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

Summary

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

Results information

Result version number	v3 (current)
This version publication date	24 December 2020
First version publication date	24 March 2016
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	111476

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

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

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	60
From 65 to 84 years	65
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Pre-assignment period milestones

Number of subjects started	125
Number of subjects completed	123

Pre-assignment subject non-completion reasons

Reason: Number of subjects	no study treatment received: 2

Period 1

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

Arms

Arm title	Overall Study Group

Arm description:

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

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

Dosage and administration details:

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

Number of subjects in period 1[1]	Overall Study Group
Started	123
Completed	1
Not completed	122
Consent withdrawn by subject	9
Death	80

Unspecified	29
Lost to follow-up	4

Notes:

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

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

Baseline characteristics

Reporting groups

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

Subject analysis sets

Subject analysis set title	GSK2132231A 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	GSK2132231A 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	GSK2132231A GS-unknown 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.

Reporting group values	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Number of subjects	71	50	2
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	66.9	62.1	60.5
standard deviation	± 13.9	± 12.6	± 6.36
Gender categorical Units: Subjects			
Female	42	23	0
Male	29	27	2

End points

End points reporting groups

Reporting group title	Overall Study 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	GSK2132231A 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	GSK2132231A 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	GSK2132231A GS-unknown Group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subset of patients with unknown status as regards GS signature, receiving the MAGE-A3 ASCI product. Gene-signature sub-grouping was based on patients having a potentially predictive gene signature, as assessed at screening.	

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

End point title	One-year overall survival rate (OSR) estimated by complete case method[1]
End point description:	
The 1-year overall survival rate (OSR) in the GS+ Population would be above 50% (target = 71%), a proportion which was reported together with its 95% confidence interval (CI). Maximum 1-year OSR of any currently available treatment in the MAGE-A3-positive population = 50% (P0). This median OS of 12 months is based on the observed median OS for MAGE-A3-positive patients, whose tumor did not present the predictive GS. The target 1-year OSR for patients presenting the predictive GS = 71% (P1). This corresponds to a median OS of 24 months when assuming an exponential distribution of OS.	
End point type	Primary
End point timeframe:	
From Month 0 to Month 12	
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	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	65	48	2	
Units: Percentage of participants				
number (confidence interval 95%)				
OSR	83.08 (71.73 to 91.24)	83.33 (69.78 to 92.52)	100 (15.81 to 100)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Primary

End point timeframe:

During the entire study period (From Month 0 to Month 49)

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	Overall Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Patients				
Any SAEs	19			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with diseases characteristics by GS

End point title	Number of patients with diseases characteristics by GS

End point description:

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

End point type	Secondary

End point timeframe:

During the entire study period (From Month 0 to Month 49)

End point values	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	71	50	2	
Units: Patients				
STAGE IIIA	0	0	0	
STAGE IIIB	11	4	1	
STAGE IIIC	21	19	1	
STAGE IV	39	27	0	
STAGE MC	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS) by GS

End point title	Progression-free survival (PFS) by GS

End point description:

From study start to Month 24, each patient being censored out of the analysis at 1st report of disease progression or death. PFS was defined and calculated as the time from first treatment to either the first progression of the disease or the date of death, whichever occurred first. In case a patient went off protocol treatment, the date of first documented progression (if applicable) was to be used as date of progression. Patients still alive with no evidence of disease progression at the time of their last visit or for whom date of first documented progression was not applicable, were censored at the time of the last examination. PFS analysis was performed using the non-parametric Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From Month 0 to Month 24

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	123	71	50	
Units: Months				
median (confidence interval 95%)				
PFS	2.8 (2.8 to 2.8)	2.8 (2.8 to 2.9)	2.8 (2.5 to 2.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimates of the Progression-free Survival (PFS) at Months 6, 12 and 24, by Gene Signature

End point title	Kaplan-Meier estimates of the Progression-free Survival (PFS) at Months 6, 12 and 24, by Gene Signature

End point description:

PFS was defined as the time from the date of registration of the patient to either the date of disease progression or the date of death (for whatever reason), whichever comes first. Patients alive and without disease progression were censored at the date of their last tumor evaluation. The PFS estimates were assessed by the Kaplan-Meier method and expressed as the percentage of patients who did not progress and were alive at a given time.

End point type	Secondary

End point timeframe:

At Month 6, Month 12 and Month 24

End point values	GSK2132231A GS+ Group	GSK2132231A GS- Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	50		
Units: Percentage of subjects				
number (confidence interval 95%)				
PFS 6M [71;50]	13.53 (6.71 to 22.75)	5 (1 to 14.22)		
PFS 12M [71;50]	6.02 (1.95 to 13.43)	5 (1 to 14.22)		
PFS 24M [71;50]	1.5 (0.13 to 7.12)	5 (1 to 14.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) by GS

End point title	Overall survival (OS) by GS

End point description:

OS was defined as defined as the time from registration of the patient until death, with patients alive at the time of analysis censored at the time of the last contact.

End point type	Secondary

End point timeframe:

Up to 5 years from the time of registration

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	123	71	50	
Units: Months				
median (confidence interval 95%)				

OS	23.9 (19.2 to 28.2)	20.6 (16.1 to 28.2)	25.8 (18.4 to 35.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to treatment failure (TTF) by GS

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

End point description:

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

End point type	Secondary

End point timeframe:

During the 24 months period (From Month 0 to Month 24).

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	123	71	50	
Units: Months				
median (confidence interval 95%)				
TTF	2.5 (2.4 to 4.1)	2.7 (2.4 to 5.4)	2.4 (2.3 to 2.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response (BOR) by GS

End point title	Best overall response (BOR) by GS

End point description:

The best overall response was the best response recorded from the start of the treatment until disease progression/recurrence, except for confirmed objective response, which was reported as BOR independently of its time of occurrence. Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0) for target lesions and assessed by MRI and/or CT: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions without any new lesions and/or progression of existing non-target lesions; Stable Disease (SD), neither sufficient shrinkage to qualify for a Partial Response nor sufficient increase to qualify for Progression of Disease (PD) without any new lesions and/or progression of existing non-target lesions; PD, >=20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions; NE = Non-evaluable response.

End point type	Secondary

End point timeframe:

During the 24 months period (From Month 0 to Month 24)

End point values	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	71	50	2	
Units: Patients				
CR	0	1	0	
PR	3	0	0	
SD	11	4	0	
SD/PR	3	0	0	
PD	51	44	2	
NE	3	1	0	
Missing	0	0	0	

Statistical analyses

No statistical analyses for this end point

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

End point title	Duration of response (CR or PR) by GS

End point description:

Duration of response was measured from the time when the measurement criteria for CR/PR (whichever was recorded first) were met until the first date that recurrent or PD was objectively documented (taking as reference for PD the smallest measurements recorded since the treatment started).
Note: As there was only one patient analyzed in the GS- Subgroup, the median duration of response was not calculated for this latter subgroup. When only 1 subject is analyzed, the lower limit (LL) and the upper limit (UL) are entered equal to the geometric mean concentration (GMC) value as the confidence interval could not be calculated with only 1 subject analyzed.

End point type	Secondary

End point timeframe:

During the 24 months period (From Month 0 to Month 24)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	4	3	1	
Units: Months				
median (confidence interval 95%)				
CR/PR	8.3 (1.9 to 8.3)	6.9 (1.9 to 9.7)	0 (0 to 0)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

During the 24 months period (From Month 0 to Month 24)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	11	4	
Units: Months				
median (confidence interval 95%)				
SD/TTP	5.4 (5.1 to 9.4)	5.4 (4.1 to 9.4)	5.4 (5.1 to 25)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of seropositive patients for anti-MAGE-A3

End point description:

Seropositive patients were those patients with anti-MAGE-A3 antibody concentrations ≥ 27 ELISA units per millilitre (EL.U/mL).

End point type	Secondary

End point timeframe:

PRE = Pre any dose, PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31) = Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18) = Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49).

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87	52	34	1
Units: Patients				
Anti-MAGE-A3, PRE [N=87;52;34;1]	7	4	3	0
Anti-MAGE-A3, PII(W4) [N=62;39;22;1]	60	37	22	1
Anti-MAGE-A3, PVI(W12) [N=52;34;17;1]	52	34	17	1
Anti-MAGE-A3, PXII(W31) [N=11;5;6;0]	11	5	6	0

Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0]	6	3	3	0
Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0]	4	4	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-MAGE-A3 antibody concentrations

End point title	Anti-MAGE-A3 antibody concentrations

End point description:

Anti-MAGE-A3 antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per millilitre (EL.U/mL). When only 1 subject is analyzed, the lower limit (LL) and the upper limit (UL) are entered equal to the geometric mean concentration (GMC) value as the confidence interval could not be calculated with only 1 subject analyzed.

End point type	Secondary

End point timeframe:

PRE = Pre any dose, PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31) = Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18) = Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49).

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87	52	34	1
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-MAGE-A3, PRE [N=87;52;34;1]	11.2 (10.3 to 12.2)	11.2 (10 to 12.5)	11.3 (9.8 to 13)	10 (10 to 10)
Anti-MAGE-A3, PII(W4) [N=62;39;22;1]	906.1 (608 to 1350.2)	728.7 (406 to 1307.9)	1385.7 (896.4 to 2142)	387 (387 to 387)
Anti-MAGE-A3, PVI(W12) [N=52;34;17;1]	6190.1 (5007.6 to 7652)	5631 (4284.9 to 7399.8)	7500.1 (5165.9 to 10889.2)	5921 (5921 to 5921)
Anti-MAGE-A3, PXII(W31) [N=11;5;6;0]	6724.2 (3978 to 11366.4)	7094.2 (2360 to 21325.5)	6430.7 (2877.3 to 14372.4)	0 (0 to 0)
Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0]	3289.8 (1575.4 to 6870)	2570.9 (480.1 to 13765.9)	4209.7 (622.4 to 28473.7)	0 (0 to 0)
Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0]	4118.6 (1557.3 to 10892.7)	4784.5 (115.5 to 198255.8)	3052 (3052 to 3052)	0 (0 to 0)
Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0]	7063.9 (3780.4 to 13199.4)	7063.9 (3780.4 to 13199.4)	0 (0 to 0)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive patients for protein D

End point title	Number of seropositive patients for protein D

End point description:

Seropositive patients were those patients with anti-PD antibody concentrations ≥ 100 EL.U/mL.

End point type	Secondary

End point timeframe:

PRE = Pre any dose, PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31) = Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18) = Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	53	34	1
Units: Patients				
Anti-PD, PRE [N=88;53;34;1]	29	20	8	1
Anti-PD, PII(W4) [N=77;46;30;1]	77	46	30	1
Anti-PD, PVI(W12) [N=52;34;17;1]	52	34	17	1
Anti-PD, PXII(W31) [N=11;5;6;0]	11	5	6	0
Anti-PD, PXVI(W54) [N=6;3;3;0]	6	3	3	0
Anti-PD, PXVII(M18) [N=3;2;1;0]	3	2	1	0
Anti-PD, PXXIV(M49) [N=4;4;0;0]	4	4	0	0

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Anti-PD antibody concentrations were presented ad geometric mean concentrations (GMTs) and expressed in EL.U/mL. When only 1 subject is analyzed, the lower limit (LL) and the upper limit (UL) are entered equal to the geometric mean concentration (GMC) value as the confidence interval could not be calculated with only 1 subject analyzed.

End point type	Secondary

End point timeframe:

PRE = Pre any dose, PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31)

= Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18)= Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	88	53	34	1
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE [N=88;53;34;1]	81.2 (68.5 to 96.2)	86.1 (68.9 to 107.5)	70.6 (54.5 to 91.5)	412 (412 to 412)
Anti-PD, PII(W4) [N=77;46;30;1]	4588 (3397.5 to 6195.7)	4196.9 (2768 to 6363.3)	5139.8 (3253.3 to 8120.2)	9167 (9167 to 9167)
Anti-PD, PVI(W12) [N=52;34;17;1]	15036.7 (12057.7 to 18751.5)	14091.9 (10763.7 to 18449.4)	16453.2 (10607.9 to 25519.6)	29553 (29553 to 29553)
Anti-PD, PXII(W31) [N=11;5;6;0]	23548.6 (15167.2 to 36561.6)	25070.5 (8468.5 to 74220)	22351.2 (13378 to 37343.1)	0 (0 to 0)
Anti-PD, PXVI(W54) [N=6;3;3;0]	12389.9 (6229 to 24644.4)	9639.2 (1286.9 to 72202.6)	15925.5 (4872 to 52057)	0 (0 to 0)
Anti-PD, PXVII(M18) [N=3;2;1;0]	11386.1 (3141.7 to 41265.3)	13839.4 (93.9 to 2040751)	7707 (7707 to 7707)	0 (0 to 0)
Anti-PD, PXXIV(M49) [N=4;4;0;0]	10546.9 (1777.2 to 62591.1)	10546.9 (1777.2 to 62591.1)	0 (0 to 0)	0 (0 to 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-MAGE-A3 antibody response

End point title	Anti-MAGE-A3 antibody response

End point description:

Anti-MAGE-A3 antibody response defined as:
For initially seronegative patients: post-vaccination antibody concentration ≥ 27 EL.U/mL.
For initially seropositive patients: post-vaccination antibody concentration ≥ 2 fold the pre-vaccination antibody concentration

End point type	Secondary

End point timeframe:

PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31) = Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18) = Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	62	39	22	1
Units: Patients				
Anti-MAGE-A3, PII(W4) [N=62;39;22;1]	60	37	22	1
Anti-MAGE-A3, PVI(W12) [N=52;34;17;1]	52	34	17	1
Anti-MAGE-A3, PXII(W31) [N=11;5;6;0]	11	5	6	0
Anti-MAGE-A3, PXVI(W54) [N=6;3;3;0]	6	3	3	0
Anti-MAGE-A3, PXVII(M18) [N=3;2;1;0]	3	2	1	0
Anti-MAGE-A3, PXXIV(M49) [N=4;4;0;0]	4	4	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD antibody response

End point title	Anti-PD antibody response

End point description:

Anti-PD antibody response defined as:
For initially seronegative patients: post-vaccination antibody concentration ≥ 100 EL.U/mL.
For initially seropositive patients: post-vaccination antibody concentration ≥ 2 fold the pre-vaccination antibody concentration

End point type	Secondary

End point timeframe:

PII(W4) = Post-Dose 2 (Week 4), PVI(W12) = Post-Dose 6 (Week 12), PXII(W31) = Post-Dose 12 (Week 31), PXVI(W54) = Post-Dose 16 (Week 54), PXVII(M18) = Post-Dose 17 (Month 18), PXXIV(M49) = Post-Dose 24 (Month 49)

End point values	Overall Study Group	GSK2132231A GS+ Group	GSK2132231A GS- Group	GSK2132231A GS-unknown Group
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	77	46	30	1
Units: Patients				
Anti-PD, PII(W4) [N=77;46;30;1]	76	45	30	1
Anti-PD, PVI(W12) [N=52;34;17;1]	52	34	17	1
Anti-PD, PXII(W31) [N=11;5;6;0]	11	5	6	0
Anti-PD, PXVI(W54) [N=6;3;3;0]	6	3	3	0
Anti-PD, PXVII(M18) [N=3;2;1;0]	3	2	1	0
Anti-PD, PXXIV(M49) [N=4;4;0;0]	4	4	0	0

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

HGB - SCR G1; SE G3	3			
HGB - SCR G1; SE G4	1			
HGB - SCR G2; SE G0	1			
HGB - SCR G2; SE G2	1			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

End point values	Overall Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Patients				
LYM - SCR G0; SE G0	67			
LYM - SCR G0; SE G1	18			
LYM - SCR G0; SE G2	3			
LYM - SCR G0; SE UNK	1			
LYM - SCR G1; SE G0	3			
LYM - SCR G1; SE G1	23			
LYM - SCR G1; SE G2	4			
LYM - SCR G2; SE G2	1			
LYM - SCR G2; SE G3	1			
LYM - SCR G3; SE G3	2			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

From study start to study end (Month 0 - Month 49), each patient being censored out of the analysis at time of death.

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

During the whole study period (From Month 0 to Month 49)

End point values	Overall Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Patients				
Any event(s)	4			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The assessed AEs were ASCI-related adverse events according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.
Grade 1 = Mild AE; Grade 2 = Moderate AE; Grade 3 = Severe AE; Grade 4 = Life-threatening or disabling AE; Grade 5 = Death due to AE.
An unsolicited AE covers any untoward medical occurrence in a clinical investigation patient temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Through 30 days after the last administration of the study treatment, approximately 49 months

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation patient temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary

End point timeframe:

Through 30 days after the last administration of the study treatment, approximately 49 months

End point values	Overall Study Group			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: Patients				
Any AE(s)	116			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs up to 30 days post treatment; SAEs during the entire study period (from Month 0 to Month 49).	
Adverse event reporting additional description:	
As planned per study protocol, safety was assessed in the overall population regardless of GS status.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

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

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

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

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

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

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

Non-serious adverse events	Overall Study Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 123 (86.99%)		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 123 (11.38%)		
occurrences (all)	20		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 123 (13.82%)		
occurrences (all)	42		
Chills			
subjects affected / exposed	21 / 123 (17.07%)		
occurrences (all)	42		
Fatigue			
subjects affected / exposed	30 / 123 (24.39%)		
occurrences (all)	110		
Influenza like illness			

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2011	The main changes in Amendment 1 concern: 1. The addition of an interim analysis for the early assessment of the predictive value of the gene signature (Statistical analysis, Section 10). The interim analysis will assess all available safety and clinical activity data at the time at least 36 enrolled patients have been followed up for one year or have died. Amongst these 36 patients, 18 should have a tumor with the predictive gene signature. The original version of the protocol specified a fixed sample size study of 51 patients with the predictive gene signature having started protocol treatment and having been followed for at least 1 year (or having died). The implementation of a group sequential test design with two stages in the amendment leads to an increase in final sample size from 51 to 53 patients with the predictive gene signature having started protocol treatment and having been followed for at least 1 year (or having died). Assumptions and details of the statistical considerations are described below in Section 10.3. Moreover, in this amendment, it has been specified that the final analysis will take place approximately one year after last patient's first visit and that updated analysis of overall survival will be performed on a yearly basis until all patients have been followed up for 5 years. 2. Contact information for reporting SAEs has been updated. 3. A new section (Section 6.3.7) has been introduced describing all the remaining Visits/procedures to be performed by patients withdrawn from study treatment. 4. An appendix was added with recommendations for biopsy collection (refer to Appendix B).
08 September 2014	Amendment 2: The main changes in Amendment 2 : • Removal of all active follow-up visits and procedures, • Removal of blood sampling for humoral immunological response and PBMC collection at the end of Cycle 4, • Clarifications regarding the decision to not perform further testing on samples already collected in the study but not tested yet, in the following sections: • Synopsis, • Objectives, • Biologicals sample handling and analysis, • Translational Research, • Secondary endpoints, • Analysis of immunogenicity, • Translational research analysis. • The section 'Final analysis' was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported