Clinical trial results:
A Multi-Center, Open-Label, Phase II Study of Ipilimumab (MDX-010) Extended-Treatment Monotherapy or Follow-up for Patients Previously Enrolled in Ipilimumab (MDX-010) Protocols

Summary

EudraCT number	2005-006083-57
Trial protocol	BE GB CZ DE AT HU FI SE IT DK ES
Global end of trial date	07 April 2014

Results information

Result version number	v1 (current)
This version publication date	01 June 2016
First version publication date	01 June 2016

Trial information

Trial identification

Sponsor protocol code	CA184-025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00162123
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	07 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To monitor the safety of ipilimumab (MDX-010) administered either as reinduction (10 mg/kg or 3 mg/kg) or as Maintenance therapy (0.3, 3 or 10 mg/kg) in this ipilimumab (MDX-010) clinical study.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	South Africa: 6
Country: Number of subjects enrolled	Ukraine: 3
Country: Number of subjects enrolled	United States: 119
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 23
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 7

Worldwide total number of subjects	248
EEA total number of subjects	91

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)	168
From 65 to 84 years	78
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 248 enrolled, 6 failed screening; 28 from study CA184-004 (2005-002126-64), 42 from CA184-007 (2005-002678-31), 67 from CA184-008 (2005-002051-41), and 103 from CA184-022 (2005-006083-57) entered the study. Of enrollees, 1 from study MDX010-08 (NCT00050102) and 9 from MDX010-15 (NCT00729950) entered maintenance as Tumor Assessment only.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	First Reinduction: Ipilimumab, 10 to 10 mg/kg

Arm description:

Subjects who initially received ipilimumab, 10 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 10 mg/kg, via 90 minute intravenous infusion, administered every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent.

Arm title	First Reinduction: Ipilimumab, 3 to 10 mg/kg

Arm description:

Subjects who initially received ipilimumab, 3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 10 mg/kg, via 90 minute intravenous infusion, administered every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent.

Arm title	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg

Arm description:

Subjects who initially received ipilimumab, 0.3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 10 mg/kg, via 90 minute intravenous infusion, administered every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent.

Arm title	First Reinduction: Ipilimumab, Other Dosage

Arm description:

Subjects who received a dose other than 10, 3, or 0.3 mg/kg ipilimumab in parent study received a first reinduction of either 3 or 10 mg/kg in current study.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg or 10 mg/kg, via 90 minute intravenous infusion, administered every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent.

Arm title	Extended Maintenance Only: Ipilimumab, 10 mg/kg

Arm description:

Subjects who received ipilimumab, 10 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (10 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 10 mg/kg, via 90 minute intravenous infusion, administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent.

Arm title	Extended Maintenance Only: Ipilimumab, 3 mg/kg

Arm description:

Subjects who received ipilimumab, 3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Arm type	Experimental

Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 3 mg/kg, via 90 minute intravenous infusion, administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent

Arm title	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg

Arm description:

Subjects who received ipilimumab, 0.3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (0.3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	BMS-734016
Other name	MDX-010
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ipilimumab 0.3 mg/kg, via 90 minute intravenous infusion, administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent

Arm title	Follow-up

Arm description:

Subjects who received ipilimumab at any dose in prior parent studies and who were deemed ineligible for other groups in the current study. Subjects did not receive any additional study treatment in current study but continued follow-up for the collection of survival data.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1[1]	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg
Started	53	34	24
Received Treatment	53	34	24
Completed	9	5	3
Not completed	44	29	21
Deterioration without progression	2	2	3
Physician decision	1	2	-
Consent withdrawn by subject	2	-	2
Disease progression	27	19	10
Not specified (after start of treatment)	-	-	-
Study drug toxicity	6	1	5
Adverse event, non-fatal	1	2	-
Death	3	3	1
Tumor assessment only (not treated)	-	-	-

Follow-up only (not treated or assessed)	-	-	-
Not specified (before treatment)	2	-	-

Number of subjects in period 1[1]	First Reinduction: Ipilimumab, Other Dosage	Extended Maintenance Only: Ipilimumab, 10 mg/kg	Extended Maintenance Only: Ipilimumab, 3 mg/kg
Started	11	45	13
Received Treatment	11	33	12
Completed	3	14	4
Not completed	8	31	9
Deterioration without progression	-	1	-
Physician decision	-	-	1
Consent withdrawn by subject	1	1	2
Disease progression	4	8	3
Not specified (after start of treatment)	-	3	-
Study drug toxicity	-	4	1
Adverse event, non-fatal	2	1	-
Death	1	1	1
Tumor assessment only (not treated)	-	-	-
Follow-up only (not treated or assessed)	-	-	-
Not specified (before treatment)	-	12	1

Number of subjects in period 1[1]	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg	Follow-up
Started	4	58
Received Treatment	4	0
Completed	0	0
Not completed	4	58
Deterioration without progression	-	-
Physician decision	1	-
Consent withdrawn by subject	1	-
Disease progression	1	-
Not specified (after start of treatment)	-	-
Study drug toxicity	1	-
Adverse event, non-fatal	-	-
Death	-	-
Tumor assessment only (not treated)	-	1
Follow-up only (not treated or assessed)	-	57
Not specified (before treatment)	-	-

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: Of 248 enrolled, 6 failed screening hence 242 subjects entered in the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	First Reinduction: Ipilimumab, 10 to 10 mg/kg
Reporting group description:	
Subjects who initially received ipilimumab, 10 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.	
Reporting group title	First Reinduction: Ipilimumab, 3 to 10 mg/kg
Reporting group description:	
Subjects who initially received ipilimumab, 3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.	
Reporting group title	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg
Reporting group description:	
Subjects who initially received ipilimumab, 0.3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.	
Reporting group title	First Reinduction: Ipilimumab, Other Dosage
Reporting group description:	
Subjects who received a dose other than 10, 3, or 0.3 mg/kg ipilimumab in parent study received a first reinduction of either 3 or 10 mg/kg in current study.	
Reporting group title	Extended Maintenance Only: Ipilimumab, 10 mg/kg
Reporting group description:	
Subjects who received ipilimumab, 10 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (10 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.	
Reporting group title	Extended Maintenance Only: Ipilimumab, 3 mg/kg
Reporting group description:	
Subjects who received ipilimumab, 3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.	
Reporting group title	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg
Reporting group description:	
Subjects who received ipilimumab, 0.3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (0.3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.	
Reporting group title	Follow-up
Reporting group description:	
Subjects who received ipilimumab at any dose in prior parent studies and who were deemed ineligible for other groups in the current study. Subjects did not receive any additional study treatment in current study but continued follow-up for the collection of survival data.	

Reporting group values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg
Number of subjects	53	34	24

Age categorical Units: Subjects			
Adult (< 65 years)	40	25	16
Adult (>= 65 years)	13	9	8
Age continuous Units: years			
arithmetic mean	55.4	58.8	56
standard deviation	± 11.74	± 9.93	± 15.33
Gender categorical Units: Subjects			
Female	21	11	4
Male	32	23	20
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	0
Black or African American	1	0	0
White	51	34	24
More than one race	1	0	0
American Indian/Alaska native	0	0	0
Other: Brazilian	0	0	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status assesses a Subject's physical ability against a 6-point scale: 0=fully active, able to carry on all predisease activities without restriction; 1=restricted in physically strenuous activity, ambulatory and able to carry out light or sedentary work; 2=ambulatory (>50% of waking hours), capable of all self care, unable to carry out any work activities; 3=capable of only limited self care, confined to bed/chair >50% of waking hours; 4=completely disabled, cannot carry on any self care, totally confined to bed/chair; 5=dead. Score ranges from 0=best to 5=worst status.			
Units: Subjects			
ECOG performance status of 0	37	22	10
ECOG performance status of 1	16	11	13
ECOG performance status of 2	0	1	1
ECOG performance status of 3	0	0	0
Not reported	0	0	0

Reporting group values	First Reinduction: Ipilimumab, Other Dosage	Extended Maintenance Only: Ipilimumab, 10 mg/kg	Extended Maintenance Only: Ipilimumab, 3 mg/kg
Number of subjects	11	45	13
Age categorical Units: Subjects			
Adult (< 65 years)	8	25	5
Adult (>= 65 years)	3	20	8
Age continuous Units: years			
arithmetic mean	57.8	60.5	59
standard deviation	± 13.72	± 12.42	± 16.65
Gender categorical Units: Subjects			
Female	1	20	5
Male	10	25	8

Race/Ethnicity, Customized Units: Subjects			
Asian	1	0	0
Black or African American	0	0	0
White	10	45	13
More than one race	0	0	0
American Indian/Alaska native	0	0	0
Other: Brazilian	0	0	0
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status assesses a Subject's physical ability against a 6-point scale: 0=fully active, able to carry on all predisease activities without restriction; 1=restricted in physically strenuous activity, ambulatory and able to carry out light or sedentary work; 2=ambulatory (>50% of waking hours), capable of all self care, unable to carry out any work activities; 3=capable of only limited self care, confined to bed/chair >50% of waking hours; 4=completely disabled, cannot carry on any self care, totally confined to bed/chair; 5=dead. Score ranges from 0=best to 5=worst status.			
Units: Subjects			
ECOG performance status of 0	9	40	12
ECOG performance status of 1	2	5	1
ECOG performance status of 2	0	0	0
ECOG performance status of 3	0	0	0
Not reported	0	0	0

Reporting group values	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg	Follow-up	Total
Number of subjects	4	58	242
Age categorical Units: Subjects			
Adult (< 65 years)	2	43	164
Adult (>= 65 years)	2	15	78
Age continuous Units: years			
arithmetic mean	65.5	56.3	
standard deviation	± 4.8	± 12.96	-
Gender categorical Units: Subjects			
Female	1	22	85
Male	3	36	157
Race/Ethnicity, Customized Units: Subjects			
Asian	0	1	2
Black or African American	0	0	1
White	4	55	236
More than one race	0	0	1
American Indian/Alaska native	0	1	1
Other: Brazilian	0	1	1
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status assesses a Subject's physical ability against a 6-point scale: 0=fully active, able to carry on all predisease activities without restriction; 1=restricted in physically strenuous activity, ambulatory and able to carry out light or sedentary work; 2=ambulatory (>50% of waking hours), capable of all self care, unable to carry out any work activities; 3=capable of only limited self care, confined to bed/chair >50% of waking hours; 4=completely disabled, cannot carry on any self care, totally confined to bed/chair; 5=dead. Score ranges from 0=best to 5=worst status.			

Units: Subjects			
ECOG performance status of 0	3	29	162
ECOG performance status of 1	1	10	59
ECOG performance status of 2	0	1	3
ECOG performance status of 3	0	1	1
Not reported	0	17	17

End points reporting groups

Reporting group title	First Reinduction: Ipilimumab, 10 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 10 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	First Reinduction: Ipilimumab, 3 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 0.3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	First Reinduction: Ipilimumab, Other Dosage

Reporting group description:

Subjects who received a dose other than 10, 3, or 0.3 mg/kg ipilimumab in parent study received a first reinduction of either 3 or 10 mg/kg in current study.

Reporting group title	Extended Maintenance Only: Ipilimumab, 10 mg/kg

Reporting group description:

Subjects who received ipilimumab, 10 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (10 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	Extended Maintenance Only: Ipilimumab, 3 mg/kg

Reporting group description:

Subjects who received ipilimumab, 3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg

Reporting group description:

Subjects who received ipilimumab, 0.3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (0.3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	Follow-up

Reporting group description:

Subjects who received ipilimumab at any dose in prior parent studies and who were deemed ineligible for other groups in the current study. Subjects did not receive any additional study treatment in current study but continued follow-up for the collection of survival data.

Primary: Number of Subjects With On-study Adverse Events (AEs), AEs Leading to Discontinuation, Serious Adverse Events (SAEs), Drug-related AEs, Immune-related AEs (irAEs), and Death as Outcome

End point title	Number of Subjects With On-study Adverse Events (AEs), AEs Leading to Discontinuation, Serious Adverse Events (SAEs), Drug-related AEs, Immune-related AEs (irAEs), and Death as Outcome[1][2]

End point description:

An AE is any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. An SAE is a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Drug-related is defined as having certain, probable, possible, or missing relationship to study drug. An IrAE is an AE characterized by a potential association with inflammation and considered by the investigator to be drug related. Grade (Gr) 1=Mild, Gr 2=Moderate, Gr 3=Severe, Gr 4=Life-threatening or disabling, Gr 5=Death. All subjects who received study drug as reinduction from 0.3, 3, or 10 mg/kg doses in parent study and 10 mg/kg in current study were evaluated.

End point type	Primary

End point timeframe:

Continuously from first dose to 70 days after last dose of study drug. For deaths, Day 1 of enrollment to 70 days after last dose of study drug.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive summary statistics were planned for this outcome measure.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

End point values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	34	24	
Units: Subjects				
AEs: Any Grade	51	33	24	
AEs: Grade 3 or 4	18	10	10	
AEs: Grade 5 (Fatal)	4	7	8	
AEs leading to discontinuation: Any grade	13	6	8	
AEs leading to discontinuation: Grade 3 or 4	9	3	6	
AEs leading to discontinuation: Grade 5 (Fatal)	1	2	1	
SAEs: Any grade	23	19	14	
SAEs: Grade 3 or 4	13	8	5	
SAEs: Grade 5 (Fatal)	4	7	8	
Drug-related AEs: Any grade	42	28	21	
Drug-related AEs: Grade 3 or 4	9	3	9	
Drug-related AEs: Grade 5 (Fatal)	0	0	0	
irAEs: Any grade	30	23	18	
irAEs: Grade 3 or 4	7	2	6	
irAEs: Grade 5 (Fatal)	0	0	0	
Deaths	36	27	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[3]

End point description:

OS was computed for all Subjects who entered this study and is defined as the time between the first dose of study therapy and death. If a subject has not died, OS was censored at the time of last contact. The analysis was performed in all the subjects who received study drug as reinduction from 0.3, 3, or 10 mg/kg doses in parent study and 10 mg/kg in current study.

End point type	Secondary

End point timeframe:

From first dose of study drug in parent study to death or date of last censoring

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

End point values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	34	24	
Units: Months				
median (confidence interval 95%)	30.8 (24.2 to 41.1)	18.7 (9.7 to 30.4)	15.2 (10.7 to 21.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Surviving at 1, 1.5, and 2 Years

End point title	Percentage of Subjects Surviving at 1, 1.5, and 2 Years[4]

End point description:

Survival rate was defined as the time from first dose of study drug to 1, 1.5, and 2 years. The analysis was performed in all the subjects who received study drug as reinduction or extended maintenance from 0.3, 3, or 10 mg/kg doses in parent study and 10 mg/kg in current study and those subjects who were followed-up.

End point type	Secondary

End point timeframe:

From first dose of study drug in parent study to up to 2 years after reinduction

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

End point values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	Extended Maintenance Only: Ipilimumab, 10 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	34	24	33
Units: Percentage of Subjects				
number (not applicable)				
At 1 year	80.93	55.88	65.63	100
At 1.5 year	71.3	50	35	100
At 2 year	63.59	38.24	30.63	91.11

End point values	Extended Maintenance Only: Ipilimumab, 3 mg/kg	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg	Follow-up	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	4	58	
Units: Percentage of Subjects				
number (not applicable)				
At 1 year	100	75	87.8	
At 1.5 year	84.62	75	79.02	
At 2 year	84.62	75	64.97	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With On-study Immune-related Adverse Events (irAEs)

End point title	Number of Subjects With On-study Immune-related Adverse Events (irAEs)[5]

End point description:

irAEs were defined as adverse events characterized by a potential association with inflammation and considered by the investigator as drug related. These prespecified terms were grouped into the following organ-specific subcategories: gastrointestinal, hepatic, skin, endocrine, neurologic, and other (includes blood, eye, immune system, investigations, infections, renal, and respiratory systems). Subjects may have 1 or more events. The analysis was performed in all the subjects who received study drug as reinduction from 0.3, 3, or 10 mg/kg doses in parent study 10 mg/kg current study.

End point type	Secondary

End point timeframe:

From first dose of study drug during reinduction to the earliest of 70 days after last dose or day before second reinduction first dose date

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

End point values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	34	24	
Units: Subjects				
Any irAE: Any grade	30	23	18	
Any irAE: Grade 3 or 4	7	2	6	
Any irAE: Grade 5 (Fatal)	0	0	0	
Gastrointestinal irAE: Any grade	11	7	14	
Gastrointestinal irAE: Grade 3 or 4	2	1	3	
Hepatic irAE: Any grade	3	0	1	
Hepatic irAE: Grade 3 or 4	2	0	1	
Endocrine irAE: Any grade	3	2	1	
Endocrine irAE: Grade 3 or 4	1	0	1	
Skin irAE: Any grade	18	18	10	
Skin irAE: Grade 3 or 4	2	1	1	
Neurologic irAE: Any grade	1	0	0	
Neurologic irAE: Grade 3 or 4	0	0	0	
Other irAE: Any grade	2	3	1	
Other irAE: Grade 3 or 4	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)[6]

End point description:

PFS was defined as the time between the date of the baseline tumor assessment in this study and the date of progression or death, whichever occurred first. The analysis was performed in all the subjects who received study drug as reinduction from 0.3, 3, or 10 mg/kg doses in parent study and 10 mg/kg in current study.

End point type	Secondary

End point timeframe:

From day of first reinduction in current study to date of progression or death, whichever occurred first

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

End point values	First Reinduction: Ipilimumab, 10 to 10 mg/kg	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	34	24	
Units: Months				
median (confidence interval 95%)	3.4 (2.6 to 7.8)	2.6 (2.6 to 2.8)	2.6 (2 to 11.1)	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Continuously from first dose to 70 days after last dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	First Reinduction: Ipilimumab, 3 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the Subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 0.3 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the Subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	First Reinduction: Ipilimumab, 10 to 10 mg/kg

Reporting group description:

Subjects who initially received ipilimumab, 10 mg/kg, in a parent study received ipilimumab, 10 mg/kg in the current study. Ipilimumab was administered as an individual open-label dose every 3 weeks for the first 10 weeks of reinduction for a total of 4 separate doses unless the subject experienced disease progression or withdrew consent. Subjects had to wait 3 weeks from the last dose of ipilimumab in a parent study to the first dose of ipilimumab in the current study.

Reporting group title	Extended Maintenance Only: Ipilimumab, 10 mg/kg

Reporting group description:

Subjects who received ipilimumab, 10 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (10 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	First Reinduction: Ipilimumab, Other Dosage

Reporting group description:

Subjects who received a dose other than 10, 3, or 0.3 mg/kg ipilimumab in parent study received a first reinduction of either 3 or 10 mg/kg in current study.

Reporting group title	Extended Maintenance Only: Ipilimumab, 3 mg/kg

Reporting group description:

Subjects who received ipilimumab, 3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg

Reporting group description:

Subjects who received ipilimumab, 0.3 mg/kg, in a parent study and who achieved extended clinical benefit received the same dose of ipilimumab (0.3 mg/kg) as maintenance in the current study. Maintenance dosing was administered every 12 weeks until disease progression, unacceptable toxicity, or withdrawal of consent. Extended maintenance was limited to 3 years.

Reporting group title	Follow-up

Reporting group description:

Subjects who received ipilimumab at any dose in prior parent studies and who were deemed ineligible for other groups in the current study. Subjects did not receive any additional study treatment in current

Serious adverse events	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	First Reinduction: Ipilimumab, 10 to 10 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 34 (55.88%)	14 / 24 (58.33%)	22 / 53 (41.51%)
number of deaths (all causes)	27	19	36
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Prostate cancer			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	5 / 34 (14.71%)	6 / 24 (25.00%)	4 / 53 (7.55%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 5	0 / 6	0 / 4
Fatigue			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchostenosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal stenosis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Confusional state			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system haemorrhage			

subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidotic hyperglycaemic coma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplegia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			

subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 1	0 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 4
Coagulopathy			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry eye			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular hyperaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital oedema			

subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	1 / 1	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	3 / 34 (8.82%)	4 / 24 (16.67%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	2 / 3	4 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	1 / 1	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 34 (0.00%)	2 / 24 (8.33%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			

subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorder			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocytic hypophysitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 15	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 34 (0.00%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extended Maintenance Only: Ipilimumab, 10 mg/kg	First Reinduction: Ipilimumab, Other Dosage	Extended Maintenance Only: Ipilimumab, 3 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 33 (36.36%)	7 / 11 (63.64%)	3 / 12 (25.00%)
number of deaths (all causes)	15	6	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malignant neoplasm progression			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cell carcinoma			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Disease progression			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchostenosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tracheal stenosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatine increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 11	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Left ventricular dysfunction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diabetic ketoacidotic hyperglycaemic coma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplegia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal cord compression			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve paralysis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry eye			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Glaucoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular hyperaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital oedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	3 / 33 (9.09%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	4 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 33 (3.03%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocytic hypophysitis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Influenza			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg	Follow-up	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	20 / 58 (34.48%)	
number of deaths (all causes)	2	31	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Malignant neoplasm progression			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastases to spine			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchostenosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal stenosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
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			
Femur fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Thoracic vertebral fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidotic hyperglycaemic coma			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Age-related macular degeneration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular hyperaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal hypomotility			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypophysitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopituitarism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocytic hypophysitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (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 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pathological fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	First Reinduction: Ipilimumab, 3 to 10 mg/kg	First Reinduction: Ipilimumab, 0.3 to 10 mg/kg	First Reinduction: Ipilimumab, 10 to 10 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 34 (94.12%)	21 / 24 (87.50%)	46 / 53 (86.79%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	4 / 53 (7.55%)
occurrences (all)	1	0	4
Hypotension			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	2	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 34 (11.76%)	1 / 24 (4.17%)	7 / 53 (13.21%)
occurrences (all)	4	1	7
Axillary pain			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	2 / 34 (5.88%)	1 / 24 (4.17%)	6 / 53 (11.32%)
occurrences (all)	2	1	7
Fatigue			
subjects affected / exposed	11 / 34 (32.35%)	10 / 24 (41.67%)	20 / 53 (37.74%)
occurrences (all)	20	11	25
Influenza like illness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	0	2

Infusion site extravasation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	3 / 53 (5.66%)
occurrences (all)	1	0	3
Pain			
subjects affected / exposed	0 / 34 (0.00%)	3 / 24 (12.50%)	2 / 53 (3.77%)
occurrences (all)	0	3	2
Pyrexia			
subjects affected / exposed	7 / 34 (20.59%)	4 / 24 (16.67%)	5 / 53 (9.43%)
occurrences (all)	8	5	6
Xerosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 34 (14.71%)	3 / 24 (12.50%)	8 / 53 (15.09%)
occurrences (all)	7	3	9
Dyspnoea			
subjects affected / exposed	7 / 34 (20.59%)	3 / 24 (12.50%)	4 / 53 (7.55%)
occurrences (all)	7	3	4
Productive cough			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1

Sleep apnoea syndrome			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	3 / 53 (5.66%)
occurrences (all)	1	1	3
Apathy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	3 / 34 (8.82%)	3 / 24 (12.50%)	1 / 53 (1.89%)
occurrences (all)	3	3	1
Libido decreased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
Amylase increased			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences (all)	1	1	2
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	0 / 53 (0.00%)
occurrences (all)	1	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Blood uric acid increased			

subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Haemoglobin decreased			
subjects affected / exposed	3 / 34 (8.82%)	2 / 24 (8.33%)	2 / 53 (3.77%)
occurrences (all)	3	2	3
Weight decreased			
subjects affected / exposed	3 / 34 (8.82%)	4 / 24 (16.67%)	5 / 53 (9.43%)
occurrences (all)	3	5	7
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Radiation skin injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	3 / 53 (5.66%)
occurrences (all)	1	3	3
Dysgeusia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences (all)	0	2	1
Headache			
subjects affected / exposed	7 / 34 (20.59%)	1 / 24 (4.17%)	6 / 53 (11.32%)
occurrences (all)	9	1	6
Migraine			

subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	2 / 34 (5.88%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	2	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 34 (5.88%)	2 / 24 (8.33%)	5 / 53 (9.43%)
occurrences (all)	2	2	6
Eye disorders			
Cataract			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Erythema of eyelid			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Iritis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Retinopathy			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	4 / 34 (11.76%)	1 / 24 (4.17%)	7 / 53 (13.21%)
occurrences (all)	4	1	7
Abdominal pain lower			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	6 / 53 (11.32%)
occurrences (all)	2	0	7
Colitis			
subjects affected / exposed	0 / 34 (0.00%)	3 / 24 (12.50%)	3 / 53 (5.66%)
occurrences (all)	0	3	3
Constipation			
subjects affected / exposed	5 / 34 (14.71%)	4 / 24 (16.67%)	6 / 53 (11.32%)
occurrences (all)	6	5	9
Diarrhea			
subjects affected / exposed	8 / 34 (23.53%)	9 / 24 (37.50%)	17 / 53 (32.08%)
occurrences (all)	9	12	36
Dry mouth			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences (all)	1	0	2
Dyspepsia			
subjects affected / exposed	0 / 34 (0.00%)	3 / 24 (12.50%)	3 / 53 (5.66%)
occurrences (all)	0	3	3
Flatulence			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 34 (0.00%)	2 / 24 (8.33%)	0 / 53 (0.00%)
occurrences (all)	0	2	0
Inguinal hernia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 34 (11.76%)	7 / 24 (29.17%)	15 / 53 (28.30%)
occurrences (all)	4	7	21

Stomatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	2 / 34 (5.88%)	2 / 24 (8.33%)	9 / 53 (16.98%)
occurrences (all)	2	2	12
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Cholecystitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences (all)	2	0	3
Blister			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences (all)	0	2	2
Eczema			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Erythema			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences (all)	0	1	2
Exfoliative rash			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	2	1	0
Hyperhidrosis			

subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	4 / 53 (7.55%)
occurrences (all)	1	2	4
Pruritus			
subjects affected / exposed	12 / 34 (35.29%)	6 / 24 (25.00%)	13 / 53 (24.53%)
occurrences (all)	18	7	16
Rash			
subjects affected / exposed	10 / 34 (29.41%)	4 / 24 (16.67%)	10 / 53 (18.87%)
occurrences (all)	10	10	16
Skin hypopigmentation			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Skin mass			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Vitiligo			
subjects affected / exposed	2 / 34 (5.88%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences (all)	2	2	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
Lymphocytic hypophysitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 34 (14.71%)	3 / 24 (12.50%)	5 / 53 (9.43%)
occurrences (all)	5	3	7
Arthritis			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Back pain			

subjects affected / exposed	6 / 34 (17.65%)	1 / 24 (4.17%)	6 / 53 (11.32%)
occurrences (all)	6	1	6
Muscle spasms			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences (all)	1	3	1
Muscle tightness			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences (all)	0	1	2
Myalgia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	2 / 53 (3.77%)
occurrences (all)	1	0	2
Pain in extremity			
subjects affected / exposed	3 / 34 (8.82%)	1 / 24 (4.17%)	3 / 53 (5.66%)
occurrences (all)	3	1	4
Musculoskeletal pain			
subjects affected / exposed	3 / 34 (8.82%)	1 / 24 (4.17%)	3 / 53 (5.66%)
occurrences (all)	3	1	4
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 34 (2.94%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	3	1	0
Cystitis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	1 / 53 (1.89%)
occurrences (all)	0	1	2
Erysipelas			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1

Nasopharyngitis			
subjects affected / exposed	0 / 34 (0.00%)	2 / 24 (8.33%)	3 / 53 (5.66%)
occurrences (all)	0	2	3
Sinusitis			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences (all)	1	2	1
Tinea cruris			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 34 (8.82%)	0 / 24 (0.00%)	3 / 53 (5.66%)
occurrences (all)	3	0	7
Urinary tract infection			
subjects affected / exposed	2 / 34 (5.88%)	1 / 24 (4.17%)	2 / 53 (3.77%)
occurrences (all)	2	1	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 34 (14.71%)	5 / 24 (20.83%)	9 / 53 (16.98%)
occurrences (all)	5	5	9
Dehydration			
subjects affected / exposed	1 / 34 (2.94%)	3 / 24 (12.50%)	3 / 53 (5.66%)
occurrences (all)	1	3	11
Hyperglycaemia			
subjects affected / exposed	1 / 34 (2.94%)	2 / 24 (8.33%)	1 / 53 (1.89%)
occurrences (all)	1	7	1
Hyperkalaemia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	3	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 34 (0.00%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 24 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			

subjects affected / exposed	1 / 34 (2.94%)	0 / 24 (0.00%)	1 / 53 (1.89%)
occurrences (all)	2	0	2
Hyponatraemia			
subjects affected / exposed	2 / 34 (5.88%)	1 / 24 (4.17%)	0 / 53 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	Extended Maintenance Only: Ipilimumab, 10 mg/kg	First Reinduction: Ipilimumab, Other Dosage	Extended Maintenance Only: Ipilimumab, 3 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 33 (84.85%)	9 / 11 (81.82%)	11 / 12 (91.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Hypertension			
subjects affected / exposed	3 / 33 (9.09%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	8	0	0
Hypotension			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 33 (6.06%)	2 / 11 (18.18%)	0 / 12 (0.00%)
occurrences (all)	2	4	0
Axillary pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	4 / 33 (12.12%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	5	0	2
Fatigue			

subjects affected / exposed	8 / 33 (24.24%)	6 / 11 (54.55%)	4 / 12 (33.33%)
occurrences (all)	11	9	5
Influenza like illness			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	6	0	1
Infusion site extravasation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Pain			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
Pyrexia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Xerosis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 33 (21.21%)	3 / 11 (27.27%)	0 / 12 (0.00%)
occurrences (all)	8	3	0
Dyspnoea			

subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Productive cough			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Apathy			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	5 / 33 (15.15%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	5	1	0
Libido decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 33 (12.12%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	6	1	0
Amylase increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 33 (15.15%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	8	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Blood creatinine increased			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Blood uric acid increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Radiation skin injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	2 / 33 (6.06%)	2 / 11 (18.18%)	0 / 12 (0.00%)
occurrences (all)	2	3	0
Dysgeusia			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 33 (15.15%)	3 / 11 (27.27%)	1 / 12 (8.33%)
occurrences (all)	5	4	3
Migraine			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 33 (12.12%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Erythema of eyelid			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Iritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Retinopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vision blurred			

subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Visual acuity reduced			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 33 (12.12%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 33 (3.03%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
Colitis			
subjects affected / exposed	4 / 33 (12.12%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	2 / 33 (6.06%)	2 / 11 (18.18%)	1 / 12 (8.33%)
occurrences (all)	3	2	1
Diarrhea			
subjects affected / exposed	16 / 33 (48.48%)	4 / 11 (36.36%)	4 / 12 (33.33%)
occurrences (all)	32	5	9
Dry mouth			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 11 (18.18%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Inguinal hernia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	5 / 33 (15.15%)	4 / 11 (36.36%)	2 / 12 (16.67%)
occurrences (all)	7	9	3
Stomatitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Vomiting			
subjects affected / exposed	2 / 33 (6.06%)	2 / 11 (18.18%)	0 / 12 (0.00%)
occurrences (all)	2	2	0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cholecystitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Alopecia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	2	1	1
Blister			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Dry skin			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Eczema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Erythema			

subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Exfoliative rash			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	10 / 33 (30.30%)	3 / 11 (27.27%)	3 / 12 (25.00%)
occurrences (all)	21	4	4
Rash			
subjects affected / exposed	6 / 33 (18.18%)	4 / 11 (36.36%)	4 / 12 (33.33%)
occurrences (all)	17	5	9
Skin hypopigmentation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Skin mass			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	0	1	2
Vitiligo			
subjects affected / exposed	3 / 33 (9.09%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Lymphocytic hypophysitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Arthritis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Back pain			
subjects affected / exposed	4 / 33 (12.12%)	2 / 11 (18.18%)	1 / 12 (8.33%)
occurrences (all)	4	4	1
Muscle spasms			
subjects affected / exposed	0 / 33 (0.00%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Muscle tightness			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	2 / 33 (6.06%)	1 / 11 (9.09%)	2 / 12 (16.67%)
occurrences (all)	3	2	2
Musculoskeletal pain			
subjects affected / exposed	3 / 33 (9.09%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Erysipelas			

subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Folliculitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Herpes zoster			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	4 / 33 (12.12%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	5	1	1
Sinusitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Tinea cruris			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	5 / 33 (15.15%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	6	0	2
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 33 (6.06%)	5 / 11 (45.45%)	2 / 12 (16.67%)
occurrences (all)	3	8	2
Dehydration			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Hypoalbuminaemia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	10	0	0
Hypocalcaemia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Hypokalaemia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Hyponatraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Extended Maintenance Only: Ipilimumab, 0.3 mg/kg	Follow-up	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	34 / 58 (58.62%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Axillary pain			

subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	12 / 58 (20.69%)	
occurrences (all)	1	12	
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Infusion site extravasation			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Local swelling			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 58 (5.17%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Xerosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 58 (1.72%)	
occurrences (all)	1	3	
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Apathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Libido decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Blood uric acid increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Blood urine present			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Radiation skin injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	

Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Migraine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Erythema of eyelid			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	0	
Iritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Photophobia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Retinopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	2 / 58 (3.45%)	
occurrences (all)	1	2	
Diarrhea			
subjects affected / exposed	0 / 4 (0.00%)	3 / 58 (5.17%)	
occurrences (all)	0	3	
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	

Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hiatus hernia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Inguinal hernia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	5 / 58 (8.62%)	
occurrences (all)	0	5	
Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Cholecystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Blister			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Dry skin			

subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Exfoliative rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	8 / 58 (13.79%)	
occurrences (all)	0	8	
Rash			
subjects affected / exposed	0 / 4 (0.00%)	6 / 58 (10.34%)	
occurrences (all)	0	6	
Skin hypopigmentation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 58 (1.72%)	
occurrences (all)	1	0	
Skin mass			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Vitiligo			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	

Lymphocytic hypophysitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 58 (1.72%)	
occurrences (all)	1	1	
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	2 / 58 (3.45%)	
occurrences (all)	1	2	
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Muscle tightness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	6 / 58 (10.34%)	
occurrences (all)	1	10	
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	3 / 58 (5.17%)	
occurrences (all)	0	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Cystitis			

subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Folliculitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	3 / 58 (5.17%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Tinea cruris			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	2 / 58 (3.45%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	

Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2006	Provided additional information regarding tumor imaging assessments and disease assessment criteria, clarified description of the 3 Phases and Groups in the trial, clarified the rollover timing and variable eligibility requirements from each parent study. Redefined secondary objectives in the 3 Subject groups. Limited the amount of reinductions per Subject to a maximum of 2 and mandated that the BMS Medical Monitor be contacted prior to the initiation of any reinduction. Simplified tumor assessment schedule. Divided Maintenance Phase Subject population into those receiving ipilimumab with tumor assessments and those having tumor assessments only.
27 February 2007	Allowed Subjects who experienced select ipilimumab-related Immune Breakthrough Events that are either completely reversible or medically manageable to receive reinduction treatment of ipilimumab at the time of progressive disease. Allowed Subjects who demonstrated defined mixed or delayed response under the parent study to continue Maintenance treatment under this rollover study. Provided more detailed description that Subjects entering into Group B from MDX010-08 or MDX010-15 would receive Tumor Assessments only until progression, when the Subject could be considered for reinduction. Redefined baseline tumor assessments for Group B Subject who entered this rollover study with continued response.
09 July 2007	Specified that in-line filters must be used when administering ipilimumab. Added immunogenicity testing. Replaced the term Immune Breakthrough Event (IBE) with the term irAE. Removed appendices for suggested work-up and treatment for IBEs and the diarrhea management algorithm and referred the protocol user to the current version of the Investigator Brochure for this information.
28 April 2008	Added periodic collection and analysis of survival data for all enrolled Subjects. Allowed the collection of survival data on Subjects who participated in the parent protocols but had not already entered this study. Allowed Subjects not available for more extensive follow-up to enter study as Group C survival follow-up only Subjects and provided for the opportunity to collect survival information on Subjects who may have died following the close of a parent study. Established the minimal follow-up requirements for Group C Survival Follow-up only Subjects.
09 September 2008	Added an exclusion criterion excluding Subjects with autoimmune disease (Subjects with documented history of inflammatory bowel disease, including ulcerative colitis and Crohn’s disease, Subjects with a history of symptomatic disease, for example, rheumatoid arthritis, systemic progressive sclerosis (scleroderma), systemic lupus erythmatosus, autoimmune vasculitis and Subjects with motor neuropathy considered of autoimmune origin (example, Gullain-Barré syndrome).
02 February 2009	Dose skipping criteria for ipilimumab was modified.
27 April 2009	Added interim analyses of efficacy and safety.
10 September 2009	Revised tumor assessment frequency for Subjects who maintained durable disease control (complete response, partial response, or stable disease) in maintenance phase for >=1 year. These Subjects could, at the discretion of the investigator, have had tumor assessments performed every 24 weeks until progressive disease, withdrawal of consent, or study closure. Clarified treatment modification section to give guidance for treatment discontinuation in the event of neurological toxicities.

06 December 2012	Addition of an Extension Phase to allow for continued dosing and collection of additional survival and outcomes data following the primary analysis database lock. Serious adverse event fax numbers and BMS medical monitor information were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated based on sponsor's decision to limit extended maintenance treatment to only 3 years from the first ipilimumab dose.

Notes: