



Clinical trial results:

An open Phase I/II study of immunization with the recMAGE-A3 + AS15 Antigen Specific Cancer Immunotherapeutic in association with dacarbazine in patients with MAGE-A3 positive unresectable and progressive metastatic cutaneous melanoma

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2008-001918-25
Trial protocol	FR BE
Global end of trial date	17 November 2014

Results information

Result version number	v1
This version publication date	13 February 2016
First version publication date	13 February 2016

Trial information

Trial identification

Sponsor protocol code	111714
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, 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	12 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 November 2014
Global end of trial reached?	Yes
Global end of trial date	17 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Co-primary objectives of this study were to characterize in the overall population and in the gene signature (GS) subsets:

- The safety of MAGE-A3 ASCI study product in association with dacarbazine in patients with MAGE-A3-positive metastatic cutaneous melanoma, with emphasis on any possible toxic effects.
- The specific humoral and cellular immune response induced by the MAGE-A3 ASCI study product in association with dacarbazine in patients with MAGE-A3-positive metastatic cutaneous melanoma.

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	26 May 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	Belgium: 10
Country: Number of subjects enrolled	France: 38
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	47
From 65 to 84 years	1
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.

Period 1

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

Arms

Arm title	MAGE-A3 Group
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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	Other name
Investigational medicinal product code	
Other name	recMAGE-A3 recombinant protein + immunological Adjuvant System
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Administration as follows: 12 administrations in Cycle 1, at 3-week intervals (Weeks 1, 4, 7, 10, 13, 16, 19, 22, 25, 28, 31 and 34) and 8 doses of a standard intravenous chemotherapy regimen consisting of dacarbazine and prophylactic anti-emetic medications administered over one hour on Weeks 1, 4, 7, 10, 13, 16, 19 and 22; 4 administrations in Cycle 2, at 6-week intervals (Weeks 38, 44, 50 and 56); 4 administrations in Cycle 3 at 3-month intervals and 4 administrations i at 6-month intervals.

Investigational medicinal product name	Darcabazine
Investigational medicinal product code	
Other name	Chemotherapy
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

During Cycle 1, 8 doses of a standard intravenous chemotherapy regimen consisting of dacarbazine administered over one hour on Weeks 1, 4, 7, 10, 13, 16, 19 and 22;

Investigational medicinal product name	Anti-emetic medication
Investigational medicinal product code	
Other name	A serotonin 5-HT3 receptor antagonist (e.g. ondansetron, dolasetron or granisetron)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administration prior to each course of chemotherapy, according to standard procedures at the site.

Investigational medicinal product name	Anti-emetic medication
Investigational medicinal product code	
Other name	A serotonin 5-HT3 receptor antagonist (e.g. ondansetron, dolasetron or granisetron)
Pharmaceutical forms	Pillules

Routes of administration	Oral use
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Dosage and administration details:

Administration at 6 hours after each course of chemotherapy, according to standard procedures at the site.

Number of subjects in period 1	MAGE-A3 Group
Started	48
Completed	1
Not completed	47
Others	6
Death	28
Lost to follow-up	2
Ongoing (unknown completion status)	11

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	48	48	
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	55.44		
standard deviation	± 15.99	-	
Gender categorical			
Units: Subjects			
Female	21	21	
Male	27	27	

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	32	15	1
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	54.8	56.1	66
standard deviation	± 15.4	± 18	± 0
Gender categorical Units: Subjects			
Female	16	5	0
Male	16	10	1

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: Number of patients reported with unsolicited adverse events (AEs) that were causally related to treatment administration by maximum grade.

End point title	Number of patients reported with unsolicited adverse events (AEs) that were causally related to treatment administration by maximum grade. ^[1]
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. Related = AE assessed by the investigator as related to the treatment.	
End point type	Primary
End point timeframe:	
Within the 31-day (Days 0-30) post-administration 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	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Patients				
Any event, Grade 3	3			
Any event, Grade 4	1			
Any Blood and lymphatic system disorders, Grade 3	1			

Any Blood and lymphatic system disorders, Grade 4	1			
Anaemia, Grade 3	0			
Anaemia, Grade 4	0			
Lymphopenia, Grade 3	0			
Lymphopenia, Grade 4	0			
Neutropenia, Grade 3	1			
Neutropenia, Grade 4	1			
Thrombocytopenia, Grade 3	0			
Thrombocytopenia, Grade 4	1			
Any Cardiac disorders, Grade 3	0			
Any Cardiac disorders, Grade 4	0			
Tachycardia, Grade 3	0			
Tachycardia, Grade 4	0			
Any Gastrointestinal disorders, Grade 3	0			
Any Gastrointestinal disorders, Grade 4	0			
Constipation, Grade 3	0			
Constipation, Grade 4	0			
Diarrhoea, Grade 3	0			
Diarrhoea, Grade 4	0			
Dyspepsia, Grade 3	0			
Dyspepsia, Grade 4	0			
Nausea, Grade 3	0			
Nausea, Grade 4	0			
Paraesthesia oral, Grade 3	0			
Paraesthesia oral, Grade 4	0			
Vomiting, Grade 3	0			
Vomiting, Grade 4	0			
Any Gen. disord. and adm. site conditions, Grade 3	1			
Any Gen. disord. and adm. site conditions, Grade 4	0			
Asthenia, Grade 3	0			
Asthenia, Grade 4	0			
Chills, Grade 3	0			
Chills, Grade 4	0			
Fatigue, Grade 3	0			
Fatigue, Grade 4	0			
Influenza like illness, Grade 3	0			
Influenza like illness, Grade 4	0			
Injection site erythema, Grade 3	0			
Injection site erythema, Grade 4	0			
Injection site inflammation, Grade 3	1			
Injection site inflammation, Grade 4	0			
Injection site oedema, Grade 3	0			
Injection site oedema, Grade 4	0			
Injection site pain, Grade 3	0			
Injection site pain, Grade 4	0			
Injection site reaction, Grade 3	0			
Injection site reaction, Grade 4	0			
Mucosal dryness, Grade 3	0			
Mucosal dryness, Grade 4	0			
Oedema peripheral, Grade 3	0			

Oedema peripheral, Grade 4	0			
Pyrexia, Grade 3	0			
Pyrexia, Grade 4	0			
Any Investigations, Grade 3	1			
Any Investigations, Grade 4	0			
Haemoglobin decreased, Grade 3	1			
Haemoglobin decreased, Grade 4	0			
Any Metabolism and nutrition disorders, Grade 3	0			
Any Metabolism and nutrition disorders, Grade 4	0			
Decreased appetite, Grade 3	0			
Decreased appetite, Grade 4	0			
Any Musculoskeletal and conn. Tiss. Diso., Grade 3	0			
Any Musculoskeletal and conn. Tiss. Diso., Grade 4	0			
Arthralgia, Grade 3	0			
Arthralgia, Grade 4	0			
Myalgia, Grade 3	0			
Myalgia, Grade 4	0			
Pain in extremity, Grade 3	0			
Pain in extremity, Grade 4	0			
Any Nervous system disorders, Grade 3	0			
Any Nervous system disorders, Grade 4	0			
Burning sensation, Grade 3	0			
Burning sensation, Grade 4	0			
Headache, Grade 3	0			
Headache, Grade 4	0			
Paraesthesia, Grade 3	0			
Paraesthesia, Grade 4	0			
Presyncope, Grade 3	0			
Presyncope, Grade 4	0			
Any Psychiatric disorders, Grade 3	0			
Any Psychiatric disorders, Grade 4	0			
Insomnia, Grade 3	0			
Insomnia, Grade 4	0			
Any Resp., thoracic and mediastinal. dis., Grade 3	0			
Any Resp., thoracic and mediastinal. dis., Grade 4	0			
Rhinitis allergic, Grade 3	0			
Rhinitis allergic, Grade 4	0			
Any Skin and subcutaneous tissue disorder, Grade 3	0			
Any Skin and subcutaneous tissue disorder, Grade 4	0			
Alopecia, Grade 3	0			
Alopecia, Grade 4	0			
Eczema, Grade 3	0			
Eczema, Grade 4	0			
Photosensitivity reaction, Grade 3	0			
Photosensitivity reaction, Grade 4	0			
Pruritus, Grade 3	0			

Pruritus, Grade 4	0			
Any Vascular disorders, Grade 3	0			
Any Vascular disorders, Grade 4	0			
Hypotension, Grade 3	0			
Hypotension, Grade 4	0			

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]
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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
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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	48			
Units: Patients				
Any SAEs	10			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of seroconverted patients for anti-MAGE-A3 ^[3]
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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	Primary
End point timeframe:	
Post Dose 4 at Week 13 (W13).	
Notes:	
[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.	

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	28	19	8	1
Units: Patients				
Anti-MAGE-A3, W13	28	19	8	1

Statistical analyses

No statistical analyses for this end point

Primary: Anti-MAGE-A3 antibody concentrations

End point title	Anti-MAGE-A3 antibody concentrations ^[4]
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	Primary
End point timeframe:	
Post Dose 4 at Week 13 (W13).	
Notes:	
[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: The scope of this primary endpoint was descriptive, no statistical analyses were conducted.	

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	28	19	8	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-MAGE-A3, W13	2778.7 (1638.3 to 4712.8)	2650.8 (1425.5 to 4929.2)	4046.9 (1206.5 to 13574.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with treatment response for anti-MAGE-A3 antibodies

End point title	Number of patients with treatment response for anti-MAGE-A3 antibodies ^[5]
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End point description:

Treatment response defined as:

For initially seronegative patients: post-administration antibody concentration ≥ 27 EL.U/mL

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

End point type	Primary
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End point timeframe:

Post Dose 4 at Week 13 (W13).

Notes:

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

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

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	28	19	8	1
Units: Patients				
Anti-MAGE-A3, W13	28	19	8	1

Statistical analyses

No statistical analyses for this end point

Primary: Anti-MAGE-A3 antibody concentrations (CMI)

End point title	Anti-MAGE-A3 antibody concentrations (CMI) ^[6]
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End point description:

Analysis of MAGE-A3 cellular response was not performed.

End point type	Primary
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End point timeframe:

Post Dose 4 at Week 13 (W13).

Notes:

[6] - 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	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	28	19	8	1
Units: Patients				
Anti-MAGE-A3, W13	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of seroconverted patients for protein D

End point title	Number of seroconverted patients for protein D ^[7]
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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 Primary

End point timeframe:

Post Dose 4 at Week 13 (W13).

Notes:

[7] - 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	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	28	19	8	19
Units: Patients				
Anti-PD, W13	28	19	8	1

Statistical analyses

No statistical analyses for this end point

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

End point title Concentrations of antibodies against protein D (Anti-PD)^[8]

End point description:

Anti-PD antibody concentrations were presented as geometric mean concentrations (GMTs) and expressed in ELISA units per millilitre (EL.U/mL). "0", "-9999" & "9999" as results when about the Unknown GS Group are placeholder values for confidence interval results being not applicable/missing.

End point type Primary

End point timeframe:

Post Dose 4 at Week 13 (W13).

Notes:

[8] - 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	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	28	19	8	1
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, W13	9979.6 (6470 to 15393)	10437 (5932.8 to 18361)	10853.6 (4823.4 to 24422.7)	2176 (-9999 to 9999)

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with treatment response for anti-PD

End point title	Number of patients with treatment response for anti-PD ^[9]
End point description: Treatment response defined as: For initially seronegative patients: post-administration antibody concentration \geq 100 EL.U/mL For initially seropositive patients: post-administration antibody concentration \geq 2 fold the pre-vaccination antibody concentration	
End point type	Primary
End point timeframe: Post Dose 4 at Week 13 (W13).	

Notes:

[9] - 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	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	28	19	8	1
Units: Patients				
Anti-PD, W13	28	19	8	1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage (%) of patients with objective tumor response (OR) to MAGE-A3 ASCI study treatment

End point title	Percentage (%) of patients with objective tumor response (OR) to MAGE-A3 ASCI study treatment
End point description: Response assessment was done based on a set of measurable lesions (MLs) identified at baseline as target lesions (TLs), and followed up until disease progression. Up to 5 MLs per organ & 10 in total were identified as TLs and measured at baseline, selected based on size (those with the longest diameter [LD]) and measurability; a sum of LDs for all TLs was calculated and reported as baseline sum LD, which was used to characterize objective tumor response (OR), OR being defined as either complete response (CR) and/or partial response (PR) post MAGE-A3 ASCI treatment. After identification, MLs and TLs were assessed as regards CR and PR definitions per Response Evaluation Criteria in Solid Tumors (RECIST) criteria. For RECIST criteria details, refer to Therasse P, et al., J Nat Cancer Inst 2000; 92: 205–216).	
End point type	Secondary
End point timeframe: From study start to study end, each patient being censored out of the analysis at 1st report of disease progression in assessed lesions	

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	48	32	15	1
Units: % of patients				
OR	4	4	0	0
CR	1	1	0	0
PR	3	3	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage (%) of patients with stable disease (SD) response to MAGE-A3 ASCI study treatment

End point title	Percentage (%) of patients with stable disease (SD) response to MAGE-A3 ASCI study treatment
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End point description:

Assessment was done based on a set of MLs identified at baseline as TLs and NTLs (see above OR endpoint) followed up until disease progression. TLs and NTLs were assessed as regards matching or not SD-related definitions, 1) SD definitions per Response Evaluation Criteria in Solid Tumors (RECIST) criteria (see above for reference) for TLs ≥ 20 mm and TLs both \geq and < 20 mm, e. a. a) for TLs: SD = Neither sufficient shrinkage to qualify as a PR nor sufficient increase to qualify as PD, taking as references the smallest sum LD since treatment start. and b) for NTLs: SD = Persistence of one or more NTL; 2) following below criteria for TLs < 20 mm e. a. a) for TLs: PR/SD = Neither sufficient shrinkage to qualify for CR nor sufficient increase, to qualify for PD taking as references the smallest sum LD since treatment start, and b) for NTLs: PR/SD = Persistence of one or more NTL.

End point type	Secondary
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End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of disease progression in assessed lesions

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	48	32	15	1
Units: % of patients				
SD	5	4	0	1
SD/PR	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of stable disease (SD) response to MAGE-A3 ASCI study treatment

End point title	Duration of stable disease (SD) response to MAGE-A3 ASCI study treatment
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End point description:

Assessment was done based on a set of MLs identified at baseline as TLs and NTLs (see above OR endpoint) followed up until disease progression. Stable disease was defined as follows: 1) In case of target lesions (TL) greater than or equal to (\geq) 20 mm: neither sufficient shrinkage to qualify for Partial Response nor sufficient increase to qualify for Progressive Disease, taking as references the sum of Longest Diameter (LD) of TL recorded previously but not necessarily at baseline; 2) In case of TL both less than 20 mm and \geq 20 mm: Neither sufficient shrinkage to qualify as a PR nor sufficient increase to qualify as PD, taking as references the smallest sum LD since the start of the treatment. The minimal time interval required between 2 measurements for determination of SD was at least 12 weeks. "-9999" & "9999" are placeholder values for confidence interval results being not applicable/missing.

End point type	Secondary
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End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of disease progression in assessed lesions

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	6	2	1	
Units: Time expressed in months				
median (confidence interval 95%)				
SD Duration	5.6 (5.3 to 8.3)	7.7 (7.2 to 8.3)	5.1 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage (%) of patients with mixed response (MxR) to MAGE-A3 ASCI study treatment

End point title	Percentage (%) of patients with mixed response (MxR) to MAGE-A3 ASCI study treatment
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End point description:

Assessment was done based on a set of MLs identified at baseline as TLs and NTLs (see above OR endpoint) followed up until disease progression. MLs were assessed as regards matching below MxR definitions. In case of evaluability per RECIST: a) MxR Type 1= at least (a.l.) 30% decrease in LD in a.l. one TL measured at baseline. Such response occurring in SD/PD status of LD of TL and without appearance of one or more new lesions = SD/PD with TL regression; b) MxR Type 2: appearance of one or more new lesions occurring in SD/PR status of LD of TL, and = SD/PR with new lesion. In case of non-evaluability per RECIST: a) MxR Type 1 = a clear decrease in diameters occurring in a.l. one TL measured at baseline. Such response occurring in SD/PD status of LD of (baseline) TL and without appearance of one or more new lesions = SD/PD with TL regression; b) MxR Type 2 = appearance of one or more new lesions occurring in SD/PR status of LD of TL = SD/PR with new lesion.

End point type	Secondary
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End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of disease progression in assessed lesions

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	48	32	15	1
Units: % of patients				
MxR: SD/PR with new lesion	10	6	4	0
MxR: SD/PD with target lesion regression	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to treatment failure (TTF), by Gene Signature

End point title	Time to treatment failure (TTF), by Gene Signature
End point description:	
TTF was defined as withdrawal from treatment with the MAGE-A3 ASCI study product due to disease progression or death. TTF 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:	
From study start to study end, each patient being censored out of the analysis at 1st report of disease progression or death	

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	32	15	1	
Units: Time expressed in months				
median (confidence interval 95%)				
TTF	2.8 (2.1 to 4.9)	2.3 (2.1 to 3)	4.3 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) for the overall population

End point title	Progression-free survival (PFS) for the overall population
End point description:	
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.	
End point type	Secondary

End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of disease progression or death

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Time expressed in months				
median (confidence interval 95%)				
PFS	2.8 (2.8 to 3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) by Gene Signature

End point title	Progression-free survival (PFS) by Gene Signature
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End point description:

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
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End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of disease progression or death

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	48	32	15	1
Units: Time expressed in months				
median (confidence interval 95%)				
PFS	2.8 (2.8 to 3)	2.8 (2.8 to 3.4)	2.8 (2.2 to 3.3)	5.1 (-9999 to 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) after slow progressive disease (SPD) by Gene Signature

End point title	Progression-free survival (PFS) after slow progressive disease (SPD) by Gene Signature
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End point description:

PFS after initial SPD was defined and calculated as the time from the time point at which the disease was the most advanced during the treatment to either a new progression of the disease or the date to death, whichever occurred first as another secondary outcome of this study. In that case, the largest diameter during the course of treatment was to be used as reference measurement. This outcome was defined to take into account the delay to induce an active immune response and the strict rules set up in this study to allow pursuing investigational treatment in case of SPD. PFS after SPD 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
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End point timeframe:

From study start to study end, each patient being censored out of the analysis at 1st report of new disease progression or death, largest diameter reported for lesions assessed during the course of treatment being used as reference measurement.

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	32	15	1	
Units: Time expressed in months				
median (confidence interval 95%)				
PFS after SPD	2.8 (2.8 to 5.3)	2.8 (2.2 to 3.3)	5.1 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) by Gene Signature

End point title	Overall survival (OS) by Gene Signature
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End point description:

OS was defined as the time from first treatment to the date of death. OS analysis was performed using the non-parametric Kaplan-Meier method. "0", "-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
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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	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	48	32	15	1
Units: Time expressed in months				
median (confidence interval 95%)				
OS	9.4 (5.8 to 15.8)	11.4 (7.3 to 17.1)	5.3 (3.3 to 10.5)	0 (-9999 to 9999)

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
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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), G1 and G2. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
ALT - SCR G0; SE G0	34			
ALT - SCR G0; SE G1	3			
ALT - SCR G0; SE G2	1			
ALT - SCR G0; SE G3	1			
ALT - SCR G0; SE G4	0			
ALT - SCR G0; SE UNK	1			
ALT - SCR G1; SE G0	3			
ALT - SCR G1; SE G1	2			
ALT - SCR G1; SE G2	1			
ALT - SCR G1; SE G3	0			
ALT - SCR G1; SE G4	0			
ALT - SCR G1; SE UNK	1			
ALT - SCR G2; SE G0	0			
ALT - SCR G2; SE G1	1			
ALT - SCR G2; SE G2	0			
ALT - SCR G2; SE G3	0			
ALT - SCR G2; SE G4	0			

ALT - SCR G2; SE UNK	0			
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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
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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, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
AST - SCR G0; SE G0	36			
AST - SCR G0; SE G1	2			
AST - SCR G0; SE G2	1			
AST - SCR G0; SE G3	0			
AST - SCR G0; SE G4	1			
AST - SCR G0; SE UNK	1			
AST - SCR G1; SE G0	2			
AST - SCR G1; SE G1	3			
AST - SCR G1; SE G2	1			
AST - SCR G1; SE G3	0			
AST - SCR G1; SE G4	0			
AST - SCR G1; SE UNK	1			

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, 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	48			
Units: Subjects				
ALK - SCR G0; SE G0	31			
ALK - SCR G0; SE G1	11			
ALK - SCR G0; SE G2	0			
ALK - SCR G0; SE G3	0			
ALK - SCR G0; SE G4	0			
ALK - SCR G0; SE UNK	1			
ALK - SCR G1; SE G0	1			
ALK - SCR G1; SE G1	3			
ALK - SCR G1; SE G2	0			
ALK - SCR G1; SE G3	0			
ALK - SCR G1; SE G4	0			
ALK - SCR G1; SE UNK	1			

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 Unknown (UNK) and Grade 0 (G0). 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	48			
Units: Subjects				
BIL - SCR UNK; SE G0	1			
BIL - SCR UNK; SE G1	0			
BIL - SCR UNK; SE G2	0			
BIL - SCR UNK; SE G3	0			
BIL - SCR UNK; SE G4	0			
BIL - SCR UNK; SE UNK	0			
BIL - SCR G0; SE G0	39			
BIL - SCR G0; SE G1	3			
BIL - SCR G0; SE G2	0			
BIL - SCR G0; SE G3	0			
BIL - SCR G0; SE G4	0			
BIL - SCR G0; SE UNK	5			

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
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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). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
CREA - SCR G0; SE G0	40			
CREA - SCR G0; SE G1	4			
CREA - SCR G0; SE G2	1			
CREA - SCR G0; SE G3	0			

CREA - SCR G0; SE G4	1			
CREA - SCR G0; SE UNK	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal gamma-glutamyl transpeptidase (GGT) values by maximum grade

End point title	Number of patients with abnormal gamma-glutamyl transpeptidase (GGT) values by maximum grade
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End point description:

The status of each patient as regards GGT 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 G3. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
GGT - SCR G0; SE G0	20			
GGT - SCR G0; SE G1	11			
GGT - SCR G0; SE G2	4			
GGT - SCR G0; SE G3	0			
GGT - SCR G0; SE G4	0			
GGT - SCR G0; SE UNK	2			
GGT - SCR G1; SE G0	2			
GGT - SCR G1; SE G1	2			
GGT - SCR G1; SE G2	0			
GGT - SCR G1; SE G3	0			
GGT - SCR G1; SE G4	0			
GGT - SCR G1; SE UNK	0			
GGT - SCR G3; SE G0	0			
GGT - SCR G3; SE G1	0			
GGT - SCR G3; SE G2	0			
GGT - SCR G3; SE G3	1			
GGT - SCR G3; SE G4	0			
GGT - SCR G3; SE UNK	0			

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
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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) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
HGB - SCR G0; SE G0	22			
HGB - SCR G0; SE G1	14			
HGB - SCR G0; SE G2	5			
HGB - SCR G0; SE G3	1			
HGB - SCR G0; SE G4	0			
HGB - SCR G0; SE UNK	2			
HGB - SCR G1; SE G0	2			
HGB - SCR G1; SE G1	2			
HGB - SCR G1; SE G2	0			
HGB - SCR G1; SE G3	0			
HGB - SCR G1; SE G4	0			
HGB - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Hypercalcemia (HCA) values by maximum grade

End point title	Number of patients with abnormal Hypercalcemia (HCA) values by maximum grade
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End point description:

The status of each patient as regards HCA 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 Unknown (UNK), Grade 0 (G0) and G1. 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	48			
Units: Subjects				
HCA - SCR UNK; SE G0	2			
HCA - SCR UNK; SE G1	1			
HCA - SCR UNK; SE G2	0			
HCA - SCR UNK; SE G3	0			
HCA - SCR UNK; SE G4	0			
HCA - SCR UNK; SE UNK	0			
HCA - SCR G0; SE G0	37			
HCA - SCR G0; SE G1	0			
HCA - SCR G0; SE G2	0			
HCA - SCR G0; SE G3	0			
HCA - SCR G0; SE G4	0			
HCA - SCR G0; SE UNK	6			
HCA - SCR G1; SE G1	1			
HCA - SCR G1; SE G2	1			
HCA - SCR G1; SE G3	0			
HCA - SCR G1; SE G4	0			
HCA - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Hyperkalemia (HKA) values by maximum grade

End point title	Number of patients with abnormal Hyperkalemia (HKA) values by maximum grade
End point description:	
The status of each patient as regards HKA 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	48			
Units: Subjects				
HKA - SCR G0; SE G0	42			
HKA - SCR G0; SE G1	2			
HKA - SCR G0; SE G2	0			
HKA - SCR G0; SE G3	0			
HKA - SCR G0; SE G4	0			
HKA - SCR G0; SE UNK	1			
HKA - SCR G1; SE G0	1			
HKA - SCR G1; SE G1	0			
HKA - SCR G1; SE G2	0			
HKA - SCR G1; SE G3	0			
HKA - SCR G1; SE G4	0			
HKA - SCR G1; SE UNK	1			
HKA - SCR G2; SE G0	1			
HKA - SCR G2; SE G1	0			
HKA - SCR G2; SE G2	0			
HKA - SCR G2; SE G3	0			
HKA - SCR G2; SE G4	0			
HKA - SCR G2; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Hyponatremia (HNA) values by maximum grade

End point title	Number of patients with abnormal Hyponatremia (HNA) values by maximum grade
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End point description:

The status of each patient as regards HNA 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, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
HNA - SCR G0; SE G0	44			
HNA - SCR G0; SE G1	0			

HNA - SCR G0; SE G2	0			
HNA - SCR G0; SE G3	0			
HNA - SCR G0; SE G4	0			
HNA - SCR G0; SE UNK	2			
HNA - SCR G1; SE G0	2			
HNA - SCR G1; SE G1	0			
HNA - SCR G1; SE G2	0			
HNA - SCR G1; SE G3	0			
HNA - SCR G1; SE G4	0			
HNA - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal hypoalbuminemia(hAL) values by maximum grade

End point title	Number of patients with abnormal hypoalbuminemia(hAL) values by maximum grade
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End point description:

The status of each patient as regards hAL 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 Unknown (UNK), Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
hAL - SCR UNK; SE G0	1			
hAL - SCR UNK; SE G1	0			
hAL - SCR UNK; SE G2	1			
hAL - SCR UNK; SE G3	0			
hAL - SCR UNK; SE G4	0			
hAL - SCR UNK; SE UNK	1			
hAL - SCR G0; SE G0	26			
hAL - SCR G0; SE G1	4			
hAL - SCR G0; SE G2	2			
hAL - SCR G0; SE G3	0			
hAL - SCR G0; SE G4	0			
hAL - SCR G0; SE UNK	4			
hAL - SCR G1; SE G1	4			
hAL - SCR G1; SE G2	3			

hAL - SCR G1; SE G3	0			
hAL - SCR G1; SE G4	0			
hAL - SCR G1; SE UNK	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal hypocalcemia(hCA) values by maximum grade

End point title	Number of patients with abnormal hypocalcemia(hCA) values by maximum grade
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End point description:

The status of each patient as regards hCA 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 Unknown (UNK), Grade 0 (G0) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
hCA - SCR UNK; SE G0	1			
hCA - SCR UNK; SE G1	1			
hCA - SCR UNK; SE G2	0			
hCA - SCR UNK; SE G3	0			
hCA - SCR UNK; SE G4	1			
hCA - SCR UNK; SE UNK	0			
hCA - SCR G0; SE G0	27			
hCA - SCR G0; SE G1	7			
hCA - SCR G0; SE G2	0			
hCA - SCR G0; SE G3	0			
hCA - SCR G0; SE G4	0			
hCA - SCR G0; SE UNK	5			
hCA - SCR G1; SE G0	0			
hCA - SCR G1; SE G1	5			
hCA - SCR G1; SE G2	0			
hCA - SCR G1; SE G3	0			
hCA - SCR G1; SE G4	0			
hCA - SCR G1; SE UNK	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal hypokalemia (hKA) values by maximum grade

End point title	Number of patients with abnormal hypokalemia (hKA) values by maximum grade
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End point description:

The status of each patient as regards hKA 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, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
hKA - SCR G0; SE G0	42			
hKA - SCR G0; SE G1	1			
hKA - SCR G0; SE G2	0			
hKA - SCR G0; SE G3	0			
hKA - SCR G0; SE G4	0			
hKA - SCR G0; SE UNK	1			
hKA - SCR G1; SE G0	3			
hKA - SCR G1; SE G1	0			
hKA - SCR G1; SE G2	0			
hKA - SCR G1; SE G3	0			
hKA - SCR G1; SE G4	0			
hKA - SCR G1; SE UNK	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal hyponatremia (hNA) values by maximum grade

End point title	Number of patients with abnormal hyponatremia (hNA) values by maximum grade
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End point description:

The status of each patient as regards hNA 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, 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	48			
Units: Subjects				
hNA - SCR G0; SE G0	33			
hNA - SCR G0; SE G1	10			
hNA - SCR G0; SE G2	0			
hNA - SCR G0; SE G3	1			
hNA - SCR G0; SE G4	0			
hNA - SCR G0; SE UNK	2			
hNA - SCR G1; SE G0	1			
hNA - SCR G1; SE G1	1			
hNA - SCR G1; SE G2	0			
hNA - SCR G1; SE G3	0			
hNA - SCR G1; SE G4	0			
hNA - SCR G1; SE UNK	0			

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
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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) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
LEU - SCR G0; SE G0	37			
LEU - SCR G0; SE G1	6			
LEU - SCR G0; SE G2	0			
LEU - SCR G0; SE G3	1			
LEU - SCR G0; SE G4	0			
LEU - SCR G0; SE UNK	2			
LEU - SCR G1; SE G0	0			
LEU - SCR G1; SE G1	1			
LEU - SCR G1; SE G2	1			
LEU - SCR G1; SE G3	0			
LEU - SCR G1; SE G4	0			
LEU - SCR G1; SE UNK	0			

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
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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) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
LYM - SCR G0; SE G0	18			
LYM - SCR G0; SE G1	13			
LYM - SCR G0; SE G2	6			
LYM - SCR G0; SE G3	0			
LYM - SCR G0; SE G4	0			
LYM - SCR G0; SE UNK	2			
LYM - SCR G1; SE G0	2			
LYM - SCR G1; SE G1	4			

LYM - SCR G1; SE G2	3			
LYM - SCR G1; SE G3	0			
LYM - SCR G1; SE G4	0			
LYM - SCR G1; SE UNK	0			

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
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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). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
NEU - SCR G0; SE G0	39			
NEU - SCR G0; SE G1	4			
NEU - SCR G0; SE G2	1			
NEU - SCR G0; SE G3	2			
NEU - SCR G0; SE G4	0			
NEU - SCR G0; SE UNK	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal Partial Thromboplastin Time (PTT) values by maximum grade

End point title	Number of patients with abnormal Partial Thromboplastin Time (PTT) values by maximum grade
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End point description:

The status of each patient as regards PTT 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, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
PTT - SCR G0; SE G0	35			
PTT - SCR G0; SE G1	3			
PTT - SCR G0; SE G2	0			
PTT - SCR G0; SE G3	1			
PTT - SCR G0; SE G4	0			
PTT - SCR G0; SE UNK	7			
PTT - SCR G1; SE G0	0			
PTT - SCR G1; SE G1	1			
PTT - SCR G1; SE G2	0			
PTT - SCR G1; SE G3	1			
PTT - SCR G1; SE G4	0			
PTT - SCR G1; SE UNK	0			

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
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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, G2, G3, G4, and Unknown (UNK).

End point type	Secondary
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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	48			
Units: Subjects				
PLT - SCR G0; SE G0	39			
PLT - SCR G0; SE G1	5			
PLT - SCR G0; SE G2	1			
PLT - SCR G0; SE G3	0			
PLT - SCR G0; SE G4	0			
PLT - SCR G0; SE UNK	2			
PLT - SCR G1; SE G0	1			
PLT - SCR G1; SE G1	0			
PLT - SCR G1; SE G2	0			
PLT - SCR G1; SE G3	0			
PLT - SCR G1; SE G4	0			
PLT - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with any adverse events (AEs) and with AEs by maximum grade

End point title	Number of patients with any adverse events (AEs) and with AEs by maximum grade
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End point description:

An AE was any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. AEs reported are here below tabulated irrespective of grade (any), as well as graded by maximum grade reported according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. Maximum grade reported and tabulated were Grade 1 (G1), G2, G3, G4 and G5.

End point type	Secondary
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End point timeframe:

Within the 31-day follow-up period post treatment administration.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Subjects				
Patients with any AEs	48			
Patients with G1 AEs	14			
Patients with G2 AEs	19			
Patients with G3 AEs	12			
Patients with G4 AEs	3			
Patients with G5 AEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with any serious adverse events (SAEs) and with AEs by maximum grade

End point title	Number of patients with any serious adverse events (SAEs) and with AEs by maximum grade
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End point description:

SAEs include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a patient, is a Grade 4 AE according to the CTCAE, version 3.0. Events which were part of the natural course of the disease under study were captured as part of the clinical activity outcome variables in this study; therefore did not need to be reported as SAEs. Progression/recurrence of the tumor 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. SAEs reported are here below tabulated irrespective of grade (any), as well as graded by maximum grade reported according to the Common Terminology Criteria (CTC) Adverse event terminology, version 3.0. Maximum grade reported and tabulated were Grade 1 (G1), G2, G3, G4 and G5.

End point type	Secondary
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End point timeframe:

Within the 31-day follow-up period post treatment administration.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Subjects				
Patients with any SAEs	10			
Patients with G1 SAEs	1			
Patients with G2 SAEs	2			
Patients with G3 SAEs	5			
Patients with G4 SAEs	2			
Patients with G5 SAEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: From screening (SCR) up to study end; AEs: Within the 31-day follow-up period post treatment administration, up to study end.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	MAGE-A3 Group
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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	10 / 48 (20.83%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			

subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 48 (4.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastroenteritis			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 48 (2.08%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 48 (2.08%)		
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	48 / 48 (100.00%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	25 / 48 (52.08%)		
occurrences (all)	25		
Injection site pain			
subjects affected / exposed	18 / 48 (37.50%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	14 / 48 (29.17%)		
occurrences (all)	14		
Injection site reaction			

subjects affected / exposed occurrences (all)	9 / 48 (18.75%) 9		
Influenza like illness subjects affected / exposed occurrences (all)	9 / 48 (18.75%) 9		
Fatigue subjects affected / exposed occurrences (all)	9 / 48 (18.75%) 9		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	22 / 48 (45.83%) 22		
Constipation subjects affected / exposed occurrences (all)	14 / 48 (29.17%) 14		
Vomiting subjects affected / exposed occurrences (all)	13 / 48 (27.08%) 13		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	11 / 48 (22.92%) 11		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 July 2008	The changes following this Amendment concern: <ul style="list-style-type: none">• The threshold value of LDH as inclusion criterion• The procedures to be performed at each visit for treatment administration
02 March 2009	The changes following this amendment concern: <ul style="list-style-type: none">• The possibility of taking a new tumor biopsy in case the results of the analysis of the biopsies originally taken are inconclusive.• Clarification that MAGE-A3 testing and gene profiling of newly dissected tumors in case of disease progression require specific informed consent by the patients.• Clarification of the number of target lesions
16 October 2009	<p>The changes following this amendment concern:</p> <ul style="list-style-type: none">• The number of patients to be enrolled has been increased from 20 to 40 in order to assess the gene profile data in patients who also receive chemotherapy. A pre-specified gene signature was identified in previous studies, but has not yet been assessed in patients receiving chemotherapy. Based on existing data, it is estimated that approximately 50% of patients will have a pre-specified gene signature. Therefore, the sample size should be doubled to have approximately 20 patients with and 20 patients without the pre-specified gene signature. Final analyses will be assessed in the overall population and in subsets with or without the pre-specified gene signature. As many patients currently enrolled in the study have agreed to allow gene profiling of their tumor sample it will remain an optional procedure.• The duration of follow-up for survival, disease progression and SAEs related to study participation and concurrent medication has been extended from 4 to 5 years after first treatment administration to obtain continued information regarding the patients' health status after the treatment phase.• Overall survival has been added as a secondary endpoint.
16 July 2010	<p>The changes following this amendment concern the avoidance of repeating procedures (biopsy and tumor imaging) during the screening phase, which may already have been performed recently prior to screening as part of local routine practice or in relation to another research study.</p> <p>It has also been made clear that any second-line therapy and not only second-line chemotherapy after the study treatment is of interest.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
18 July 2014	Early end of trial notification after termination of long term follow up due to lack of scientific justification to continue collect information.	-

Notes:

Limitations and caveats

None reported