



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	v2
This version publication date	02 November 2016
First version publication date	28 July 2016
Version creation reason	<ul style="list-style-type: none">• New data added to full data set To add Cohort 1 results and update Cohort 2 results with September 2015 data cut-off date

Trial information**Trial identification**

Sponsor protocol code	GO29293
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02108652
WHO universal trial number (UTN)	-
Other trial identifiers	Genentech Inc.: IMvigor 210

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	14 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	No
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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.

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	Canada: 25
Country: Number of subjects enrolled	Spain: 26
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	United States: 309
Worldwide total number of subjects	429
EEA total number of subjects	95

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)	147
From 65 to 84 years	274
85 years and over	8

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The analysis included data up to cutoff date 14 September 2015.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Treatment-naive Cisplatin Ineligible Participants

Arm description:

Participants with advanced disease who were treatment-naive for advanced urothelial carcinoma and cisplatin ineligible received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until disease progression per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) criteria 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 (\pm 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 (\pm 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (\pm 10) minutes.

Arm title	Cohort 2: Participants With Second-line or Beyond Treatments
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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 mg via 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 (\pm 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 (\pm 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (\pm 10) minutes.

Number of subjects in period 1	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments
Started	119	310
Completed	0	0
Not completed	119	310
Consent withdrawn by subject	6	8
Death	46	193
Ongoing at data cutoff 14 September 2015	67	108
Unspecified	-	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Treatment-naive Cisplatin Ineligible Participants
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Reporting group description:

Participants with advanced disease who were treatment-naive for advanced urothelial carcinoma and cisplatin ineligible received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until disease progression per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) criteria or unmanageable toxicity.

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

Reporting group values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments	Total
Number of subjects	119	310	429
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	71.8	65.6	
standard deviation	± 8.9	± 10.1	-
Gender categorical Units: Subjects			
Female	23	69	92
Male	96	241	337

End points

End points reporting groups

Reporting group title	Cohort 1: Treatment-naive Cisplatin Ineligible Participants
Reporting group description:	
Participants with advanced disease who were treatment-naive for advanced urothelial carcinoma and cisplatin ineligible received atezolizumab 1200 milligrams (mg) via intravenous (IV) infusion on Day 1 of 21-day cycles until disease progression per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) criteria or unmanageable toxicity.	
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.	

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. Objective response-evaluable population included Intent-to-Treat (ITT) participants who had measurable disease per RECIST v1.1 at baseline. ITT population included all participants who received any amount of study drug.	
End point type	Primary
End point timeframe:	
Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 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 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second- line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (confidence interval 95%)	19.3 (12.66 to 27.58)	14.5 (10.79 to 18.94)		

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 (Applicable Only to Cohort 2)

End point title	Percentage of Participants With a Confirmed Objective Response of CR or PR as Assessed by the Investigator According Modified RECIST (Applicable Only to Cohort 2) ^{[2][3]}
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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 $\geq 30\%$ 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
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 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.

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Per planned analysis, this endpoint was applicable only to Cohort 2.

End point values	Cohort 2: Participants With Second- line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	310			
Units: percentage of participants				
number (confidence interval 95%)	18.7 (14.52 to 23.5)			

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
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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 $\geq 30\%$ 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. Objective response-evaluable population. Here, '9999' and '99999' signifies that median duration of response and the upper limit for the Full Range were not reached at a median follow up of 11.2 months on study, respectively.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: months				
median (full range (min-max))	9999 (2 to 99999)	9999 (2 to 99999)		

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
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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 RECIST v1.1. 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 $\geq 30\%$ decrease in sum of LD of target lesions in reference to Baseline sum LD. Cohort 2 ITT population. Here, '9999' and '99999' signifies that median duration of response and the upper limit for the Full Range were not reached at a median follow up of 11.2 months on study, respectively.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: months				
median (full range (min-max))	9999 (2 to 99999)	9999 (2.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2)

End point title	Duration of Response as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2) ^[4]
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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 $\geq 30\%$ decrease in sum of LD of target lesions in reference to Baseline sum LD. Cohort 2 objective response-evaluable population. Here, '9999' and '99999' signifies that median duration of response and the upper limit for the Full Range were not reached at a median follow up of 11.7 months on study, respectively.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per planned analysis, this endpoint was applicable only to Cohort 2.

End point values	Cohort 2: Participants With Second-line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	310			
Units: months				
median (full range (min-max))	9999 (2.1 to 99999)			

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
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End point description:

Tumor response was assessed by the IRF according to RECIST v1.1. Disease progression or PD was defined as $\geq 20\%$ 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. ITT population.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (not applicable)	68.1	84.2		

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
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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 $\geq 20\%$ 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. ITT population.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second- line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: months				
median (confidence interval 95%)	2.4 (2.1 to 4.14)	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
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End point description:

Tumor response was assessed by the investigator according to RECIST v1.1. Disease progression or PD was defined as $\geq 20\%$ 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. ITT population.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second- line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (not applicable)	63	84.8		

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
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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 $\geq 20\%$ 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. ITT population.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: months				
median (confidence interval 95%)	4.17 (2.3 to 5.75)	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 (Applicable Only to Cohort 2)

End point title	Percentage of Participants With Death or Disease Progression as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2) ^[5]
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End point description:

Tumor response was assessed by the investigator according to modified RECIST. Disease progression or PD was defined as $\geq 20\%$ 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
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per planned analysis, this endpoint was applicable only to Cohort 2.

End point values	Cohort 2: Participants With Second- line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	310			
Units: percentage of participants				
number (not applicable)	80			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2)

End point title	PFS as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2) ^[6]
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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 $\geq 20\%$ 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
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per planned analysis, this endpoint was applicable only to Cohort 2.

End point values	Cohort 2: Participants With Second- line or Beyond Treatments			
Subject group type	Reporting group			
Number of subjects analysed	310			
Units: months				
median (confidence interval 95%)	2.69 (2.14 to 3.88)			

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
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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 $\geq 30\%$ 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. Objective response-evaluable population.

End point type	Secondary
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End point timeframe:

Baseline, every 9 weeks for the first 12 months, thereafter every 12 weeks until confirmed disease progression or death, whichever occurred first (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (confidence interval 95%)	22.7 (15.52 to 31.27)	16.1 (12.21 to 20.71)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Died

End point title	Percentage of Participants Who Died
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End point description:

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

End point type	Secondary
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End point timeframe:

Baseline until death (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (not applicable)	38.7	62.3		

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. 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 14 September 2015, up to maximum length of follow-up of 15.24 months)	

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: months				
median (confidence interval 95%)	10.58 (8.08 to 99999)	7.92 (6.6 to 9.26)		

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:	
ITT population.	
End point type	Secondary
End point timeframe:	
1-year	

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	119	310		
Units: percentage of participants				
number (confidence interval 95%)	49.29 (36.29 to 62.3)	35.6 (29.87 to 41.32)		

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
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End point description:

The pharmacokinetic (PK) evaluable population was defined as participants who received any dose of atezolizumab treatment and had PK data at timepoints that were sufficient to determine PK parameters. Here, number of participants analyzed = participants who were evaluable for this outcome.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hours) and 30 minutes post-dose on Day 1 of Cycle 1 (Cycle length = 21 days)

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	300		
Units: microgram(s)/milliliter (mcg/mL)				
arithmetic mean (standard deviation)	386 (± 118)	364 (± 120)		

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
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End point description:

PK evaluable population. Here, number of participants analyzed = participants who were evaluable for

this outcome. "n" = participants who were evaluable at specified timepoint.

End point type	Secondary
End point timeframe:	
Pre-dose (0 hours) on Day 1 of Cycles 1, 2, 3, 4, 8 (Cycle length = 21 days)	

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	117	303		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Pre-dose Cycle 1 (n=117, 303)	0 (± 0)	0.0252 (± 0.429)		
Pre-dose Cycle 2 (n=106, 269)	77.7 (± 35.3)	74.2 (± 29.9)		
Pre-dose Cycle 3 (n=57, 146)	117 (± 48.8)	120 (± 59.5)		
Pre-dose Cycle 4 (n=66, 186)	159 (± 68.4)	147 (± 77.7)		
Pre-dose Cycle 8 (n=47, 108)	169 (± 110)	188 (± 76.1)		

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:	
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 (Cycle length = 21 days) and at treatment discontinuation (data cutoff date 14 September 2015, up to maximum length of follow-up of 15.24 months)	

End point values	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	276		
Units: percentage of participants				
number (not applicable)	47.7	42		

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 14 September 2015 (up to maximum length of follow-up of 15.24 months)

Adverse event reporting additional description:

Safety Evaluable Population

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Cohort 1: Treatment-naive Cisplatin Ineligible Participants
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Reporting group description:

Participants with advanced disease who were treatment-naive for advanced urothelial carcinoma and cisplatin ineligible received atezolizumab 1200 mg via IV infusion on Day 1 of 21-day cycles until disease progression per RECIST v1.1 criteria or unmanageable toxicity.

Reporting group title	Cohort 2: Participants With Second-line or Beyond Treatments
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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 disease progression per RECIST v1.1 criteria or unmanageable toxicity.

	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments	
Serious adverse events			
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 119 (35.29%)	150 / 310 (48.39%)	
number of deaths (all causes)	46	193	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 119 (0.84%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 119 (0.84%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular compression			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Renal stone removal			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	2 / 119 (1.68%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cyst			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 119 (1.68%)	7 / 310 (2.26%)	
occurrences causally related to treatment / all	1 / 2	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Immobile			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Vaginal haemorrhage			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penile pain			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
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			
Bronchial obstruction			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 119 (0.84%)	7 / 310 (2.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 119 (0.00%)	8 / 310 (2.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 119 (0.84%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	2 / 119 (1.68%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ilium fracture			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm ruptured			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site thrombosis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			

subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Diplegia			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 119 (1.68%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node pain			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain lower			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 119 (0.00%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 119 (1.68%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecal incontinence			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 119 (0.84%)	4 / 310 (1.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	3 / 119 (2.52%)	5 / 310 (1.61%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	4 / 119 (3.36%)	7 / 310 (2.26%)	
occurrences causally related to treatment / all	0 / 5	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 119 (0.00%)	4 / 310 (1.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 119 (1.68%)	11 / 310 (3.55%)	
occurrences causally related to treatment / all	0 / 2	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydroureter			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	3 / 119 (2.52%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 119 (0.84%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 119 (0.84%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
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 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 119 (0.84%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis of male external genital			

organ			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 119 (0.84%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 119 (0.00%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	3 / 119 (2.52%)	7 / 310 (2.26%)	
occurrences causally related to treatment / all	1 / 3	1 / 7	
deaths causally related to treatment / all	1 / 1	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 119 (0.84%)	21 / 310 (6.77%)
occurrences causally related to treatment / all	0 / 1	0 / 21
deaths causally related to treatment / all	0 / 0	0 / 0
Spinal cord infection		
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Urinary tract infection pseudomonal		
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Urosepsis		
subjects affected / exposed	1 / 119 (0.84%)	3 / 310 (0.97%)
occurrences causally related to treatment / all	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Biliary sepsis		
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Influenza		
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Meningoencephalitis herpetic		
subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Retroperitoneal infection		
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal infection		

subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 119 (1.68%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 119 (0.84%)	4 / 310 (1.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 119 (0.00%)	4 / 310 (1.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: Treatment-naive Cisplatin Ineligible Participants	Cohort 2: Participants With Second-line or Beyond Treatments	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 119 (87.39%)	272 / 310 (87.74%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	7 / 119 (5.88%)	11 / 310 (3.55%)	
occurrences (all)	8	11	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed occurrences (all)	9 / 119 (7.56%) 10	21 / 310 (6.77%) 34	
Chills subjects affected / exposed occurrences (all)	9 / 119 (7.56%) 11	29 / 310 (9.35%) 32	
Fatigue subjects affected / exposed occurrences (all)	53 / 119 (44.54%) 68	151 / 310 (48.71%) 195	
Oedema peripheral subjects affected / exposed occurrences (all)	15 / 119 (12.61%) 18	39 / 310 (12.58%) 48	
Pain subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 6	27 / 310 (8.71%) 34	
Pyrexia subjects affected / exposed occurrences (all)	16 / 119 (13.45%) 17	64 / 310 (20.65%) 80	
Influenza like illness subjects affected / exposed occurrences (all)	3 / 119 (2.52%) 3	16 / 310 (5.16%) 32	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	11 / 119 (9.24%) 11	48 / 310 (15.48%) 60	
Cough subjects affected / exposed occurrences (all)	13 / 119 (10.92%) 14	45 / 310 (14.52%) 59	
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	8 / 119 (6.72%) 8	18 / 310 (5.81%) 18	
Anxiety subjects affected / exposed occurrences (all)	9 / 119 (7.56%) 11	14 / 310 (4.52%) 14	
Depression			

subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 6	12 / 310 (3.87%) 12	
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	7 / 119 (5.88%) 7	23 / 310 (7.42%) 26	
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	10 / 119 (8.40%) 15	15 / 310 (4.84%) 20	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	8 / 119 (6.72%) 14	13 / 310 (4.19%) 20	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 8	11 / 310 (3.55%) 11	
Blood creatinine increased subjects affected / exposed occurrences (all)	17 / 119 (14.29%) 21	17 / 310 (5.48%) 25	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	10 / 119 (8.40%) 13	25 / 310 (8.06%) 29	
Dizziness subjects affected / exposed occurrences (all)	10 / 119 (8.40%) 14	18 / 310 (5.81%) 19	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	18 / 119 (15.13%) 24	46 / 310 (14.84%) 63	
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	8 / 119 (6.72%) 9	33 / 310 (10.65%) 39	
Constipation subjects affected / exposed occurrences (all)	16 / 119 (13.45%) 20	71 / 310 (22.90%) 82	

Diarrhoea			
subjects affected / exposed	23 / 119 (19.33%)	60 / 310 (19.35%)	
occurrences (all)	27	76	
Dry mouth			
subjects affected / exposed	4 / 119 (3.36%)	21 / 310 (6.77%)	
occurrences (all)	4	21	
Nausea			
subjects affected / exposed	24 / 119 (20.17%)	78 / 310 (25.16%)	
occurrences (all)	30	94	
Vomiting			
subjects affected / exposed	17 / 119 (14.29%)	54 / 310 (17.42%)	
occurrences (all)	20	72	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	20 / 119 (16.81%)	41 / 310 (13.23%)	
occurrences (all)	23	56	
Rash			
subjects affected / exposed	7 / 119 (5.88%)	32 / 310 (10.32%)	
occurrences (all)	10	41	
Dry skin			
subjects affected / exposed	6 / 119 (5.04%)	14 / 310 (4.52%)	
occurrences (all)	6	14	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	7 / 119 (5.88%)	36 / 310 (11.61%)	
occurrences (all)	7	48	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	7 / 119 (5.88%)	5 / 310 (1.61%)	
occurrences (all)	7	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	13 / 119 (10.92%)	51 / 310 (16.45%)	
occurrences (all)	16	61	
Pain in extremity			

subjects affected / exposed occurrences (all)	8 / 119 (6.72%) 9	27 / 310 (8.71%) 32	
Back pain subjects affected / exposed occurrences (all)	15 / 119 (12.61%) 17	43 / 310 (13.87%) 54	
Muscular weakness subjects affected / exposed occurrences (all)	4 / 119 (3.36%) 5	24 / 310 (7.74%) 36	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	16 / 119 (13.45%) 19	49 / 310 (15.81%) 56	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 7	11 / 310 (3.55%) 11	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	26 / 119 (21.85%) 31	82 / 310 (26.45%) 104	
Hyperglycaemia subjects affected / exposed occurrences (all)	8 / 119 (6.72%) 10	14 / 310 (4.52%) 15	
Hyperkalaemia subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 7	6 / 310 (1.94%) 7	
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 119 (2.52%) 3	16 / 310 (5.16%) 22	
Hyponatraemia subjects affected / exposed occurrences (all)	9 / 119 (7.56%) 11	14 / 310 (4.52%) 17	

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