------------------|----------------------|--|--|
| Subject group type                     | Subject analysis set     | Subject analysis set |  |  |
| Number of subjects analysed            | 20                       | 25                   |  |  |
| Units: CD4 T-cells per million T-cells |                          |                      |  |  |
| median (inter-quartile range (Q1-Q3))  |                          |                      |  |  |
| CD4[2+] T-cells, Month 0 (N=20;23)     | 134.5 (42.8 to 329.7)    | 112 (39.3 to 151.5)  |  |  |
| CD4[2+] T-cells, Month 1 (N=19;25)     | 498.1 (336.1 to 652.4)   | 53.9 (1 to 179.4)    |  |  |
| CD4[2+] T-cells, Month 2 (N=20;21)     | 832.1 (536.2 to 1303.6)  | 58.9 (22.7 to 139.4) |  |  |
| CD4[2+] T-cells, Month 13 (N=18;19)    | 332.9 (114.9 to 604.6)   | 51.2 (1 to 288.6)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine response for gE-specific CD4[2+] T-cells

|                 |  |
|-----------------|--|
| End point title | Number of subjects with vaccine response for gE-specific CD4[2+] T-cells |
|-----------------|--|

End point description:

Vaccine response for gE-specific CD4[2+] T-cells was defined as:

- For initially subjects with pre-vaccination T cell frequencies below the threshold, at least a 2-fold increase as compared to the threshold (2x320 Events/10E6 CD4+ T cells);
- For initially subjects with pre-vaccination T cell frequencies above the threshold, at least a 2-fold increase as compared to pre-vaccination T cell frequencies.

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

End point timeframe:

At Months 1, 2 and 13

| End point values                    | GSK1437173A-<br>PreChemo | Placebo-<br>PreChemo |  |  |
|-------------------------------------|--------------------------|----------------------|--|--|
| Subject group type                  | Subject analysis set     | Subject analysis set |  |  |
| Number of subjects analysed         | 19                       | 23                   |  |  |
| Units: Subjects                     |                          |                      |  |  |
| CD4[2+] T-cells, Month 1 (N=19;23)  | 5                        | 0                    |  |  |
| CD4[2+] T-cells, Month 2 (N=19;20)  | 11                       | 0                    |  |  |
| CD4[2+] T-cells, Month 13 (N=17;16) | 3                        | 0                    |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any, Grade 3 and related unsolicited adverse events (AEs) |
|-----------------|---|

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. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

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

End point timeframe:

During the 30-day (Days 0-29) post-vaccination period

| End point values            | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 117               | 115             |  |  |
| Units: Subjects             |                   |                 |  |  |
| Any AE(s)                   | 100               | 103             |  |  |
| Grade 3 AE(s)               | 18                | 15              |  |  |
| Related AE(s)               | 10                | 9               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any and related serious adverse events (SAEs)

|                 |   |
|-----------------|---|
| End point title | Number of subjects with any and related serious adverse events (SAEs) |
|-----------------|---|

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. Related = SAE assessed by the investigator as causally related to the study vaccination.

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

End point timeframe:

From Dose 1 up to 30 days post last vaccination period

| <b>End point values</b>     | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 117               | 115             |  |  |
| Units: Subjects             |                   |                 |  |  |
| Any SAE(s)                  | 16                | 14              |  |  |
| Related SAE(s)              | 0                 | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and related potential Immune Mediated Diseases (pIMDs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any and related potential Immune Mediated Diseases (pIMDs) |
|-----------------|--|

End point description:

Potential immune-mediated diseases (pIMDs) are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. Any = occurrence of the symptom regardless of intensity grade. Related = pIMDs assessed by the investigator as causally related to the study vaccination.

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

End point timeframe:

From first vaccination up to 30 days post last vaccination

| <b>End point values</b>     | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 117               | 115             |  |  |
| Units: Subjects             |                   |                 |  |  |
| Any pIMD(s)                 | 0                 | 0               |  |  |
| Related pIMD(s)             | 0                 | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and Grade 3 solicited local symptoms

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any and Grade 3 solicited local symptoms |
|-----------------|--|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3



redness/swelling = redness/swelling spreading beyond 100 millimeters (mm) of injection site.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| During the 7-day (Days 0-6) post-vaccination period following each dose and across doses |           |

| End point values                           | GSK1437173A Group | Placebo Group   |  |  |
|--|-------------------|-----------------|--|--|
| Subject group type                         | Reporting group   | Reporting group |  |  |
| Number of subjects analysed                | 112               | 110             |  |  |
| Units: Subjects                            |                   |                 |  |  |
| Any Pain, Dose 1 (N=112;110)               | 83                | 2               |  |  |
| Grade 3 Pain, Dose 1 (N=112;110)           | 8                 | 0               |  |  |
| Any Redness, Dose 1 (N=112;110)            | 33                | 0               |  |  |
| Grade 3 Redness, Dose 1 (N=112;110)        | 2                 | 0               |  |  |
| Any Swelling, Dose 1 (N=112;110)           | 15                | 1               |  |  |
| Grade 3 Swelling, Dose 1 (N=112;110)       | 0                 | 0               |  |  |
| Any Pain, Dose 2 (N=98;105)                | 52                | 5               |  |  |
| Grade 3 Pain, Dose 2 (N=98;105)            | 4                 | 0               |  |  |
| Any Redness, Dose 2 (N=98;105)             | 20                | 0               |  |  |
| Grade 3 Redness, Dose 2 (N=98;105)         | 0                 | 0               |  |  |
| Any Swelling, Dose 2 (N=98;105)            | 8                 | 0               |  |  |
| Grade 3 Swelling, Dose 2 (N=98;105)        | 0                 | 0               |  |  |
| Any Pain, Across doses (N=112;110)         | 90                | 7               |  |  |
| Grade 3 Pain, Across doses (N=112;110)     | 11                | 0               |  |  |
| Any Redness, Across doses (N=112;110)      | 40                | 0               |  |  |
| Grade 3 Redness, Across doses (N=112;110)  | 2                 | 0               |  |  |
| Any Swelling, Across doses (N=112;110)     | 18                | 1               |  |  |
| Grade 3 Swelling, Across doses (N=112;110) | 0                 | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with pIMDs

|  |                               |
|--|-------------------------------|
| End point title  | Number of subjects with pIMDs |
| End point description:   |                               |
| pIMDs are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. |                               |
| End point type   | Secondary                     |
| End point timeframe:   |                               |
| From 30 days post last vaccination up to study end at Month 13   |                               |

| End point values            | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 117               | 115             |  |  |
| Units: Subjects             |                   |                 |  |  |
| Any pIMD(s)                 | 0                 | 1               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with SAE(s)

|   |                                |
|---|--------------------------------|
| End point title   | Number of subjects with SAE(s) |
| End point description:<br>SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. Related = SAE assessed by the investigator as causally related to the study vaccination. |                                |
| End point type  | Secondary                      |
| End point timeframe:<br>From 30 days post last vaccination up to study end at Month 13  |                                |

| End point values            | GSK1437173A Group | Placebo Group   |  |  |
|-----------------------------|-------------------|-----------------|--|--|
| Subject group type          | Reporting group   | Reporting group |  |  |
| Number of subjects analysed | 117               | 115             |  |  |
| Units: Subjects             |                   |                 |  |  |
| Any SAE(s)                  | 30                | 31              |  |  |
| Related SAE(s)              | 0                 | 0               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Anti-gE antibody concentrations

|   |                                 |
|---|---------------------------------|
| End point title   | Anti-gE antibody concentrations |
| End point description:<br>Antibody concentrations are presented as geometric mean concentrations (GMCs), expressed in millinternational units per milliliter (mIU/mL). The reference seropositivity cut-off value was equal to or above ( $\geq$ ) 97 mIU/mL. |                                 |
| End point type  | Secondary                       |
| End point timeframe:<br>At Months 0, 1, 6 and 13  |                                 |

| <b>End point values</b>                  | GSK1437173A Group            | Placebo Group             |  |  |
|--|------------------------------|---------------------------|--|--|
| Subject group type                       | Reporting group              | Reporting group           |  |  |
| Number of subjects analysed              | 87                           | 97                        |  |  |
| Units: mIU/mL                            |                              |                           |  |  |
| geometric mean (confidence interval 95%) |                              |                           |  |  |
| Anti-gE, Month 0 (N=87;94)               | 1049.8 (865.8 to 1273)       | 1116.7 (918.4 to 1358)    |  |  |
| Anti-gE, Month 1 (N=85;97)               | 24793.1 (18747.8 to 32787.6) | 1107.2 (920 to 1332.6)    |  |  |
| Anti-gE, Month 6 (N=42;43)               | 7730.4 (5358.4 to 11152.2)   | 1380.2 (1066.3 to 1786.6) |  |  |
| Anti-gE, Month 13 (N=68;70)              | 4477.3 (3482.4 to 5756.3)    | 1064.7 (845.9 to 1340.1)  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 7-day post-vaccination period; Unsolicited AEs: during the 30-day post-vaccination period; SAEs: during the entire study period (from Month 0 up to Month 13).

Adverse event reporting additional description:

Individual SAEs remain blinded as long as the study is ongoing.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | GSK1437173A Group |
|-----------------------|-------------------|

Reporting group description:

Subjects received the first dose of GSK 1437173A at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of GSK 1437173A vaccine was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

|                       |               |
|-----------------------|---------------|
| Reporting group title | Placebo Group |
|-----------------------|---------------|

Reporting group description:

Subjects received the first dose of placebo at least 10 days (up to 1 month) before start of chemotherapy cycle or at the first day (allowing a window of +/- 1 day) of the first (or second) chemotherapy cycle. The second dose of placebo was administered between 1 and 2 months after the first vaccination and at the first day (allowing a window of +/- 1 day) of a subsequent cycle of chemotherapy. The study products were administered intramuscularly into a deltoid muscle. The choice of and use of chemotherapy, or any other medication related to the patients' current conditions, were based on the local standard of care for the patients.

| Serious adverse events  | GSK1437173A Group | Placebo Group     |  |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                   |                   |  |
| subjects affected / exposed   | 36 / 117 (30.77%) | 42 / 115 (36.52%) |  |
| number of deaths (all causes)                                       | 12                | 11                |  |
| number of deaths resulting from adverse events                      |                   |                   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |  |
| Adenocarcinoma of colon   |                   |                   |  |
| subjects affected / exposed   | 1 / 117 (0.85%)   | 0 / 115 (0.00%)   |  |
| occurrences causally related to treatment / all                     | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 1             | 0 / 0             |  |
| Breast cancer recurrent   |                   |                   |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholangiocarcinoma                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Colon cancer                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Colorectal cancer                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Colorectal cancer metastatic                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Head and neck cancer                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Liposarcoma                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Lung neoplasm malignant                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| Malignant melanoma                              |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metastases to central nervous system            |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metastases to liver                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Non-small cell lung cancer                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Ovarian cancer                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Prostate cancer                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Rectal cancer metastatic                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Squamous cell carcinoma of lung                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Tongue neoplasm malignant stage unspecified     |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Tumour haemorrhage                                   |                 |                 |  |
| subjects affected / exposed                          | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Uterine leiomyosarcoma                               |                 |                 |  |
| subjects affected / exposed                          | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Vascular disorders                                   |                 |                 |  |
| Superior vena cava occlusion                         |                 |                 |  |
| subjects affected / exposed                          | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Thrombosis   |                 |                 |  |
| subjects affected / exposed                          | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Surgical and medical procedures                      |                 |                 |  |
| Abdominal hernia repair                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Death  |                 |                 |  |
| subjects affected / exposed                          | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Mucosal inflammation                                 |                 |                 |  |
| subjects affected / exposed                          | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Pyrexia   |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Immune system disorders                         |                 |                 |  |
| Drug hypersensitivity                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Bronchial obstruction                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pleural effusion                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory failure                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Gastrostomy failure                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lumbar vertebral fracture                       |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Cardiac arrest                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac failure congestive                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Myocardial infarction                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Bladder cancer                                  |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Hepatic encephalopathy                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Seizure   |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Anaemia   |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 3 / 115 (2.61%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| Febrile neutropenia                             |                 |                 |  |
| subjects affected / exposed                     | 6 / 117 (5.13%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 8           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neutropenia                                     |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 4 / 115 (3.48%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 4           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Pancytopenia                                    |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombocytopenia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Constipation                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diarrhoea                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dysphagia                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Enteritis                                       |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mouth ulceration                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nausea  |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Odynophagia                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Oesophagitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Cholangitis acute                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Rash  |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin haemorrhage                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Renal and urinary disorders                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Acute kidney injury                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Hydronephrosis                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endocrine disorders                             |                 |                 |  |
| Autoimmune thyroiditis                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Arthralgia                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal chest pain                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Anal abscess                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bacteraemia                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Candida infection                               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clostridium bacteriaemia                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Clostridium difficile infection                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Device related sepsis                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulitis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Epiglottitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastroenteritis                                 |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Hepatitis c                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infected dermal cyst                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Kidney infection                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lower respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung infection                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nasopharyngitis                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neutropenic sepsis                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oral candidiasis                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Pleural infection                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 117 (0.85%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Respiratory tract infection                     |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 3 / 117 (2.56%) | 2 / 115 (1.74%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Staphylococcal infection                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Upper respiratory tract infection               |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urosepsis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 117 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Diabetic ketoacidosis                           |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypokalaemia                                    |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hyponatraemia                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 117 (0.85%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malnutrition                                    |                 |                 |  |
| subjects affected / exposed                     | 2 / 117 (1.71%) | 0 / 115 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | GSK1437173A Group  | Placebo Group      |  |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                    |                    |  |
| subjects affected / exposed                           | 115 / 117 (98.29%) | 106 / 115 (92.17%) |  |
| Nervous system disorders                              |                    |                    |  |
| Dysgeusia   |                    |                    |  |
| subjects affected / exposed                           | 1 / 117 (0.85%)    | 6 / 115 (5.22%)    |  |
| occurrences (all)                                     | 1                  | 6                  |  |
| Headache  |                    |                    |  |
| subjects affected / exposed                           | 43 / 117 (36.75%)  | 40 / 115 (34.78%)  |  |
| occurrences (all)                                     | 61                 | 52                 |  |
| Blood and lymphatic system disorders                  |                    |                    |  |
| Neutropenia   |                    |                    |  |
| subjects affected / exposed                           | 11 / 117 (9.40%)   | 13 / 115 (11.30%)  |  |
| occurrences (all)                                     | 12                 | 15                 |  |
| General disorders and administration site conditions  |                    |                    |  |
| Asthenia  |                    |                    |  |
| subjects affected / exposed                           | 30 / 117 (25.64%)  | 29 / 115 (25.22%)  |  |
| occurrences (all)                                     | 34                 | 33                 |  |
| Chills  |                    |                    |  |
| subjects affected / exposed                           | 39 / 117 (33.33%)  | 25 / 115 (21.74%)  |  |
| occurrences (all)                                     | 48                 | 30                 |  |



|                             |                   |                   |  |
|-----------------------------|-------------------|-------------------|--|
| Fatigue                     |                   |                   |  |
| subjects affected / exposed | 78 / 117 (66.67%) | 68 / 115 (59.13%) |  |
| occurrences (all)           | 118               | 109               |  |
| Mucosal inflammation        |                   |                   |  |
| subjects affected / exposed | 9 / 117 (7.69%)   | 6 / 115 (5.22%)   |  |
| occurrences (all)           | 11                | 8                 |  |
| Pain                        |                   |                   |  |
| subjects affected / exposed | 90 / 117 (76.92%) | 7 / 115 (6.09%)   |  |
| occurrences (all)           | 139               | 7                 |  |
| Pyrexia                     |                   |                   |  |
| subjects affected / exposed | 22 / 117 (18.80%) | 9 / 115 (7.83%)   |  |
| occurrences (all)           | 23                | 9                 |  |
| Swelling                    |                   |                   |  |
| subjects affected / exposed | 18 / 117 (15.38%) | 1 / 115 (0.87%)   |  |
| occurrences (all)           | 23                | 1                 |  |
| Redness                     |                   |                   |  |
| subjects affected / exposed | 40 / 117 (34.19%) | 0 / 115 (0.00%)   |  |
| occurrences (all)           | 40                | 0                 |  |
| Shivering                   |                   |                   |  |
| subjects affected / exposed | 39 / 117 (33.33%) | 25 / 115 (21.74%) |  |
| occurrences (all)           | 39                | 25                |  |
| Fever                       |                   |                   |  |
| subjects affected / exposed | 20 / 117 (17.09%) | 5 / 115 (4.35%)   |  |
| occurrences (all)           | 20                | 5                 |  |
| Gastrointestinal disorders  |                   |                   |  |
| Constipation                |                   |                   |  |
| subjects affected / exposed | 16 / 117 (13.68%) | 11 / 115 (9.57%)  |  |
| occurrences (all)           | 19                | 11                |  |
| Diarrhoea                   |                   |                   |  |
| subjects affected / exposed | 9 / 117 (7.69%)   | 10 / 115 (8.70%)  |  |
| occurrences (all)           | 12                | 10                |  |
| Dyspepsia                   |                   |                   |  |
| subjects affected / exposed | 6 / 117 (5.13%)   | 13 / 115 (11.30%) |  |
| occurrences (all)           | 6                 | 13                |  |
| Gastrointestinal disorder   |                   |                   |  |

|  |                         |                         |  |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed<br>occurrences (all)                       | 49 / 117 (41.88%)<br>74 | 51 / 115 (44.35%)<br>63 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)             | 31 / 117 (26.50%)<br>36 | 28 / 115 (24.35%)<br>33 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)           | 10 / 117 (8.55%)<br>10  | 14 / 115 (12.17%)<br>16 |  |
| Skin and subcutaneous tissue disorders                                 |                         |                         |  |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)           | 21 / 117 (17.95%)<br>21 | 22 / 115 (19.13%)<br>22 |  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)           | 43 / 117 (36.75%)<br>58 | 1 / 115 (0.87%)<br>1    |  |
| Musculoskeletal and connective tissue disorders                        |                         |                         |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)            | 60 / 117 (51.28%)<br>88 | 31 / 115 (26.96%)<br>45 |  |
| Metabolism and nutrition disorders                                     |                         |                         |  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 9 / 117 (7.69%)<br>12   | 5 / 115 (4.35%)<br>5    |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 19 November 2012 | <p>The primary objective for immunogenicity response (based on Geometric Mean [GM] ratios) following the HZ/su vaccination compared to placebo will now be evaluated only in the PreChemo Groups.</p> <p>The secondary objectives have now been qualified to evaluate immunogenicity in either the PreChemo Groups (Vaccine Response Rates [VRR] in anti-gE humoral immunogenicity responses and VRR and GM ratio in gE-specific Cellular-Mediated Immunity [CMI]) or in all study subjects (VRR and GM ratio in anti-gE humoral immunogenicity responses).</p> <p>The CMI sub-cohort will now only be recruited in the PreChemo Groups.</p> <p>The timepoint for evaluation of the primary objective for safety/reactogenicity has been reworded for clarity ('up to 30 days post last vaccination' instead of 'up to month 2').</p> |
| 11 August 2014   | <p>The cut-off of the gE-specific ELISA assay has been changed from 18 to 97 mIU/mL.</p> <p>The definition of the according-to-protocol (ATP) cohort for safety was updated. (Section 9.4.2)</p> <p>Statistical section was updated to describe the descriptive cell-mediated immune (CMI) response analysis, to clarify other descriptive analysis for immunogenicity and safety. (Section 9.5.3)</p>  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported