Clinical trial results:
A double-blind, randomized, placebo-controlled Phase III study to assess the efficacy of recMAGE-A3 + AS15 Antigen-Specific Cancer Immunotherapeutic as adjuvant therapy in patients with resectable MAGE-A3-positive Non-Small Cell Lung Cancer

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	2007-001283-73
Trial protocol	BE DE IE FI ES SI FR SE GR IT LV AT NL HU CZ EE GB
Global end of trial date	23 September 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	109493

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00480025
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	08 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 December 2013
Global end of trial reached?	Yes
Global end of trial date	23 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this Phase III study is to demonstrate the clinical efficacy (in terms of disease-free survival) of recMAGE-A3 + AS15 versus placebo in NSCLC after complete surgical resection.
three co-primary objectives are considered:
•Objective A: Efficacy in the overall population;
•Objective B: Efficacy in the population of patients who did not receive adjuvant chemotherapy (no-CT population).
•Objective C: Efficacy in the population of patients presenting the potentially favourable gene signature.

Protection of trial subjects:

Patients were observed closely for at least 30 minutes following treatment, with appropriate medical treatment readily available in case of a rare anaphylactic reaction. MAGE-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 =< 38°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	04 October 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	8 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 10

Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Brazil: 21
Country: Number of subjects enrolled	Canada: 37
Country: Number of subjects enrolled	Netherlands: 24
Country: Number of subjects enrolled	Norway: 22
Country: Number of subjects enrolled	Poland: 166
Country: Number of subjects enrolled	Spain: 86
Country: Number of subjects enrolled	Sweden: 12
Country: Number of subjects enrolled	United Kingdom: 83
Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Belgium: 35
Country: Number of subjects enrolled	Czech Republic: 50
Country: Number of subjects enrolled	Estonia: 57
Country: Number of subjects enrolled	Finland: 9
Country: Number of subjects enrolled	France: 107
Country: Number of subjects enrolled	Germany: 268
Country: Number of subjects enrolled	Greece: 97
Country: Number of subjects enrolled	Hungary: 57
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Italy: 113
Country: Number of subjects enrolled	China: 159
Country: Number of subjects enrolled	Hong Kong: 10
Country: Number of subjects enrolled	India: 13
Country: Number of subjects enrolled	Israel: 16
Country: Number of subjects enrolled	Japan: 210
Country: Number of subjects enrolled	Korea, Republic of: 108
Country: Number of subjects enrolled	Russian Federation: 55
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	Taiwan: 31
Country: Number of subjects enrolled	Thailand: 20
Country: Number of subjects enrolled	Ukraine: 22
Country: Number of subjects enrolled	United States: 343
Worldwide total number of subjects	2312
EEA total number of subjects	1220

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)	1251
From 65 to 84 years	1055
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

A total of 2315 patients were screened towards participation in the study. For 3 of these subjects informed consent forms issues were reported, and thus only 2312 subjects were considered for analyses/results Out of these 2312 subjects, 2272 were treated with at least one dose of treatment, either MAGE-A3 ASCI study product or placebo solution.

Pre-assignment

Screening details:

2312 patients signed informed consent forms and were screened. Out of these, 2272 patients received at least one dose of study treatment (1515 received MAGE-A3 ASCI and 757 received placebo).

Pre-assignment period milestones

Number of subjects started	2312
Number of subjects completed	2272

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Study treatment not administered: 40

Period 1

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

Blinding implementation details:

Because the final establishment of the gene expression signature classifier by testing the samples on the training set was to only start after a positive interim analysis or after the final analysis of DFS in the overall/no-CT population, Disease Free Survival (DFS) in the GS+ population was to be analyzed at a later time point. Therefore, the Sponsor, investigators and patients should remain blinded to the treatment assignment until analysis of DFS in the GS+ population.

Arms

Are arms mutually exclusive?	Yes
Arm title	MAGE-A3 Total/TTP-T Group

Arm description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Arm type	Experimental
Investigational medicinal product name	recMAGE-A3 recombinant protein formulated in AS15 adjuvant
Investigational medicinal product code	recMAGE-A3 + AS15
Other name	MAGE-A3 ASCI, MAGE-A3 ASCI product, GSK1572932A
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Up to 13 doses via intramuscular injections in the deltoid or lateral region of the thigh preferably alternating on right and left side.

Arm title	Placebo Total/TTP-T Group

Arm description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in

the treatment group as per treatment actually received.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Sucrose reconstituted with an oil-in-water emulsion
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Up to 13 doses via intramuscular injections in the deltoid or lateral region of the thigh preferably alternating on right and left side.

Number of subjects in period 1[1]	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group
Started	1515	757
Completed	763	388
Not completed	752	369
Adverse event, non-fatal	44	12
Disease Progression / Recurrence	449	224
SAE including intercurrent illness	76	42
Unspecified	70	29
Protocol deviation	12	7
Patients remaining ongoing at Data Lock Point	101	55

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: Out of the 2312 enrolled patients, not all started treatment, hence only a part (2272) started the trial.

Baseline characteristics

Reporting groups

Reporting group title	MAGE-A3 Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Reporting group title	Placebo Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Reporting group values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group	Total
Number of subjects	1515	757	2272
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	63.1	63.4	
standard deviation	± 8.96	± 9.15	-
Gender categorical Units: Subjects			
Female	370	179	549
Male	1145	578	1723

Subject analysis sets

Subject analysis set title	MAGE-A3 CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had received adjuvant chemotherapy prior to randomization (CT Population).

Subject analysis set title	Placebo CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had received adjuvant chemotherapy prior to randomization (CT Population).

Subject analysis set title	MAGE-A3 No-CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had not received adjuvant chemotherapy prior to randomization (No-CT Population).

Subject analysis set title	Placebo No-CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had not received adjuvant chemotherapy prior to randomization (No-CT Population).

Reporting group values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group	MAGE-A3 No-CT/TTP-R Group
Number of subjects	785	391	730
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	61.1	61.1	65.3
standard deviation	± 8.27	± 8.65	± 9.16

Gender categorical Units: Subjects			
Female	600	97	185
Male	185	294	545

Reporting group values	Placebo No-CT/TTP-R Group		
Number of subjects	366		
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	65.8		
standard deviation	± 9.07		
Gender categorical Units: Subjects			
Female	82		
Male	284		

End points reporting groups

Reporting group title	MAGE-A3 Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Reporting group title	Placebo Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Subject analysis set title	MAGE-A3 CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had received adjuvant chemotherapy prior to randomization (CT Population).

Subject analysis set title	Placebo CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had received adjuvant chemotherapy prior to randomization (CT Population).

Subject analysis set title	MAGE-A3 No-CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had not received adjuvant chemotherapy prior to randomization (No-CT Population).

Subject analysis set title	Placebo No-CT/TTP-R Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the TTP as Randomized (TTP-R), e. a. patients in treatment group randomized based on below stratification (1) & minimization (2, 3, 4, 5 & 6) factors (10% randomness, equal weight to each minimization factor): 1) Chemotherapy (CT) vs. no -CT; 2) number of CT cycles received if any (1, 2 vs. 3, 4); 3) AJCC 6.0 disease stage (IB vs. II vs. IIIA); 4) Type of lymph-node sampling (minimal vs. systematic radical mediastinal lymphadenectomy); 5) Eastern Co-operative Oncology Group (ECOG) status (0, 1 vs. 2); 6) Smoking status (100 cigarettes [c] a lifetime vs. >100 c & current smoker vs. >100 c & past smoker). Patients in this sub-group consisted solely of patients who had not received

adjuvant chemotherapy prior to randomization (No-CT Population).

Primary: Person year rate (PYAR) as regards disease-free survival (DFS) in the overall population

End point title	Person year rate (PYAR) as regards disease-free survival (DFS) in the overall population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Primary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFS PYAR – Overall Population	0.17	0.168		

Statistical analyses

Statistical analysis title	DFS Comparing MAGE-A3 vs placebo – All Patients

Statistical analysis description:

Analysis compared DFS PYAR between groups for period from 1st treatment dose to DLP. A Cox model was used to evaluate treatment efficacy (TE). TE was calculated as PYAR in MAGE-A3 Total/TTP-R (PYAR1) divided by PYAR in Placebo Total/TTP-R (PYAR2), and weighed for adjustment factors. This comparison in all patients (overall population) also included taking into account stratification by previous CT vs. No-CT treatment and weighing using randomization-minimization factors (RMF) as regressors.

Comparison groups	MAGE-A3 Total/TTP-T Group v Placebo Total/TTP-T Group
Number of subjects included in analysis	2272
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.7379 [2]
Method	Regression, Cox
Parameter estimate	TE
Point estimate	1.024

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.891
upper limit	1.177

Notes:

[1] - RMF taken into account included: 1) Number of chemotherapy cycles received (1, 2 vs. 3, 4), if any; 2) Pathological stage of the disease (IB vs. II vs. IIIA); 3) Type of lymph-node sampling (minimal lymph-node sampling vs. systematic radical mediastinal lymphadenectomy); 4) ECOG performance status randomization (0, 1 vs. 2); 5) Smoking status (100 cigarettes a lifetime vs. > 100 cigarettes and current smoker vs. > 100 cigarettes and past smoker).
[2] - 2-sided p-value of Likelihood Ratio test from RMF-adjusted Cox regression, Efron method used to handle ties. Overall population objective reached if p-value < 2%/4% in absence/presence of statistically significant effect in No-CT patients per TTP-R.

Primary: Person year rate (PYAR) as regards disease-free survival (DFS) in the No-CT population

End point title	Person year rate (PYAR) as regards disease-free survival (DFS) in the No-CT population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Primary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 No-CT/TTP-R Group	Placebo No-CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	730	366		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFS PYAR – No-CT Population	0.169	0.178		

Statistical analyses

Statistical analysis title	DFS Comparing MAGE-A3 vs placebo – No-CT Patients

Statistical analysis description:

Analysis compared DFS PYAR between groups for the period from 1st treatment dose to DLP. A Cox model was used to evaluate treatment efficacy (TE). TE was calculated as PYAR in MAGE-A3 No-CT/TTP-R (PYAR1) divided by PYAR in Placebo No-CT/TTP-R (PYAR2) and weighed for adjustment factors. This comparison in all patients (overall population) also included taking into account weighing using randomization-minimization factors (RMF) as regressors.

Comparison groups	MAGE-A3 No-CT/TTP-R Group v Placebo No-CT/TTP-R Group

Number of subjects included in analysis	1096
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.7572 [4]
Method	Regression, Cox
Parameter estimate	TE
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.797
upper limit	1.179

Notes:

[3] - RMF included: 1) Number of chemotherapy cycles received (1, 2 vs. 3, 4), if any; 2) Pathological stage of the disease (IB vs. II vs. IIIA); 3) Type of lymph-node sampling (minimal lymph-node sampling vs. systematic radical mediastinal lymphadenectomy); 4) ECOG performance status randomization (0, 1 vs. 2); 5) Smoking status (100 cigarettes a lifetime vs. > 100 cigarettes and current smoker vs. > 100 cigarettes and past smoker).
[4] - 2-sided p-value of Likelihood Ratio test from RMF-adjusted Cox regression, Efron method used to handle ties. No-CT population objective reached if p-value < 2.56%/4% in absence/presence of statistically significant effect in No-CT patients per TTP-R.

Secondary: Person year rate (PYAR) as regards disease-free survival (DFS) in the CT population

End point title	Person year rate (PYAR) as regards disease-free survival (DFS) in the CT population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	785	391		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFS PYAR – CT Population	0.172	0.158		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards overall-survival (OS) in the overall population

End point title	Person year rate (PYAR) as regards overall-survival (OS) in the overall population

End point description:

OS was defined as the time interval from randomization to the date of death, irrespective of the cause of death. Patients still alive were censored at the last visit they were known to be alive. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Median PYAR (= median n/T)				
number (not applicable)				
OS PYAR – Overall Population	0.082	0.081		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards overall-survival (OS) in the No-CT population

End point title	Person year rate (PYAR) as regards overall-survival (OS) in the No-CT population

End point description:

OS was defined as the time interval from randomization to the date of death, irrespective of the cause of death. Patients still alive were censored at the last visit they were known to be alive. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 No-CT/TTP-R Group	Placebo No-CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	730	366		
Units: Median PYAR (= median n/T)				
number (not applicable)				
OS PYAR – No-CT Population	0.084	0.086		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards overall-survival (OS) in the CT population

End point title	Person year rate (PYAR) as regards overall-survival (OS) in the CT population

End point description:

OS was defined as the time interval from randomization to the date of death, irrespective of the cause of death. Patients still alive were censored at the last visit they were known to be alive. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	785	391		
Units: Median PYAR (= median n/T				
number (not applicable)				
OS PYAR – CT Population	0.08	0.076		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the Overall population

End point title	Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the Overall population

End point description:

LCSS was defined as the time interval from randomization to the date of death due to lung cancer. Deaths due to other or unknown causes were censored at the date of death. PYAR = n (=number of

subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Median PYAR (= median n/T)				
number (not applicable)				
LCSS PYAR – Overall Population	0.064	0.061		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the No-CT population

End point title	Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the No-CT population

End point description:

LCSS was defined as the time interval from randomization to the date of death due to lung cancer. Deaths due to other or unknown causes were censored at the date of death. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 No-CT/TTP-R Group	Placebo No-CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	730	366		
Units: Median PYAR (= median n/T)				
number (not applicable)				
LCSS PYAR – No-CT Population	0.064	0.06		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the CT population

End point title	Person year rate (PYAR) as regards lung-cancer specific survival (LCSS) in the CT population

End point description:

LCSS was defined as the time interval from randomization to the date of death due to lung cancer. Deaths due to other or unknown causes were censored at the date of death. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median OS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	785	391		
Units: Median PYAR (= median n/T)				
number (not applicable)				
LCSS PYAR – CT Population	0.063	0.063		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the overall population

End point title	Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the overall population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. Median DFS KMEs in % were obtained non-parametrically by Kaplan-Meier method and confidence intervals (CIs) calculated using the Greenwood formula for standard error computation.

End point type	Secondary

End point timeframe:

KME assessed at 2, 3, 4 and 5-year (Y) post Dose 1 of treatment. Follow-up period was from administration of 1st dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014.

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Median KME in %				
number (confidence interval 95%)				
DFS KME at 2Y – Overall Population	65.57 (63.08 to 67.95)	65.5 (61.94 to 68.81)		
DFS KME at 3Y – Overall Population	59.97 (57.3 to 62.53)	60.42 (56.62 to 64)		
DFS KME at 4Y – Overall Population	56.72 (53.8 to 59.54)	57.19 (53.07 to 61.1)		
DFS KME at 5Y – Overall Population	51.73 (47.66 to 55.64)	49.56 (42.87 to 55.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the No-CT population

End point title	Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the No-CT population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. Median DFS KMEs in % were obtained non-parametrically by Kaplan-Meier method and confidence intervals (CIs) calculated using the Greenwood formula for standard error computation.

End point type	Secondary

End point timeframe:

KME assessed at 2, 3, 4 and 5-year (Y) post Dose 1 of treatment Follow-up period was from administration of 1st dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014.

End point values	MAGE-A3 No-CT/TTP-R Group	Placebo No-CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	730	366		
Units: Median KME in %				
number (confidence interval 95%)				

DFS KME at 2Y – No-CT Population	66.03 (62.39 to 69.4)	63.96 (58.72 to 68.72)		
DFS KME at 3Y – No-CT Population	59.6 (55.7 to 63.27)	57.62 (52.02 to 62.81)		
DFS KME at 4Y – No-CT Population	55.4 (51.06 to 59.52)	54.85 (48.98 to 60.33)		
DFS KME at 5Y – No-CT Population	49.72 (43.44 to 55.67)	44.59 (34.64 to 54.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the CT population

End point title	Kaplan-Meier estimate (KME) of 2, 3, 4 and 5-year as regards disease-free survival (DFS) in the CT population

End point description:

DFS = time interval from randomization to 1st evidence of recurrence/death, if occurring before. All recurrence types were included, including local, regional & distant metastasis & 2nd primary lung cancer (i.e. local recurrence, defined as a tumor within same lung or at bronchial stump; regional recurrence, involving a clinically or radiologically manifest disease in mediastinum or supraclavicular nodes; & distant recurrence [any tumor arising in contralateral lung or outside hemithorax]). Deaths occurring without prior documentation of recurrence were considered as event & not censored. If no event occurred by time of analysis, time to event was censored at last assessment date of patient. New 1ry cancers outside lungs were not considered as event. Median DFS KMEs in % were obtained non-parametrically by Kaplan-Meier method and confidence intervals (CIs) calculated using the Greenwood formula for standard error computation.

End point type	Secondary

End point timeframe:

KME assessed at 2, 3, 4 and 5-year (Y) post Dose 1 of treatment. Follow-up period was from administration of 1st dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014.

End point values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	785	391		
Units: Median KME in %				
number (confidence interval 95%)				
DFS KME at 2Y – CT Population	65.17 (61.67 to 68.43)	66.94 (61.98 to 71.41)		
DFS KME at 3Y – CT Population	60.39 (56.68 to 63.89)	63.09 (57.84 to 67.87)		
DFS KME at 4Y – CT Population	58.17 (54.22 to 61.9)	59.3 (53.33 to 64.76)		
DFS KME at 5Y – CT Population	53.64 (48.28 to 58.7)	54.8 (46.44 to 62.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the overall population

End point title	Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the overall population

End point description:

DFSS was defined as the interval from randomization to the date of disease recurrence or death due to lung cancer. Patients who had died due to another cause than lung cancer were censored on their date of death and patients alive at the time of analysis were censored on the date of last assessment. Patients with no assessment post-randomization were censored on the date of randomization. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFSS PYAR – Overall Population	0.159	0.154		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the No-CT population

End point title	Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the No-CT population

End point description:

DFSS was defined as the interval from randomization to the date of disease recurrence or death due to lung cancer. Patients who had died due to another cause than lung cancer were censored on their date of death and patients alive at the time of analysis were censored on the date of last assessment. Patients with no assessment post-randomization were censored on the date of randomization. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 No-CT/TTP-R Group	Placebo No-CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	730	366		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFSS PYAR – No-CT Population	0.155	0.159		

Statistical analyses

No statistical analyses for this end point

Secondary: Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the CT population

End point title	Person year rate (PYAR) as regards disease-free specific survival (DFSS) in the CT population

End point description:

DFSS was defined as the interval from randomization to the date of disease recurrence or death due to lung cancer. Patients who had died due to another cause than lung cancer were censored on their date of death and patients alive at the time of analysis were censored on the date of last assessment. Patients with no assessment post-randomization were censored on the date of randomization. PYAR = n (=number of subjects reported with at least 1 event) divided by T (=sum of follow-up period [in years] censored at 1st occurrence of event in group). Median DFS estimates were obtained non-parametrically by Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Period of follow-up was from administration of first dose of MAGE-A3 ASCI study product/placebo solution to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 CT/TTP-R Group	Placebo CT/TTP-R Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	785	391		
Units: Median PYAR (= median n/T)				
number (not applicable)				
DFSS PYAR – CT Population	0.162	0.149		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-Melanoma AntiGEn (MAGE)-A3

antibodies (Anti-MAGE-A3 S+)

End point title	Number of subjects seropositive for anti-Melanoma AntiGEn (MAGE)-A3 antibodies (Anti-MAGE-A3 S+)

End point description:

A seropositive subject for anti-MAGE-A3 antibodies was a subject with anti-MAGE-A3 antibodies >= the seropositivity cut-off of 27 Enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/mL).

End point type	Secondary

End point timeframe:

Pre-treatment (PRE), at Weeks (W) 6 and 12, at Months (M) 9, 12, 18 and 30 and at one year after treatment concluding time point, i.e. at follow-up visit 2 at W120 added of one year (At 12M post W120)

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1184	614		
Units: Subjects				
Anti-MAGE-A3 S+, PRE (N=1184;614)	105	53		
Anti-MAGE-A3 S+, W6 (N=945;548)	929	43		
Anti-MAGE-A3 S+, W12 (N=925;491)	921	42		
Anti-MAGE-A3 S+, M9 (N=633;352)	631	30		
Anti-MAGE-A3 S+, M12 (N=538;279)	536	19		
Anti-MAGE-A3 S+, M18 (N=420;229)	419	15		
Anti-MAGE-A3 S+, M30 (N=384;222)	383	17		
Anti-MAGE-A3 S+, at 12M post W120 (N=76;47)	75	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of humoral responders as regards anti-Melanoma AntiGEn (MAGE)-A3 antibodies (Anti-MAGE-A3 HR)

End point title	Number of humoral responders as regards anti-Melanoma AntiGEn (MAGE)-A3 antibodies (Anti-MAGE-A3 HR)

End point description:

A seropositive/seronegative subject for anti-MAGE-A3 antibodies was a subject with anti-MAGE-A3 antibodies >=/< the seropositivity cut-off of 27 Enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/mL). A humoral responder as regards anti-MAGE-A3 antibodies was defined as 1) for initially seronegative patients, a patient with post-administration Anti-MAGE-A3 antibody concentration >= 27 EL.U/mL; 2) for initially seropositive patients: post-treatment administration antibody concentration >= 2 fold the pre-treatment antibody concentration.

End point type	Secondary

End point timeframe:

At Weeks (W) 6 and 12, at Months (M) 9, 12, 18 and 30 and at one year after treatment concluding time point, i.e. at follow-up visit 2 at W120 added of one year (at 12M post W120)

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	942	548		
Units: Subjects				
Anti-MAGE-A3 HR, W6 (N=942;548)	922	10		
Anti-MAGE-A3 HR, W12 (N=920;491)	916	15		
Anti-MAGE-A3 HR, M9 (N=630;352)	627	13		
Anti-MAGE-A3 HR, M12 (N=537;279)	534	6		
Anti-MAGE-A3 HR, M18 (N=420;229)	417	7		
Anti-MAGE-A3 HR, M30 (N=382;222)	380	8		
Anti-MAGE-A3 HR, at 12M post W120 (N=76;47)	75	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-protein D (PD) antibodies (Anti-PD S+)

End point title	Number of subjects seropositive for anti-protein D (PD) antibodies (Anti-PD S+)

End point description:

A seropositive subject for anti-PD antibodies was a subject with anti-PD antibodies >= the seropositivity cut-off of 100 Enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/mL).

End point type	Secondary

End point timeframe:

Pre-treatment (PRE), at Weeks (W) 6 and 12, at Months (M) 9, 12, 18 and 30 and at one year after treatment concluding time point, i.e. at follow-up visit 2 at W120 added of one year (at 12M post W120)

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1096	554		
Units: Subjects				
Anti-PD S+, PRE (N=1096;554)	381	210		
Anti-PD S+, W6 (N=967;493)	958	195		
Anti-PD S+, W12 (N=864;436)	860	176		
Anti-PD S+, M9 (N=582;311)	580	133		
Anti-PD S+, M12 (N=485;243)	483	101		
Anti-PD S+, M18 (N=376;197)	375	77		
Anti-PD S+, M30 (N=358;189)	357	75		
Anti-PD S+, at 12M post W120 (N=78;46)	77	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of humoral responders as regards anti-protein D (PD) antibodies (Anti-PD HR)

End point title	Number of humoral responders as regards anti-protein D (PD) antibodies (Anti-PD HR)

End point description:

A seropositive/seronegative subject for anti-PD antibodies was a subject with anti-PD antibodies ≥/< the seropositivity cut-off of 100 Enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/mL). A humoral responder as regards anti-PD antibodies was defined as 1) for initially seronegative patients, a patient with post-administration anti-PD antibody concentration ≥ 100 EL.U/mL; 2) for initially seropositive patients: post-administration antibody concentration ≥ 2 fold the pre-vaccination antibody concentration.

End point type	Secondary

End point timeframe:

At Weeks (W) 6 and 12, at Months (M) 9, 12, 18 and 30 and at one year after treatment concluding time point, i.e. at follow-up visit 2 at W120 added of one year (at 12M post W120)

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	962	490		
Units: Subjects				
Anti-PD HR, W6 (N=962;490)	945	27		
Anti-PD HR, W12 (N=859;432)	853	35		
Anti-PD HR, M9 (N=579;307)	575	26		
Anti-PD HR, M12 (N=482;240)	479	19		
Anti-PD HR, M18 (N=374;194)	370	21		
Anti-PD HR, M30 (N=354;186)	352	17		
Anti-PD HR, at 12M post W120 (N=78;46)	77	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Health-related quality of life (HQL) scores

End point title	Health-related quality of life (HQL) scores

End point description:

HQL was assessed using the EQ-5D generic health state classification and valuation system. The number and percentage of patients with each score within each dimension of the EQ-5D questionnaire (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) were tabulated at each assessment for each group. Resulting descriptive mean and standard deviation (SD) for the EQ-5D Utility Value (EQ-5D UV) were tabulated. Note that analysis was performed solely on patients who were offered to participate to these analyses, that is, patients enrolled who consented to study participation after Protocol Amendment 1 became effective at their study site and for whom valid EQ-5D data were available. Valid EQ-5D data were defined as questionnaires assessed 1) on day of treatment administration and before administration for time points with a treatment administration; or 2) on day after treatment administration for W0, W6 and W12; or 3) during follow-up visits or at time of recurrence.

End point type	Secondary

End point timeframe:

At Week (W) 0 on day of treatment (DoT) (W0 DoT), W0 on day post treatment (DpT) (W0 DpT), W6 DoT, W6 DpT, W12 DoT, W12 DpT, Month (M) 6, M9, M12, M24, 6M post W120, at recurrence, and at 12M post W120.

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	103		
Units: EQ-5D UV				
arithmetic mean (standard deviation)				
EQ-5D UV, At W0 DoT (N=226;103)	0.83 (± 0.152)	0.823 (± 0.189)		
EQ-5D UV, At W0 DpT (N=206;93)	0.788 (± 0.182)	0.838 (± 0.177)		
EQ-5D UV, At W6 DoT (N=215;99)	0.837 (± 0.182)	0.825 (± 0.191)		
EQ-5D UV, At W6 DpT (N=188;94)	0.798 (± 0.205)	0.835 (± 0.176)		
EQ-5D UV, At W12 DoT (N=201;97)	0.848 (± 0.158)	0.811 (± 0.236)		
EQ-5D UV, At W12 DpT (N=186;87)	0.841 (± 0.152)	0.831 (± 0.211)		
EQ-5D UV, At M6 (N=176;84)	0.847 (± 0.182)	0.825 (± 0.236)		
EQ-5D UV, At M9 (N=173;81)	0.84 (± 0.197)	0.81 (± 0.219)		
EQ-5D UV, At M12 (N=146;69)	0.857 (± 0.166)	0.824 (± 0.214)		
EQ-5D UV, At M24 (N=102;50)	0.855 (± 0.179)	0.865 (± 0.145)		
EQ-5D UV, At 6M post W120 (N=7;3)	0.723 (± 0.298)	0.679 (± 0.073)		
EQ-5D UV, At recurrence (N=41;14)	0.662 (± 0.343)	0.785 (± 0.159)		
EQ-5D UV, At 12M post W120 (N=16;5)	0.753 (± 0.199)	0.777 (± 0.395)		

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

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
ALT - SCR UNK; DLP G0	1	0		
ALT - SCR UNK; DLP G1	1	1		
ALT - SCR UNK; DLP G2	0	0		
ALT - SCR UNK; DLP G3	0	0		
ALT - SCR UNK; DLP G4	0	0		
ALT - SCR UNK; DLP UNK	3	1		
ALT - SCR G0; DLP G0	1133	588		
ALT - SCR G0; DLP G1	162	77		
ALT - SCR G0; DLP G2	17	8		
ALT - SCR G0; DLP G3	7	7		
ALT - SCR G0; DLP G4	1	1		
ALT - SCR G0; DLP UNK	113	37		
ALT - SCR G1; DLP G0	34	14		
ALT - SCR G1; DLP G1	32	17		
ALT - SCR G1; DLP G2	4	3		
ALT - SCR G1; DLP G3	1	2		
ALT - SCR G1; DLP G4	0	0		
ALT - SCR G1; DLP UNK	4	1		
ALT - SCR G2; DLP G0	0	0		
ALT - SCR G2; DLP G1	1	0		
ALT - SCR G2; DLP G2	1	0		
ALT - SCR G2; DLP G3	0	0		
ALT - SCR G2; DLP G4	0	0		
ALT - SCR G2; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of patients with abnormal alanine 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 DLP 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), G1 and G2. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
AST - SCR UNK; DLP G0	12	4		
AST - SCR UNK; DLP G1	5	2		
AST - SCR UNK; DLP G2	0	0		
AST - SCR UNK; DLP G3	0	0		
AST - SCR UNK; DLP G4	0	0		
AST - SCR UNK; DLP UNK	5	2		
AST - SCR G0; DLP G0	1170	579		
AST - SCR G0; DLP G1	136	84		
AST - SCR G0; DLP G2	6	4		
AST - SCR G0; DLP G3	8	5		
AST - SCR G0; DLP G4	2	1		
AST - SCR G0; DLP UNK	111	37		
AST - SCR G1; DLP G0	26	19		
AST - SCR G1; DLP G1	25	16		
AST - SCR G1; DLP G2	5	2		
AST - SCR G1; DLP G3	0	1		
AST - SCR G1; DLP G4	0	0		
AST - SCR G1; DLP UNK	2	1		
AST - SCR G2; DLP G0	0	0		
AST - SCR G2; DLP G1	0	0		
AST - SCR G2; DLP G2	0	0		
AST - SCR G2; DLP G3	1	0		
AST - SCR G2; DLP G4	0	0		
AST - SCR G2; DLP UNK	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal alkaline phosphatase (ALKP) values by maximum grade

End point title	Number of patients with abnormal alkaline phosphatase (ALKP) values by maximum grade

End point description:

The status of each patient as regards ALKP laboratory values at baseline (SCR) up to DLP 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), G1 and G2. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
ALKP - SCR UNK; DLP G0	21	3		
ALKP - SCR UNK; DLP G1	0	0		
ALKP - SCR UNK; DLP G2	0	0		
ALKP - SCR UNK; DLP G3	1	0		
ALKP - SCR UNK; DLP G4	0	0		
ALKP - SCR UNK; DLP UNK	5	3		
ALKP - SCR G0; DLP G0	1121	569		
ALKP - SCR G0; DLP G1	99	63		
ALKP - SCR G0; DLP G2	3	2		
ALKP - SCR G0; DLP G3	1	0		
ALKP - SCR G0; DLP G4	0	0		
ALKP - SCR G0; DLP UNK	107	39		
ALKP - SCR G1; DLP G0	63	35		
ALKP - SCR G1; DLP G1	79	38		
ALKP - SCR G1; DLP G2	1	0		
ALKP - SCR G1; DLP G3	1	0		
ALKP - SCR G1; DLP G4	0	0		
ALKP - SCR G1; DLP UNK	11	4		
ALKP - SCR G2; DLP G0	0	0		
ALKP - SCR G2; DLP G1	2	1		
ALKP - SCR G2; DLP G2	0	0		
ALKP - SCR G2; DLP G3	0	0		
ALKP - SCR G2; DLP G4	0	0		
ALKP - SCR G2; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The status of each patient as regards BIL laboratory values at baseline (SCR) up to DLP 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 DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
BIL - SCR UNK; DLP G0	9	2		
BIL - SCR UNK; DLP G1	1	0		
BIL - SCR UNK; DLP G2	0	0		
BIL - SCR UNK; DLP G3	0	0		
BIL - SCR UNK; DLP G4	0	0		
BIL - SCR UNK; DLP UNK	4	2		
BIL - SCR G0; DLP G0	1275	661		
BIL - SCR G0; DLP G1	74	28		
BIL - SCR G0; DLP G2	11	9		
BIL - SCR G0; DLP G3	1	2		
BIL - SCR G0; DLP G4	1	0		
BIL - SCR G0; DLP UNK	114	37		
BIL - SCR G1; DLP G0	10	5		
BIL - SCR G1; DLP G1	8	9		
BIL - SCR G1; DLP G2	5	1		
BIL - SCR G1; DLP G3	1	0		
BIL - SCR G1; DLP G4	0	0		
BIL - SCR G1; DLP UNK	1	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 DLP 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), G1 and G2. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
CREA - SCR UNK; DLP G0	2	0		
CREA - SCR UNK; DLP G1	0	0		
CREA - SCR UNK; DLP G2	0	0		
CREA - SCR UNK; DLP G3	0	0		
CREA - SCR UNK; DLP G4	2	0		
CREA - SCR UNK; DLP UNK	1139	577		
CREA - SCR G0; DLP G0	126	74		
CREA - SCR G0; DLP G1	9	3		
CREA - SCR G0; DLP G2	3	1		
CREA - SCR G0; DLP G3	1	0		
CREA - SCR G0; DLP G4	103	32		
CREA - SCR G0; DLP UNK	27	14		
CREA - SCR G1; DLP G0	72	44		
CREA - SCR G1; DLP G1	11	6		
CREA - SCR G1; DLP G2	0	0		
CREA - SCR G1; DLP G3	1	0		
CREA - SCR G1; DLP G4	6	4		
CREA - SCR G1; DLP UNK	0	0		
CREA - SCR G2; DLP G0	7	2		
CREA - SCR G2; DLP G1	6	0		
CREA - SCR G2; DLP G2	0	0		
CREA - SCR G2; DLP G3	0	0		
CREA - SCR G2; DLP G4	0	0		
CREA - SCR G2; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The status of each patient as regards HGB laboratory values at baseline (SCR) up to DLP 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), G1, G2 and G3. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
HGB - SCR UNK; DLP G0	3	0		
HGB - SCR UNK; DLP G1	1	0		
HGB - SCR UNK; DLP G2	0	0		
HGB - SCR UNK; DLP G3	0	0		
HGB - SCR UNK; DLP G4	0	0		
HGB - SCR UNK; DLP UNK	3	0		
HGB - SCR G0; DLP G0	534	274		
HGB - SCR G0; DLP G1	70	26		
HGB - SCR G0; DLP G2	9	5		
HGB - SCR G0; DLP G3	1	1		
HGB - SCR G0; DLP G4	0	2		
HGB - SCR G0; DLP UNK	50	19		
HGB - SCR G1; DLP G0	342	187		
HGB - SCR G1; DLP G1	310	142		
HGB - SCR G1; DLP G2	17	14		
HGB - SCR G1; DLP G3	6	3		
HGB - SCR G1; DLP G4	2	0		
HGB - SCR G1; DLP UNK	49	15		
HGB - SCR G2; DLP G0	29	30		
HGB - SCR G2; DLP G1	63	31		
HGB - SCR G2; DLP G3	12	3		
HGB - SCR G2; DLP G4	1	3		
HGB - SCR G2; DLP UNK	1	0		
HGB - SCR G3; DLP G0	6	0		
HGB - SCR G3; DLP G1	2	1		
HGB - SCR G3; DLP G2	3	1		
HGB - SCR G3; DLP G3	1	0		
HGB - SCR G3; DLP G4	0	0		
HGB - SCR G3; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The status of each patient as regards LEU laboratory values at baseline (SCR) up to DLP 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), G1, G2 and G3. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
LEU - SCR UNK; DLP G0	1	0		
LEU - SCR UNK; DLP G1	0	0		
LEU - SCR UNK; DLP G2	0	0		
LEU - SCR UNK; DLP G3	0	0		
LEU - SCR UNK; DLP G4	0	0		
LEU - SCR UNK; DLP UNK	1	0		
LEU - SCR G0; DLP G0	1259	652		
LEU - SCR G0; DLP G1	45	29		
LEU - SCR G0; DLP G2	4	2		
LEU - SCR G0; DLP G3	2	0		
LEU - SCR G0; DLP G4	6	2		
LEU - SCR G0; DLP UNK	98	32		
LEU - SCR G1; DLP G0	54	24		
LEU - SCR G1; DLP G1	21	5		
LEU - SCR G1; DLP G2	2	1		
LEU - SCR G1; DLP G3	0	0		
LEU - SCR G1; DLP G4	0	1		
LEU - SCR G1; DLP UNK	4	0		
LEU - SCR G2; DLP G0	13	6		
LEU - SCR G2; DLP G1	3	2		
LEU - SCR G2; DLP G2	2	0		
LEU - SCR G2; DLP G3	0	0		
LEU - SCR G2; DLP G4	0	0		
LEU - SCR G2; DLP UNK	0	0		
LEU - SCR G3; DLP G0	0	1		
LEU - SCR G3; DLP G1	0	0		
LEU - SCR G3; DLP G2	0	0		
LEU - SCR G3; DLP G3	0	0		
LEU - SCR G3; DLP G4	0	0		
LEU - SCR G3; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The status of each patient as regards LYM laboratory values at baseline (SCR) up to DLP 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), G1, G2 and G3. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
LYM - SCR UNK; DLP G0	12	3		
LYM - SCR UNK; DLP G1	3	1		
LYM - SCR UNK; DLP G2	0	0		
LYM - SCR UNK; DLP G3	0	0		
LYM - SCR UNK; DLP G4	0	0		
LYM - SCR UNK; DLP UNK	4	2		
LYM - SCR G0; DLP G0	999	518		
LYM - SCR G0; DLP G1	160	89		
LYM - SCR G0; DLP G2	40	16		
LYM - SCR G0; DLP G3	5	0		
LYM - SCR G0; DLP G4	0	0		
LYM - SCR G0; DLP UNK	96	35		
LYM - SCR G1; DLP G0	47	27		
LYM - SCR G1; DLP G1	86	42		
LYM - SCR G1; DLP G2	15	4		
LYM - SCR G1; DLP G3	1	4		
LYM - SCR G1; DLP G4	2	0		
LYM - SCR G1; DLP UNK	20	5		
LYM - SCR G2; DLP G0	3	1		
LYM - SCR G2; DLP G1	7	2		
LYM - SCR G2; DLP G2	4	3		
LYM - SCR G2; DLP G3	2	1		
LYM - SCR G2; DLP G4	0	0		
LYM - SCR G2; DLP UNK	0	1		
LYM - SCR G3; DLP G0	4	1		
LYM - SCR G3; DLP G1	1	2		
LYM - SCR G3; DLP G2	3	0		
LYM - SCR G3; DLP G3	1	0		
LYM - SCR G3; DLP G4	0	0		
LYM - SCR G3; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The status of each patient as regards NEU laboratory values at baseline (SCR) up to DLP 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), G1, G2, G3 and G4. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
NEU - SCR UNK; DLP G0	12	3		
NEU - SCR UNK; DLP G1	0	0		
NEU - SCR UNK; DLP G2	0	0		
NEU - SCR UNK; DLP G3	0	0		
NEU - SCR UNK; DLP G4	0	0		
NEU - SCR UNK; DLP UNK	1	2		
NEU - SCR G0; DLP G0	1200	625		
NEU - SCR G0; DLP G1	47	28		
NEU - SCR G0; DLP G2	1	3		
NEU - SCR G0; DLP G3	2	1		
NEU - SCR G0; DLP G4	3	1		
NEU - SCR G0; DLP UNK	111	37		
NEU - SCR G1; DLP G0	56	23		
NEU - SCR G1; DLP G1	31	10		
NEU - SCR G1; DLP G2	3	1		
NEU - SCR G1; DLP G3	0	0		
NEU - SCR G1; DLP G4	0	0		
NEU - SCR G1; DLP UNK	3	2		
NEU - SCR G2; DLP G0	32	16		
NEU - SCR G2; DLP G1	5	1		

NEU - SCR G2; DLP G2	2	2		
NEU - SCR G2; DLP G3	0	0		
NEU - SCR G2; DLP G4	0	0		
NEU - SCR G2; DLP UNK	1	1		
NEU - SCR G3; DLP G0	3	1		
NEU - SCR G3; DLP G1	0	0		
NEU - SCR G3; DLP G2	0	0		
NEU - SCR G3; DLP G3	0	0		
NEU - SCR G3; DLP G4	0	0		
NEU - SCR G3; DLP UNK	0	0		
NEU - SCR G4; DLP G0	1	0		
NEU - SCR G4; DLP G1	0	0		
NEU - SCR G4; DLP G2	1	0		
NEU - SCR G4; DLP G3	0	0		
NEU - SCR G4; DLP G4	0	0		
NEU - SCR G4; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with abnormal platelets (PLA) values by maximum grade

End point title	Number of patients with abnormal platelets (PLA) values by maximum grade

End point description:

The status of each patient as regards PLA laboratory values at baseline (SCR) up to DLP 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), G1 and G3. CTC grade statuses reported at DLP were G0, G1, G2, G3, G4, and UNK.

End point type	Secondary

End point timeframe:

Period of follow-up was from screening (SCR) to data lock point (DLP) on 23 January 2014

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
PLA - SCR UNK; DLP G0	1	1		
PLA - SCR UNK; DLP G1	0	0		
PLA - SCR UNK; DLP G2	0	0		
PLA - SCR UNK; DLP G3	0	0		
PLA - SCR UNK; DLP G4	0	0		
PLA - SCR UNK; DLP UNK	1	0		
PLA - SCR G0; DLP G0	1275	648		
PLA - SCR G0; DLP G1	78	38		

PLA - SCR G0; DLP G2	6	2		
PLA - SCR G0; DLP G3	1	0		
PLA - SCR G0; DLP G4	7	2		
PLA - SCR G0; DLP UNK	98	35		
PLA - SCR G1; DLP G0	22	16		
PLA - SCR G1; DLP G1	17	10		
PLA - SCR G1; DLP G2	2	4		
PLA - SCR G1; DLP G3	1	0		
PLA - SCR G1; DLP G4	0	0		
PLA - SCR G1; DLP UNK	5	0		
PLA - SCR G3; DLP G0	1	1		
PLA - SCR G3; DLP G1	0	0		
PLA - SCR G3; DLP G2	0	0		
PLA - SCR G3; DLP G3	0	0		
PLA - SCR G3; DLP G4	0	0		
PLA - SCR G3; DLP UNK	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with any adverse events (AEs) and with AEs by maximum grade reported – Up to data lock point (DLP)

End point title	Number of patients with any adverse events (AEs) and with AEs by maximum grade reported – Up to data lock point (DLP)

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, 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. Any here below is defined as irrespective of CTC grade reported.

End point type	Secondary

End point timeframe:

Within the 31-day follow-up period post treatment administration, up to data lock point (DLP) on 23 January 2014.

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
Patients with any AEs	1369	556		
Patients with G1 AEs	563	225		
Patients with G2 AEs	560	209		
Patients with G3 AEs	184	88		
Patients with G4 AEs	49	26		
Patients with G5 AEs	13	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with serious adverse events (SAEs) – Up to data lock point (DLP)

End point title	Number of patients with serious adverse events (SAEs) – Up to data lock point (DLP)

End point description:

A SAE is any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, was a congenital anomaly/birth defect in the offspring of a study subject, or was a Grade 4 AE according to CTC for Adverse Events, Version 3.0. Events part of natural course of lung cancer (i.e., disease progression, recurrence) were captured towards clinical efficacy assessment (CEA) and were not reported as SAEs. Death due to a progressive disease was similarly recorded towards CEA, but not as an SAE. However, if progression of lung cancer disease was greater than normally be expected, or if investigators considered that there was a causal relationship between treatment or protocol design/procedures and disease progression/ recurrence, then it was reported as SAE. Any new cancer (non-related to lung cancer) was reported as SAE.

End point type	Secondary

End point timeframe:

From screening (SCR) up to data lock point (DLP) on 23 January 2014.

End point values	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1515	757		
Units: Subjects				
Patient(s) with SAE(s)	330	164		

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 database freeze on 23 January 2014 (DLP); AEs: Within the 31-day follow-up period post treatment administration, up to DLP.

Adverse event reporting additional description:

Results presented per group consist of a summary of the events (SAEs and AEs other than SAEs, respectively) reported, compiling overall number of subjects

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	MAGE-A3 Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of MAGE-A3 ASCI, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Reporting group title	Placebo Total/TTP-T Group

Reporting group description:

Patients received up to 13 doses (D) of placebo, 5 Ds every 3 weeks followed by 8 Ds every 12 weeks. Patients are as per the Total Treated population (TTP) as Treated, or TTP-T, which included patients in the treatment group as per treatment actually received.

Serious adverse events	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	330 / 1515 (21.78%)	164 / 757 (21.66%)	
number of deaths (all causes)	30	17	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	4 / 1515 (0.26%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	8 / 1515 (0.53%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign oesophageal neoplasm			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	2 / 1515 (0.13%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder transitional cell carcinoma			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma stage ii			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen’s disease			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 1515 (0.07%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brenner tumour			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma in situ of skin			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemangioma			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatofibrosarcoma protuberans			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse large b-cell lymphoma			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			

subjects affected / exposed	2 / 1515 (0.13%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stromal tumour			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lentigo maligna			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant peritoneal neoplasm			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to central nervous system			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian cancer metastatic			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian fibroma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	8 / 1515 (0.53%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer recurrent			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			

subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of pharynx			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal cancer			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	5 / 1515 (0.33%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	4 / 1515 (0.26%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bleeding varicose vein			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic shock			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pelvic venous thrombosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	2 / 1515 (0.13%)	5 / 757 (0.66%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral embolism			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	3 / 1515 (0.20%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	2 / 1515 (0.13%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 3	
Euthanasia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Impaired healing			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mass			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorder			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchostenosis			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Acute respiratory failure			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Alveolitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoea			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Asthma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopleural fistula			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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	6 / 1515 (0.40%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	4 / 1515 (0.26%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	7 / 1515 (0.46%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary granuloma			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			

subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 1515 (0.00%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	17 / 1515 (1.12%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	0 / 18	1 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood uric acid increased			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 1515 (0.07%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	6 / 1515 (0.40%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site pain			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Procedural complication			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	2 / 1515 (0.13%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adams-stokes syndrome			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	3 / 1515 (0.20%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 1515 (0.26%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Atrial flutter			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			

subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure			
subjects affected / exposed	5 / 1515 (0.33%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 1515 (0.07%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac fibrillation			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac flutter			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	4 / 1515 (0.26%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	3 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial ischaemia			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Silent myocardial infarction			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Brain injury			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 1515 (0.13%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebrovascular accident			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia alzheimer’s type			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 1515 (0.26%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 1515 (0.13%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unresponsive to stimuli			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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	7 / 1515 (0.46%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersplenism			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic thrombocytopenic purpura			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis microscopic			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal stenosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			

subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 1515 (0.07%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	5 / 1515 (0.33%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			

subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	7 / 1515 (0.46%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic necrosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatitis chronic			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis chronic			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	3 / 1515 (0.20%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	4 / 1515 (0.26%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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			
Angioedema			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytoclastic vasculitis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash pruritic			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Glomerulonephritis rapidly progressive			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematuria			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	5 / 1515 (0.33%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ureteric dilatation			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibromyalgia			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lumbar spinal stenosis			
subjects affected / exposed	1 / 1515 (0.07%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	3 / 1515 (0.20%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic sclerosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis b			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis streptococcal			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest wall abscess			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Citrobacter infection			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Diverticulitis			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	0 / 1515 (0.00%)	2 / 757 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis b			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	3 / 1515 (0.20%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	5 / 1515 (0.33%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	4 / 1515 (0.26%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	26 / 1515 (1.72%)	15 / 757 (1.98%)	
occurrences causally related to treatment / all	0 / 27	1 / 16	
deaths causally related to treatment / all	0 / 5	1 / 4	
Pneumonia bacterial			
subjects affected / exposed	4 / 1515 (0.26%)	4 / 757 (0.53%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia haemophilus			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonas aeruginosa			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Post procedural infection			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Q fever			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rickettsiosis			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	5 / 1515 (0.33%)	3 / 757 (0.40%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Staphylococcal bacteraemia			

subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 1515 (0.07%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 1515 (0.26%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pericarditis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 1515 (0.13%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			

subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	2 / 1515 (0.13%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Insulin-requiring type 2 diabetes mellitus			
subjects affected / exposed	0 / 1515 (0.00%)	1 / 757 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic alkalosis			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder			
subjects affected / exposed	1 / 1515 (0.07%)	0 / 757 (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: 5 %

Non-serious adverse events	MAGE-A3 Total/TTP-T Group	Placebo Total/TTP-T Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1354 / 1515 (89.37%)	533 / 757 (70.41%)	
Nervous system disorders			
Headache			
subjects affected / exposed	130 / 1515 (8.58%)	40 / 757 (5.28%)	
occurrences (all)	239	50	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	92 / 1515 (6.07%)	26 / 757 (3.43%)	
occurrences (all)	199	55	

Chills			
subjects affected / exposed	118 / 1515 (7.79%)	7 / 757 (0.92%)	
occurrences (all)	249	16	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	243 / 1515 (16.04%)	50 / 757 (6.61%)	
occurrences (all)	578	85	
Influenza like illness			
subjects affected / exposed	197 / 1515 (13.00%)	23 / 757 (3.04%)	
occurrences (all)	680	39	
Injection site erythema			
subjects affected / exposed	103 / 1515 (6.80%)	3 / 757 (0.40%)	
occurrences (all)	343	3	
Injection site pain			
subjects affected / exposed	477 / 1515 (31.49%)	35 / 757 (4.62%)	
occurrences (all)	1873	73	
Injection site reaction			
subjects affected / exposed	273 / 1515 (18.02%)	14 / 757 (1.85%)	
occurrences (all)	1353	17	
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	237 / 1515 (15.64%)	13 / 757 (1.72%)	
occurrences (all)	578	25	
Pyrexia			
subjects affected / exposed	529 / 1515 (34.92%)	38 / 757 (5.02%)	
occurrences (all)	1720	49	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	76 / 1515 (5.02%)	31 / 757 (4.10%)	
occurrences (all)	110	42	
Nausea			
subjects affected / exposed	108 / 1515 (7.13%)	36 / 757 (4.76%)	
occurrences (all)	177	45	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	131 / 1515 (8.65%)	71 / 757 (9.38%)	
occurrences (all)	155	80	
Dyspnoea			
subjects affected / exposed	82 / 1515 (5.41%)	46 / 757 (6.08%)	
occurrences (all)	90	51	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	119 / 1515 (7.85%)	6 / 757 (0.79%)	
occurrences (all)	257	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	106 / 1515 (7.00%)	31 / 757 (4.10%)	
occurrences (all)	162	35	
Myalgia			
subjects affected / exposed	183 / 1515 (12.08%)	20 / 757 (2.64%)	
occurrences (all)	588	23	
Pain in extremity			
subjects affected / exposed	125 / 1515 (8.25%)	24 / 757 (3.17%)	
occurrences (all)	251	29	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	79 / 1515 (5.21%)	28 / 757 (3.70%)	
occurrences (all)	112	30	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2010	Amendment 1 included the following changes: 1) Evaluation of efficacy of study treatment in GS+ vs GS- population was upgraded to secondary objective of the trial; 2) Analysis of impact of study treatment on patients' health-related Quality of Life or utility was added as new secondary objective along with corresponding endpoints; 3) New, optional translational research was added including pharmacogenetic testing, DNA demethylation analysis & antigen spreading; 4) Recording of autoimmune diseases as AEs of specific interest was included in protocol & a list of types of diseases/disorders with potential autoimmune causality to be considered established; 5) Hematology & biochemistry safety laboratory tests were added for Week 12 visit; 6) Allowed concomitant medication was changed: a) systemic corticosteroids was prohibited only when prescribed for chronic treatment (more than 7 consecutive days [D]), b) immunoglobulins &/or any blood products administration was allowed provided a minimum of 7D between immunoglobulins &/or blood products & study treatment administration; 7) Study treatment postponement was allowed to permit influenza vaccination in framework of imposed influenza vaccination programs to allow a minimum of 7D between influenza vaccine & study treatment administration; 8) Clarifications were added to protocol (e.g. allowed time intervals for scans, randomization & surgery, clarifications on acceptance of scans, etc.) without changing study procedures; 9) Country specific appendices were included for countries also participating in PRAME-AS15-NSC-001 (ADJ) (GSK ID: 113174) study to allow simultaneous screening for both studies, i.e. both MAGE-A3 & PRAME expression could be tested on the tumor samples. 10) Japan was added as participating country & an appendix with Japan specific requirements was added. 11) Certain information was updated, e.g. contact numbers for emergency code breaking & SAE reporting, description of the ECOG performance status.
18 October 2011	Amendment 2 included the following changes: 1) After trial initiation, a GS at the tumor site associated with a clinical response to MAGE-A3 ASCI was identified in 2 trials in melanoma and lung cancer. This opens the possibility to identify patients likely to benefit from MAGE-A3 ASCI. To clinically validate these GS biomarkers, DFS analysis in patients presenting the GS was added as co-primary (1ry) objective; 2) At the time of the initially planned 1st interim analysis (IA) there would not have been enough events reported in GS+ population to conclude on relevance of GS selection approach. Clinical validation of GS could only be performed on data set available at time of 2nd IA or final analysis (FA). It was decided to remove 1st efficacy IA; 3) In addition, secondary (2ry) endpoints to evaluate OS & lung-cancer-related survival in GS+ and GS- patients were added; 4) Other 2ry objectives were clarified in accordance with addition of above co-1ry objective; 5) Alpha levels assigned to objectives A and B were adapted to take into account correlation between test statistics for no-CT and overall; 6) A weighted Bonferroni-Holm strategy using the closure principle was put in place in case of efficacy claims at the FA; 7) The Wald test was replaced by Likelihood Ratio test as primary test in Cox models, due to that a slight increase in 1-sided type I error is expected when using an unbalanced design together with Wald test; 8) It was clarified that at time of the analyses, 2-sided p-values will be reported & design considerations adapted using 2-sided significance levels; 9) To validate predictive value of GS, an interaction test between MAGE-A3 ASCI vs placebo & GS status was planned; 10) A new criterion for study treatment postponement to allow recovery of possibly related CTC grade ≥ 2 AEs was added; 11) IDMC responsibilities were modified to accommodate that an independent statistician (vs the sponsor) was to provide the FA for review by the IDMC.

06 June 2012	Protocol Amendment 3 included the following changes: 1) At the European Medicines Agency's (EMA) request, GSK Biologicals updated its procedure for emergency unblinding during the conduct of a clinical study; 2) According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resided solely with the investigator and consequently, the investigator would have full authority to break the treatment code. Wording in the protocol was adapted accordingly; 3) To ensure the availability of images that could be valuable to the accurate assessment of a patient's disease status, instructions that GSK could collect for review any imaging performed within the scope of this trial and not only images that are related to the identification of recurrences were included; 4) Clarification that at the concluding examination following a recurrence, any tumor assessment performed at the visit showing recurrence did not have to be repeated; 5) Some corrections were made, i.e. footnote cross references, clinical cut off for anti-MAGE-A3 antibodies enzyme-linked immunosorbent assay (ELISA), the power to detect a differential effect in the GS+ population for validation of the gene profile.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 April 2014	The study was terminated early on 1 April 2014 following assessment of the lack of efficacy of the MAGE-A3 ASCI study product by the IDMC for the study, as the first two co-primary objectives (DFS in the overall population and DFS in the No-CT population) were not reached. The third co-primary objective, i.e. DFS in the test set of the GS+ population, could not be assessed as no GS classifier could be identified in the training set. The final analysis presented in this summary was performed on all the data collected up to the data lock point (DLP) of 23 January 2014. No follow-up analysis was performed including additional data collected until the end of the study as these were very limited data. Safety data were recorded after the data lock point of the Final Analysis. These safety data are not reported in the safety section of this summary and are as follows for the period spreading from DLP to study end (23 September 2014): 1) For this entire period of assessment, SAEs were additionally reported by 7 and 3 patients in the MAGE-A3 and Placebo groups, respectively, none of these SAEs having a fatal outcome and one of them reported in the MAGE-A3 Group (MedDRA preferred term: mediastinitis) being assessed by the investigators as related to MAGE-A3 ASCI study product; and 2) during the 31-day periods following each treatment administration, at least one AE was reported by 38 and 15 patients in MAGE-A3 and Placebo groups, respectively. Overall these additional safety data did not alter the rates of AEs as displayed in this summary.	-

Notes:

Limitations and caveats

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

Objective C to demonstrate clinical efficacy in terms of DFS of the MAGE-A3 product versus placebo in NSCLC after complete surgical resection in the GS+ population could not be evaluated as no GS classifier could be identified in the training set.

Notes: