Clinical trial results:
A Phase II, Multicenter, Single-Arm Study of Atezolizumab in Patients With Locally Advanced or Metastatic Urothelial Bladder Cancer

Summary

EudraCT number	2013-005486-39
Trial protocol	DE IT ES NL FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	28 July 2016
First version publication date	28 July 2016

Trial information

Trial identification

Sponsor protocol code	GO29293

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02108652
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.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	Interim
Date of interim/final analysis	05 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 May 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study was to evaluate the efficacy of atezolizumab in participants with locally advanced or metastatic urothelial carcinoma.

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Netherlands: 11
Country: Number of subjects enrolled	United States: 210
Worldwide total number of subjects	311
EEA total number of subjects	81

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)	126
From 65 to 84 years	181
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only Cohort 2 primary analysis data are included with cutoff date 5 May 2015. Per planned analysis, the primary analysis of Cohort 2 was performed approximately 6 months after the last participant in Cohort 2 had been enrolled. Cohort 1 data will be posted later, anticipated posting date 14 Sep 2016.

Period 1

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

Arms

Arm title	Cohort 2: Participants With Second-line or Beyond Treatments

Arm description:

Participants who had disease progression during or following treatment with at least one platinum-containing chemotherapy regimen in the metastatic setting received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until loss of clinical benefit or unmanageable toxicity.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	MPDL3280A
Other name	Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants were administered 1200 mg atezolizumab by IV infusion by trained medical staff at the clinical site. The initial dose of atezolizumab was delivered over 60 (± 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 (± 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (± 10) minutes.

Number of subjects in period 1	Cohort 2: Participants With Second-line or Beyond Treatments
Started	311
Completed	0
Not completed	311
Physician decision	1
Consent withdrawn by subject	9
Progression of Disease	5
Death	141
Unspecified	2
Lost to follow-up	1

Ongoing at data cutoff 5 May 2014	152

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 2: Participants With Second-line or Beyond Treatments

Reporting group description:

Participants who had disease progression during or following treatment with at least one platinum-containing chemotherapy regimen in the metastatic setting received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until loss of clinical benefit or unmanageable toxicity.

Reporting group values	Cohort 2: Participants With Second-line or Beyond Treatments	Total	
Number of subjects	311	311	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 65.7 ± 10.1	 -	
Gender categorical Units: Subjects			
Female	69	69	
Male	242	242	

End points

End points reporting groups

Reporting group title	Cohort 2: Participants With Second-line or Beyond Treatments

Reporting group description:

Participants who had disease progression during or following treatment with at least one platinum-containing chemotherapy regimen in the metastatic setting received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until loss of clinical benefit or unmanageable toxicity.

Primary: Percentage of Participants With a Confirmed Objective Response of Complete Response (CR) or Partial Response (PR) as Assessed by the Independent Review Facility (IRF) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

End point title	Percentage of Participants With a Confirmed Objective Response of Complete Response (CR) or Partial Response (PR) as Assessed by the Independent Review Facility (IRF) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)[1]

End point description:

Tumor response was assessed by the IRF according to RECIST v1.1. CR was defined as disappearance of all target and non-target lesions and (if applicable) normalization of tumor marker levels. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<) 10 millimeters (mm). PR was defined as greater than or equal to (≥) 30 percent (%) decrease in sum of longest diameter (LD) of target lesions in reference to Baseline sum LD. Response was to be confirmed ≥4 weeks after the initial assessment of CR or PR. The percentage of participants with a confirmed objective response of CR or PR was reported. The exact 95% confidence interval (CI) was calculated using the Clopper-Pearson method. Cohort 2 objective response-evaluable population included Intent-to-treat (ITT) participants who had measurable disease per RECIST v1.1 at baseline. Cohort 2 ITT population included all participants from Cohort 2 who received any amount of study drug.

End point type	Primary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

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: No statistical analysis was planned for this end point.

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (confidence interval 95%)	15.1 (11.3 to 19.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With a Confirmed Objective Response of CR or PR as Assessed by the Investigator According Modified RECIST

End point title	Percentage of Participants With a Confirmed Objective Response of CR or PR as Assessed by the Investigator According Modified RECIST[2]

End point description:

Tumor response was assessed by the investigator according to modified RECIST. CR was defined as disappearance of all target and non-target lesions and no new measurable or unmeasurable lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. Response was to be confirmed ≥4 weeks after the initial assessment of CR or PR. The percentage of participants with a confirmed objective response of CR or PR was reported. The exact 95% CI was calculated using the Clopper-Pearson method. Cohort 2 objective response-evaluable population.

End point type	Primary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this end point.

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (confidence interval 95%)	18.3 (14.2 to 23.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the IRF According to RECIST v1.1

End point title	Duration of Response as Assessed by the IRF According to RECIST v1.1

End point description:

Duration of response was defined as the time from the initial occurrence of documented CR or PR (whichever occurred first) until documented disease progression or death due to any cause on study, whichever occurred first. Tumor response was assessed by the IRF according to RECIST v1.1. CR was defined as disappearance of all target and non-target lesions and (if applicable) normalization of tumor marker levels. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. Response was to be confirmed ≥4 weeks after the initial assessment of CR or PR. Cohort 2 objective response-evaluable population. Here, '2.99999' signifies that median duration of response was not reached at a median follow up of 7.1 months on study. Full range values are censored.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (full range (min-max))	2.99999 (2.1 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the Investigator According to RECIST v1.1

End point title	Duration of Response as Assessed by the Investigator According to RECIST v1.1

End point description:

Duration of response was defined as the time from the initial occurrence of documented CR or PR (whichever occurred first) until documented disease progression or death due to any cause on study, whichever occurred first. Tumor response was assessed by the investigator according to modified RECIST. CR was defined as disappearance of all target and non-target lesions and no new measurable or unmeasurable lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. Cohort 2 ITT population. Here, "2.99999" signifies that the median duration of response was not reached at a median follow up of 7.1 months on study. Full range values are censored values.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (full range (min-max))	2.99999 (1.6 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the Investigator According to Modified RECIST

End point title	Duration of Response as Assessed by the Investigator According to Modified RECIST

End point description:

Duration of response was defined as the time from the initial occurrence of documented CR or PR (whichever occurred first) until documented disease progression or death due to any cause on study, whichever occurred first. Tumor response was assessed by the investigator according to modified RECIST. CR was defined as disappearance of all target and non-target lesions and no new measurable or unmeasurable lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. Cohort 2 objective response-evaluable population. Here, "2.99999" signifies that the median duration of response was not reached at a median follow up of 7.1 months on study. Full range values are censored.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (full range (min-max))	2.99999 (1.6 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Death or Disease Progression as Assessed by the IRF According to RECIST v1.1

End point title	Percentage of Participants With Death or Disease Progression as Assessed by the IRF According to RECIST v1.1

End point description:

Tumor response was assessed by the IRF according to RECIST v1.1. Disease progression or PD was defined as ≥20% increase in sum LD in reference to the smallest on-study sum LD, or the appearance of new lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The percentage of participants who died or experienced PD was reported. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (not applicable)	77.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) as Assessed by the IRF According to RECIST v1.1

End point title	Progression-Free Survival (PFS) as Assessed by the IRF According to RECIST v1.1

End point description:

PFS was defined as the time from start of treatment to the first event of death or PD. Tumor response was assessed by the IRF according to RECIST v1.1. Disease progression or PD was defined as ≥20% increase in sum LD in reference to the smallest on-study sum LD, or the appearance of new lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (confidence interval 95%)	2.1 (2.07 to 2.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Death or Disease Progression as Assessed by the Investigator According to RECIST v1.1

End point title	Percentage of Participants With Death or Disease Progression as Assessed by the Investigator According to RECIST v1.1

End point description:

Tumor response was assessed by the investigator according to RECIST v1.1. Disease progression or PD was defined as ≥20% increase in sum LD in reference to the smallest on-study sum LD, or the appearance of new lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The percentage of participants who died or experienced PD was reported. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (not applicable)	78.1			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by the Investigator According to RECIST v1.1

End point title	PFS as Assessed by the Investigator According to RECIST v1.1

End point description:

PFS was defined as the time from start of treatment to the first event of death or PD. Tumor response was assessed by the investigator according to RECIST v1.1. Disease progression or PD was defined as ≥20% increase in sum LD in reference to the smallest on-study sum LD, or the appearance of new lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (full range (min-max))	2.1 (2.07 to 2.23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Death or Disease Progression as Assessed by the Investigator According to Modified RECIST

End point title	Percentage of Participants With Death or Disease Progression as Assessed by the Investigator According to Modified RECIST

End point description:

Tumor response was assessed by the investigator according to modified RECIST. Disease progression or PD was defined as ≥20% increase in sum LD in reference to the smallest on-study sum LD. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The percentage of participants who died or experienced PD was reported. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (not applicable)	73.3			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by the Investigator According to Modified RECIST

End point title	PFS as Assessed by the Investigator According to Modified RECIST

End point description:

PFS was defined as the time from start of treatment to the first event of death or PD. Tumor response was assessed by the investigator according to modified RECIST. Disease progression or PD was defined

as ≥20% increase in sum LD in reference to the smallest on-study sum LD. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (full range (min-max))	2.73 (2.14 to 3.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Confirmed Objective Response of CR or PR as Assessed by the Investigator According RECIST v1.1

End point title	Percentage of Participants With a Confirmed Objective Response of CR or PR as Assessed by the Investigator According RECIST v1.1

End point description:

Tumor response was assessed by the investigator according to RECIST v1.1. CR was defined as disappearance of all target and non-target lesions and (if applicable) normalization of tumor marker levels. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. Response was to be confirmed ≥4 weeks after the initial assessment of CR or PR. The percentage of participants with a confirmed objective response of CR or PR was reported. The exact 95% CI was calculated using the Clopper-Pearson method. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline, every 9 weeks for the first 12 months, until confirmed disease progression or death, whichever occurred first (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (confidence interval 95%)	16.1 (12.2 to			

20.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died

End point description:

The percentage of participants who died from any cause was reported. Cohort 2 ITT population.

End point type	Secondary

End point timeframe:

Baseline until death (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (not applicable)	45.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from start of treatment to the time of death from any cause on study. Cohort 2 ITT population. Here, "99999" signifies that the upper limit of the 95% CI was not calculable because an insufficient number of participants reached the event at the final time point for assessment.

End point type	Secondary

End point timeframe:

Baseline until death (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: months				
median (confidence interval 95%)	7.89 (6.7 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive at 1-year

End point title	Percentage of Participants Alive at 1-year

End point description:

Cohort 2 ITT population. Here, "99999" signifies that 1-year overall survival was not evaluable because it was not yet reached. Participants had not yet been on the study for a year as of the data cutoff.

End point type	Secondary

End point timeframe:

1-year

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	311			
Units: percentage of participants				
number (not applicable)	99999			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab

End point description:

Per planned analysis, the pharmacokinetic data will be analyzed and reported for all participants (Cohorts 1 and 2 combined). Data have not been analyzed separately for each cohort.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (Cycle length = 21 days)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: microgram(s)/milliliter (mcg/mL)				
arithmetic mean (standard deviation)	()			

Notes:

[3] - PK data will be analyzed for all participants (Cohorts 1 and 2 combined), anticipated date Sep 2016.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Serum Concentration (Cmin) of Atezolizumab

End point description:

Per planned analysis, the pharmacokinetic data will be analyzed and reported for all participants (Cohorts 1 and 2 combined). Data have not been analyzed separately for each cohort.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 2, 4, 8 (Cycle length = 21 days)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: mcg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[4] - PK data will be analyzed for all participants (Cohorts 1 and 2 combined), anticipated date Sep 2016.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Positive for Anti-therapeutic Antibodies (ATA) to Atezolizumab

End point title	Percentage of Participants Positive for Anti-therapeutic Antibodies (ATA) to Atezolizumab

End point description:

Cohort 2 Safety Evaluable Population included all participants who received any amount of study drug.

Here, number of participants analyzed = participants for whom ATA samples were available.

End point type	Secondary

End point timeframe:

Day 1 of all cycles and at treatment discontinuation (data cutoff date 05 May 2015, up to maximum length of follow-up of 10.61 months)

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	275			
Units: percentage of participants				
number (not applicable)	41.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug until data cutoff date 05 May 2015 (up to maximum length of follow-up of 10.61 months)

Adverse event reporting additional description:

Cohort 2 Safety Evaluable Population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Cohort 2: Participants With Second-line or Beyond Treatments

Reporting group description:

Participants who had disease progression during or following treatment with at least one platinum-containing chemotherapy regimen in the metastatic setting received atezolizumab 1200 mg via IV infusion on Day 1 of 21-day cycles until loss of clinical benefit or unmanageable toxicity.

Serious adverse events	Cohort 2: Participants With Second-line or Beyond Treatments		
Total subjects affected by serious adverse events			
subjects affected / exposed	141 / 311 (45.34%)		
number of deaths (all causes)	141		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 311 (0.96%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Hypotension				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Vascular compression				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	3 / 311 (0.96%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic cyst				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pain				
subjects affected / exposed	3 / 311 (0.96%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	8 / 311 (2.57%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Immobile				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Pelvic pain				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vaginal haemorrhage				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Bronchial obstruction				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				

subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hiccups				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	3 / 311 (0.96%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	6 / 311 (1.93%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	7 / 311 (2.25%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				

subjects affected / exposed	3 / 311 (0.96%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Brain natriuretic peptide increased				

subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Troponin increased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Hip fracture				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ilium fracture				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				

subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stoma site haemorrhage				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm ruptured				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				

subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Diplegia			
subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraplegia			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			

subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lymph node pain			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 311 (1.93%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Faecal incontinence			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			

subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	4 / 311 (1.29%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haemorrhage				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	5 / 311 (1.61%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vomiting				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholestasis				

subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	7 / 311 (2.25%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	10 / 311 (3.22%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	4 / 311 (1.29%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Hydroureter				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstructive uropathy				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				

subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureteric obstruction			
subjects affected / exposed	2 / 311 (0.64%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	6 / 311 (1.93%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Muscular weakness				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 311 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis of male external genital organ				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Kidney infection				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 311 (1.61%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyelonephritis				
subjects affected / exposed	3 / 311 (0.96%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	6 / 311 (1.93%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Spinal cord infection				
subjects affected / exposed	1 / 311 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	19 / 311 (6.11%)		
occurrences causally related to treatment / all	0 / 19		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 311 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	3 / 311 (0.96%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	6 / 311 (1.93%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	4 / 311 (1.29%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	3 / 311 (0.96%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 2: Participants With Second-line or Beyond Treatments		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	263 / 311 (84.57%)		
Investigations			
Weight decreased			

subjects affected / exposed	22 / 311 (7.07%)		
occurrences (all)	24		
Nervous system disorders			
Dizziness			
subjects affected / exposed	16 / 311 (5.14%)		
occurrences (all)	17		
Headache			
subjects affected / exposed	24 / 311 (7.72%)		
occurrences (all)	28		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	41 / 311 (13.18%)		
occurrences (all)	56		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 311 (5.47%)		
occurrences (all)	28		
Chills			
subjects affected / exposed	26 / 311 (8.36%)		
occurrences (all)	29		
Fatigue			
subjects affected / exposed	143 / 311 (45.98%)		
occurrences (all)	182		
Oedema peripheral			
subjects affected / exposed	36 / 311 (11.58%)		
occurrences (all)	43		
Pain			
subjects affected / exposed	23 / 311 (7.40%)		
occurrences (all)	29		
Pyrexia			
subjects affected / exposed	58 / 311 (18.65%)		
occurrences (all)	69		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	33 / 311 (10.61%)		
occurrences (all)	39		

Constipation subjects affected / exposed occurrences (all)	63 / 311 (20.26%) 70		
Diarrhoea subjects affected / exposed occurrences (all)	55 / 311 (17.68%) 68		
Dry mouth subjects affected / exposed occurrences (all)	16 / 311 (5.14%) 16		
Nausea subjects affected / exposed occurrences (all)	71 / 311 (22.83%) 87		
Vomiting subjects affected / exposed occurrences (all)	50 / 311 (16.08%) 67		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	38 / 311 (12.22%) 47		
Dyspnoea subjects affected / exposed occurrences (all)	42 / 311 (13.50%) 53		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	39 / 311 (12.54%) 49		
Rash subjects affected / exposed occurrences (all)	30 / 311 (9.65%) 37		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	16 / 311 (5.14%) 16		
Renal and urinary disorders Haematuria			

subjects affected / exposed occurrences (all)	35 / 311 (11.25%) 45		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 43 / 311 (13.83%) 49 39 / 311 (12.54%) 47 20 / 311 (6.43%) 26 21 / 311 (6.75%) 24		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	 42 / 311 (13.50%) 47		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 79 / 311 (25.40%) 93		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2014	The protocol was amended to clarify the dose modification guidelines as to the management of immune-related adverse events (e.g., dermatologic toxicity, endocrine toxicity). Additionally, the protocol was modified to discontinue Cohort 1 participants (first-line cisplatin ineligible) from the study who develop RECIST v1.1 progression because of the possibility that they may benefit from non-cisplatin based regimens (e.g., carboplatin-based regimens).
27 September 2014	The protocol was amended in order to detail changes in the duration of treatment for participants receiving atezolizumab. Participants in Cohort 1 would receive treatment with atezolizumab until progression. Participants in Cohort 2 would receive treatment with atezolizumab until lack of clinical benefit. Participants would no longer stop treatment at 16 cycles. The re-treatment period and related text were removed.
06 February 2015	The protocol was amended to specify a longer washout period for participants who received prior anti-cytotoxic T lymphocyte-associated antigen 4 (anti−CTLA-4) treatment. Additionally, primary efficacy analysis was updated: activity in participants in Cohorts 1 and 2 will be analyzed separately with separate alpha spending for each cohort. The analysis of data from Cohort 1 participants will analyze overall response rate RECIST v1.1 in a hierarchical fashion on the basis of programmed death−ligand 1 (PD-L1) immunohistochemistry (IHC) and will not include the modified RECIST v1.1. In Cohort 2, the hierarchical fixed-sequence testing procedure on the three populations will be sequentially performed and alternate between the IRF−assessed objective response rate (ORR) according to RECIST v1.1 and the investigator-assessed ORR according to modified RECIST.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported