



## Clinical trial results:

**A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of recMAGE-A3 + AS15 ASCI as adjuvant therapy in patients with MAGE-A3 positive resected stage III melanoma**

### Summary

|                          |   |
|--------------------------|---|
| EudraCT number           | 2008-002447-16                            |
| Trial protocol           | IE DE BE CZ FR NL IT SE EE ES AT GR BG GB |
| Global end of trial date | 15 March 2016                             |

### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 22 February 2021   |
| First version publication date | 15 October 2016  |
| Version creation reason        | • Correction of full data set<br>Alignment in the endpoints and safety sections. |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 111482 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00796445 |
| 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 Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 15 March 2016     |
| Is this the analysis of the primary completion data? | Yes               |
| Primary completion date                              | 01 September 2015 |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 15 March 2016     |
| Was the trial ended prematurely?                     | Yes               |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the clinical efficacy in terms of disease-free survival (DFS) of recMAGE-A3 + AS15 ASCI compared to placebo in the overall study population of patients with completely resected stage III cutaneous melanoma with macroscopic lymph node involvement;  
To demonstrate the clinical efficacy in terms of DFS of the recMAGE-A3 + AS15 ASCI compared to placebo in the population presenting the potentially favorable gene expression signature.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Study products were administered by qualified and trained personnel. Study products were administered only to eligible subjects that had no contraindications to any components of the study products.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 December 2008 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Argentina: 5       |
| Country: Number of subjects enrolled | Australia: 126     |
| Country: Number of subjects enrolled | Austria: 29        |
| Country: Number of subjects enrolled | Belgium: 25        |
| Country: Number of subjects enrolled | Brazil: 6          |
| Country: Number of subjects enrolled | Bulgaria: 20       |
| Country: Number of subjects enrolled | Canada: 4          |
| Country: Number of subjects enrolled | Czech Republic: 40 |
| Country: Number of subjects enrolled | Estonia: 10        |
| Country: Number of subjects enrolled | France: 303        |
| Country: Number of subjects enrolled | Germany: 184       |
| Country: Number of subjects enrolled | Greece: 7          |
| Country: Number of subjects enrolled | Ireland: 15        |
| Country: Number of subjects enrolled | Israel: 4          |
| Country: Number of subjects enrolled | Italy: 96          |
| Country: Number of subjects enrolled | Japan: 7           |
| Country: Number of subjects enrolled | Mexico: 3          |

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Netherlands: 21        |
| Country: Number of subjects enrolled | Norway: 14             |
| Country: Number of subjects enrolled | Poland: 69             |
| Country: Number of subjects enrolled | Romania: 3             |
| Country: Number of subjects enrolled | Russian Federation: 63 |
| Country: Number of subjects enrolled | Serbia: 6              |
| Country: Number of subjects enrolled | Spain: 13              |
| Country: Number of subjects enrolled | Sweden: 11             |
| Country: Number of subjects enrolled | Taiwan: 2              |
| Country: Number of subjects enrolled | Ukraine: 44            |
| Country: Number of subjects enrolled | United Kingdom: 12     |
| Country: Number of subjects enrolled | United States: 209     |
| Worldwide total number of subjects   | 1351                   |
| EEA total number of subjects         | 872                    |

Notes:

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### Subjects enrolled per age group

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 958 |
| From 65 to 84 years                       | 384 |
| 85 years and over                         | 9   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Out of 1351 patients enrolled, 6 did not receive treatment and were excluded, hence 1345 patients were included in the Total treated population (895 in MAGE-A3 Group, 450 in Placebo Group). Between the final and follow-up analyses, 1 patient (in MAGE-A3 Group) had an invalid ICF and was not included in the follow-up analysis, which included 1344 patients

### Pre-assignment period milestones

|                              |      |
|------------------------------|------|
| Number of subjects started   | 1351 |
| Number of subjects completed | 1345 |

### Pre-assignment subject non-completion reasons

|                            |                          |
|----------------------------|--------------------------|
| Reason: Number of subjects | No treatment received: 6 |
|----------------------------|--------------------------|

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall Study (overall period)  |
| Is this the baseline period? | Yes                             |
| Allocation method            | Randomised - controlled         |
| Blinding used                | Double blind                    |
| Roles blinded                | Subject, Investigator, Assessor |

### Arms

|                              |                            |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes                        |
| <b>Arm title</b>             | MAGE-A3 (as treated) Group |

Arm description:

Patients who received up to 13 doses of recMAGE-A3 + AS15 ASCI.

|  |  |
|--|--|
| Arm type                               | Experimental   |
| Investigational medicinal product name | recMAGE-A3 recombinant protein formulated in AS15 adjuvant |
| Investigational medicinal product code | recMAGE-A3 + AS15  |
| Other name                             | GSK 2132231A, ASCI   |
| Pharmaceutical forms                   | Powder and solvent for suspension for injection            |
| Routes of administration               | Intramuscular use  |

Dosage and administration details:

The study product was administered intramuscularly in 13 doses over 27 months: 5 doses of placebo at 3-week intervals, followed by 8 doses of placebo at 12-week intervals.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Placebo (as treated) Group |
|------------------|----------------------------|

Arm description:

Patients who received up to 13 doses of placebo.

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

Dosage and administration details:

The study product was administered intramuscularly in 13 doses over 27 months: 5 doses of placebo at 3-week intervals, followed by 8 doses of placebo at 12-week intervals.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | <b>MAGE-A3 (as treated) Group</b> | <b>Placebo (as treated) Group</b> |
|---|-----------------------------------|-----------------------------------|
| Started   | 895                               | 450                               |
| Completed   | 310                               | 158                               |
| Not completed                                       | 585                               | 292                               |
| Adverse event, serious fatal                        | 10                                | 5                                 |
| Consent withdrawn by subject                        | 18                                | 9                                 |
| Adverse event, non-fatal                            | 4                                 | -                                 |
| Invalid informed consent form                       | 1                                 | -                                 |
| Unspecified   | 10                                | 7                                 |
| Disease progression/recurrence                      | 537                               | 268                               |
| Protocol deviation                                  | 5                                 | 3                                 |

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Notes:

[1] - 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: Out of the subjects enrolled in the trial, only the ones who received treatment according to the protocol started the study.

## Baseline characteristics

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | MAGE-A3 (as treated) Group |
|-----------------------|----------------------------|

Reporting group description:

Patients who received up to 13 doses of recMAGE-A3 + AS15 ASCI.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Placebo (as treated) Group |
|-----------------------|----------------------------|

Reporting group description:

Patients who received up to 13 doses of placebo.

| Reporting group values             | MAGE-A3 (as treated) Group | Placebo (as treated) Group | Total |
|------------------------------------|----------------------------|----------------------------|-------|
| Number of subjects                 | 895                        | 450                        | 1345  |
| Age categorical<br>Units: Subjects |                            |                            |       |
| Age continuous                     |                            |                            |       |
| Age continuous description         |                            |                            |       |
| Units: years                       |                            |                            |       |
| arithmetic mean                    | 56                         | 56.2                       |       |
| standard deviation                 | ± 13.51                    | ± 13.66                    | -     |
| Gender categorical                 |                            |                            |       |
| Gender categorical description     |                            |                            |       |
| Units: Subjects                    |                            |                            |       |
| Female                             | 345                        | 188                        | 533   |
| Male                               | 550                        | 262                        | 812   |

## End points

### End points reporting groups

|   |                               |
|---|-------------------------------|
| Reporting group title   | MAGE-A3 (as treated) Group    |
| Reporting group description:<br>Patients who received up to 13 doses of recMAGE-A3 + AS15 ASCI.   |                               |
| Reporting group title   | Placebo (as treated) Group    |
| Reporting group description:<br>Patients who received up to 13 doses of placebo.  |                               |
| Subject analysis set title  | GS+ MAGE-A3 Sub-Group         |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Subset of patients with the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as assessed at screening.    |                               |
| Subject analysis set title  | GS+ Placebo Sub-Group         |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Subset of patients with the pre-specified gene signature, receiving placebo. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as assessed at screening.                     |                               |
| Subject analysis set title  | GS- MAGE-A3 Sub-Group         |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Subset of patients without the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as assessed at screening. |                               |
| Subject analysis set title  | GS- Placebo Sub-Group         |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Subset of patients without the pre-specified gene signature, receiving placebo. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as assessed at screening.                  |                               |
| Subject analysis set title  | MAGE-A3 (as randomized) Group |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Patients who were allocated by the randomization system for receiving up to 13 doses of recMAGE-A3 + AS15 ASCI.  |                               |
| Subject analysis set title  | Placebo (as randomized) Group |
| Subject analysis set type   | Sub-group analysis            |
| Subject analysis set description:<br>Patients who were allocated by the randomization system for receiving up to 13 doses of placebo.   |                               |

### Primary: Disease Free Survival (DFS)

|   |                             |
|---|-----------------------------|
| End point title   | Disease Free Survival (DFS) |
| End point description:<br>DFS = time to event from randomization to the date of first disease recurrence or the date of death (whatever cause), whichever occurred first. DFS expressed as person-year rate i.e number of patients with at least one event over the sum of follow-up periods (in years), until first occurrence of a recurrence/death. Types of recurrence to be considered as an event included loco-regional and distant metastases. Any death occurring without prior documentation of tumor recurrence was considered as an event. If no event occurred by the time of analysis, then time to event was censored at the last assessment date of the patient. Any new primary cancer at another site, including second primary melanoma, was not considered as a recurrence and had to be reported as a Serious Adverse Event. The analysis was performed on the Total Treated population - as randomized, which included patients in the treatment groups as allocated by the randomization system at the start of the study. |                             |
| End point type  | Primary                     |

End point timeframe:

At Final analysis (Month 30 = Year 2.5) and at follow-up analysis (up to Year 5)

| End point values                                   | GS+ MAGE-A3<br>Sub-Group | GS+ Placebo<br>Sub-Group | GS- MAGE-A3<br>Sub-Group | GS- Placebo<br>Sub-Group |
|--|--------------------------|--------------------------|--------------------------|--------------------------|
| Subject group type                                 | Subject analysis set     | Subject analysis set     | Subject analysis set     | Subject analysis set     |
| Number of subjects analysed                        | 200                      | 116                      | 255                      | 126                      |
| Units: First events per person-year                |                          |                          |                          |                          |
| number (not applicable)                            |                          |                          |                          |                          |
| DFS, Final analysis (N=200,116,255,126,893,452)    | 0.5                      | 0.46                     | 0.437                    | 0.442                    |
| DFS, Follow-up analysis(N=200,116,255,126,892,452) | 0.345                    | 0.335                    | 0.316                    | 0.319                    |

| End point values                                   | MAGE-A3 (as<br>randomized)<br>Group | Placebo (as<br>randomized)<br>Group |  |  |
|--|-------------------------------------|-------------------------------------|--|--|
| Subject group type                                 | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed                        | 893                                 | 452                                 |  |  |
| Units: First events per person-year                |                                     |                                     |  |  |
| number (not applicable)                            |                                     |                                     |  |  |
| DFS, Final analysis (N=200,116,255,126,893,452)    | 0.505                               | 0.478                               |  |  |
| DFS, Follow-up analysis(N=200,116,255,126,892,452) | 0.366                               | 0.345                               |  |  |

## Statistical analyses

| Statistical analysis title  | Statistical analysis 1  |
|---|---|
| Statistical analysis description:<br>At Final analysis (Month 30 = Year 2.5).<br>The aim of this analysis was to demonstrate the clinical efficacy in terms of disease-free survival (DFS) of recMAGE-A3 + AS15 ASCI compared to placebo in the overall study population of patients with completely resected stage III cutaneous melanoma with macroscopic lymph node involvement. |   |
| Comparison groups   | MAGE-A3 (as randomized) Group v Placebo (as randomized) Group |
| Number of subjects included in analysis   | 1345  |
| Analysis specification  | Pre-specified   |
| Analysis type   | non-inferiority   |
| P-value   | = 0.8566  |
| Method  | Regression, Cox   |
| Parameter estimate  | Hazard ratio (HR)   |
| Point estimate  | 1.013   |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.879   |
| upper limit         | 1.169   |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

At Final analysis (Month 30 = Year 2.5).

The aim of this analysis was to demonstrate the clinical efficacy in terms of DFS of the recMAGE-A3 + AS15 ASCI compared to placebo in the population presenting the potentially favorable gene expression signature.

|   |   |
|---|---|
| Comparison groups                       | GS+ Placebo Sub-Group v GS+ MAGE-A3 Sub-Group |
| Number of subjects included in analysis | 316   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | non-inferiority                               |
| P-value                                 | = 0.4821                                      |
| Method                                  | Regression, Cox                               |
| Parameter estimate                      | Hazard ratio (HR)                             |
| Point estimate                          | 1.111   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 0.828   |
| upper limit                             | 1.491   |

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

At Final analysis (Month 30 = Year 2.5).

The aim of this analysis was to demonstrate the clinical efficacy in terms of DFS of the recMAGE-A3 + AS15 ASCI compared to placebo in the population without the potentially favorable gene expression signature.

|   |   |
|---|---|
| Comparison groups                       | GS- Placebo Sub-Group v GS- MAGE-A3 Sub-Group |
| Number of subjects included in analysis | 381   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | non-inferiority                               |
| P-value                                 | = 0.5375                                      |
| Method                                  | Regression, Cox                               |
| Parameter estimate                      | Hazard ratio (HR)                             |
| Point estimate                          | 0.915   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 0.691   |
| upper limit                             | 1.212   |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical analysis 4  |
| Statistical analysis description:  |   |
| At Follow-up analysis (Up to Year 5).  |   |
| The aim of this analysis was to demonstrate the clinical efficacy in terms of disease-free survival (DFS) of recMAGE-A3 + AS15 ASCI compared to placebo in the overall study population of patients with completely resected stage III cutaneous melanoma with macroscopic lymph node involvement. |   |
| Comparison groups  | MAGE-A3 (as randomized) Group v Placebo (as randomized) Group |
| Number of subjects included in analysis  | 1345  |
| Analysis specification   | Pre-specified   |
| Analysis type  | non-inferiority   |
| P-value  | = 0.7534  |
| Method   | Regression, Cox   |
| Parameter estimate   | Hazard ratio (HR)   |
| Point estimate   | 1.023   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.89  |
| upper limit  | 1.175   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical analysis 5                        |
| Statistical analysis description:   |   |
| At Follow-up analysis (Up to Year 5).   |   |
| The aim of this analysis was to demonstrate the clinical efficacy in terms of DFS of the recMAGE-A3 + AS15 ASCI compared to placebo in the population presenting the potentially favorable gene expression signature. |   |
| Comparison groups   | GS+ Placebo Sub-Group v GS+ MAGE-A3 Sub-Group |
| Number of subjects included in analysis   | 316   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | non-inferiority                               |
| P-value   | = 0.5385                                      |
| Method  | Regression, Cox                               |
| Parameter estimate  | Hazard ratio (HR)                             |
| Point estimate  | 1.094   |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | 0.821   |
| upper limit   | 1.457   |

|  |                        |
|--|------------------------|
| <b>Statistical analysis title</b>  | Statistical analysis 6 |
| Statistical analysis description:  |                        |
| At Follow-up analysis (Up to Year 5).  |                        |
| The aim of this analysis was to demonstrate the clinical efficacy in terms of DFS of the recMAGE-A3 + AS15 ASCI compared to placebo in the population without the potentially favorable gene expression signature. |                        |

|   |   |
|---|---|
| Comparison groups                       | GS- Placebo Sub-Group v GS- MAGE-A3 Sub-Group |
| Number of subjects included in analysis | 381   |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | non-inferiority                               |
| P-value                                 | = 0.5419                                      |
| Method                                  | Regression, Cox                               |
| Parameter estimate                      | Hazard ratio (HR)                             |
| Point estimate                          | 0.918   |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 0.698   |
| upper limit                             | 1.207   |

### Secondary: Overall Survival (OS)

|  |                       |
|--|-----------------------|
| End point title  | Overall Survival (OS) |
| End point description:   |                       |
| Overall Survival (OS) was defined as the time to event from randomization to the date of death, irrespective of the cause of death; OS was expressed as the person-year rate i.e. the number of patients with death over the sum of the follow-up periods in years; Patients alive at the time of the analysis were censored on the date last known to be alive. The analysis was performed on the Total Treated population - as randomized, which included patients in the treatment groups as allocated by the randomization system at the start of the study. |                       |
| End point type   | Secondary             |
| End point timeframe:   |                       |
| At final analysis (Month 30 = Year 2.5) and Follow-up analysis (Up to Year 5).   |                       |

| End point values                                      | GS+ MAGE-A3 Sub-Group | GS+ Placebo Sub-Group | GS- MAGE-A3 Sub-Group | GS- Placebo Sub-Group |
|---|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                    | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed                           | 200                   | 116                   | 255                   | 126                   |
| Units: Events per person-year                         |                       |                       |                       |                       |
| number (not applicable)                               |                       |                       |                       |                       |
| OS, Final analysis<br>(N=200,116,255,126,893,452)     | 0.172                 | 0.188                 | 0.165                 | 0.151                 |
| OS, Follow-up analysis<br>(N=200,116,255,126,892,452) | 0.146                 | 0.153                 | 0.132                 | 0.12                  |

| End point values                                  | MAGE-A3 (as randomized) Group | Placebo (as randomized) Group |  |  |
|---|-------------------------------|-------------------------------|--|--|
| Subject group type                                | Subject analysis set          | Subject analysis set          |  |  |
| Number of subjects analysed                       | 893                           | 452                           |  |  |
| Units: Events per person-year                     |                               |                               |  |  |
| number (not applicable)                           |                               |                               |  |  |
| OS, Final analysis<br>(N=200,116,255,126,893,452) | 0.177                         | 0.165                         |  |  |

|   |       |      |  |  |
|---|-------|------|--|--|
| OS, Follow-up analysis<br>(N=200,116,255,126,892,452) | 0.146 | 0.14 |  |  |
|---|-------|------|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Disease-free specific survival (DFSS)

|                 |                                       |
|-----------------|---------------------------------------|
| End point title | Disease-free specific survival (DFSS) |
|-----------------|---------------------------------------|

End point description:

Disease Free Specific Survival (DFSS) was defined as the time to event from randomization to the date of first recurrence of disease or date of death due to melanoma (cause as assessed by investigator), whichever occurred first. DFSS was expressed as the person-year rate i.e. the number of patients with at least one event over the sum of the follow-up periods in years. Patients who died due to a cause other than the disease under study and patients alive at the time of analysis were censored on the date of last assessment (visit or tumor assessment). The analysis was performed on the Total Treated population - as randomized, which included patients in the treatment groups as allocated by the randomization system at the start of the study.

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

End point timeframe:

At Final analysis (Month 30 = Year 2.5)

| End point values                    | GS+ MAGE-A3<br>Sub-Group | GS+ Placebo<br>Sub-Group | GS- MAGE-A3<br>Sub-Group | GS- Placebo<br>Sub-Group |
|-------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Subject group type                  | Subject analysis set     | Subject analysis set     | Subject analysis set     | Subject analysis set     |
| Number of subjects analysed         | 200                      | 116                      | 255                      | 126                      |
| Units: First events per person-year |                          |                          |                          |                          |
| number (not applicable)             | 0.5                      | 0.46                     | 0.434                    | 0.442                    |

| End point values                    | MAGE-A3 (as<br>randomized)<br>Group | Placebo (as<br>randomized)<br>Group |  |  |
|-------------------------------------|-------------------------------------|-------------------------------------|--|--|
| Subject group type                  | Subject analysis set                | Subject analysis set                |  |  |
| Number of subjects analysed         | 893                                 | 452                                 |  |  |
| Units: First events per person-year |                                     |                                     |  |  |
| number (not applicable)             | 0.499                               | 0.478                               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Distant metastasis-free survival (DMFS)

|                 |   |
|-----------------|---|
| End point title | Distant metastasis-free survival (DMFS) |
|-----------------|---|

**End point description:**

Distant Metastasis Free Survival (DMFS) was defined as the time to event from randomization to the date of first distant metastasis or date of death, whichever occurred first. DMFS was expressed as the person-year rate i.e. the number of patients with at least one event over the sum of the follow-up periods in year. Patients alive and without distant metastases were censored at the date of last assessment (visit or tumor assessment, or date of last tumor assessment as documented during the yearly contact follow-up period). The analysis was performed on the Total Treated population - as randomized, which included patients in the treatment groups as allocated by the randomization system at the start of the study.

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

**End point timeframe:**

At Final analysis (Month 30 = Year 2.5)

| End point values                    | GS+ MAGE-A3 Sub-Group | GS+ Placebo Sub-Group | GS- MAGE-A3 Sub-Group | GS- Placebo Sub-Group |
|-------------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                  | Subject analysis set  | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed         | 200                   | 116                   | 255                   | 126                   |
| Units: First events per person-year |                       |                       |                       |                       |
| number (not applicable)             | 0.388                 | 0.337                 | 0.334                 | 0.307                 |

| End point values                    | MAGE-A3 (as randomized) Group | Placebo (as randomized) Group |  |  |
|-------------------------------------|-------------------------------|-------------------------------|--|--|
| Subject group type                  | Subject analysis set          | Subject analysis set          |  |  |
| Number of subjects analysed         | 893                           | 452                           |  |  |
| Units: First events per person-year |                               |                               |  |  |
| number (not applicable)             | 0.387                         | 0.342                         |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Health-related quality of life**

|                 |                                |
|-----------------|--------------------------------|
| End point title | Health-related quality of life |
|-----------------|--------------------------------|

**End point description:**

The assessment of health-related quality of life was restricted to patients who consented to study participation after Protocol Amendment 1 became effective at their study site, and for whom a validated version of the Euro Quality of Life-5D (EQ-5D) questionnaire was available in their native language. The EQ-5D comprises a 5-dimensional descriptive system (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), where each item has 3 levels and together they define 243 possible health states. For each health state, a value (utility) was determined by using an additive algorithm. These utility scores were calculated for each patient at each timepoint at which an EQ-5D questionnaire was completed. The score had a maximum value of 1.0 corresponding to full health level, while lower scores, down to a minimum value of 0.0 reflected degradation in the health-related quality of life.

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

**End point timeframe:**

At Week 0, 6, 12 [on the day of and on the day after treatment administration (TA)], at Month 6, 9, 12, 24, at the Concluding visit (Month 30) + 6 months and +12 Months and at disease recurrence

| End point values                              | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|---|----------------------------|----------------------------|--|--|
| Subject group type                            | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed                   | 245                        | 118                        |  |  |
| Units: Units on a scale                       |                            |                            |  |  |
| arithmetic mean (standard deviation)          |                            |                            |  |  |
| EQ-5D, W0 day of TA (N=245;118)               | 0.842 (± 0.182)            | 0.861 (± 0.159)            |  |  |
| EQ-5D, W0 day after TA (N=195;94)             | 0.773 (± 0.182)            | 0.873 (± 0.141)            |  |  |
| EQ-5D, W6 day of TA (N=234;118)               | 0.853 (± 0.183)            | 0.865 (± 0.173)            |  |  |
| EQ-5D, W6 day after TA (N=198;96)             | 0.722 (± 0.245)            | 0.867 (± 0.174)            |  |  |
| EQ-5D, W12 day of TA (N=193;96)               | 0.873 (± 0.158)            | 0.887 (± 0.138)            |  |  |
| EQ-5D, W12 day after TA (N=162;77)            | 0.788 (± 0.17)             | 0.888 (± 0.126)            |  |  |
| EQ-5D, M6 (N=144;75)                          | 0.879 (± 0.146)            | 0.9 (± 0.156)              |  |  |
| EQ-5D, M9 (N=130;77)                          | 0.891 (± 0.134)            | 0.876 (± 0.194)            |  |  |
| EQ-5D, M12 (N=113;67)                         | 0.891 (± 0.157)            | 0.899 (± 0.149)            |  |  |
| EQ-5D, M24 (N=62;36)                          | 0.894 (± 0.132)            | 0.881 (± 0.15)             |  |  |
| EQ-5D, Concluding visit + 6 months (N=1;2)    | 0.727 (± 0)                | 0.568 (± 0.074)            |  |  |
| EQ-5D, Concluding visit + 12 months (N=30;10) | 0.791 (± 0.264)            | 0.648 (± 0.344)            |  |  |
| EQ-5D, Disease recurrence (N=76;35)           | 0.752 (± 0.261)            | 0.815 (± 0.197)            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-MAGE-A3 antibody concentrations above the cut-off values

|  |   |
|--|---|
| End point title  | Number of subjects with Anti-MAGE-A3 antibody concentrations above the cut-off values |
| End point description:<br>The cut-off value was 27 ELISA units per millilitre (EL.U/mL).                 |   |
| End point type   | Secondary   |
| End point timeframe:<br>At Weeks 0, 6, 12, 36, 48, 72, 120 (Concluding visit) and at Week 120 + 6 months |   |

| End point values                                  | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|---|----------------------------|----------------------------|--|--|
| Subject group type                                | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed                       | 629                        | 316                        |  |  |
| Units: Subjects                                   |                            |                            |  |  |
| Anti-MAGE-A3, W0 (N=629;316)                      | 25                         | 19                         |  |  |
| Anti-MAGE-A3, W6 (N=482;271)                      | 478                        | 22                         |  |  |
| Anti-MAGE-A3, W12 (N=425;230)                     | 424                        | 13                         |  |  |
| Anti-MAGE-A3, W36 (N=259;131)                     | 259                        | 6                          |  |  |
| Anti-MAGE-A3, W48 (N=224;113)                     | 224                        | 5                          |  |  |
| Anti-MAGE-A3, W72 (N=178;85)                      | 178                        | 4                          |  |  |
| Anti-MAGE-A3, W120 (N=257;140)                    | 257                        | 10                         |  |  |
| Anti-MAGE-A3, Concluding visit+6 months (N=70;36) | 70                         | 1                          |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-MAGE-A3 antibody geometric mean concentration

|   |  |
|---|--|
| End point title   | Anti-MAGE-A3 antibody geometric mean concentration |
| End point description:  |  |
| Geometric mean concentration (GMC) was expressed as ELISA units per millilitre (EL.U/mL). |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| At Weeks 0, 6, 12, 36, 48, 72, 120 (Concluding visit) and at Week 120 + 6 months          |  |

| End point values                         | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|--|----------------------------|----------------------------|--|--|
| Subject group type                       | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed              | 629                        | 316                        |  |  |
| Units: EL.U/mL                           |                            |                            |  |  |
| geometric mean (confidence interval 95%) |                            |                            |  |  |
| Anti-MAGE-A3, W0 (N=629;316)             | 11 (10.6 to 11.4)          | 11.4 (10.7 to 12.1)        |  |  |
| Anti-MAGE-A3, W6 (N=482;271)             | 1451.6 (1290.9 to 1632.3)  | 11.9 (11 to 12.9)          |  |  |
| Anti-MAGE-A3, W12 (N=425;230)            | 4031.6 (3738.7 to 4347.4)  | 11.3 (10.6 to 12.1)        |  |  |
| Anti-MAGE-A3, W36 (N=259;131)            | 2189.6 (2000.4 to 2396.7)  | 11.4 (10.4 to 12.4)        |  |  |
| Anti-MAGE-A3, W48 (N=224;113)            | 2243.4 (2034.4 to 2473.8)  | 11.3 (10.2 to 12.6)        |  |  |
| Anti-MAGE-A3, W72 (N=178;85)             | 2489.4 (2221.8 to 2789.4)  | 11.2 (10 to 12.5)          |  |  |

|   |                           |                     |  |  |
|---|---------------------------|---------------------|--|--|
| Anti-MAGE-A3, W120 (N=257;140)                    | 3109.7 (2827.4 to 3420.2) | 12.7 (10.9 to 14.8) |  |  |
| Anti-MAGE-A3, Concluding visit+6 months (N=70;36) | 1293.4 (1056.3 to 1583.7) | 10.8 (9.9 to 11.8)  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with Anti-MAGE-A3 antibody response

|                 |  |
|-----------------|--|
| End point title | Number of subjects with Anti-MAGE-A3 antibody response |
|-----------------|--|

End point description:

Treatment response defined as: - For initially seronegative patients: post-treatment antibody concentration  $\geq 27$  EL.U/mL; - For initially seropositive patients: post-treatment antibody concentration  $\geq 2$  fold the pre-treatment antibody concentration.

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

End point timeframe:

At Weeks 6, 12, 36, 48, 72, 120 (Concluding visit) and at Week 120 + 6 months

| End point values                                  | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|---|----------------------------|----------------------------|--|--|
| Subject group type                                | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed                       | 482                        | 271                        |  |  |
| Units: Subjects                                   |                            |                            |  |  |
| Anti-MAGE-A3, W6 (N=482;271)                      | 476                        | 9                          |  |  |
| Anti-MAGE-A3, W12 (N=425;230)                     | 424                        | 4                          |  |  |
| Anti-MAGE-A3, W36 (N=259;131)                     | 259                        | 2                          |  |  |
| Anti-MAGE-A3, W48 (N=224;113)                     | 224                        | 2                          |  |  |
| Anti-MAGE-A3, W72 (N=178;85)                      | 178                        | 2                          |  |  |
| Anti-MAGE-A3, W120 (N=257;140)                    | 257                        | 6                          |  |  |
| Anti-MAGE-A3, Concluding visit+6 months (N=70;36) | 70                         | 1                          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any adverse events (AEs)

|                 |  |
|-----------------|--|
| End point title | Number of subjects with any 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.



|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Within the 31-day (Days 0-30) follow-up period after treatment |           |

| End point values            | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|-----------------------------|----------------------------|----------------------------|--|--|
| Subject group type          | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed | 895                        | 450                        |  |  |
| Units: Subjects             | 822                        | 333                        |  |  |

## Statistical analyses

No statistical analyses for this end point

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

|   |   |  |
|---|---|--|
| End point title   | Number of subjects with any 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. |   |  |
| End point type  | Secondary   |  |
| End point timeframe:  |   |  |
| From Day 0 up to study end (up to 5 years)  |   |  |

| End point values            | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|-----------------------------|----------------------------|----------------------------|--|--|
| Subject group type          | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed | 895                        | 450                        |  |  |
| Units: Subjects             | 129                        | 64                         |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with potential immune-mediated disorders(pIMDs)

|  |  |
|--|--|
| End point title  | Number of subjects with potential immune-mediated disorders(pIMDs) |
| End point description:   |  |
| Potential Immune-Mediated Disorders (pIMDs) were to be collected up to 5 years after first treatment administration or study withdrawal. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| From Day 0 up to study end (up to 5 years)   |  |

| End point values            | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|-----------------------------|----------------------------|----------------------------|--|--|
| Subject group type          | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed | 895                        | 450                        |  |  |
| Units: Subjects             | 33                         | 23                         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with abnormal haematological and biochemical parameters

|                 |  |
|-----------------|--|
| End point title | Number of subjects with abnormal haematological and biochemical parameters |
|-----------------|--|

End point description:

Laboratory abnormalities belong to hematological and biochemical parameters such as: alanine aminotransferase [ALT], asparatate aminostransferase [AST], alkaline phoshatase [AP], bilirubin [BIL], creatinine [CREA], hemoglobin [HGB], leukocytes [LEU], lymphopenia [LYMPH], neutrophils [NEU], platelets [PLA]. Parameter grades (Grade [G] 0, 1, 2, 3, 4, Unknown) were compared to each baseline parameter grade (G Unknown, 0, 1, 2, 3), as defined by the Common Terminology Criteria for Adverse Events (CTCAE), version 3.0 of August 9, 2006.

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

End point timeframe:

Within the 31-day (Days 0-30) post-treatment period

| End point values                   | MAGE-A3 (as treated) Group | Placebo (as treated) Group |  |  |
|------------------------------------|----------------------------|----------------------------|--|--|
| Subject group type                 | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed        | 894                        | 450                        |  |  |
| Units: Subjects                    |                            |                            |  |  |
| ALT, Unknown - G0 (N=894,450)      | 3                          | 2                          |  |  |
| ALT, Unknown - G1 (N=894,450)      | 1                          | 0                          |  |  |
| ALT, Unknown - G3 (N=894,450)      | 0                          | 0                          |  |  |
| ALT, Unknown - G4 (N=894,450)      | 0                          | 0                          |  |  |
| ALT, Unknown - Unknown (N=894,450) | 2                          | 0                          |  |  |
| ALT, G0 - G0 (N=894,450)           | 625                        | 337                        |  |  |
| ALT, G0 - G1 (N=894,450)           | 98                         | 30                         |  |  |
| ALT, G0 - G2 (N=894,450)           | 10                         | 4                          |  |  |
| ALT, G0 - G3 (N=894,450)           | 3                          | 4                          |  |  |
| ALT, G0 - G4 (N=894,450)           | 0                          | 0                          |  |  |
| ALT, G0 - Unknown (N=894,450)      | 36                         | 18                         |  |  |
| ALT, G1 - G0 (N=894,450)           | 45                         | 22                         |  |  |
| ALT, G1 - G1 (N=894,450)           | 49                         | 25                         |  |  |
| ALT, G1 - G2 (N=894,450)           | 14                         | 4                          |  |  |
| ALT, G1 - G3 (N=894,450)           | 1                          | 2                          |  |  |

|                                   |     |     |  |  |
|-----------------------------------|-----|-----|--|--|
| ALT, G1 - G4 (N=894,450)          | 0   | 0   |  |  |
| ALT, G1 - Unknown (N=894,450)     | 2   | 1   |  |  |
| ALT, G2 - G0 (N=894,450)          | 1   | 1   |  |  |
| ALT, G2 - G1 (N=894,450)          | 2   | 0   |  |  |
| ALT, G2 - G2 (N=894,450)          | 1   | 0   |  |  |
| ALT, G2 - G3 (N=894,450)          | 0   | 0   |  |  |
| ALT, G2 - G4 (N=894,450)          | 0   | 0   |  |  |
| ALT, G2 - Unknown (N=894,450)     | 0   | 0   |  |  |
| ALT, G3 - G0 (N=894,450)          | 0   | 0   |  |  |
| ALT, G3 - G1 (N=894,450)          | 0   | 0   |  |  |
| ALT, G3 - G2 (N=894,450)          | 0   | 0   |  |  |
| ALT, G3 - G3 (N=894,450)          | 0   | 0   |  |  |
| ALT, G3 - G4 (N=894,450)          | 0   | 0   |  |  |
| ALT, G3 - Unknown (N=894,450)     | 1   | 0   |  |  |
| ALT, Total - G0 (N=894,450)       | 674 | 362 |  |  |
| ALT, Total - G1 (N=894,450)       | 150 | 55  |  |  |
| ALT, Total - G2 (N=894,450)       | 25  | 8   |  |  |
| ALT, Total - G3 (N=894,450)       | 4   | 6   |  |  |
| ALT, Total - G4 (N=894,450)       | 0   | 0   |  |  |
| ALT, Total - Unknown (N=894,450)  | 41  | 19  |  |  |
| AST, G0 - G0 (N=894,450)          | 701 | 356 |  |  |
| AST, G0 - G1 (N=894,450)          | 88  | 37  |  |  |
| AST, G0 - G2 (N=894,450)          | 5   | 3   |  |  |
| AST, G0 - G3 (N=894,450)          | 3   | 4   |  |  |
| AST, G0 - G4 (N=894,450)          | 0   | 0   |  |  |
| AST, G0 - Unknown (N=894,450)     | 40  | 19  |  |  |
| AST, G1 - G0 (N=894,450)          | 24  | 15  |  |  |
| AST, G1 - G1 (N=894,450)          | 18  | 11  |  |  |
| AST, G1 - G2 (N=894,450)          | 3   | 1   |  |  |
| AST, G1 - G3 (N=894,450)          | 2   | 0   |  |  |
| AST, G1 - G4 (N=894,450)          | 0   | 0   |  |  |
| AST, G1 - Unknown (N=894,450)     | 1   | 1   |  |  |
| AST, G2 - G0 (N=894,450)          | 0   | 0   |  |  |
| AST, G2 - G1 (N=894,450)          | 0   | 0   |  |  |
| AST, G2 - G2 (N=894,450)          | 1   | 0   |  |  |
| AST, G2 - G3 (N=894,450)          | 0   | 0   |  |  |
| AST, G2 - G4 (N=894,450)          | 0   | 0   |  |  |
| AST, G2 - Unknown (N=894,450)     | 1   | 0   |  |  |
| AST, Total - G0 (N=894,450)       | 728 | 374 |  |  |
| AST, Total - G1 (N=894,450)       | 107 | 48  |  |  |
| AST, Total - G2 (N=894,450)       | 9   | 4   |  |  |
| AST, Total - G3 (N=894,450)       | 5   | 4   |  |  |
| AST, Total - G4 (N=894,450)       | 0   | 0   |  |  |
| AST, Total - Unknown (N=894,450)  | 45  | 20  |  |  |
| AP, Unknown - G0 (N=894,450)      | 9   | 6   |  |  |
| AP, Unknown - G1 (N=894,450)      | 0   | 1   |  |  |
| AP, Unknown - G2 (N=894,450)      | 1   | 0   |  |  |
| AP, Unknown - G3 (N=894,450)      | 0   | 0   |  |  |
| AP, Unknown - G4 (N=894,450)      | 0   | 0   |  |  |
| AP, Unknown - Unknown (N=894,450) | 2   | 0   |  |  |
| AP, G0 - G0 (N=894,450)           | 749 | 378 |  |  |
| AP, G0 - G1 (N=894,450)           | 56  | 18  |  |  |

|                                    |     |     |  |  |
|------------------------------------|-----|-----|--|--|
| AP, G0 - G2 (N=894,450)            | 3   | 4   |  |  |
| AP, G0 - G3 (N=894,450)            | 2   | 1   |  |  |
| AP, G0 - G4 (N=894,450)            | 0   | 0   |  |  |
| AP, G0 - Unknown (N=894,450)       | 38  | 18  |  |  |
| AP, G1 - G0 (N=894,450)            | 18  | 13  |  |  |
| AP, G1 - G1 (N=894,450)            | 14  | 9   |  |  |
| AP, G1 - G2 (N=894,450)            | 0   | 0   |  |  |
| AP, G1 - G3 (N=894,450)            | 0   | 0   |  |  |
| AP, G1 - G4 (N=894,450)            | 0   | 0   |  |  |
| AP, G1 - Unknown (N=894,450)       | 2   | 2   |  |  |
| AP, Total - G0 (N=894,450)         | 776 | 397 |  |  |
| AP, Total - G1 (N=894,450)         | 70  | 28  |  |  |
| AP, Total - G2 (N=894,450)         | 4   | 4   |  |  |
| AP, Total - G3 (N=894,450)         | 2   | 1   |  |  |
| AP, Total - G4 (N=894,450)         | 0   | 0   |  |  |
| AP, Total - Unknown (N=894,450)    | 42  | 20  |  |  |
| BIL, Unknown - G0 (N=894,450)      | 7   | 5   |  |  |
| BIL, Unknown - G1 (N=894,450)      | 1   | 0   |  |  |
| BIL, Unknown - G2 (N=894,450)      | 0   | 0   |  |  |
| BIL, Unknown - G3 (N=894,450)      | 0   | 0   |  |  |
| BIL, Unknown - G4 (N=894,450)      | 0   | 0   |  |  |
| BIL, Unknown - Unknown (N=894,450) | 1   | 1   |  |  |
| BIL, G0 - G0 (N=894,450)           | 771 | 383 |  |  |
| BIL, G0 - G1 (N=894,450)           | 33  | 21  |  |  |
| BIL, G0 - G2 (N=894,450)           | 3   | 2   |  |  |
| BIL, G0 - G3 (N=894,450)           | 0   | 1   |  |  |
| BIL, G0 - G4 (N=894,450)           | 0   | 0   |  |  |
| BIL, G0 - Unknown (N=894,450)      | 44  | 19  |  |  |
| BIL, G1 -G0 (N=894,450)            | 11  | 3   |  |  |
| BIL, G1 - G1 (N=894,450)           | 10  | 5   |  |  |
| BIL, G1 -G2 (N=894,450)            | 9   | 4   |  |  |
| BIL, G1 - G3 (N=894,450)           | 0   | 0   |  |  |
| BIL, G1 - G4 (N=894,450)           | 0   | 0   |  |  |
| BIL, G1 - Unknown (N=894,450)      | 3   | 2   |  |  |
| BIL, G2 - G0 (N=894,450)           | 0   | 0   |  |  |
| BIL, G2 - G1 (N=894,450)           | 0   | 2   |  |  |
| BIL, G2 - G2 (N=894,450)           | 0   | 2   |  |  |
| BIL, G2 - G3 (N=894,450)           | 0   | 0   |  |  |
| BIL, G2 - G4 (N=894,450)           | 0   | 0   |  |  |
| BIL, G2 - Unknown (N=894,450)      | 1   | 0   |  |  |
| BIL, Total - G0 (N=894,450)        | 789 | 391 |  |  |
| BIL, Total - G1 (N=894,450)        | 44  | 28  |  |  |
| BIL, Total - G2 (N=894,450)        | 12  | 8   |  |  |
| BIL, Total - G3 (N=894,450)        | 0   | 1   |  |  |
| BIL, Total - G4 (N=894,450)        | 0   | 0   |  |  |
| BIL, Total - Unknown (N=894,450)   | 49  | 22  |  |  |
| CREA, Unknown - G0 (N=894,450)     | 2   | 1   |  |  |
| CREA, Unknown - G1 (N=894,450)     | 0   | 0   |  |  |
| CREA, Unknown - G2 (N=894,450)     | 0   | 0   |  |  |
| CREA, Unknown - G3 (N=894,450)     | 0   | 0   |  |  |
| CREA, Unknown - G4 (N=894,450)     | 0   | 0   |  |  |

|                                     |     |     |  |  |
|-------------------------------------|-----|-----|--|--|
| CREA, Unknown - Unknown (N=894,450) | 1   | 0   |  |  |
| CREA, G0 - G0 (N=894,450)           | 789 | 391 |  |  |
| CREA, G0 - G1 (N=894,450)           | 31  | 19  |  |  |
| CREA, G0 - G2 (N=894,450)           | 0   | 1   |  |  |
| CREA, G0 - G3 (N=894,450)           | 0   | 1   |  |  |
| CREA, G0 - G4 (N=894,450)           | 0   | 0   |  |  |
| CREA, G0 - Unknown (N=894,450)      | 36  | 19  |  |  |
| CREA, G1 - G0 (N=894,450)           | 8   | 6   |  |  |
| CREA, G1 - G1 (N=894,450)           | 19  | 12  |  |  |
| CREA, G1 - G2 (N=894,450)           | 3   | 0   |  |  |
| CREA, G1 - G3 (N=894,450)           | 0   | 0   |  |  |
| CREA, G1 - G4 (N=894,450)           | 0   | 0   |  |  |
| CREA, G1 - Unknown (N=894,450)      | 4   | 0   |  |  |
| CREA, G2 - G0 (N=894,450)           | 0   | 0   |  |  |
| CREA, G2 - G1 (N=894,450)           | 0   | 0   |  |  |
| CREA, G2 - G2 (N=894,450)           | 1   | 0   |  |  |
| CREA, G2 - G3 (N=894,450)           | 0   | 0   |  |  |
| CREA, G2 - G4 (N=894,450)           | 0   | 0   |  |  |
| CREA, G2 - Unknown (N=894,450)      | 0   | 0   |  |  |
| CREA, Total - G0 (N=894,450)        | 799 | 398 |  |  |
| CREA, Total - G1 (N=894,450)        | 50  | 31  |  |  |
| CREA, Total - G2 (N=894,450)        | 4   | 1   |  |  |
| CREA, Total - G3 (N=894,450)        | 0   | 1   |  |  |
| CREA, Total - G4 (N=894,450)        | 0   | 0   |  |  |
| CREA, Total - Unknown (N=894,450)   | 41  | 19  |  |  |
| HGB, Unknown - G0 (N=894,450)       | 2   | 1   |  |  |
| HGB, Unknown - G1 (N=894,450)       | 1   | 0   |  |  |
| HGB, Unknown - G2 (N=894,450)       | 0   | 0   |  |  |
| HGB, Unknown - G3 (N=894,450)       | 0   | 0   |  |  |
| HGB, Unknown - G4 (N=894,450)       | 0   | 0   |  |  |
| HGB, Unknown - Unknown (N=894,450)  | 0   | 0   |  |  |
| HGB, G0 - G0 (N=894,450)            | 636 | 326 |  |  |
| HGB, G0 - G1 (N=894,450)            | 78  | 28  |  |  |
| HGB, G0 - G2 (N=894,450)            | 7   | 3   |  |  |
| HGB, G0 - G3 (N=894,450)            | 2   | 1   |  |  |
| HGB, G0 - G4 (N=894,450)            | 0   | 0   |  |  |
| HGB, G0 - Unknown (N=894,450)       | 35  | 17  |  |  |
| HGB, G1 - G0 (N=894,450)            | 39  | 27  |  |  |
| HGB, G1 - G1 (N=894,450)            | 77  | 41  |  |  |
| HGB, G1 - G2 (N=894,450)            | 7   | 2   |  |  |
| HGB, G1 - G3 (N=894,450)            | 1   | 0   |  |  |
| HGB, G1 - G4 (N=894,450)            | 1   | 0   |  |  |
| HGB, G1 - Unknown (N=894,450)       | 4   | 3   |  |  |
| HGB, G2 - G0 (N=894,450)            | 1   | 1   |  |  |
| HGB, G2 - G1 (N=894,450)            | 1   | 0   |  |  |
| HGB, G2 - G2 (N=894,450)            | 2   | 0   |  |  |
| HGB, G2 - G3 (N=894,450)            | 0   | 0   |  |  |
| HGB, G2 - G4 (N=894,450)            | 0   | 0   |  |  |
| HGB, G2 - Unknown (N=894,450)       | 0   | 0   |  |  |
| HGB, Total - G0 (N=894,450)         | 678 | 355 |  |  |
| HGB, Total - G1 (N=894,450)         | 157 | 69  |  |  |

|   |     |     |  |  |
|---|-----|-----|--|--|
| HGB, Total - G2 (N=894,450)             | 16  | 5   |  |  |
| HGB, Total - G3 (N=894,450)             | 3   | 1   |  |  |
| HGB, Total - G4 (N=894,450)             | 1   | 0   |  |  |
| HGB, Total - Unknown (N=894,450)        | 39  | 20  |  |  |
| LEU, Unknown - G0 (N=894,450)           | 2   | 1   |  |  |
| LEU, Unknown - G1 (N=894,450)           | 1   | 0   |  |  |
| LEU, Unknown - G2 (N=894,450)           | 0   | 0   |  |  |
| LEU, Unknown - G3 (N=894,450)           | 0   | 0   |  |  |
| LEU, Unknown - G4 (N=894,450)           | 0   | 0   |  |  |
| LEU, Unknown - Unknown (N=894,450)      | 0   | 0   |  |  |
| LEU, G0 - G0 (N=894,450)                | 762 | 382 |  |  |
| LEU, G0 - G1 (N=894,450)                | 53  | 31  |  |  |
| LEU, G0 - G2 (N=894,450)                | 4   | 2   |  |  |
| LEU, G0 - G3 (N=894,450)                | 0   | 0   |  |  |
| LEU, G0 - G4 (N=894,450)                | 2   | 0   |  |  |
| LEU, G0 - Unknown (N=894,450)           | 39  | 18  |  |  |
| LEU, G1 - G0 (N=894,450)                | 13  | 8   |  |  |
| LEU, G1 - G1 (N=894,450)                | 15  | 6   |  |  |
| LEU, G1 - G2 (N=894,450)                | 1   | 1   |  |  |
| LEU, G1 - G3 (N=894,450)                | 0   | 0   |  |  |
| LEU, G1 - G4 (N=894,450)                | 0   | 0   |  |  |
| LEU, G1 - Unknown (N=894,450)           | 0   | 1   |  |  |
| LEU, G2 - G0 (N=894,450)                | 0   | 0   |  |  |
| LEU, G2 - G1 (N=894,450)                | 1   | 0   |  |  |
| LEU, G2 - G2 (N=894,450)                | 0   | 0   |  |  |
| LEU, G2 - G3 (N=894,450)                | 1   | 0   |  |  |
| LEU, G2 - G4 (N=894,450)                | 0   | 0   |  |  |
| LEU, G2 - Unknown (N=894,450)           | 0   | 0   |  |  |
| LEU, Total - G0 (N=894,450)             | 777 | 391 |  |  |
| LEU, Total - G1 (N=894,450)             | 70  | 37  |  |  |
| LEU, Total - G2 (N=894,450)             | 5   | 3   |  |  |
| LEU, Total - G3 (N=894,450)             | 1   | 0   |  |  |
| LEU, Total - G4 (N=894,450)             | 2   | 0   |  |  |
| LEU, Total - Unknown (N=894,450)        | 39  | 19  |  |  |
| LYMPH, Unknown - G0 (N=894,450)         | 8   | 1   |  |  |
| LYMPH, Unknown - G1 (N=894,450)         | 2   | 2   |  |  |
| LYMPH, Unknown - G2 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, Unknown - G3 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, Unknown - G4 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, Unknown - Unknown<br>(N=894,450) | 0   | 0   |  |  |
| LYMPH, G0 - G0 (N=894,450)              | 633 | 303 |  |  |
| LYMPH, G0 - G1 (N=894,450)              | 93  | 57  |  |  |
| LYMPH, G0 - G2 (N=894,450)              | 17  | 8   |  |  |
| LYMPH, G0 - G3 (N=894,450)              | 4   | 0   |  |  |
| LYMPH, G0 - G4 (N=894,450)              | 0   | 0   |  |  |
| LYMPH, G0 - Unknown (N=894,450)         | 38  | 22  |  |  |
| LYMPH, G1 - G0 (N=894,450)              | 29  | 9   |  |  |
| LYMPH, G1 - G1 (N=894,450)              | 49  | 37  |  |  |
| LYMPH, G1 - G2 (N=894,450)              | 4   | 6   |  |  |
| LYMPH, G1 - G3 (N=894,450)              | 4   | 0   |  |  |
| LYMPH, G1 - G4 (N=894,450)              | 0   | 0   |  |  |

|                                    |     |     |  |  |
|------------------------------------|-----|-----|--|--|
| LYMPH, G1 - Unknown (N=894,450)    | 4   | 0   |  |  |
| LYMPH, G2 - G0 (N=894,450)         | 1   | 1   |  |  |
| LYMPH, G2 - G1 (N=894,450)         | 4   | 1   |  |  |
| LYMPH, G2 - G2 (N=894,450)         | 2   | 2   |  |  |
| LYMPH, G2 - G3 (N=894,450)         | 2   | 0   |  |  |
| LYMPH, G2 - G4 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, G2 - Unknown (N=894,450)    | 0   | 0   |  |  |
| LYMPH, G3 - G0 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, G3 - G1 (N=894,450)         | 0   | 1   |  |  |
| LYMPH, G3 - G2 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, G3 - G3 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, G3 - G4 (N=894,450)         | 0   | 0   |  |  |
| LYMPH, G3 - Unknown (N=894,450)    | 0   | 0   |  |  |
| LYMPH, Total - G0 (N=894,450)      | 671 | 314 |  |  |
| LYMPH, Total - G1 (N=894,450)      | 148 | 98  |  |  |
| LYMPH, Total - G2 (N=894,450)      | 23  | 16  |  |  |
| LYMPH, Total - G3 (N=894,450)      | 10  | 0   |  |  |
| LYMPH, Total - G4 (N=894,450)      | 0   | 0   |  |  |
| LYMPH, Total - Unknown (N=894,450) | 42  | 22  |  |  |
| NEU, Unknown - G0 (N=894,450)      | 6   | 1   |  |  |
| NEU, Unknown - G1 (N=894,450)      | 0   | 1   |  |  |
| NEU, Unknown - G2 (N=894,450)      | 0   | 0   |  |  |
| NEU, Unknown - G3 (N=894,450)      | 0   | 0   |  |  |
| NEU, Unknown - G4 (N=894,450)      | 0   | 0   |  |  |
| NEU, Unknown - Unknown (N=894,450) | 0   | 0   |  |  |
| NEU, G0 - G0 (N=894,450)           | 781 | 393 |  |  |
| NEU, G0 - G1 (N=894,450)           | 39  | 16  |  |  |
| NEU, G0 - G2 (N=894,450)           | 9   | 2   |  |  |
| NEU, G0 - G3 (N=894,450)           | 0   | 0   |  |  |
| NEU, G0 - G4 (N=894,450)           | 1   | 0   |  |  |
| NEU, G0 - Unknown (N=894,450)      | 43  | 22  |  |  |
| NEU, G1 - G0 (N=894,450)           | 7   | 10  |  |  |
| NEU, G1 - G1 (N=894,450)           | 6   | 3   |  |  |
| NEU, G1 - G2 (N=894,450)           | 1   | 2   |  |  |
| NEU, G1 - G3 (N=894,450)           | 0   | 0   |  |  |
| NEU, G1 - G4 (N=894,450)           | 0   | 0   |  |  |
| NEU, G1 - Unknown (N=894,450)      | 0   | 0   |  |  |
| NEU, G2 - G0 (N=894,450)           | 0   | 0   |  |  |
| NEU, G2 - G1 (N=894,450)           | 1   | 0   |  |  |
| NEU, G2 - G2 (N=894,450)           | 0   | 0   |  |  |
| NEU, G2 - G3 (N=894,450)           | 0   | 0   |  |  |
| NEU, G2 - G4 (N=894,450)           | 0   | 0   |  |  |
| NEU, G2 - Unknown (N=894,450)      | 0   | 0   |  |  |
| NEU, Total - G0 (N=894,450)        | 794 | 404 |  |  |
| NEU, Total - G1 (N=894,450)        | 46  | 20  |  |  |
| NEU, Total - G2 (N=894,450)        | 10  | 4   |  |  |
| NEU, Total - G3 (N=894,450)        | 0   | 0   |  |  |
| NEU, Total - G4 (N=894,450)        | 1   | 0   |  |  |
| NEU, Total - Unknown (N=894,450)   | 43  | 22  |  |  |
| PLA, Unknown - G0 (N=894,450)      | 4   | 1   |  |  |
| PLA, Unknown - G1 (N=894,450)      | 0   | 0   |  |  |
| PLA, Unknown - G2 (N=894,450)      | 0   | 0   |  |  |

|                                    |     |     |  |  |
|------------------------------------|-----|-----|--|--|
| PLA, Unknown - G3 (N=894,450)      | 0   | 0   |  |  |
| PLA, Unknown - G4 (N=894,450)      | 0   | 0   |  |  |
| PLA, Unknown - Unknown (N=894,450) | 0   | 0   |  |  |
| PLA, G0 - G0 (N=894,450)           | 796 | 390 |  |  |
| PLA, G0 - G1 (N=894,450)           | 34  | 25  |  |  |
| PLA, G0 - G2 (N=894,450)           | 0   | 1   |  |  |
| PLA, G0 - G3 (N=894,450)           | 0   | 0   |  |  |
| PLA, G0 - G4 (N=894,450)           | 1   | 3   |  |  |
| PLA, G0 - Unknown (N=894,450)      | 36  | 17  |  |  |
| PLA, G1 - G0 (N=894,450)           | 4   | 1   |  |  |
| PLA, G1 - G1 (N=894,450)           | 15  | 10  |  |  |
| PLA, G1 - G2 (N=894,450)           | 1   | 0   |  |  |
| PLA, G1 - G3 (N=894,450)           | 0   | 0   |  |  |
| PLA, G1 - G4 (N=894,450)           | 0   | 0   |  |  |
| PLA, G1 - Unknown (N=894,450)      | 3   | 2   |  |  |
| PLA, Total - G0 (N=894,450)        | 804 | 392 |  |  |
| PLA, Total - G1 (N=894,450)        | 49  | 35  |  |  |
| PLA, Total - G2 (N=894,450)        | 1   | 1   |  |  |
| PLA, Total - G3 (N=894,450)        | 0   | 0   |  |  |
| PLA, Total - G4 (N=894,450)        | 1   | 3   |  |  |
| PLA, Total - Unknown (N=894,450)   | 39  | 19  |  |  |
| AST, Unknown - G0 (N=894, 450)     | 3   | 3   |  |  |
| AST, Unknown - G1 (N=894,450)      | 1   | 0   |  |  |
| AST, Unknown - G2 (N=894,450)      | 0   | 0   |  |  |
| AST, Unknown - G3 (N=894,450)      | 0   | 0   |  |  |
| AST, Unknown - G4 (N=894,450)      | 0   | 0   |  |  |
| AST, Unknown - Unknown (N=894,450) | 3   | 0   |  |  |
| ALT, Unknown - G2 (N=894,450)      | 0   | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs): Within the 31-day (Days 0-30) follow-up period after treatment. Serious Adverse Events: from Day 0 up to study end (up to 5 years).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Placebo (as treated) Group |
|-----------------------|----------------------------|

Reporting group description:

Patients who received up to 13 doses of placebo.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | MAGE-A3 (as treated) Group |
|-----------------------|----------------------------|

Reporting group description:

Patients who received up to 13 doses of recMAGE-A3 + AS15 ASCI.

| Serious adverse events  | Placebo (as treated) Group | MAGE-A3 (as treated) Group |  |
|---|----------------------------|----------------------------|--|
| Total subjects affected by serious adverse events                   |                            |                            |  |
| subjects affected / exposed   | 64 / 450 (14.22%)          | 129 / 895 (14.41%)         |  |
| number of deaths (all causes)                                       | 1                          | 5                          |  |
| number of deaths resulting from adverse events                      | 0                          | 0                          |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                            |                            |  |
| Basal cell carcinoma  |                            |                            |  |
| subjects affected / exposed   | 13 / 450 (2.89%)           | 25 / 895 (2.79%)           |  |
| occurrences causally related to treatment / all                     | 0 / 14                     | 0 / 34                     |  |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                      |  |
| Bladder transitional cell carcinoma                                 |                            |                            |  |
| subjects affected / exposed   | 1 / 450 (0.22%)            | 0 / 895 (0.00%)            |  |
| occurrences causally related to treatment / all                     | 0 / 1                      | 0 / 0                      |  |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                      |  |
| Clear cell renal cell carcinoma                                     |                            |                            |  |
| subjects affected / exposed   | 0 / 450 (0.00%)            | 1 / 895 (0.11%)            |  |
| occurrences causally related to treatment / all                     | 0 / 0                      | 0 / 1                      |  |
| deaths causally related to treatment / all                          | 0 / 0                      | 0 / 0                      |  |
| Endometrial adenocarcinoma  |                            |                            |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Focal nodular hyperplasia                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Glioblastoma                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Invasive lobular breast carcinoma               |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lentigo maligna                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphoma  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malignant melanoma                              |                 |                 |  |
| subjects affected / exposed                     | 3 / 450 (0.67%) | 9 / 895 (1.01%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 9           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malignant melanoma in situ                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Malignant melanoma stage i                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Non-hodgkin's lymphoma                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Papillary thyroid cancer                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polycythaemia vera                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Porocarcinoma                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostate cancer                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostatic adenoma                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal cell carcinoma                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Squamous cell carcinoma of skin                 |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                      | 3 / 450 (0.67%) | 6 / 895 (0.67%) |  |
| occurrences causally related to treatment / all  | 0 / 3           | 0 / 9           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Superficial spreading melanoma stage unspecified |                 |                 |  |
| subjects affected / exposed                      | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Thyroid cancer                                   |                 |                 |  |
| subjects affected / exposed                      | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Urinary tract neoplasm                           |                 |                 |  |
| subjects affected / exposed                      | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Uterine leiomyoma                                |                 |                 |  |
| subjects affected / exposed                      | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Vascular disorders                               |                 |                 |  |
| Aortic aneurysm                                  |                 |                 |  |
| subjects affected / exposed                      | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Deep vein thrombosis                             |                 |                 |  |
| subjects affected / exposed                      | 1 / 450 (0.22%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all  | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Haematoma  |                 |                 |  |
| subjects affected / exposed                      | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           |  |
| Hypertension                                     |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Intermittent claudication                            |                 |                 |  |
| subjects affected / exposed                          | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Lymphocele   |                 |                 |  |
| subjects affected / exposed                          | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Lymphoedema  |                 |                 |  |
| subjects affected / exposed                          | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Peripheral arterial occlusive disease                |                 |                 |  |
| subjects affected / exposed                          | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Thrombosis   |                 |                 |  |
| subjects affected / exposed                          | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Chest pain   |                 |                 |  |
| subjects affected / exposed                          | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Device dislocation                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Impaired healing                                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oedema peripheral                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pyrexia   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Immune system disorders                         |                 |                 |  |
| Sarcoidosis                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Reproductive system and breast disorders        |                 |                 |  |
| Ovarian cyst                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Chronic obstructive pulmonary disease           |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 3 / 895 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Organising pneumonia                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pleural effusion                                |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary oedema                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Respiratory failure                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vocal cord polyp                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                           |                 |                 |  |
| Major depression                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mental disorder                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Mental status changes                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Suicide attempt                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                           | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| <b>Investigations</b>                                 |                 |                 |  |
| Blood alkaline phosphatase increased                  |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| Gamma-glutamyltransferase increased                   |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| Transaminases increased                               |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| <b>Injury, poisoning and procedural complications</b> |                 |                 |  |
| Asbestosis  |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| Contrast media reaction                               |                 |                 |  |
| subjects affected / exposed                           | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| Electric shock  |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |
| Femur fracture  |                 |                 |  |
| subjects affected / exposed                           | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Humerus fracture                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Patella fracture                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Periprosthetic fracture                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Post procedural fistula                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Post procedural haematoma                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Postoperative hernia                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Radius fracture                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tendon rupture                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Tibia fracture                                  |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |
| Angina pectoris                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrioventricular block                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Atrioventricular block second degree            |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bradycardia                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac arrest                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Cardiac failure                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Cardiac failure acute                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Coronary artery disease                         |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Intracardiac thrombus                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ischaemic cardiomyopathy                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Left ventricular failure                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| 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 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Myocardial ischaemia                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Cerebral haemorrhage                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Cerebrovascular accident                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Meningism                                       |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Multiple sclerosis                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polyneuropathy                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Psychomotor skills impaired                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Subarachnoid haemorrhage                        |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Blood and lymphatic system disorders            |                 |                 |  |
| Anaemia   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Disseminated intravascular coagulation          |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Haemolytic uraemic syndrome                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Leukopenia                                      |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphadenitis                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphadenopathy                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neutropenia                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombocytopenia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Thrombocytopenic purpura                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ear and labyrinth disorders                     |                 |                 |  |
| Vertigo   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vertigo positional                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Eye disorders                                   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Retinal detachment                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinal vascular thrombosis                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Retinopathy                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vision blurred                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Abdominal pain                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Diverticulum                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dysphagia                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Ileal perforation                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Inguinal hernia                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Large intestine perforation                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nausea  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pancreatitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Umbilical hernia                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Vomiting  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatobiliary disorders                         |                 |                 |  |
| Autoimmune hepatitis                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bile duct obstruction                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bile duct stone                                 |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholecystitis chronic                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cholelithiasis                                  |                 |                 |  |
| subjects affected / exposed                     | 2 / 450 (0.44%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatic steatosis                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hepatitis acute                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hydrocholecystis                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Jaundice  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Skin and subcutaneous tissue disorders          |                 |                 |  |
| Actinic elastosis                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Dermal cyst                                     |                 |                 |  |



|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Bladder neck sclerosis                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nephrolithiasis                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Renal failure                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary retention                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| 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 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Basedow's disease                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphocytic hypophysitis                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Polyglandular autoimmune syndrome               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| type ii   |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lumbar spinal stenosis                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Neck pain                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Osteoarthritis                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pain in extremity                               |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Synovial cyst                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Abscess limb                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Appendicitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis                                      |                 |                 |  |
| subjects affected / exposed                     | 5 / 450 (1.11%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cellulitis enterococcal                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cystitis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endocarditis bacterial                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Erysipelas                                      |                 |                 |  |
| subjects affected / exposed                     | 5 / 450 (1.11%) | 7 / 895 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 1 / 9           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Escherichia urinary tract infection             |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| H1n1 influenza                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Localised infection                             |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung infection                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymph node abscess                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lymphangitis                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pharyngitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pilonidal cyst                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia haemophilus                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Post procedural infection                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Postoperative abscess                           |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Prostatitis Escherichia coli                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Sepsis  |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 2 / 895 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Streptococcal infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Subcutaneous abscess                            |                 |                 |  |
| subjects affected / exposed                     | 1 / 450 (0.22%) | 0 / 895 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urinary tract infection                         |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Urosepsis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Wound infection                                 |                 |                 |  |
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Metabolism and nutrition disorders              |                 |                 |  |
| Dehydration                                     |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 450 (0.00%) | 1 / 895 (0.11%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Placebo (as treated)<br>Group | MAGE-A3 (as<br>treated) Group |  |
|---|-------------------------------|-------------------------------|--|
| Total subjects affected by non-serious adverse events |                               |                               |  |
| subjects affected / exposed                           | 327 / 450 (72.67%)            | 819 / 895 (91.51%)            |  |
| Nervous system disorders                              |                               |                               |  |
| Headache  |                               |                               |  |
| subjects affected / exposed                           | 55 / 450 (12.22%)             | 205 / 895 (22.91%)            |  |
| occurrences (all)                                     | 128                           | 550                           |  |
| General disorders and administration site conditions  |                               |                               |  |
| Asthenia  |                               |                               |  |
| subjects affected / exposed                           | 46 / 450 (10.22%)             | 149 / 895 (16.65%)            |  |
| occurrences (all)                                     | 68                            | 354                           |  |
| Chills  |                               |                               |  |
| subjects affected / exposed                           | 15 / 450 (3.33%)              | 179 / 895 (20.00%)            |  |
| occurrences (all)                                     | 23                            | 432                           |  |
| Fatigue   |                               |                               |  |
| subjects affected / exposed                           | 63 / 450 (14.00%)             | 210 / 895 (23.46%)            |  |
| occurrences (all)                                     | 116                           | 490                           |  |
| Influenza like illness                                |                               |                               |  |
| subjects affected / exposed                           | 30 / 450 (6.67%)              | 261 / 895 (29.16%)            |  |
| occurrences (all)                                     | 46                            | 902                           |  |
| Injection site erythema                               |                               |                               |  |
| subjects affected / exposed                           | 3 / 450 (0.67%)               | 90 / 895 (10.06%)             |  |
| occurrences (all)                                     | 3                             | 241                           |  |
| Injection site oedema                                 |                               |                               |  |
| subjects affected / exposed                           | 3 / 450 (0.67%)               | 48 / 895 (5.36%)              |  |
| occurrences (all)                                     | 5                             | 134                           |  |
| Injection site pain                                   |                               |                               |  |
| subjects affected / exposed                           | 22 / 450 (4.89%)              | 325 / 895 (36.31%)            |  |
| occurrences (all)                                     | 37                            | 1057                          |  |

|   |                        |                            |  |
|---|------------------------|----------------------------|--|
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all) | 6 / 450 (1.33%)<br>9   | 160 / 895 (17.88%)<br>500  |  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                    | 19 / 450 (4.22%)<br>26 | 191 / 895 (21.34%)<br>480  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                 | 35 / 450 (7.78%)<br>44 | 380 / 895 (42.46%)<br>1240 |  |
| Gastrointestinal disorders  |                        |                            |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)               | 19 / 450 (4.22%)<br>26 | 46 / 895 (5.14%)<br>61     |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                  | 32 / 450 (7.11%)<br>43 | 123 / 895 (13.74%)<br>266  |  |
| Skin and subcutaneous tissue disorders                                      |                        |                            |  |
| Erythema<br>subjects affected / exposed<br>occurrences (all)                | 10 / 450 (2.22%)<br>10 | 138 / 895 (15.42%)<br>297  |  |
| Musculoskeletal and connective tissue disorders                             |                        |                            |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)              | 31 / 450 (6.89%)<br>43 | 84 / 895 (9.39%)<br>165    |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                 | 23 / 450 (5.11%)<br>39 | 188 / 895 (21.01%)<br>456  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)       | 26 / 450 (5.78%)<br>28 | 115 / 895 (12.85%)<br>207  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment  |
|---------------|--|
| 22 April 2014 | Immune related gene signatures have been recently reported as having a possible prognostic value in melanoma [Messina, 2012; Sivendran, 2014]. Similarly, a prognostic gene signature has been identified in the training set (Refer to Figure 4 and Section 10.3) of this study. As this prognostic gene signature is independent from other clinical covariates it will also be included as an additional covariate in the Cox model for the primary analyses in the gene signature sub-group (test set).<br>Other minor corrections have been made. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date              | Interruption  | Restart date |
|-------------------|---|--------------|
| 08 September 2015 | The study was terminated early following assessment of the two co-primary endpoints showed the lack of efficacy of the study product. | -            |

Notes:

### Limitations and caveats

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

The study was terminated early following assessment of the two co-primary endpoints showed the lack of efficacy of the study product.

Notes: