



Clinical trial results:

An open Phase II study to assess the clinical activity and safety of recMAGE-A3 + AS15 cancer immunotherapeutic in patients with metastatic cutaneous melanoma, and to explore its immunogenic properties, including their relation to tumor infiltration, genomics and proteomics

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	2008-001301-42
Trial protocol	FR BE
Global end of trial date	03 November 2014

Results information

Result version number	v1
This version publication date	03 March 2016
First version publication date	03 March 2016

Trial information

Trial identification

Sponsor protocol code	111473
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00896480
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	06 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 November 2014
Global end of trial reached?	Yes
Global end of trial date	03 November 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Clinical Activity - To characterize in patients with MAGE-A3-positive metastatic cutaneous melanoma: The clinical activity of the MAGE-A3 ASCI study treatment in terms of objective response (OR), stable disease (SD) and mixed response (MR)*

The clinical activity of the MAGE-A3 ASCI study treatment in terms of time to treatment failure (TTF)*
The safety of the MAGE-A3 ASCI study treatment.

Immunogenicity - To document the humoral and cellular immune response induced by the MAGE-A3 ASCI study treatment.

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. VMAGE-A3 ASCI/placebo were administered by qualified and trained personnel, only to eligible subjects with no contraindications to any components of these products. During treatment, the following was checked to assess need to postpone treatment: acute disease at time of administration; any systemic grade ≥ 2 Common Terminology Criteria Adverse Event related or possibly related to treatment; fever, defined as an oral, axillary or tympanic temperature $\geq 38^{\circ}\text{C}$; need for influenza vaccine, immunoglobulins and/or any blood products; any medical reason exposing the patient to unacceptable risk. Patients were required to discontinue treatment in case of evidence of disease relapse/occurrence of second primary lung cancer; treatment with either investigational or non-registered product other than MAGE-A3 ASCI study product or other anticancer treatments; anaphylactic reaction following treatment administration; any intolerable adverse event; clinical signs or symptoms indicative of any autoimmune disorder, except vitiligo; appearance of any confirmed or suspected immunosuppressive or immunodeficient condition, or any condition requiring use of any immunosuppressive agent or systemic corticosteroids prescribed for chronic use; inability of the patient to complete study evaluations due to unforeseen circumstances; other conditions indicating the patient's best interest to be withdrawn from treatment. In addition, between the end of the 120-weeks treatment phase, the following follow-up (FU) of patients was also planned: 1) an active FU for survival, recurrence, serious adverse events related to treatment & SAEs related to study participation and concurrent GSK medication of up to 5 years from the 1st treatment, and 2) annual contacts up to 10 years after 1st treatment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 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: 9
Country: Number of subjects enrolled	France: 15

Worldwide total number of subjects	24
EEA total number of subjects	24

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)	11
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

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
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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	recMAGE-A3 recombinant protein formulated in AS15 adjuvant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Administration as follows:

-Cycle 1 (ending Week 13): 6 doses at 2-week intervals (Weeks 1, 3, 5, 7, 9 and 11)

-Cycle 2 (ending Week 32): 6 doses at 3-week intervals (Weeks 15, 18, 21, 24, 27 and 30)

-Cycle 3 (ending Week 54): 4 doses at 6-week intervals (Weeks 34, 40, 46 and 52)

-Cycle 4: 4 doses at 12-week intervals, starting 12 weeks after end of Cycle 3, followed by, after an interruption of treatment of 6 months, 4 doses at 24-week intervals. All analyses were performed on the overall study population (MAGE3 Group) as well as in the subsets of patients with or without the pre-specified gene signature (GS+ or GS- groups) and in one patient with unknown status as regards GS signature (Unknown Group).

Number of subjects in period 1	MAGE-A3 Group
Started	24
Completed	0
Not completed	24
Withdrawn	20
Ongoing (unknown completion status)	4

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	24	24	
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	65.4		
standard deviation	± 12.4	-	
Gender categorical Units: Subjects			
Female	17	17	
Male	7	7	

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 gene signature positive for two biopsies, as assessed at screening.

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

Subject analysis set description:

Subset of patients the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a gene signature positive for only one biopsies, as assessed at screening.

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

Subject analysis set description:

Subset of patients the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a gene signature negative for both biopsies, as

Reporting group values	GS+/+ Group	GS+/- Group	GS- Group
Number of subjects	8	8	8
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 standard deviation	70.1 ± 13.4	66.3 ± 12.7	59.9 ± 10.1
Gender categorical Units: Subjects			
Female	5	5	7
Male	3	3	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 gene signature positive for two biopsies, as assessed at screening.	
Subject analysis set title	GS+/- Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of patients the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a gene signature positive for only one biopsies, as assessed at screening.	
Subject analysis set title	GS- Group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of patients the pre-specified gene signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a gene signature negative for both biopsies, as assessed at screening.	

Primary: 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 ^[1]
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 (= SD/PR with new lesion). In case of non-evaluability per RECIST (due to LD<20mm): 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	Primary
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	

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group	GS+/+ Group	GS+/- Group	GS- Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	8	8	8
Units: Patients				
Best response CR	2	2	0	0
Best response PR	2	1	1	0
Best response MR (SD/PR)	2	1	1	0
Best response MR (SD/PD)	3	2	0	1
Best response SD	1	0	0	1
Best response SD/PD	0	0	0	0
Best response PD (SPD)	4	1	1	2
Best response PD (SPD/MR)	10	1	5	4
Best response NE	0	0	0	0

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage (%) of patients with best objective tumor response (OR) to MAGE-A3 ASCI study treatment ^[2]
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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 MLs 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. All other lesions (or sites of disease) were to be identified as non-target lesions (NTL) and were to also be recorded and measured at baseline. 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	Primary
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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

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group	GS+/+ Group	GS+/- Group	GS- Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	8	8	8
Units: Patients				
Best response CR	2	2	0	0
Best response PR	2	1	1	0
Best response SD	2	0	1	1
Best response SD/PR	1	1	0	0
Best response PD	17	4	6	7

Best response NE	0	0	0	0
Best objective response Yes	4	3	1	0
Best objective response No	20	5	7	8
Disease Control Yes	7	4	2	1
Disease Control No	17	4	6	7

Statistical analyses

No statistical analyses for this end point

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

End point title	Time to treatment failure (TTF), by Gene Signature ^[3]
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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	Primary
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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

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	GS+/+ Group	GS+/- Group	GS- Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	8	8	8	
Units: Time expressed in months				
median (confidence interval 95%)				
TTF	14.8 (2.3 to 9999)	2.3 (0.5 to 15)	2.4 (0.5 to 4.6)	

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 ^[4]
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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 EL.U/mL.

End point type	Primary
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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

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group	GS+/+ Group	GS+/- Group	GS- Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	7	5	6
Units: Patients				
Anti-MAGE-A3, PRE [N=18;7;5;6]	3	1	1	1
Anti-MAGE-A3, PI (D2) [N=17;7;4;6]	3	1	1	1
Anti-MAGE-A3, PI (D7) [N=18;7;5;6]	4	1	2	1
Anti-MAGE-A3, PI (D15) [N=17;7;5;5]	9	3	3	3
Anti-MAGE-A3, PII (D16) [N=15;7;3;5]	8	3	2	3
Anti-MAGE-A3, PII (W5) [N=16;7;4;5]	16	7	4	5
Anti-MAGE-A3, PV (W11) [N=12;4;4;4]	12	4	4	4
Anti-MAGE-A3, PVI (W13) [N=16;7;4;5]	16	7	4	5
Anti-MAGE-A3, PVIII (W21) [N=10;7;2;1]	10	7	2	1
Anti-MAGE-A3, PXII (W32) [N=10;7;2;1]	10	7	2	1
Anti-MAGE-A3, PXVI (W54) [N=5;4;1;0]	5	4	1	0
Anti-MAGE-A3, PXVII (V21+3M) [N=3;3;0;0]	3	3	0	0
Anti-MAGE-A3, PXVIII (V22+2W) [N=2;1;1;0]	2	1	1	0
Anti-MAGE-A3, PXIX (V24+3M) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXX (V25+2W) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXX (V25+6M) [N=2;1;1;0]	2	1	1	0
Anti-MAGE-A3, PXXI (V27+2W) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXI (V27+6M) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXII (V29+2W) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXIII (V31+2W) [N=2;2;0;0]	2	2	0	0
Anti-MAGE-A3, CCL [N=5;2;0;3]	5	2	0	3

Statistical analyses

No statistical analyses for this end point

Primary: Anti-MAGE-A3 antibody concentrations

End point title	Anti-MAGE-A3 antibody concentrations ^[5]
End point description:	
Anti-MAGE-A3 antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per millilitre (EL.U/mL). A seropositive patient was defined as a patient whose concentration greater than or equal to 27 EL.U/mL.	
End point type	Primary

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

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group	GS+/+ Group	GS+/- Group	GS- Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	7	5	6
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-MAGE-A3, PRE [N=18;7;5;6]	14.2 (9.5 to 21.4)	13.9 (6.2 to 31.4)	15.3 (4.7 to 49.9)	13.8 (6.1 to 31.3)
Anti-MAGE-A3, PI (D2) [N=17;7;4;6]	14.6 (9.5 to 22.6)	13.9 (6.2 to 30.8)	16.8 (3.2 to 86.8)	14.2 (5.8 to 34.7)
Anti-MAGE-A3, PI (D7) [N=18;7;5;6]	16.6 (11.1 to 24.7)	16.1 (6.9 to 37.4)	18.7 (5.9 to 59.2)	15.5 (7.3 to 32.7)
Anti-MAGE-A3, PI (D15) [N=17;7;5;5]	56.6 (24.8 to 129)	48.5 (11.6 to 202.6)	72 (7.4 to 699.2)	55.1 (5.9 to 512.2)
Anti-MAGE-A3, PII (D16) [N=15;7;3;5]	65.1 (25.5 to 166.6)	55.4 (11.8 to 260.6)	102.4 (0.7 to 15279.4)	62.2 (5.8 to 662.9)
Anti-MAGE-A3, PII (W5) [N=16;7;4;5]	1865.7 (906.6 to 3839.3)	1396.9 (234.5 to 8321.5)	4120.2 (2093 to 8111)	1484.1 (736.8 to 2989.6)
Anti-MAGE-A3, PV (W11) [N=12;4;4;4]	6312.1 (4177.9 to 9536.4)	4161.6 (1542.3 to 11229.3)	9775.9 (3065.3 to 31177.1)	6181.6 (3414.2 to 11191.8)
Anti-MAGE-A3, PVI (W13) [N=16;7;4;5]	9080.5 (7030.9 to 11727.6)	7797.4 (4564.5 to 13320.2)	13789.3 (7278.1 to 26125.3)	8046.1 (7249.1 to 8930.8)
Anti-MAGE-A3, PVIII (W21) [N=10;7;2;1]	8540.2 (5768.3 to 12644)	7400.3 (4304 to 12724.1)	12544.5 (371.2 to 423881.3)	10790 (10790 to 10790)
Anti-MAGE-A3, PXII (W32) [N=10;7;2;1]	6826.9 (4728.9 to 9855.8)	6128 (3601.6 to 10426.5)	8384.1 (459.4 to 153006.6)	9641 (9641 to 9641)
Anti-MAGE-A3, PXVI (W54) [N=5;4;1;0]	7429.9 (4876.9 to 11319.3)	6542.6 (4660.3 to 9185.1)	12357 (12357 to 12357)	0 (0 to 0)
Anti-MAGE-A3, PXVII (V21+3M) [N=3;3;0;0]	3539.3 (2578.1 to 4859)	3539.3 (2578.1 to 4859)	0 (0 to 0)	0 (0 to 0)
Anti-MAGE-A3, PXVIII (V22+2W) [N=2;1;1;0]	5972.3 (24 to 1485256)	3869 (3869 to 3869)	9219 (9219 to 9219)	0 (0 to 0)
Anti-MAGE-A3, PXIX (V24+3M) [N=3;2;1;0]	5512.4 (1673 to 18163)	4260 (452.7 to 40086)	9230 (9230 to 9230)	0 (0 to 0)
Anti-MAGE-A3, PXX (V25+2W) [N=3;2;1;0]	6523.7 (1713.7 to 24834.3)	4804.1 (1467.6 to 15725.7)	12030 (12030 to 12030)	0 (0 to 0)
Anti-MAGE-A3, PXX (V25+6M) [N=2;1;1;0]	3429.1 (0.2 to 67399712)	1575 (1575 to 1575)	7466 (7466 to 7466)	0 (0 to 0)
Anti-MAGE-A3, PXXI (V27+2W) [N=3;2;1;0]	5459.7 (1022.8 to 29145.2)	3699.8 (2894.3 to 4729.5)	11889 (11889 to 11889)	0 (0 to 0)
Anti-MAGE-A3, PXXI (V27+6M) [N=3;2;1;0]	3010.6 (288.7 to 31395.3)	1754.4 (351.7 to 8751.9)	8865 (8865 to 8865)	0 (0 to 0)
Anti-MAGE-A3, PXXII (V29+2W) [N=3;2;1;0]	4657.1 (529.4 to 40967)	3077.8 (5.3 to 1801276)	10663 (10663 to 10663)	0 (0 to 0)

Anti-MAGE-A3, PXXIII (V31+2W) [N=2;2;0;0]	2248.7 (226.4 to 22332.9)	2248.7 (226.4 to 22332.9)	0 (0 to 0)	0 (0 to 0)
Anti-MAGE-A3, CCL [N=5;2;0;3]	6972.9 (2571.8 to 18905.3)	4057.1 (0.1 to 135760000)	0 (0 to 0)	10004.8 (4092.9 to 24455.9)

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 ^[6]
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End point description:

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

For initially seropositive patients: post-administration antibody concentration $\geq$ 2 fold the pre-vaccination antibody concentration

End point type	Primary
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End point timeframe:

From Dose 2 to Study End

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group	GS+/+ Group	GS+/- Group	GS- Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	7	5	6
Units: Patients				
Anti-MAGE-A3, PI (D2) [N=17;7;4;6]	0	0	0	0
Anti-MAGE-A3, PI (D7) [N=18;7;5;6]	1	0	1	0
Anti-MAGE-A3, PI (D15) [N=17;7;5;5]	9	3	3	3
Anti-MAGE-A3, PII (D16) [N=15;7;3;5]	8	3	2	3
Anti-MAGE-A3, PII (W5) [N=16;7;4;5]	16	7	4	5
Anti-MAGE-A3, PV (W11) [N=12;4;4;4]	12	4	4	4
Anti-MAGE-A3, PVI (W13) [N=16;7;4;5]	16	7	4	5
Anti-MAGE-A3, PVIII (W21) [N=10;7;2;1]	10	7	2	1
Anti-MAGE-A3, PXII (W32) [N=10;7;2;1]	10	7	2	1
Anti-MAGE-A3, PXVI (W54) [N=5;4;1;0]	5	4	1	0
Anti-MAGE-A3, PXVII (V21+3M) [N=3;3;0;0]	3	3	0	0
Anti-MAGE-A3, PXVIII (V22+2W) [N=2;1;1;0]	2	1	1	0
Anti-MAGE-A3, PXIX (V24+3M) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXX (V25+2W) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXX (V25+6M) [N=2;1;1;0]	2	1	1	0
Anti-MAGE-A3, PXXI (V27+2W) [N=3;2;1;0]	3	2	1	0

Anti-MAGE-A3, PXXI (V27+6M) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXII (V29+2W) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXIII (V31+2W) [N=2;2;0;0]	2	2	0	0
Anti-MAGE-A3, CCL [N=5;2;0;3]	5	2	0	3

Statistical analyses

No statistical analyses for this end point

Primary: mean of Anti-MAGE-A3 specific CD4+ and CD8+ T-cells concentrations after immunization

End point title	mean of Anti-MAGE-A3 specific CD4+ and CD8+ T-cells concentrations after immunization ^[7]
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End point description:

A patient was considered as a cellular mediated immune (CMI) responder if there was an increased amount of antigen-specific T-cells after immunization as compared to the patient's baseline value. These specific T-cells included the CD4+ or CD8+ T-cells producing cytokines and/or presenting cytolytic activity (or other, following the updated method of detection), and/or specific CD4+ or CD8+ T-cells presenting a particular phenotype (effector/memory).

End point type	Primary
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End point timeframe:

From study start to study end

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: T cell				
geometric mean (confidence interval 95%)				
CD4.TNFα (+) + IFNγ (+) PRE	1.05 (0.98 to 1.11)			
CD8.TNFα (+) + IFNγ (+) PRE	1.01 (0.99 to 1.03)			
CD4.TNFα (+) + IFNγ (+) PII(W5)	3.36 (2.2 to 5.13)			
CD8.TNFα (+) + IFNγ (+) PII(W5)	1 (1 to 1)			
CD4.TNFα (+) + IFNγ (+) PVI(W13)	5.35 (2.42 to 11.79)			
CD8.TNFα (+) + IFNγ (+) PVI(W13)	1 (1 to 1)			
CD4.TNFα (+) + IFNγ (+) PXII(W32)	5.29 (2.09 to 13.37)			
CD8.TNFα (+) + IFNγ (+) PXII(W32)	1.04 (0.99 to 1.09)			
CD4.TNFα (+) + IFNγ (+) PXVI(W54)	2.83 (1.04 to 7.68)			
CD8.TNFα (+) + IFNγ (+) PXVI(W54)	1 (1 to 1)			

CD4.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	2.62 (0.07 to 92.58)			
CD8.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	1 (1 to 1)			
CD4.TNFα (+) + IFNγ (+) PXX(V25+2W)	2.13 (0.29 to 15.91)			
CD8.TNFα (+) + IFNγ (+) PXX(V25+2W)	1.05 (0.86 to 1.28)			
CD4.TNFα (+) + IFNγ (+) CCL	2.42 (0 to 185163.6)			
CD8.TNFα (+) + IFNγ (+) CCL	1 (1 to 1)			
CD4.TNFα (+) + IFNγ (+) At any time point	0 (0 to 0)			
CD8.TNFα (+) + IFNγ (+) At any time point	0 (0 to 0)			

Statistical analyses

No statistical analyses for this end point

Primary: CD4+ and CD8+ T cell frequency ≥ 1.24 cut-off

End point title	CD4+ and CD8+ T cell frequency ≥ 1.24 cut-off ^[8]
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End point description:

A patient was considered as a cellular mediated immune (CMI) responder if there was an increased amount of antigen-specific T-cells after immunization as compared to the patient's baseline value. These specific T-cells included the CD4+ or CD8+ T-cells producing cytokines and/or presenting cytolytic activity (or other, following the updated method of detection), and/or specific CD4+ or CD8+ T-cells presenting a particular phenotype (effector/memory).

End point type	Primary
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End point timeframe:

From study start to study end

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Patients				
CD4.TNFα (+) + IFNγ (+) PRE	1			
CD8.TNFα (+) + IFNγ (+) PRE	1			
CD4.TNFα (+) + IFNγ (+) PII(W5)	15			
CD8.TNFα (+) + IFNγ (+) PII(W5)	0			
CD4.TNFα (+) + IFNγ (+) PVI(W13)	11			
CD8.TNFα (+) + IFNγ (+) PVI(W13)	0			
CD4.TNFα (+) + IFNγ (+) PXII(W32)	9			
CD8.TNFα (+) + IFNγ (+) PXII(W32)	2			
CD4.TNFα (+) + IFNγ (+) PXVI(W54)	4			
CD8.TNFα (+) + IFNγ (+) PXVI(W54)	0			
CD4.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	2			

CD8.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	0			
CD4.TNFα (+) + IFNγ (+) PXX(V25+2W)	2			
CD8.TNFα (+) + IFNγ (+) PXX(V25+2W)	1			
CD4.TNFα (+) + IFNγ (+) CCL	1			
CD8.TNFα (+) + IFNγ (+) CCL	0			
CD4.TNFα (+) + IFNγ (+) At any time point	15			
CD8.TNFα (+) + IFNγ (+) At any time point	3			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with a cellular response (Anti-MAGE-A3 specific CD4+ and CD8+ T-cells concentrations after immunization)

End point title	Number of patients with a cellular response (Anti-MAGE-A3 specific CD4+ and CD8+ T-cells concentrations after immunization) ^[9]
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End point description:

A patient was considered as a cellular mediated immune (CMI) responder if there was an increased amount of antigen-specific T-cells after immunization as compared to the patient's baseline value. These specific T-cells included the CD4+ or CD8+ T-cells producing cytokines and/or presenting cytolytic activity (or other, following the updated method of detection), and/or specific CD4+ or CD8+ T-cells presenting a particular phenotype (effector/memory). Analysis of MAGE-A3 cellular response was not performed. So the numbers presented for them are placeholder values.

End point type	Primary
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End point timeframe:

From week 5 to study end

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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Patients				
CD4.TNFα (+) + IFNγ (+) PII(W5)	5			
CD8.TNFα (+) + IFNγ (+) PII(W5)	0			
CD4.TNFα (+) + IFNγ (+) PVI(W13)	8			
CD8.TNFα (+) + IFNγ (+) PVI(W13)	0			
CD4.TNFα (+) + IFNγ (+) PXII(W32)	4			
CD8.TNFα (+) + IFNγ (+) PXII(W32)	0			
CD4.TNFα (+) + IFNγ (+) PXVI(W54)	2			
CD8.TNFα (+) + IFNγ (+) PXVI(W54)	0			
CD4.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	0			
CD8.TNFα (+) + IFNγ (+) PXVIII(V22+2W)	0			

CD4.TNFα (+) + IFNγ (+) PXX(V25+2W)	1			
CD8.TNFα (+) + IFNγ (+) PXX(V25+2W)	0			
CD4.TNFα (+) + IFNγ (+) CCL	1			
CD8.TNFα (+) + IFNγ (+) CCL	0			
CD4.TNFα (+) + IFNγ (+) At any time point	12			
CD8.TNFα (+) + IFNγ (+) At any time point	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients reported with ASCI-related grade3/4 adverse events (AEs) according to the Common Terminology Criteria (CTCAE) version 3.0.

End point title	Number of patients reported with ASCI-related grade3/4 adverse events (AEs) according to the Common Terminology Criteria (CTCAE) version 3.0. ^[10]
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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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. AEs may include pre- or post-treatment events that occur as a result of protocol-mandated procedures (i.e. invasive procedures, modification of patient's previous therapeutic regimen). Related = AE assessed by the investigator as related to the treatment.

End point type	Primary
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End point timeframe:

Within the 31-day (Days 0-30) post-administration periods.

Notes:

[10] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Any event, Grade 3	0			
Any event, 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) ^[11]
End point description:	
Serious adverse events (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. 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:

[11] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Any SAEs	2			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[12]
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	Primary
End point timeframe:	
From study start to study end, each patient being censored out of the analysis at time of death.	

Notes:

[12] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
ALT - SCR G0; SE G0	20			
ALT - SCR G0; SE G1	3			
ALT - SCR G0; SE G2	0			
ALT - SCR G0; SE G3	1			
ALT - SCR G0; SE G4	0			
ALT - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[13]
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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 was Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[13] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
AST - SCR G0; SE G0	19			
AST - SCR G0; SE G1	5			
AST - SCR G0; SE G2	0			
AST - SCR G0; SE G3	0			
AST - SCR G0; SE G4	0			
AST - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[14]
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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 Unknown (UNK) and Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[14] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
ALK - SCR UNK; SE G0	0			
ALK - SCR UNK; SE G1	0			
ALK - SCR UNK; SE G2	0			
ALK - SCR UNK; SE G3	0			
ALK - SCR UNK; SE G4	0			
ALK - SCR UNK; SE UNK	1			
ALK - SCR G0; SE G0	17			
ALK - SCR G0; SE G1	6			
ALK - SCR G0; SE G2	0			
ALK - SCR G0; SE G3	0			
ALK - SCR G0; SE G4	0			
ALK - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[15]
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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 was Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[15] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
BIL - SCR G0; SE G0	24			
BIL - SCR G0; SE G1	0			
BIL - SCR G0; SE G2	0			
BIL - SCR G0; SE G3	0			
BIL - SCR G0; SE G4	0			
BIL - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[16]
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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) and G1. CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[16] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
CREA - SCR G0; SE G0	20			
CREA - SCR G0; SE G1	2			
CREA - SCR G0; SE G2	0			
CREA - SCR G0; SE G3	0			
CREA - SCR G0; SE G4	0			
CREA - SCR G0; SE UNK	1			
CREA - SCR G1; SE G0	0			
CREA - SCR G1; SE G1	0			

CREA - SCR G1; SE G2	1			
CREA - SCR G1; SE G3	0			
CREA - SCR G1; SE UNK	0			
CREA - SCR G1; SE G4	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[17]
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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 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	Primary
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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.

Notes:

[17] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
GGT - SCR UNK; SE G0	0			
GGT - SCR UNK; SE G1	1			
GGT - SCR UNK; SE G2	0			
GGT - SCR UNK; SE G3	0			
GGT - SCR UNK; SE G4	0			
GGT - SCR UNK; SE UNK	0			
GGT - SCR G0; SE G0	17			
GGT - SCR G0; SE G1	2			
GGT - SCR G0; SE G2	1			
GGT - SCR G0; SE G3	0			
GGT - SCR G0; SE G4	0			
GGT - SCR G0; SE UNK	0			
GGT - SCR G1; SE G0	0			
GGT - SCR G1; SE G1	2			
GGT - SCR G1; SE G2	0			
GGT - SCR G1; SE G3	1			
GGT - SCR G1; SE G4	0			
GGT - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[18]
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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	Primary
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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.

Notes:

[18] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
HGB - SCR G0; SE G0	14			
HGB - SCR G0; SE G1	9			
HGB - SCR G0; SE G2	0			
HGB - SCR G0; SE G3	0			
HGB - SCR G0; SE G4	0			
HGB - SCR G0; SE UNK	0			
HGB - SCR G1; SE G0	0			
HGB - SCR G1; SE G1	1			
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

Primary: 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 ^[19]
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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	Primary
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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.

Notes:

[19] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
HCA - SCR UNK; SE G0	3			
HCA - SCR UNK; SE G1	0			
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	15			
HCA - SCR G0; SE G1	3			
HCA - SCR G0; SE G2	0			
HCA - SCR G0; SE G3	0			
HCA - SCR G0; SE G4	0			
HCA - SCR G0; SE UNK	0			
HCA - SCR G1; SE G0	1			
HCA - SCR G1; SE G1	2			
HCA - SCR G1; SE G2	0			
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

Primary: 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 ^[20]
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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 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	Primary
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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.

Notes:

[20] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
HKA - SCR UNK; SE G0	2			
HKA - SCR UNK; SE G1	0			
HKA - SCR UNK; SE G2	0			
HKA - SCR UNK; SE G3	0			
HKA - SCR UNK; SE G4	0			
HKA - SCR UNK; SE UNK	0			
HKA - SCR G0; SE G0	17			
HKA - SCR G0; SE G1	3			
HKA - SCR G0; SE G2	1			
HKA - SCR G0; SE G3	0			
HKA - SCR G0; SE G4	0			
HKA - SCR G0; SE UNK	0			
HKA - SCR G1; SE G0	0			
HKA - SCR G1; SE G1	0			
HKA - SCR G1; SE G2	1			
HKA - SCR G1; SE G3	0			
HKA - SCR G1; SE G4	0			
HKA - SCR G1; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[21]
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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 Unknown (UNK) and Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[21] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
HNA - SCR UNK; SE G0	2			
HNA - SCR UNK; SE G1	0			
HNA - SCR UNK; SE G2	0			
HNA - SCR UNK; SE G3	0			
HNA - SCR UNK; SE G4	0			
HNA - SCR UNK; SE UNK	0			
HNA - SCR G0; SE G0	19			
HNA - SCR G0; SE G1	3			
HNA - SCR G0; SE G2	0			
HNA - SCR G0; SE G3	0			
HNA - SCR G0; SE G4	0			
HNA - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[22]
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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) and Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[22] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
hAL - SCR UNK; SE G0	1			
hAL - SCR UNK; SE G1	1			

hAL - SCR UNK; SE G2	0			
hAL - SCR UNK; SE G3	0			
hAL - SCR UNK; SE G4	0			
hAL - SCR UNK; SE UNK	0			
hAL - SCR G0; SE G0	21			
hAL - SCR G0; SE G1	0			
hAL - SCR G0; SE G2	0			
hAL - SCR G0; SE G3	0			
hAL - SCR G0; SE G4	0			
hAL - SCR G0; SE UNK	1			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[23]
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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	Primary
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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.

Notes:

[23] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
hCA - SCR UNK; SE G0	3			
hCA - SCR UNK; SE G1	0			
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	18			
hCA - SCR G0; SE G1	2			
hCA - SCR G0; SE G2	0			
hCA - SCR G0; SE G3	0			
hCA - SCR G0; SE G4	0			
hCA - SCR G0; SE UNK	0			
hCA - SCR G1; SE G0	0			

hCA - SCR G1; SE G1	1			
hCA - SCR G1; SE G2	0			
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

Primary: 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 ^[24]
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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 Unknown (UNK) and Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[24] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
hKA - SCR UNK; SE G0	2			
hKA - SCR UNK; SE G1	0			
hKA - SCR UNK; SE G2	0			
hKA - SCR UNK; SE G3	0			
hKA - SCR UNK; SE G4	0			
hKA - SCR UNK; SE UNK	0			
hKA - SCR G0; SE G0	19			
hKA - SCR G0; SE G1	3			
hKA - SCR G0; SE G2	0			
hKA - SCR G0; SE G3	0			
hKA - SCR G0; SE G4	0			
hKA - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[25]
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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 Unknown (UNK) and Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[25] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
hNA - SCR UNK; SE G0	2			
hNA - SCR UNK; SE G1	0			
hNA - SCR UNK; SE G2	0			
hNA - SCR UNK; SE G3	0			
hNA - SCR UNK; SE G4	0			
hNA - SCR UNK; SE UNK	0			
hNA - SCR G0; SE G0	18			
hNA - SCR G0; SE G1	4			
hNA - SCR G0; SE G2	0			
hNA - SCR G0; SE G3	0			
hNA - SCR G0; SE G4	0			
hNA - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[26]
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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	Primary
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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.

Notes:

[26] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
LEU - SCR G0; SE G0	21			
LEU - SCR G0; SE G1	2			
LEU - SCR G0; SE G2	0			
LEU - SCR G0; SE G3	0			
LEU - SCR G0; SE G4	0			
LEU - SCR G0; SE UNK	0			
LEU - SCR G1; SE G0	1			
LEU - SCR G1; SE G1	0			
LEU - SCR G1; SE G2	0			
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

Primary: 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 ^[27]
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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	Primary
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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.

Notes:

[27] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
LYM - SCR G0; SE G0	17			
LYM - SCR G0; SE G1	0			
LYM - SCR G0; SE G2	3			
LYM - SCR G0; SE G3	0			
LYM - SCR G0; SE G4	0			
LYM - SCR G0; SE UNK	0			
LYM - SCR G1; SE G0	1			
LYM - SCR G1; SE G1	3			
LYM - SCR G1; SE G2	0			
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

Primary: 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 ^[28]
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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 was Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[28] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
NEU - SCR G0; SE G0	21			
NEU - SCR G0; SE G1	2			
NEU - SCR G0; SE G2	1			
NEU - SCR G0; SE G3	0			
NEU - SCR G0; SE G4	0			
NEU - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[29]
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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 was Grade 0 (G0). CTC grade statuses reported at SE were G0, G1, G2, G3, G4, and Unknown (UNK).

End point type	Primary
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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.

Notes:

[29] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
PLT - SCR G0; SE G0	24			
PLT - SCR G0; SE G1	0			
PLT - SCR G0; SE G2	0			
PLT - SCR G0; SE G3	0			
PLT - SCR G0; SE G4	0			
PLT - SCR G0; SE UNK	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with any AE(s) and with AEs by maximum grade, related to treatment administration

End point title	Number of patients with any AE(s) and with AEs by maximum grade, related to treatment administration ^[30]
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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	Primary
End point timeframe:	
Within the 31-day follow-up period post treatment administration.	

Notes:

[30] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Patients with any AEs	23			
Patients with G1 AEs	11			
Patients with G2 AEs	12			
Patients with G3 AEs	0			
Patients with G4 AEs	0			
Patients with G5 AEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[31]
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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	Primary
End point timeframe:	
Within the 31-day follow-up period post treatment administration.	

Notes:

[31] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Patients with any AEs	24			
Patients with G1 AEs	6			

Patients with G2 AEs	15			
Patients with G3 AEs	0			
Patients with G4 AEs	0			
Patients with G5 AEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: 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 ^[32]
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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	Primary
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End point timeframe:

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

Notes:

[32] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Patients with any SAEs	2			
Patients with G1 SAEs	0			
Patients with G2 SAEs	1			
Patients with G3 SAEs	1			
Patients with G4 SAEs	0			
Patients with G5 SAEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with any serious adverse events (SAEs) and with AEs by maximum grade, related to treatment administration

End point title	Number of patients with any serious adverse events (SAEs) and with AEs by maximum grade, related to treatment administration ^[33]
-----------------	--

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	Primary
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End point timeframe:

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

Notes:

[33] - 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: This outcome was descriptive, hence no statistical analyses were performed.

End point values	MAGE-A3 Group			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Patients with any SAEs	0			
Patients with G1 SAEs	0			
Patients with G2 SAEs	0			
Patients with G3 SAEs	0			
Patients with G4 SAEs	0			
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	18.0
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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	2 / 24 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic malignant melanoma			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	1 / 24 (4.17%)		
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	24 / 24 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic malignant melanoma			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Metastatic pain			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	31		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	40		
Injection site reaction			
subjects affected / exposed	12 / 24 (50.00%)		
occurrences (all)	50		
Pyrexia			
subjects affected / exposed	10 / 24 (41.67%)		
occurrences (all)	31		
Asthenia			
subjects affected / exposed	9 / 24 (37.50%)		
occurrences (all)	19		
Fatigue			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	13		
Influenza like illness			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	40		
Chills			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	8		

Injection site erythema subjects affected / exposed occurrences (all)	4 / 24 (16.67%) 7		
Discomfort subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 10		
Administration site pain subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 4		
Injection site induration subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 7		
Ulcer subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	7 / 24 (29.17%) 17		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Vomiting subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 3		
Dyspnoea subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		

Hyperhidrosis subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Pruritus subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 7		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 3		
Myalgia subjects affected / exposed occurrences (all)	3 / 24 (12.50%) 18		
Back pain subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Groin pain subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Infections and infestations			
Skin infection subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 24 (8.33%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 March 2009	The changes following this amendment concern: • The possibility of taking a new tumor biopsy in case the results of the analysis of the biopsies originally taken are inconclusive. • The description of the AJCC staging system for cutaneous melanoma • The AJCC staging system for cutaneous melanoma • The time window for tumor imaging at screening • The expected time for completing patient recruitment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported