



Clinical trial results:

An open, single-arm trial to assess the clinical activity of recMAGE-A3 + AS15 in patients with unresectable MAGE-A3-positive metastatic cutaneous melanoma

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2008-004007-64 |
| Trial protocol | DE IE FR ES IT FI |
| Global end of trial date | 16 September 2015 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 24 March 2016 |
| First version publication date | 24 March 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 111476 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00942162 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 01 April 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 April 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 September 2015 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical activity of the MAGE-A3 ASCI study product in terms of the 1-year overall survival rate (OSR) in patients with MAGE-A3-positive, unresectable stage III or stage IV M1a melanoma tumors presenting the predictive GS.

Protection of trial subjects:

The patients will be observed closely for at least 30 minutes following the administration of treatments, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 14 August 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Poland: 11 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | France: 24 |
| Country: Number of subjects enrolled | Germany: 29 |
| Country: Number of subjects enrolled | Ireland: 4 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Russian Federation: 6 |
| Country: Number of subjects enrolled | United States: 24 |
| Worldwide total number of subjects | 125 |
| EEA total number of subjects | 95 |

Notes:

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) | 60 |
| From 65 to 84 years | 65 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 125 |
| Number of subjects completed | 123 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--------------------------------|
| Reason: Number of subjects | no study treatment received: 2 |
|----------------------------|--------------------------------|

Period 1

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

Arms

| | |
|-----------|---------------|
| Arm title | MAGE-A3 Group |
|-----------|---------------|

Arm description:

Patients planned to receive intramuscularly up to 24 doses of MAGE-A3 ASCI (the study product), in 4 cycles.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Immunotherapeutic GSK2132231A |
| Investigational medicinal product code | |
| Other name | recMAGE-A3 recombinant protein + immunological Adjuvant System |
| Pharmaceutical forms | Powder and suspension for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

6 administrations in Cycle 1, at 2-week intervals (Weeks 0, 2, 4, 6, 8 and 10); 6 administrations in Cycle 2, at 3-week intervals (Weeks 14, 17, 20, 23, 26 and 29); 4 administrations in Cycle 3 at 6-week intervals (Weeks 33, 39, 45 and 51) and 4 administrations in Cycle 4 at 3-months (12-weeks) intervals, followed by 4 further administrations at 6-months (24-weeks) intervals at Months 15, 18, 21, 24, 30, 36, 42, and 48.

| Number of subjects in period 1 ^[1] | MAGE-A3 Group |
|---|---------------|
| Started | 123 |
| Completed | 1 |
| Not completed | 122 |
| Consent withdrawn by subject | 9 |
| Death | 80 |

| | |
|-------------------|----|
| Unspecified | 29 |
| Lost to follow-up | 4 |

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: While 125 subjects were enrolled, only 123 started the study, as 2 subjects did not receive treatment and were excluded.

Baseline characteristics

Reporting groups

| | |
|--|---------------|
| Reporting group title | MAGE-A3 Group |
| Reporting group description: Patients planned to receive intramuscularly up to 24 doses of MAGE-A3 ASCI (the study product), in 4 cycles. | |

| Reporting group values | MAGE-A3 Group | Total | |
|---|---------------|-------|--|
| Number of subjects | 123 | 123 | |
| Age categorical Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous Units: years | | | |
| arithmetic mean | 64.9 | | |
| standard deviation | ± 13.45 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 65 | 65 | |
| Male | 58 | 58 | |

Subject analysis sets

| | |
|----------------------------|--------------------|
| Subject analysis set title | GS+ Group |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

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

Subject analysis set description:

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 | Unknown GS Group |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Subset of patients with unknown status as regards GS signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as

| Reporting group values | GS+ Group | GS- Group | Unknown GS Group |
|--|-----------|-----------|------------------|
| Number of subjects | 71 | 50 | 2 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 66.9 | 62.1 | 60.5 |
| standard deviation | ± 13.9 | ± 12.6 | ± 6.36 |
| Gender categorical Units: Subjects | | | |
| Female | 42 | 23 | 0 |
| Male | 29 | 27 | 2 |

End points

End points reporting groups

| | |
|--|--------------------|
| Reporting group title | MAGE-A3 Group |
| Reporting group description: Patients planned to receive intramuscularly up to 24 doses of MAGE-A3 ASCI (the study product), in 4 cycles. | |
| Subject analysis set title | GS+ Group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: 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- Group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: 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 | Unknown GS Group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subset of patients with unknown status as regards GS 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. | |

Primary: One-year overall survival rate (OSR) estimated by complete case method

| | |
|---|---|
| End point title | One-year overall survival rate (OSR) estimated by complete case method ^[1] |
| End point description: The 1-year overall survival rate (OSR) in the GS+ Population would be above 50% (target = 71%), a proportion which was reported together with its 95% confidence interval (CI). Maximum 1-year OSR of any currently available treatment in the MAGE-A3-positive population = 50% (P0). This median OS of 12 months is based on the observed median OS for MAGE-A3-positive patients, whose tumor did not present the predictive GS. The target 1-year OSR for patients presenting the predictive GS = 71% (P1). This corresponds to a median OS of 24 months when assuming an exponential distribution of OS. | |
| End point type | Primary |
| End point timeframe: Study period. | |

Notes:

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

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | GS+ Group | GS- Group | Unknown GS Group | |
|----------------------------------|------------------------|------------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 65 | 48 | 2 | |
| Units: Rate | | | | |
| number (confidence interval 95%) | | | | |
| OSR | 83.08 (71.73 to 91.24) | 83.33 (69.78 to 92.52) | 100 (15.81 to 100) | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients reported with serious adverse events (SAEs)

| | |
|-----------------|---|
| End point title | Number of patients reported with serious adverse events (SAEs) ^[2] |
|-----------------|---|

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. Events which were part of the natural course of the disease under study (i.e., disease progression, recurrence) were captured as part of the clinical activity outcome variables in this study; therefore these did not need to be reported as SAEs. Progression/recurrence of the tumor in a patient was recorded as part of the clinical assessment data collection, and deaths due to progressive disease was recorded on a specific form, but not as an SAE. However, if the investigator considered that there was a causal relationship between treatment or protocol design/procedures and the disease progression/recurrence, then the event was reported as an SAE. Any new primary cancer (non-related to the cancer under study) was reported as an SAE.

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

End point timeframe:

During the entire study period.

Notes:

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

Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| Any SAEs | 19 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with diseases characteristics by GS

| | |
|-----------------|--|
| End point title | Number of patients with diseases characteristics by GS |
|-----------------|--|

End point description:

Cancer staging (characteristics and categories) as by the categorization by the AJCC Cancer Staging Manual 2002.

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

End point timeframe:

Study period.

| End point values | GS+ Group | GS- Group | Unknown GS Group | |
|-----------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 71 | 50 | 2 | |
| Units: Patients | | | | |
| OSR STAGE IIIA | 0 | 0 | 0 | |
| OSR STAGE IIIB | 11 | 4 | 1 | |
| OSR STAGE IIIC | 21 | 19 | 1 | |
| OSR STAGE IV | 39 | 27 | 0 | |
| OSR STAGE MC | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) by GS

| | |
|--|---------------------------------------|
| End point title | Progression-free survival (PFS) by GS |
| End point description: | |
| From study start to study end, each patient being censored out of the analysis at 1st report of disease progression or death. PFS was defined and calculated as the time from first treatment to either the first progression of the disease or the date of death, whichever occurred first. In case a patient went off protocol treatment, the date of first documented progression (if applicable) was to be used as date of progression. Patients still alive with no evidence of disease progression at the time of their last visit or for whom date of first documented progression was not applicable, were censored at the time of the last examination. PFS analysis was performed using the non-parametric Kaplan-Meier method. "-9999" & "9999" as results when about the Unknown GS Group are placeholder values for confidence interval results being not applicable/missing. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 24 months period. | |

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | |
|----------------------------------|------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 123 | 71 | 50 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| PFS | 2.8 (2.8 to 2.8) | 2.8 (2.8 to 2.9) | 2.8 (2.5 to 2.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS rate

| | |
|--|-----------|
| End point title | PFS rate |
| End point description: PFS was defined as the time from the date of registration of the patient to either the date of disease progression or the date of death (for whatever reason), whichever comes first. Patients alive and without disease progression were censored at the date of their last tumor evaluation. | |
| End point type | Secondary |
| End point timeframe: At 6, 12, and 24 months. | |

| End point values | GS+ Group | GS- Group | | |
|----------------------------------|-----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 71 | 50 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| PFS 6M [71;50] | 13.53 (6.71 to 22.75) | 5 (1 to 14.22) | | |
| PFS 12M [71;50] | 6.02 (1.95 to 13.43) | 5 (1 to 14.22) | | |
| PFS 24M [71;50] | 1.5 (0.13 to 7.12) | 5 (1 to 14.22) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) by GS

| | |
|---|-----------------------------|
| End point title | Overall survival (OS) by GS |
| End point description: OS was defined as defined as the time from registration of the patient until death, with patients alive at the time of analysis censored at the time of the last contact. | |
| End point type | Secondary |
| End point timeframe: During the 24 months period. | |

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | |
|----------------------------------|---------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 123 | 71 | 50 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| OS | 23.9 (19.2 to 28.2) | 20.6 (16.1 to 28.2) | 25.8 (18.4 to 35.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to treatment failure (TTF) by GS

| | |
|-----------------|---------------------------------------|
| End point title | Time to treatment failure (TTF) by GS |
|-----------------|---------------------------------------|

End point description:

The TTF was defined as the time from registration of the patient until the date of the last treatment administration, irrespective of the reason for study treatment discontinuation.

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

End point timeframe:

During the 24 months period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | |
|----------------------------------|------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 123 | 71 | 50 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| TTF | 2.5 (2.4 to 4.1) | 2.7 (2.4 to 5.4) | 2.4 (2.3 to 2.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response (BOR) by GS

| | |
|-----------------|-----------------------------------|
| End point title | Best overall response (BOR) by GS |
|-----------------|-----------------------------------|

End point description:

The best overall response was the best response recorded from the start of the treatment until disease progression/recurrence, except for confirmed objective response, which was reported as BOR independently of its time of occurrence.

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

End point timeframe:

During the 24 months period.

| End point values | GS+ Group | GS- Group | Unknown GS Group | |
|-----------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 71 | 50 | 2 | |
| Units: Patients | | | | |
| CR | 0 | 1 | 0 | |
| PR | 3 | 0 | 0 | |
| SD | 11 | 4 | 0 | |
| SD/PR | 3 | 0 | 0 | |
| PD | 51 | 44 | 2 | |
| NE | 3 | 1 | 0 | |
| Missing | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (CR or PR) by GS

| | |
|---|---------------------------------------|
| End point title | Duration of response (CR or PR) by GS |
| End point description: | |
| Duration of response was measured from the time when the measurement criteria for CR/PR (whichever was recorded first) were met until the first date that recurrent or PD was objectively documented (taking as reference for PD the smallest measurements recorded since the treatment started). | |
| Note: As there was only one patient analysed in the GS- Subgroup, the median duration of response was not calculated for this latter subgroup. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 24 months period. | |

| End point values | MAGE-A3 Group | GS+ Group | | |
|----------------------------------|------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| CR/PR | 8.3 (1.9 to 8.3) | 6.9 (1.9 to 9.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of stable disease (SD), or Time-to-Progression (TTP) by GS

| | |
|-----------------|---|
| End point title | Duration of stable disease (SD), or Time-to-Progression (TTP) by GS |
|-----------------|---|

End point description:

The duration of stable disease (SD), or TTP, was tabulated for patients whose best response was SD. The minimal time interval required between 2 measurements for determination of SD was 12 weeks.

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

End point timeframe:

During the 24 months period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | |
|----------------------------------|------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 15 | 11 | 4 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| SD/TTP | 5.4 (5.1 to 9.4) | 5.4 (4.1 to 9.4) | 5.4 (5.1 to 25) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted patients for anti-MAGE-A3

| | |
|-----------------|---|
| End point title | Number of seroconverted patients for anti-MAGE-A3 |
|-----------------|---|

End point description:

Seroconversion was defined as a concentration of antibodies assessed that was greater than the cut-off value for a patient whose concentration of such antibodies was below the cut-off level before the initiation of treatment. Seroconverted patients were those patients with anti-MAGE-A3 antibody concentrations ≥ 27 .

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

End point timeframe:

Study period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|---------------------------------------|-----------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 52 | 34 | 1 |
| Units: Patients | | | | |
| Anti-MAGE-A3, PRE [N=87;52;34;1] | 7 | 4 | 3 | 0 |
| Anti-MAGE-A3, PII(W4) [N=62;39;22;1] | 60 | 37 | 22 | 1 |
| Anti-MAGE-A3, PVI(W12) [N=52;34;17;1] | 52 | 34 | 17 | 1 |
| Anti-MAGE-A3, PXII(W31) [N=11;5;6;0] | 11 | 5 | 6 | 0 |
| Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0] | 6 | 3 | 3 | 0 |
| Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0] | 3 | 2 | 1 | 0 |
| Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0] | 4 | 4 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-MAGE-A3 antibody concentrations

| | |
|-----------------|--------------------------------------|
| End point title | Anti-MAGE-A3 antibody concentrations |
|-----------------|--------------------------------------|

End point description:

Anti-MAGE-A3 antibody concentrations were presented as geometric mean concentrations (GMTs) and expressed in ELISA units per millilitre (EL.U/mL)

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

End point timeframe:

Study period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|--|----------------------------|----------------------------|----------------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 52 | 34 | 1 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-MAGE-A3, PRE [N=87;52;34;1] | 11.2 (10.3 to 12.2) | 11.2 (10 to 12.5) | 11.3 (9.8 to 13) | 10 (10 to 10) |
| Anti-MAGE-A3, PII(W4) [N=62;39;22;1] | 906.1 (608 to 1350.2) | 728.7 (406 to 1307.9) | 1385.7 (896.4 to 2142) | 387 (387 to 387) |
| Anti-MAGE-A3, PVI(W12) [N=52;34;17;1] | 6190.1 (5007.6 to 7652) | 5631 (4284.9 to 7399.8) | 7500.1 (5165.9 to 10889.2) | 5921 (5921 to 5921) |
| Anti-MAGE-A3, PXII(W31) [N=11;5;6;0] | 6724.2 (3978 to 11366.4) | 7094.2 (2360 to 21325.5) | 6430.7 (2877.3 to 14372.4) | 0 (0 to 0) |
| Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0] | 3289.8 (1575.4 to 6870) | 2570.9 (480.1 to 13765.9) | 4209.7 (622.4 to 28473.7) | 0 (0 to 0) |
| Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0] | 4118.6 (1557.3 to 10892.7) | 4784.5 (115.5 to 198255.8) | 3052 (3052 to 3052) | 0 (0 to 0) |
| Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0] | 7063.9 (3780.4 to 13199.4) | 7063.9 (3780.4 to 13199.4) | 0 (0 to 0) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted patients for protein D

| | |
|-----------------|--|
| End point title | Number of seroconverted patients for protein D |
|-----------------|--|

End point description:

Seroconversion was defined as a concentration of antibodies assessed that was greater than the cut-off value for a patient whose concentration of such antibodies was below the cut-off level before the initiation of treatment. Seroconverted patients were those patients with anti-PD antibody concentrations ≥ 100 EL.U/mL

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

End point timeframe:

Study period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|----------------------------------|-----------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 88 | 53 | 34 | 1 |
| Units: Patients | | | | |
| Anti-PD, PRE [N=88;53;34;1] | 29 | 20 | 8 | 1 |
| Anti-PD, PII(W4) [N=77;46;30;1] | 77 | 46 | 30 | 1 |
| Anti-PD, PVI(W12) [N=52;34;17;1] | 52 | 34 | 17 | 1 |
| Anti-PD, PXII(W31) [N=11;5;6;0] | 11 | 5 | 6 | 0 |
| Anti-PD, PXVI(W54) [N=6;3;3;0] | 6 | 3 | 3 | 0 |
| Anti-PD, PXVII(M18) [N=3;2;1;0] | 3 | 2 | 1 | 0 |
| Anti-PD, PXXIV(M49) [N=4;4;0;0] | 4 | 4 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (Anti-PD)

| | |
|-----------------|--|
| End point title | Concentrations of antibodies against protein D (Anti-PD) |
|-----------------|--|

End point description:

Anti-PD antibody concentrations were presented as geometric mean concentrations (GMTs) and expressed in ELISA units per millilitre (EL.U/mL)

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

End point timeframe:

Study period.

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|--|---------------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 88 | 53 | 34 | 1 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD, PRE [N=88;53;34;1] | 81.2 (68.5 to 96.2) | 86.1 (68.9 to 107.5) | 70.6 (54.5 to 91.5) | 412 (412 to 412) |

| | | | | |
|----------------------------------|------------------------------|------------------------------|------------------------------|------------------------|
| Anti-PD, PII(W4) [N=77;46;30;1] | 4588 (3397.5 to 6195.7) | 4196.9 (2768 to 6363.3) | 5139.8 (3253.3 to 8120.2) | 9167 (9167 to 9167) |
| Anti-PD, PVI(W12) [N=52;34;17;1] | 15036.7 (12057.7 to 18751.5) | 14091.9 (10763.7 to 18449.4) | 16453.2 (10607.9 to 25519.6) | 29553 (29553 to 29553) |
| Anti-PD, PXII(W31) [N=11;5;6;0] | 23548.6 (15167.2 to 36561.6) | 25070.5 (8468.5 to 74220) | 22351.2 (13378 to 37343.1) | 0 (0 to 0) |
| Anti-PD, PXVI(W54) [N=6;3;3;0] | 12389.9 (6229 to 24644.4) | 9639.2 (1286.9 to 72202.6) | 15925.5 (4872 to 52057) | 0 (0 to 0) |
| Anti-PD, PXVII(M18) [N=3;2;1;0] | 11386.1 (3141.7 to 41265.3) | 13839.4 (93.9 to 2040751) | 7707 (7707 to 7707) | 0 (0 to 0) |
| Anti-PD, PXXIV(M49) [N=4;4;0;0] | 10546.9 (1777.2 to 62591.1) | 10546.9 (1777.2 to 62591.1) | 0 (0 to 0) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-MAGE-A3 antibody response

| | |
|-----------------|--------------------------------|
| End point title | Anti-MAGE-A3 antibody response |
|-----------------|--------------------------------|

End point description:

Anti-MAGE-A3 antibody response defined as:

For initially seronegative patients: post-vaccination antibody concentration ≥ 27 EU/mL

For initially seropositive patients: post-vaccination antibody concentration ≥ 2 fold the pre-vaccination antibody concentration

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

End point timeframe:

From Week 4 to Month 49

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|---------------------------------------|-----------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 62 | 39 | 22 | 1 |
| Units: Patients | | | | |
| Anti-MAGE-A3, PII(W4) [N=62;39;22;1] | 60 | 37 | 22 | 1 |
| Anti-MAGE-A3, PVI(W12) [N=52;34;17;1] | 52 | 34 | 17 | 1 |
| Anti-MAGE-A3, PXII(W31) [N=11;5;6;0] | 11 | 5 | 6 | 0 |
| Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0] | 6 | 3 | 3 | 0 |
| Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0] | 3 | 2 | 1 | 0 |
| Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0] | 4 | 4 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD antibody response

| | |
|-----------------|---------------------------|
| End point title | Anti-PD antibody response |
|-----------------|---------------------------|

End point description:

Anti-PD antibody response defined as:

For initially seronegative patients: post-vaccination antibody concentration ≥ 100 EU/mL

For initially seropositive patients: post-vaccination antibody concentration ≥ 2 fold the pre-vaccination antibody concentration

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

End point timeframe:

From Week 4 to Month 49

| End point values | MAGE-A3 Group | GS+ Group | GS- Group | Unknown GS Group |
|----------------------------------|-----------------|----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 77 | 46 | 30 | 1 |
| Units: Patients | | | | |
| Anti-PD, PII(W4) [N=77;46;30;1] | 76 | 45 | 30 | 1 |
| Anti-PD, PVI(W12) [N=52;34;17;1] | 52 | 34 | 17 | 1 |
| Anti-PD, PXII(W31) [N=11;5;6;0] | 11 | 5 | 6 | 0 |
| Anti-PD, PXVI(W54) [N=6;3;3;0] | 6 | 3 | 3 | 0 |
| Anti-PD, PXVII(M18) [N=3;2;1;0] | 3 | 2 | 1 | 0 |
| Anti-PD, PXXIV(M49) [N=4;4;0;0] | 4 | 4 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Alanine aminotransferase (ALT) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Alanine aminotransferase (ALT) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards ALT laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| ALT - SCR G0; SE G0 | 100 | | | |
| ALT - SCR G0; SE G1 | 8 | | | |
| ALT - SCR G0; SE G2 | 1 | | | |
| ALT - SCR G0; SE G3 | 1 | | | |
| ALT - SCR G0; SE UNK | 1 | | | |
| ALT - SCR G1; SE G0 | 3 | | | |
| ALT - SCR G1; SE G1 | 8 | | | |
| ALT - SCR G1; SE G2 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Aspartate aminotransferase (AST) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Aspartate aminotransferase (AST) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards AST laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| AST - SCR G0; SE G0 | 101 | | | |
| AST - SCR G0; SE G1 | 12 | | | |
| AST - SCR G0; SE UNK | 1 | | | |
| AST - SCR G1; SE G0 | 6 | | | |
| AST - SCR G1; SE G1 | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Alkaline Phosphatase (ALK) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Alkaline Phosphatase (ALK) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards ALK laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| ALK - SCR G0; SE G0 | 103 | | | |
| ALK - SCR G0; SE G1 | 7 | | | |
| ALK - SCR G0; SE UNK | 1 | | | |
| ALK - SCR G1; SE G0 | 5 | | | |
| ALK - SCR G1; SE G1 | 7 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Bilirubine (BIL) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Bilirubine (BIL) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards BIL laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| BIL - SCR G0; SE G0 | 113 | | | |
| BIL - SCR G0; SE G1 | 5 | | | |
| BIL - SCR G0; SE UNK | 1 | | | |
| BIL - SCR G1; SE G0 | 2 | | | |
| BIL - SCR G2; SE G1 | 1 | | | |
| BIL - SCR G2; SE G2 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Creatinine (CREA) values by maximum grade

| | |
|-----------------|--|
| End point title | Number of patients with abnormal Creatinine (CREA) values by maximum grade |
|-----------------|--|

End point description:

The status of each patient as regards CREA laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| CREA - SCR G0; SE G0 | 105 | | | |
| CREA - SCR G0; SE G1 | 7 | | | |
| CREA - SCR G0; SE UNK | 1 | | | |
| CREA - SCR G1; SE G0 | 1 | | | |
| CREA - SCR G1; SE G1 | 6 | | | |
| CREA - SCR G1; SE G2 | 2 | | | |
| CREA - SCR G2; SE G2 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Hemoglobin (HGB) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Hemoglobin (HGB) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards HGB laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| HGB - SCR G0; SE G0 | 61 | | | |
| HGB - SCR G0; SE G1 | 30 | | | |
| HGB - SCR G0; SE G2 | 1 | | | |
| HGB - SCR G0; SE G3 | 1 | | | |
| HGB - SCR G0; SE UNK | 1 | | | |
| HGB - SCR G1; SE G0 | 1 | | | |
| HGB - SCR G1; SE G1 | 16 | | | |
| HGB - SCR G1; SE G2 | 6 | | | |
| HGB - SCR G1; SE G3 | 3 | | | |
| HGB - SCR G1; SE G4 | 1 | | | |
| HGB - SCR G2; SE G0 | 1 | | | |
| HGB - SCR G2; SE G2 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Leukocytes (LEU) values by maximum grade

| | |
|-----------------|---|
| End point title | Number of patients with abnormal Leukocytes (LEU) values by maximum grade |
|-----------------|---|

End point description:

The status of each patient as regards LEU laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2, G4, and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| LEU - SCR G0; SE G0 | 99 | | | |
| LEU - SCR G0; SE G1 | 10 | | | |
| LEU - SCR G0; SE G2 | 1 | | | |
| LEU - SCR G0; SE G4 | 1 | | | |
| LEU - SCR G0; SE UNK | 1 | | | |
| LEU - SCR G1; SE G0 | 6 | | | |
| LEU - SCR G1; SE G1 | 3 | | | |
| LEU - SCR G1; SE G2 | 1 | | | |
| LEU - SCR G2; SE G1 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Lymphopenia (LYM) values by maximum grade

| | |
|-----------------|--|
| End point title | Number of patients with abnormal Lymphopenia (LYM) values by maximum grade |
|-----------------|--|

End point description:

The status of each patient as regards LYM laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1, G2 and G3. CTC grade statuses reported at SE were G0, G1, G2, G3 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| LYM - SCR G0; SE G0 | 67 | | | |
| LYM - SCR G0; SE G1 | 18 | | | |
| LYM - SCR G0; SE G2 | 3 | | | |
| LYM - SCR G0; SE UNK | 1 | | | |
| LYM - SCR G1; SE G0 | 3 | | | |

| | | | | |
|---------------------|----|--|--|--|
| LYM - SCR G1; SE G1 | 23 | | | |
| LYM - SCR G1; SE G2 | 4 | | | |
| LYM - SCR G2; SE G2 | 1 | | | |
| LYM - SCR G2; SE G3 | 1 | | | |
| LYM - SCR G3; SE G3 | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Neutrophils (NEU) values by maximum grade

| | |
|-----------------|--|
| End point title | Number of patients with abnormal Neutrophils (NEU) values by maximum grade |
|-----------------|--|

End point description:

The status of each patient as regards NEU laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2, G3 and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| NEU - SCR G0; SE G0 | 108 | | | |
| NEU - SCR G0; SE G1 | 4 | | | |
| NEU - SCR G0; SE G2 | 1 | | | |
| NEU - SCR G0; SE UNK | 1 | | | |
| NEU - SCR G1; SE G0 | 2 | | | |
| NEU - SCR G1; SE G1 | 5 | | | |
| NEU - SCR G1; SE G3 | 1 | | | |
| NEU - SCR G2; SE G1 | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Platelets (PLT) values by maximum grade

| | |
|-----------------|--|
| End point title | Number of patients with abnormal Platelets (PLT) values by maximum grade |
|-----------------|--|

End point description:

The status of each patient as regards PLT laboratory values at baseline (SCR) up to study end (SE) was collected and graded according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. The post-treatment values were presented by worst grade versus baseline grade. SCR CTC grade statuses reported were Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1, G4, and Unknown (UNK).

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

End point timeframe:

From study start to study end, each patient being censored out of the analysis at time of death.

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| PLT - SCR G0; SE G0 | 112 | | | |
| PLT - SCR G0; SE G1 | 5 | | | |
| PLT - SCR G0; SE G4 | 1 | | | |
| PLT - SCR G0; SE UNK | 1 | | | |
| PLT - SCR G1; SE G1 | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with autoimmune diseases or immune-mediated inflammatory disorders

| | |
|-----------------|---|
| End point title | Number of patients with autoimmune diseases or immune-mediated inflammatory disorders |
|-----------------|---|

End point description:

Auto-immune diseases or immune-mediated inflammatory disorders were tabulated during the whole duration of the study (up to 30 days after the last administration of the study treatment).

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

End point timeframe:

During the whole study period

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| Any event(s) | 4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients reported with unsolicited adverse events (AEs) by maximum grade.

| | |
|-----------------|---|
| End point title | Number of patients reported with unsolicited adverse events (AEs) by maximum grade. |
|-----------------|---|

End point description:

The assessed AEs were ASCI-related grade 3/4 adverse events according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. An unsolicited AE covers any untoward medical occurrence in a clinical investigation patient 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.

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

End point timeframe:

Up to 30 days after the last administration of the study treatment

| End point values | MAGE-A3 Group | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| Any event, Grade 1 | 52 | | | |
| Any event, Grade 2 | 35 | | | |
| Any event, Grade 3 | 21 | | | |
| Any event, Grade 4 | 5 | | | |
| Any event, Grade 5 | 3 | | | |
| Any event, Grade Any | 116 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients reported with unsolicited AE(s)

| | |
|-----------------|--|
| End point title | Number of patients reported with unsolicited AE(s) |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation patient 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.

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

End point timeframe:

Up to 30 days after the last administration of the study treatment

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | MAGE-A3 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 123 | | | |
| Units: Patients | | | | |
| Any AE(s) | 116 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs up to 30 days post vaccination; SAEs during the entire study period.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | MAGE-A3 Group |
|-----------------------|---------------|

Reporting group description:

Patients planned to receive intramuscularly up to 24 doses of MAGE-A3 ASCI (the study product), in 4 cycles.

| Serious adverse events | MAGE-A3 Group | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 123 (15.45%) | | |
| number of deaths (all causes) | 3 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Laceration | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vascular disorders | | | |
| Lymphoedema | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|-----------------|--|--|
| Hypotonia | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Multi-organ failure | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Gastrointestinal disorders | | | |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric ulcer perforation | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 123 (1.63%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal colic | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 123 (0.81%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | MAGE-A3 Group | | |
|--|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 116 / 123 (94.31%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 14 / 123 (11.38%) | | |
| occurrences (all) | 20 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 17 / 123 (13.82%) | | |
| occurrences (all) | 42 | | |
| Chills | | | |
| subjects affected / exposed | 21 / 123 (17.07%) | | |
| occurrences (all) | 42 | | |
| Fatigue | | | |
| subjects affected / exposed | 30 / 123 (24.39%) | | |
| occurrences (all) | 110 | | |
| Influenza like illness | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 15 / 123 (12.20%) | | |
| occurrences (all) | 46 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 21 / 123 (17.07%) | | |
| occurrences (all) | 53 | | |
| Injection site pain | | | |
| subjects affected / exposed | 60 / 123 (48.78%) | | |
| occurrences (all) | 193 | | |
| Injection site reaction | | | |
| subjects affected / exposed | 9 / 123 (7.32%) | | |
| occurrences (all) | 38 | | |
| Pain | | | |
| subjects affected / exposed | 11 / 123 (8.94%) | | |
| occurrences (all) | 11 | | |
| Pyrexia | | | |
| subjects affected / exposed | 41 / 123 (33.33%) | | |
| occurrences (all) | 155 | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 10 / 123 (8.13%) | | |
| occurrences (all) | 22 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 13 / 123 (10.57%) | | |
| occurrences (all) | 32 | | |
| Nausea | | | |
| subjects affected / exposed | 15 / 123 (12.20%) | | |
| occurrences (all) | 35 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 123 (6.50%) | | |
| occurrences (all) | 10 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 7 / 123 (5.69%) | | |
| occurrences (all) | 20 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|-------------------|--|--|
| Arthralgia | | | |
| subjects affected / exposed | 9 / 123 (7.32%) | | |
| occurrences (all) | 12 | | |
| Myalgia | | | |
| subjects affected / exposed | 12 / 123 (9.76%) | | |
| occurrences (all) | 96 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 18 / 123 (14.63%) | | |
| occurrences (all) | 25 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 27 January 2011 | <p>The main changes in Amendment 1 concern:</p> <ol style="list-style-type: none">1. The addition of an interim analysis for the early assessment of the predictive value of the gene signature (Statistical analysis, Section 10). The interim analysis will assess all available safety and clinical activity data at the time at least 36 enrolled patients have been followed up for one year or have died. Amongst these 36 patients, 18 should have a tumor with the predictive gene signature. The original version of the protocol specified a fixed sample size study of 51 patients with the predictive gene signature having started protocol treatment and having been followed for at least 1 year (or having died). The implementation of a group sequential test design with two stages in the amendment leads to an increase in final sample size from 51 to 53 patients with the predictive gene signature having started protocol treatment and having been followed for at least 1 year (or having died). Assumptions and details of the statistical considerations are described below in Section 10.3. Moreover, in this amendment, it has been specified that the final analysis will take place approximately one year after last patient's first visit and that updated analysis of overall survival will be performed on a yearly basis until all patients have been followed up for 5 years.2. Contact information for reporting SAEs has been updated.3. A new section (Section 6.3.7) has been introduced describing all the remaining Visits/procedures to be performed by patients withdrawn from study treatment.4. An appendix was added with recommendations for biopsy collection (refer to Appendix B). |
| 08 September 2014 | <p>Amendment 2: The main changes in Amendment 2 :</p> <ul style="list-style-type: none">• Removal of all active follow-up visits and procedures,• Removal of blood sampling for humoral immunological response and PBMC collection at the end of Cycle 4,• Clarifications regarding the decision to not perform further testing on samples already collected in the study but not tested yet, in the following sections:<ul style="list-style-type: none">• Synopsis,• Objectives,• Biologicals sample handling and analysis,• Translational Research,• Secondary endpoints,• Analysis of immunogenicity,• Translational research analysis.• The section 'Final analysis' was updated. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported