



Clinical trial results:

A Phase 2, Open-Label, Randomized Study to Evaluate the Efficacy and Safety of GS-5745 Combined with Nivolumab versus Nivolumab Alone in Subjects with Unresectable or Recurrent Gastric or Gastroesophageal Junction Adenocarcinoma

Summary

EudraCT number	2016-001402-41
Trial protocol	DE HU GB BE ES IT
Global end of trial date	23 August 2019

Results information

Result version number	v2 (current)
This version publication date	03 October 2020
First version publication date	03 September 2020
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Updated the time frame for the primary outcome measure.

Trial information

Trial identification

Sponsor protocol code	GS-US-296-2013
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02864381
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	23 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 November 2017
Global end of trial reached?	Yes
Global end of trial date	23 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate and compare the efficacy of andecaliximab (GS-5745) in combination with nivolumab versus nivolumab alone in adults with recurrent gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	United States: 28
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Hungary: 3
Worldwide total number of subjects	144
EEA total number of subjects	109

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)	90
From 65 to 84 years	54
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Australia, Europe, and the United States. The first participant was screened on 01 September 2016. The last study visit occurred on 23 August 2019.

Pre-assignment

Screening details:

187 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Andecaliximab + Nivolumab

Arm description:

Andecaliximab 800 mg administered via intravenous (IV) infusion plus nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 34 weeks at the time of the primary efficacy analysis; up to 101 weeks at the time of the safety follow-up analysis).

Arm type	Experimental
Investigational medicinal product name	Andecaliximab
Investigational medicinal product code	
Other name	GS-5745
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

800 mg administered via IV infusion every 2 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg administered via IV infusion every 2 weeks

Arm title	Nivolumab
------------------	-----------

Arm description:

Nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 41 weeks at the time of the primary efficacy analysis; up to 97 weeks at the time of the safety follow-up analysis).

Arm type	Active comparator
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg administered via IV infusion every 2 weeks

Number of subjects in period 1	Andecaliximab + Nivolumab	Nivolumab
Started	72	72
Completed	0	0
Not completed	72	72
Withdrew Consent	5	6
Reason Unknown	7	3
Death	58	61
Investigator's Discretion	1	-
Protocol Violation	-	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups

Reporting group title	Andecaliximab + Nivolumab
Reporting group description:	
Andecaliximab 800 mg administered via intravenous (IV) infusion plus nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 34 weeks at the time of the primary efficacy analysis; up to 101 weeks at the time of the safety follow-up analysis).	
Reporting group title	Nivolumab
Reporting group description:	
Nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 41 weeks at the time of the primary efficacy analysis; up to 97 weeks at the time of the safety follow-up analysis).	

Reporting group values	Andecaliximab + Nivolumab	Nivolumab	Total
Number of subjects	72	72	144
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	58	59	
standard deviation	± 12.1	± 11.8	-
Gender categorical			
Units: Subjects			
Female	23	22	45
Male	49	50	99
Race			
Not Permitted=local regulators did not allow collection of race information.			
Units: Subjects			
Asian	1	1	2
Black	2	0	2
White	55	61	116
Not Permitted	12	8	20
Other	2	2	4
Ethnicity			
Not Permitted=local regulators did not allow collection of ethnicity information.			
Units: Subjects			
Hispanic or Latino	2	3	5
Not Hispanic or Latino	59	61	120
Not Permitted	11	8	19

End points

End points reporting groups

Reporting group title	Andecaliximab + Nivolumab
Reporting group description: Andecaliximab 800 mg administered via intravenous (IV) infusion plus nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 34 weeks at the time of the primary efficacy analysis; up to 101 weeks at the time of the safety follow-up analysis).	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 41 weeks at the time of the primary efficacy analysis; up to 97 weeks at the time of the safety follow-up analysis).	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description: ORR was defined as the percentage of participants with confirmed overall best response of complete response (CR) or partial response (PR) after starting study drug but before starting any new chemotherapy or radiotherapy as assessed by the investigator according to Response Criteria in Solid Tumors (RECIST) version 1.1. CR was defined as the disappearance of all target lesions and disappearance of all non-target lesions and normalization of tumor marker level. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. The Intent-to-treat Analysis Set included all participants who were randomized in the study.	
End point type	Primary
End point timeframe: Up to 41 weeks	

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	72		
Units: percentage of participants				
number (confidence interval 95%)	9.7 (4.0 to 19.0)	6.9 (2.3 to 15.5)		

Statistical analyses

Statistical analysis title	Andecaliximab+Nivolumab vs Nivolumab
Comparison groups	Andecaliximab + Nivolumab v Nivolumab

Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8 ^[1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	6.1

Notes:

[1] - P-value is derived from Cochran-Mantel-Haenszel (CMH) test stratified by programmed death ligand 1 (PD-L1) stratification factor status. Odds ratio is derived from CMH test stratified by PD-L1 stratus, the Nivolumab alone arm serves as the reference.

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
-----------------	---------------------------------

End point description:

PFS was defined as the interval in months from the date of randomization to the earlier of the first documentation of definitive disease progression or death from any cause. The first definitive progressive disease (PD) was defined as the first radiation therapy, the first clinical PD, and the first confirmed imaging PD, whichever came first. Participants without PD or death and participants with PD after starting new anti-cancer therapy are censored at the last tumor assessment date. Participants in the Intent-to-treat Analysis Set were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Andecaliximab + Nivolumab median follow-up time: 7.0 months; Nivolumab median follow-up time: 7.1 months

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	72		
Units: months				
median (confidence interval 95%)	1.840 (1.807 to 2.004)	1.856 (1.741 to 1.906)		

Statistical analyses

Statistical analysis title	Andecaliximab+Nivolumab vs Nivolumab
Comparison groups	Andecaliximab + Nivolumab v Nivolumab
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.306 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.836

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.589
upper limit	1.189

Notes:

[2] - P-value is derived from log-rank test stratified by PD-L1 stratification factor status. Hazard ratio is derived from Cox model stratified by PD-L1 stratification factor status, the Nivolumab alone arm serves as the reference.

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
-----------------	-----------------------

End point description:

OS was defined as the interval from the date of randomization to death from any cause. 99999=not applicable (NA). Upper 95% Confidence Interval (CI) were not estimable due to the low number of participants with events. Surviving participants are censored at the last date known alive. Participants in the Intent-to-treat Analysis Set were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Andecaliximab + Nivolumab median follow-up time: 7.0 months; Nivolumab median follow-up time: 7.0 months

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	72		
Units: months				
median (confidence interval 95%)	7.162 (4.797 to 99999)	5.881 (3.483 to 10.908)		

Statistical analyses

Statistical analysis title	Andecaliximab+Nivolumab vs Nivolumab
Comparison groups	Andecaliximab + Nivolumab v Nivolumab
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.312 ^[3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.786
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.491
upper limit	1.257

Notes:

[3] - P-value is derived from log-rank test stratified by PD-L1 stratification factor status. Hazard ratio is derived from Cox model stratified by PD-L1 stratification factor status, the Nivolumab alone arm serves as the reference.

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
-----------------	----------------------------

End point description:

DOR was defined as the interval from the date of the first response (complete or partial response) was achieved to the earlier of the first documentation of definitive disease progression or death from any cause. 99999=NA. Median and Upper 95% CI were not estimable due to the low number of participants with events. Participants in the Intent-to-treat Analysis Set who achieved CR or PR were analyzed.

End point type	Secondary
----------------	-----------

End point timeframe:

Andecaliximab + Nivolumab median follow-up time: 7.0 months; Nivolumab median follow-up time: 7.1 months

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	5		
Units: months				
median (confidence interval 95%)	99999 (1.807 to 99999)	99999 (2.037 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)

End point title	Percentage of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)
-----------------	--

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study participants administered a medicinal product, which does not necessarily have a causal relationship with the treatment. TEAEs are events that are defined as AEs with onset dates on or after the first dose of andecaliximab/nivolumab and up to 30 days after permanent discontinuation of andecaliximab or 5 months after permanent discontinuation of nivolumab, or led to premature discontinuation of andecaliximab or nivolumab. The Safety Analysis Set included all participants who received at least 1 dose of study drug.

End point type	Secondary
----------------	-----------

End point timeframe:

Andecaliximab: First dose date up to last dose (maximum: 101 weeks) + 30 days; Nivolumab: First dose date up to last dose (maximum: 101 weeks) + 5 months

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	70		
Units: percentage of participants				
number (not applicable)	98.6	97.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants who Experienced Treatment-emergent Laboratory Abnormalities

End point title	Percentage of Participants who Experienced Treatment-emergent Laboratory Abnormalities
-----------------	--

End point description:

Treatment-emergent (Chemistry, Hematology, Coagulation, and Urinalysis) laboratory abnormalities were graded per Common Terminology Criteria for Adverse Events (CTCAE), Version 4.03 where: 0=None, 1=Mild, 2=Moderate, 3=Severe, 4=Potentially Life Threatening. Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point, up to and including the date of the last dose of andecaliximab plus 30 days or nivolumab plus 5 months. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment-emergent. Percentage of participants with any postbaseline Grade 1 or higher laboratory abnormality is reported. Participants in the Safety Analysis Set with available data were analyzed. aPTT = activated partial thromboplastin time, INR = international normalized ratio.

End point type	Secondary
----------------	-----------

End point timeframe:

Andecaliximab: First dose date up to last dose (maximum: 101 weeks) + 30 days; Nivolumab: First dose date up to last dose (maximum: 101 weeks) + 5 months

End point values	Andecaliximab + Nivolumab	Nivolumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	70		
Units: percentage of participants				
number (not applicable)				
Alanine Aminotransferase Increased (n=70, 70)	20.0	27.1		
Alkaline Phosphatase Increased	45.1	40.0		
Aspartate Aminotransferase Increased (n=70, 70)	30.0	28.6		
Blood Bilirubin Increased	8.5	11.4		
Chronic Kidney Disease	16.9	25.7		
Creatinine Increased	1.4	7.1		
Hyperglycemia	22.5	18.6		
Hyperkalemia (n=70, 70)	7.1	5.7		
Hypermagnesemia	2.8	1.4		
Hypoalbuminemia	35.2	38.6		
Hypoglycemia	11.3	4.3		
Hypokalemia (n=70, 70)	10.0	11.4		

Hypomagnesemia	5.6	4.3		
Hyponatremia	28.2	40.0		
Hypophosphatemia	11.3	8.6		
Lipase Increased	11.3	8.6		
Serum Amylase Increased	9.9	7.1		
aPTT Prolonged (n=39, 31)	2.6	19.4		
INR Increased (n=39, 32)	2.6	12.5		
Anemia (n=71, 69)	53.5	56.5		
Lymphocytes, Typical Count Decreased (n=71, 69)	35.2	27.5		
Lymphocytes, Typical Count Increased (n=71, 69)	4.2	0		
Neutrophil Count Decreased (n=71, 69)	5.6	5.8		
Platelet Count Decreased (n=71, 69)	8.5	5.8		
White Blood Cell Decreased (n=71, 69)	9.9	7.2		
Proteinuria (Dipstick) (n=68, 67)	29.4	31.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths: Andecaliximab + Nivolumab median follow-up time 28.2 months; Nivolumab median follow-up time 28.4 months; AEs: Andecaliximab: First dose to last dose (maximum: 101 weeks) + 30 days; Nivolumab: First dose to last dose (maximum: 101 weeks) + 5 months

Adverse event reporting additional description:

Deaths: The Intent-to Treat Analysis Set included all participants who were randomized in the study.
Adverse Events: The Safety Analysis Set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Andecaliximab + Nivolumab
-----------------------	---------------------------

Reporting group description:

Andecaliximab 800 mg administered via intravenous (IV) infusion plus nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 34 weeks at the time of the primary efficacy analysis; up to 101 weeks at the time of the safety follow-up analysis).

Reporting group title	Nivolumab
-----------------------	-----------

Reporting group description:

Nivolumab 3 mg/kg administered via IV infusion every 2 weeks until disease progression, unacceptable toxicity, or withdrawal of consent (up to 41 weeks at the time of the primary efficacy analysis; up to 97 weeks at the time of the safety follow-up analysis).

Serious adverse events	Andecaliximab + Nivolumab	Nivolumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 71 (59.15%)	38 / 70 (54.29%)	
number of deaths (all causes)	61	62	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Euthanasia			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
General physical health deterioration			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Complication associated with device			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 71 (2.82%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory failure			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Productive cough			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 71 (1.41%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood magnesium decreased subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transaminases increased subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular fibrillation subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Cerebral haemorrhage subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 71 (7.04%)	4 / 70 (5.71%)	
occurrences causally related to treatment / all	2 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal disorder			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 71 (4.23%)	6 / 70 (8.57%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	3 / 71 (4.23%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	3 / 71 (4.23%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	4 / 71 (5.63%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 71 (4.23%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	3 / 70 (4.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	3 / 71 (4.23%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	3 / 71 (4.23%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			

subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Melaena			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastric perforation			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastric stenosis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			

subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal failure			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (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			
Back pain			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 71 (1.41%)	3 / 70 (4.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	

Sepsis			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Device related infection			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			

subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 71 (1.41%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdiaphragmatic abscess			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 71 (2.82%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dehydration			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 71 (1.41%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			

subjects affected / exposed	0 / 71 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 71 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Andecaliximab + Nivolumab	Nivolumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 71 (92.96%)	62 / 70 (88.57%)	
Investigations			
Weight decreased			
subjects affected / exposed	5 / 71 (7.04%)	7 / 70 (10.00%)	
occurrences (all)	5	8	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	
occurrences (all)	4	4	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 71 (5.63%)	4 / 70 (5.71%)	
occurrences (all)	4	4	
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 71 (7.04%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 71 (8.45%)	8 / 70 (11.43%)	
occurrences (all)	6	9	
Headache			
subjects affected / exposed	6 / 71 (8.45%)	6 / 70 (8.57%)	
occurrences (all)	6	7	
Paraesthesia			

subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	4 / 70 (5.71%) 4	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	14 / 71 (19.72%) 16	14 / 70 (20.00%) 18	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	22 / 71 (30.99%) 27	25 / 70 (35.71%) 29	
Asthenia subjects affected / exposed occurrences (all)	21 / 71 (29.58%) 29	12 / 70 (17.14%) 12	
Pyrexia subjects affected / exposed occurrences (all)	10 / 71 (14.08%) 11	4 / 70 (5.71%) 5	
Oedema peripheral subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 6	6 / 70 (8.57%) 6	
Chest pain subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	4 / 70 (5.71%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	27 / 71 (38.03%) 34	17 / 70 (24.29%) 20	
Vomiting subjects affected / exposed occurrences (all)	22 / 71 (30.99%) 30	18 / 70 (25.71%) 21	
Constipation subjects affected / exposed occurrences (all)	18 / 71 (25.35%) 20	18 / 70 (25.71%) 21	
Abdominal pain subjects affected / exposed occurrences (all)	11 / 71 (15.49%) 11	16 / 70 (22.86%) 21	
Diarrhoea			

subjects affected / exposed	14 / 71 (19.72%)	9 / 70 (12.86%)	
occurrences (all)	18	23	
Dysphagia			
subjects affected / exposed	12 / 71 (16.90%)	8 / 70 (11.43%)	
occurrences (all)	13	9	
Abdominal pain upper			
subjects affected / exposed	11 / 71 (15.49%)	2 / 70 (2.86%)	
occurrences (all)	13	2	
Ascites			
subjects affected / exposed	7 / 71 (9.86%)	4 / 70 (5.71%)	
occurrences (all)	8	4	
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 71 (8.45%)	2 / 70 (2.86%)	
occurrences (all)	7	2	
Dry mouth			
subjects affected / exposed	2 / 71 (2.82%)	5 / 70 (7.14%)	
occurrences (all)	2	5	
Dyspepsia			
subjects affected / exposed	5 / 71 (7.04%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Abdominal distension			
subjects affected / exposed	4 / 71 (5.63%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	10 / 71 (14.08%)	9 / 70 (12.86%)	
occurrences (all)	10	10	
Cough			
subjects affected / exposed	4 / 71 (5.63%)	8 / 70 (11.43%)	
occurrences (all)	5	8	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 71 (4.23%)	6 / 70 (8.57%)	
occurrences (all)	4	6	
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3	9 / 70 (12.86%) 9	
Anxiety subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 5	2 / 70 (2.86%) 2	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	11 / 71 (15.49%) 11	5 / 70 (7.14%) 6	
Arthralgia subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 5	6 / 70 (8.57%) 6	
Myalgia subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3	4 / 70 (5.71%) 4	
Muscle spasms subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0	4 / 70 (5.71%) 4	
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 71 (9.86%) 7	1 / 70 (1.43%) 1	
Oral candidiasis subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 4	4 / 70 (5.71%) 4	
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4	0 / 70 (0.00%) 0	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	24 / 71 (33.80%) 29	20 / 70 (28.57%) 26	
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 6	7 / 70 (10.00%) 8	

Dehydration			
subjects affected / exposed	2 / 71 (2.82%)	5 / 70 (7.14%)	
occurrences (all)	2	5	
Hyponatraemia			
subjects affected / exposed	2 / 71 (2.82%)	5 / 70 (7.14%)	
occurrences (all)	2	5	
Hyperkalaemia			
subjects affected / exposed	2 / 71 (2.82%)	4 / 70 (5.71%)	
occurrences (all)	2	4	
Hypoalbuminaemia			
subjects affected / exposed	1 / 71 (1.41%)	4 / 70 (5.71%)	
occurrences (all)	1	4	
Hypomagnesaemia			
subjects affected / exposed	4 / 71 (5.63%)	1 / 70 (1.43%)	
occurrences (all)	5	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2016	<ul style="list-style-type: none">• Modified eligibility tissue requirements for PD-L1 stratification and made a new pretreatment biopsy optional.• Updated chemistry analytes that were tested by the central laboratory.• Clarified urine pregnancy procedures in the schedule of assessments.• Modified eligibility requirements based on central labs.• Clarified dosing information for nivolumab in the Dosage and Administration Section.
02 August 2016	<ul style="list-style-type: none">• Added Thyroid function tests to the schedule of assessments and the body of the protocol to maintain consistency with protocol.• Added an exclusion criterion to exclude participants with history of bone marrow, stem cell, or allogenic organ transplantation.
16 June 2017	Updated the section regarding Discontinuation Criteria for nivolumab to refer to the local nivolumab Summary of Product Characteristics (SmPC) for dose adjustments, AE management guidance, and discontinuation criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported