Clinical trial results:
A double blind, randomized, placebo controlled phase II study to assess the efficacy of recPRAME +AS15 Antigen-Specific Cancer Immunotherapeutic as adjuvant therapy in patients with resected PRAME-positive, Non-Small Cell Lung Cancer

Summary

EudraCT number	2012-002790-55
Trial protocol	EE GB DE
Global end of trial date	24 August 2016

Results information

Result version number	v1 (current)
This version publication date	30 August 2017
First version publication date	30 August 2017

Trial information

Trial identification

Sponsor protocol code	116389

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01853878
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 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 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	20 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of the recPRAME versus placebo in terms of disease-free survival (DFS)

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 63
Country: Number of subjects enrolled	France: 40
Country: Number of subjects enrolled	Germany: 131
Country: Number of subjects enrolled	Japan: 123
Country: Number of subjects enrolled	Korea, Republic of: 33
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Russian Federation: 64
Country: Number of subjects enrolled	United Kingdom: 115
Country: Number of subjects enrolled	United States: 96
Worldwide total number of subjects	681
EEA total number of subjects	365

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	294
From 65 to 84 years	381
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Am ong 681 enrolled patients, 358 were reported with positive PRAME expression results (out of whom 221 patients were not randomized for screening failures reasons) and 4 patients didn’t receive any study product dose.

Pre-assignment period milestones

Number of subjects started	681
Number of subjects completed	133

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No treatment received: 4
Reason: Number of subjects	positive PRAME expression results: 358
Reason: Number of subjects	Unspecified: 186

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2302032A Group

Arm description:

The patients received 13 administrations of the GSK2302032A product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Arm type	Experimental
Investigational medicinal product name	recPRAME + AS15 Antigen-Specific Cancer Immunotherapeutic
Investigational medicinal product code	PRAME ASCI
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The patients received 13 administrations of the product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Arm title	Placebo group

Arm description:

The patients received 13 administrations of a placebo, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Arm type	Placebo

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

Dosage and administration details:

The patients received 13 administrations of the product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Number of subjects in period 1[1]	GSK2302032A Group	Placebo group
Started	86	47
Completed	23	3
Not completed	63	44
Migrated/moved from the study area	1	-
Consent withdrawn by subject	3	1
Adverse event, non-fatal	2	-
Unspecified	55	43
Recurrence	2	-

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: Am ong 681 enrolled patients, 358 were reported with positive PRAME expression results (out of whom 221 patients were not randomized for screening failures reasons) and 4 patients didn’t receive any study product dose.

Baseline characteristics

Reporting groups	
Reporting group title	GSK2302032A Group
Reporting group description:	
The patients received 13 administrations of the GSK2302032A product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.	
Reporting group title	Placebo group
Reporting group description:	
The patients received 13 administrations of a placebo, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.	

Reporting group values	GSK2302032A Group	Placebo group	Total
Number of subjects	86	47	133
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 64.5 ± 8.68	 62.7 ± 9.28	 -
Gender categorical Units: Subjects			
Female	26	13	39
Male	60	34	94

End points

End points reporting groups

Reporting group title	GSK2302032A Group

Reporting group description:

The patients received 13 administrations of the GSK2302032A product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Reporting group title	Placebo group

Reporting group description:

The patients received 13 administrations of a placebo, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Primary: Time to occurrence of any recurrence of disease

End point title	Time to occurrence of any recurrence of disease

End point description:

Time to occurrence of any recurrence of disease is expressed in terms of rate: Person-year rate in each group = number of patients reporting at least one recurrence of disease (n)/ sum of follow-up period expressed in years (T[year)]) As a consequence of the decision to stop the PRAME-AS15-NSC-002 (ADJ) study, not all data were available for a full analysis. The median follow-up time was 10.3 months in the GSK2302032A group and 5.7 months in the Placebo group.

End point type	Primary

End point timeframe:

During the entire study (From Week 1 to Week 112)

End point values	GSK2302032A Group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	47		
Units: Months				
number (not applicable)				
Months	82.86	14.93		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Estimates of Hazard Ratio (HR) and their 95% Confidence Interval (CI) were obtained by Cox regression modelling.The Likelihood ratio test was used to compare the groups. The Cox proportional hazard regression was stratified by previous treatment (CT vs. no-CT) and disease stage.

Comparison groups	Placebo group v GSK2302032A Group

Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.1422
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	4.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	35.167

Notes:

[1] - P-value of the Wald test from a Cox regression model to test H0 = { HR=1} (Y = Time to Event)

Secondary: Number of patients with any Adverse Events

End point title	Number of patients with any Adverse Events

End point description:

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

End point type	Secondary

End point timeframe:

Up to 30 days post last dose of study product administration

End point values	GSK2302032A Group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	47		
Units: Participants				
Participants	78	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with any abnormal hematological and biochemical parameters

End point title	Number of patients with any abnormal hematological and biochemical parameters

End point description:

Hematological and biochemical parameters assessed were tabulated by maximum grade versus baseline, by CTC = Common Terminology Criteria and by the type of abnormality (e.g. inrcreased, decreased, prolonged, etc.). Some parameters (e.g. Anemia) already comprise within their defintion the type of abnormality presented. Due to character constraints, some parameteres were abbreviated as follows: Activated partial thromboplastin=APT; Alanine aminotransferase=ALT.

End point type	Secondary

End point timeframe:
For the whole study duration (Day 0 to Week 112)

End point values	GSK2302032A Group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	47		
Units: Participants				
APT time prolonged Grade 1	26	8		
APT time prolonged Grade 2	1	0		
APT time prolonged Grade 3	0	0		
APT time prolonged Grade 4	0	0		
APT time prolonged Grade 5	0	0		
APT prolonged Unknown	1	2		
ALT increased Grade 1	17	6		
ALT increased Grade 2	1	0		
ALT increased Grade 3	0	0		
ALT increased Grade 4	0	0		
ALT increased Grade 5	0	0		
ALT increased Unknown	0	1		
Alkaline Phosphatase increased Grade 1	17	5		
Alkaline Phosphatase increased Grade 2	0	0		
Alkaline Phosphatase increased Grade 3	0	0		
Alkaline Phosphatase increased Grade 4	0	0		
Alkaline Phosphatase increased Grade 5	0	0		
Alkaline Phosphatase increased Unknown	0	1		
Anemia Grade 1	36	17		
Anemia Grade 2	0	2		
Anemia Grade 3	0	0		
Anemia Grade 4	0	0		
Anemia Grade 5	0	0		
Anemia Unknown	1	1		
Aspartate aminotransferase increased Grade 1	15	5		
Aspartate aminotransferase increased Grade 2	0	0		
Aspartate aminotransferase increased Grade 3	0	0		
Aspartate aminotransferase increased Grade 4	0	0		
Aspartate aminotransferase increased Grade 5	0	0		
Aspartate aminotransferase increased Unknown	0	1		
Blood bilirubin increased Grade 1	7	2		
Blood bilirubin increased Grade 2	1	1		
Blood bilirubin increased Grade 3	0	0		
Blood bilirubin increased Grade 4	0	0		
Blood bilirubin increased Grade 5	0	0		
Blood bilirubin increased Unknown	0	1		
Creatinine increased Grade 1	15	7		

Creatinine increased Grade 2	3	0		
Creatinine increased Grade 3	0	0		
Creatinine increased Grade 4	0	0		
Creatinine increased Grade 5	0	0		
Creatinine increased Unknown	0	1		
Gamma-glutamyl transferase increased Grade 1	14	11		
Gamma-glutamyl transferase increased Grade 2	7	1		
Gamma-glutamyl transferase increased Grade 3	2	0		
Gamma-glutamyl transferase increased Grade 4	0	0		
Gamma-glutamyl transferase increased Grade 5	0	0		
Gamma-glutamyl transferase increased Unknown	0	2		
Hemoglobin increased Grade 1	5	1		
Hemoglobin increased Grade 2	1	0		
Hemoglobin increased Grade 3	0	0		
Hemoglobin increased Grade 4	0	0		
Hemoglobin increased Grade 5	0	0		
Hemoglobin increased Unknown	0	1		
Hyperkalemia Grade 1	22	12		
Hyperkalemia Grade 2	4	1		
Hyperkalemia Grade 3	1	0		
Hyperkalemia Grade 4	0	0		
Hyperkalemia Grade 5	0	0		
Hyperkalemia Unknown	0	1		
Hypernatremia Grade 1	13	6		
Hypernatremia Grade 2	4	1		
Hypernatremia Grade 3	0	0		
Hypernatremia Grade 4	0	0		
Hypernatremia Grade 5	0	0		
Hypernatremia Unknown	0	1		
Hypoalbuminemia Grade 1	18	10		
Hypoalbuminemia Grade 2	3	0		
Hypoalbuminemia Grade 3	0	0		
Hypoalbuminemia Grade 4	0	0		
Hypoalbuminemia Grade 5	0	0		
Hypoalbuminemia Unknown	0	2		
Hypokalemia Grade 1	3	1		
Hypokalemia Grade 2	0	0		
Hypokalemia Grade 3	0	0		
Hypokalemia Grade 4	0	0		
Hypokalemia Grade 5	0	0		
Hypokalemia Unknown	0	1		
Hyponatremia Grade 1	10	6		
Hyponatremia Grade 2	0	0		
Hyponatremia Grade 3	1	0		
Hyponatremia Grade 4	0	0		
Hyponatremia Grade 5	0	0		
Hyponatremia Unknown	0	1		
Lymphocyte count decreased Grade 1	19	8		

Lymphocyte count decreased Grade 2	3	2		
Lymphocyte count decreased Grade 3	2	0		
Lymphocyte count decreased Grade 4	0	0		
Lymphocyte count decreased Grade 5	0	0		
Lymphocyte count decreased Unknown	0	1		
Lymphocyte count increased Grade 1	0	0		
Lymphocyte count increased Grade 2	2	0		
Lymphocyte count increased Grade 3	0	0		
Lymphocyte count increased Grade 4	0	0		
Lymphocyte count increased Grade 5	0	0		
Lymphocyte count increased Unknown	0	1		
Neutrophil count decreased Grade 1	9	7		
Neutrophil count decreased Grade 2	4	1		
Neutrophil count decreased Grade 3	0	0		
Neutrophil count decreased Grade 4	0	0		
Neutrophil count decreased Grade 5	0	0		
Neutrophil count decreased Unknown	0	1		
Platelet count decreased Grade 1	6	1		
Platelet count decreased Grade 2	1	0		
Platelet count decreased Grade 3	0	0		
Platelet count decreased Grade 4	0	0		
Platelet count decreased Grade 5	0	0		
Platelet count decreased Unknown	0	1		
White blood cell decreased Grade 1	7	4		
White blood cell decreased Grade 2	1	0		
White blood cell decreased Grade 3	0	0		
White blood cell decreased Grade 4	0	0		
White blood cell decreased Grade 5	0	0		
White blood cell decreased Unknown	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of Serious Adverse Events (SAEs)

End point title	Occurrence of Serious Adverse Events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. An event that was part of the natural course of the disease under study (i.e., disease progression, recurrence) was captured in the study as an efficacy measure; therefore it did not need to be reported as an SAE.

End point type	Secondary

End point timeframe:

During the entire study (From Week 1 to Week 112)

End point values	GSK2302032A Group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	47		
Units: Participants				
Participants	14	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse events: 30 days post study treatment administration. Serious adverse events (SAEs): throughout the study (i.e. up to Week 112).

Adverse event reporting additional description:

An event that was part of the natural course of the disease under study (i.e., disease progression, recurrence) was captured in the study as an efficacy measure; therefore it did not need to be reported as an SAE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	GSK2302032A Group

Reporting group description:

The patients received 13 administrations GSK2302032A product, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Reporting group title	Placebo group

Reporting group description:

The patients received 13 administrations of a placebo, as per the following schedule: For the first five doses: 1 dose every 3 weeks. For the remaining 8 doses: 1 dose every 12 weeks.

Serious adverse events	GSK2302032A Group	Placebo group	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 86 (16.28%)	0 / 47 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			

subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 86 (2.33%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			

subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 86 (2.33%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhagic pneumonia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sepsis			
subjects affected / exposed	1 / 86 (1.16%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2.13 %

Non-serious adverse events	GSK2302032A Group	Placebo group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 86 (90.70%)	21 / 47 (44.68%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 86 (4.65%)	3 / 47 (6.38%)	
occurrences (all)	4	3	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 86 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 86 (6.98%)	0 / 47 (0.00%)	
occurrences (all)	11	0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 86 (3.49%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 86 (3.49%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
Chills			
subjects affected / exposed	6 / 86 (6.98%)	1 / 47 (2.13%)	
occurrences (all)	21	1	
Influenza like illness			
subjects affected / exposed	16 / 86 (18.60%)	2 / 47 (4.26%)	
occurrences (all)	59	3	
Fatigue			

subjects affected / exposed	14 / 86 (16.28%)	7 / 47 (14.89%)	
occurrences (all)	35	10	
Injection site erythema			
subjects affected / exposed	18 / 86 (20.93%)	1 / 47 (2.13%)	
occurrences (all)	31	1	
Injection site pain			
subjects affected / exposed	49 / 86 (56.98%)	1 / 47 (2.13%)	
occurrences (all)	175	2	
Injection site reaction			
subjects affected / exposed	12 / 86 (13.95%)	0 / 47 (0.00%)	
occurrences (all)	42	0	
Injection site swelling			
subjects affected / exposed	6 / 86 (6.98%)	0 / 47 (0.00%)	
occurrences (all)	16	0	
Malaise			
subjects affected / exposed	5 / 86 (5.81%)	0 / 47 (0.00%)	
occurrences (all)	15	0	
Pain			
subjects affected / exposed	4 / 86 (4.65%)	1 / 47 (2.13%)	
occurrences (all)	8	1	
Pyrexia			
subjects affected / exposed	35 / 86 (40.70%)	1 / 47 (2.13%)	
occurrences (all)	132	5	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 86 (5.81%)	1 / 47 (2.13%)	
occurrences (all)	11	1	
Nausea			
subjects affected / exposed	6 / 86 (6.98%)	2 / 47 (4.26%)	
occurrences (all)	7	2	
Stomatitis			
subjects affected / exposed	0 / 86 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	3 / 86 (3.49%)	0 / 47 (0.00%)	
occurrences (all)	7	0	

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 86 (3.49%)	2 / 47 (4.26%)	
occurrences (all)	3	2	
Dyspnoea			
subjects affected / exposed	2 / 86 (2.33%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Rhinitis allergic			
subjects affected / exposed	0 / 86 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 86 (1.16%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	1 / 86 (1.16%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 86 (3.49%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	4 / 86 (4.65%)	0 / 47 (0.00%)	
occurrences (all)	7	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 86 (1.16%)	2 / 47 (4.26%)	
occurrences (all)	2	3	
Cystitis			
subjects affected / exposed	0 / 86 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	1 / 86 (1.16%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Upper respiratory tract infection			

subjects affected / exposed	3 / 86 (3.49%)	2 / 47 (4.26%)	
occurrences (all)	3	2	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 86 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 86 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2014	A comprehensive review of the Phase III results, together with all other available clinical and laboratory data with various recombinant proteins tested in different diseases and settings now suggests that the anticancer activity of this technology may well be limited to a subgroup of Stage III melanoma patients with a specific predictive gene signature. A few patients in early metastatic melanoma also appear to benefit from this type of treatment. There is no evidence to believe that the PRAME ASCI can be successful relative to the MAGE-A3 ASCI because: • The PRAME ASCI and MAGE-A3 ASCI are produced from the same technology platform i.e. a recombinant protein adjuvanted with AS15, and both ASCIs share the same theoretical mechanism of action. • The PRAME ASCI has shown similar clinical efficacy in the metastatic melanoma setting compared to MAGE-A3 ASCI. • The PRAME ASCI has a similar immunogenicity profile relative to MAGE-A3 ASCI in the lung adjuvant setting. Consequently, GSK Biologicals has decided to stop further development of recPRAME + AS15 as a standalone treatment for cancer patients. This decision is not motivated by any safety concern as confirmed by the IDMC on 20 June 2014. In light of this decision, no further patients were randomized to the study and enrolled patients not yet treated were not to start their treatment as of 18 July 2014. Primary and secondary objectives will not be assessed as planned. All clinical and safety data collected in the study will be analysed descriptively. By default, for each biological sample already collected in the scope of this study and not tested yet, testing will not be performed except if a scientific rationale remains relevant despite the premature termination of the study. In this case, testing will be done in compliance with the protocol and ICF signed by the patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

As of 18 July 2014, the recruitment was stopped and the study was unblinded. For patients randomized to the placebo group, no further protocol visits were to be performed except for the concluding visit and no further doses were to be administered.

Notes: