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	28 February 2023

Results information

Result version number	v4 (current)
This version publication date	11 February 2024
First version publication date	28 July 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO29293

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02108652
WHO universal trial number (UTN)	-
Other trial identifiers	Genentech Inc.: IMvigor 210, ClinicalTrials.gov (NCT Number) for Cohort 1: NCT02951767

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	Final
Date of interim/final analysis	28 February 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 February 2023
Was the trial ended prematurely?	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.

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	73

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 28 February 2023.

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 (± 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.

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 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 (± 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 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	11	16
Physician decision	1	6
Non-Compliance	-	1
Progression of Disease	-	1
Study Terminated By Sponsor	9	31
Death	96	253
Lost to follow-up	2	2

Baseline characteristics

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.	

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 until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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 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%)	22.7 (15.5 to 31.3)	15.8 (11.9 to 20.4)		

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]

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 until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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 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: No statistical analysis for this endpoint.

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%)	19.7 (15.4 to 24.6)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

DOR 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. Objective response-evaluable population. Number of participants analyzed = participants who were evaluable for this outcome. Here, '9999' and '99999' signifies that median DOR and the upper limit for the Full Range were not reached at the time of data cutoff date 04 July 2016, respectively.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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	27	49		
Units: months				
median (full range (min-max))	9999 (3.7 to 99999)	9999 (2.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

DOR 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 ≥30% decrease in sum of LD of target lesions in reference to Baseline sum LD. ITT population. Here, number of participants analyzed = participants who were evaluable for this outcome. Here, '9999' and '99999' signifies that median DOR and the upper limit for the Full Range were not reached at the time of data cutoff date 04 July 2016, respectively.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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	30	51		
Units: months				
median (full range (min-max))	9999 (4.3 to 99999)	20.50 (2.1 to 20.5)		

Statistical analyses

No statistical analyses for this end point

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

End point title	DOR as Assessed by the Investigator According to Modified RECIST (Applicable Only to Cohort 2)[4]

End point description:

DOR 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, number of participants analyzed = participants who were evaluable for this outcome.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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: No statistical analysis 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	61			
Units: months				
median (full range (min-max))	20.50 (2.1 to 20.5)			

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. ITT population.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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)	73.9	88.4		

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. ITT population.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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)	71.4	89.7		

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. ITT population.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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%)	2.69 (2.10 to 4.17)	2.10 (2.07 to 2.14)		

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. ITT population.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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)	2.10 (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 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]

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 until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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: No statistical analysis 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	310			
Units: percentage of participants				
number (not applicable)	87.1			

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. ITT population.

End point type	Secondary

End point timeframe:

Baseline until death (data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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)	49.6	72.9		

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]

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 until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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: No statistical analysis 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	310			
Units: months				
median (confidence interval 95%)	2.56 (2.14 to 3.61)			

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. Objective response-evaluable population.

End point type	Secondary

End point timeframe:

Baseline until confirmed disease progression or death, whichever occurred first (assessed at every 9 weeks for the first 12 months, thereafter every 12 weeks until data cutoff date 04 July 2016, up to maximum length of follow-up of 24.48 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%)	25.2 (17.7 to 34.0)	16.5 (12.5 to 21.1)		

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%)	57.2 (48.2 to 66.3)	36.9 (31.4 to 42.3)		

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 04 July 2016, up to maximum length of follow-up of 24.48 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%)	15.9 (10.4 to 99999)	7.9 (6.7 to 9.3)		

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:

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

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

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 04 July 2016, up to maximum length of follow-up of 24.48 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	42.4		

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 28 February 2023 (up to approximately 105 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	MPDL3280A COHORT1 INFUSION

Reporting group description:

Participants with advanced disease who are treatment-naive for advanced urothelial carcinoma and cisplatin ineligible will receive 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	MPDL3280A COHORT2 INFUSION

Reporting group description:

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

Serious adverse events	MPDL3280A COHORT1 INFUSION	MPDL3280A COHORT2 INFUSION	
Total subjects affected by serious adverse events			
subjects affected / exposed	49 / 119 (41.18%)	155 / 310 (50.00%)	
number of deaths (all causes)	96	253	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
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	
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	
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	
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	
Vascular disorders			
HYPOTENSION			
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	
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	
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	
EMBOLISM			
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	
Surgical and medical procedures			
URETERAL STENT INSERTION			
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 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			
NON-CARDIAC CHEST PAIN			
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	

SYSTEMIC INFLAMMATORY RESPONSE 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	
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	
PYREXIA			
subjects affected / exposed	1 / 119 (0.84%)	8 / 310 (2.58%)	
occurrences causally related to treatment / all	1 / 1	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	0 / 119 (0.00%)	4 / 310 (1.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
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	
ASTHENIA			
subjects affected / exposed	2 / 119 (1.68%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
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	
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	
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	
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			
RESPIRATORY DISTRESS			

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	
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	
PLEURAL EFFUSION			
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%)	10 / 310 (3.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 119 (0.00%)	5 / 310 (1.61%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
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	
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	
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	
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	
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 119 (0.84%)	8 / 310 (2.58%)	
occurrences causally related to treatment / all	0 / 1	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
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	
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	
DELIRIUM			
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	
MENTAL STATUS CHANGES			
subjects affected / exposed	2 / 119 (1.68%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
THROMBOSIS IN DEVICE			
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			

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	
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	
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	
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	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	
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	
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	
Injury, poisoning and procedural complications			
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	
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	
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	
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	
SPINAL COMPRESSION 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	
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	
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	
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	
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	
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	
Cardiac disorders			
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	
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	
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	
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			
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	
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	
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	
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	
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	
TRANSIENT ISCHAEMIC ATTACK			

subjects affected / exposed	1 / 119 (0.84%)	0 / 310 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIPLEGIA			
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	
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	
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	
LYMPH NODE 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	
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	
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			
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	

AUTOIMMUNE COLITIS			
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	
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 / 1	
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	
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	
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	
ANAL 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	
SUBILEUS			
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	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	
RECTAL 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	
ABDOMINAL HERNIA			
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	
ABDOMINAL PAIN LOWER			
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	
INTESTINAL PERFORATION			
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	
COLITIS			
subjects affected / exposed	2 / 119 (1.68%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	1 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	3 / 119 (2.52%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	5 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	3 / 119 (2.52%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 3	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			

subjects affected / exposed	1 / 119 (0.84%)	3 / 310 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
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	
HYPERBILIRUBINAEMIA			
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	
CHOLECYSTITIS			
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	
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	
ERYTHEMA			
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	
DERMATITIS PSORIASIFORM			
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	
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	4 / 119 (3.36%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 5	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER PERFORATION			
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	
HAEMATURIA			
subjects affected / exposed	1 / 119 (0.84%)	12 / 310 (3.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 12	
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	
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	
RENAL FAILURE			
subjects affected / exposed	3 / 119 (2.52%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYDRONEPHROSIS			
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	
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	
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	
URETERIC 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	
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			
MUSCULAR WEAKNESS			
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	
FLANK 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	
OSTEOPOROSIS			
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	
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	
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	

BACK PAIN			
subjects affected / exposed	1 / 119 (0.84%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 10	
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	
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	
Infections and infestations			
BRONCHITIS			
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	
POST PROCEDURAL INFECTION			
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	
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	
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	
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 119 (0.00%)	1 / 310 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
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	
PNEUMONIA			
subjects affected / exposed	2 / 119 (1.68%)	7 / 310 (2.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	3 / 119 (2.52%)	9 / 310 (2.90%)	
occurrences causally related to treatment / all	1 / 3	1 / 9	
deaths causally related to treatment / all	1 / 1	0 / 0	
SKIN 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	
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	
BURSITIS INFECTIVE STAPHYLOCOCCAL			
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	
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 119 (3.36%)	23 / 310 (7.42%)	
occurrences causally related to treatment / all	0 / 4	0 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE 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	
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	
PYELONEPHRITIS			
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	
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	
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	
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	
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	
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	
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	
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	
CELLULITIS			
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	
KIDNEY INFECTION			
subjects affected / exposed	0 / 119 (0.00%)	2 / 310 (0.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
HYPONATRAEMIA			
subjects affected / exposed	1 / 119 (0.84%)	5 / 310 (1.61%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERKALAEMIA			
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	
DEHYDRATION			
subjects affected / exposed	3 / 119 (2.52%)	6 / 310 (1.94%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAILURE TO THRIVE			
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	
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	MPDL3280A COHORT1 INFUSION	MPDL3280A COHORT2 INFUSION	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 119 (92.44%)	289 / 310 (93.23%)	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	7 / 119 (5.88%)	13 / 310 (4.19%)	
occurrences (all)	8	13	
General disorders and administration site conditions			
CHILLS			
subjects affected / exposed	11 / 119 (9.24%)	34 / 310 (10.97%)	
occurrences (all)	16	37	
OEDEMA PERIPHERAL			
subjects affected / exposed	23 / 119 (19.33%)	52 / 310 (16.77%)	
occurrences (all)	30	63	
ASTHENIA			
subjects affected / exposed	12 / 119 (10.08%)	23 / 310 (7.42%)	
occurrences (all)	18	37	
PYREXIA			
subjects affected / exposed	21 / 119 (17.65%)	70 / 310 (22.58%)	
occurrences (all)	24	90	
PAIN			
subjects affected / exposed	7 / 119 (5.88%)	27 / 310 (8.71%)	
occurrences (all)	8	34	
FATIGUE			
subjects affected / exposed	64 / 119 (53.78%)	164 / 310 (52.90%)	
occurrences (all)	87	228	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	5 / 119 (4.20%)	17 / 310 (5.48%)	
occurrences (all)	6	65	

Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	7 / 119 (5.88%)	7 / 310 (2.26%)	
occurrences (all)	8	9	
Respiratory, thoracic and mediastinal disorders			
NASAL CONGESTION			
subjects affected / exposed	7 / 119 (5.88%)	21 / 310 (6.77%)	
occurrences (all)	8	22	
DYSPNOEA			
subjects affected / exposed	18 / 119 (15.13%)	55 / 310 (17.74%)	
occurrences (all)	18	74	
COUGH			
subjects affected / exposed	25 / 119 (21.01%)	59 / 310 (19.03%)	
occurrences (all)	29	86	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	7 / 119 (5.88%)	15 / 310 (4.84%)	
occurrences (all)	7	16	
INSOMNIA			
subjects affected / exposed	12 / 119 (10.08%)	22 / 310 (7.10%)	
occurrences (all)	12	22	
CONFUSIONAL STATE			
subjects affected / exposed	7 / 119 (5.88%)	11 / 310 (3.55%)	
occurrences (all)	10	11	
ANXIETY			
subjects affected / exposed	11 / 119 (9.24%)	18 / 310 (5.81%)	
occurrences (all)	12	18	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	12 / 119 (10.08%)	28 / 310 (9.03%)	
occurrences (all)	13	34	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	10 / 119 (8.40%)	16 / 310 (5.16%)	
occurrences (all)	17	24	
ASPARTATE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	10 / 119 (8.40%)	15 / 310 (4.84%)	
occurrences (all)	26	22	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	8 / 119 (6.72%)	19 / 310 (6.13%)	
occurrences (all)	12	20	
BLOOD CREATININE INCREASED			
subjects affected / exposed	22 / 119 (18.49%)	22 / 310 (7.10%)	
occurrences (all)	35	38	
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	7 / 119 (5.88%)	5 / 310 (1.61%)	
occurrences (all)	13	14	
Nervous system disorders			
NEUROPATHY PERIPHERAL			
subjects affected / exposed	6 / 119 (5.04%)	10 / 310 (3.23%)	
occurrences (all)	6	14	
DIZZINESS			
subjects affected / exposed	10 / 119 (8.40%)	26 / 310 (8.39%)	
occurrences (all)	13	29	
HEADACHE			
subjects affected / exposed	13 / 119 (10.92%)	30 / 310 (9.68%)	
occurrences (all)	17	37	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	25 / 119 (21.01%)	56 / 310 (18.06%)	
occurrences (all)	39	72	
Gastrointestinal disorders			
VOMITING			
subjects affected / exposed	24 / 119 (20.17%)	61 / 310 (19.68%)	
occurrences (all)	29	83	
CONSTIPATION			
subjects affected / exposed	21 / 119 (17.65%)	85 / 310 (27.42%)	
occurrences (all)	35	102	
ABDOMINAL PAIN			
subjects affected / exposed	14 / 119 (11.76%)	44 / 310 (14.19%)	
occurrences (all)	15	54	
NAUSEA			

subjects affected / exposed	29 / 119 (24.37%)	86 / 310 (27.74%)	
occurrences (all)	35	114	
DIARRHOEA			
subjects affected / exposed	31 / 119 (26.05%)	69 / 310 (22.26%)	
occurrences (all)	50	103	
DRY MOUTH			
subjects affected / exposed	5 / 119 (4.20%)	24 / 310 (7.74%)	
occurrences (all)	5	25	
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	10 / 119 (8.40%)	20 / 310 (6.45%)	
occurrences (all)	10	21	
RASH MACULO-PAPULAR			
subjects affected / exposed	6 / 119 (5.04%)	13 / 310 (4.19%)	
occurrences (all)	6	14	
PRURITUS			
subjects affected / exposed	23 / 119 (19.33%)	54 / 310 (17.42%)	
occurrences (all)	39	77	
RASH			
subjects affected / exposed	14 / 119 (11.76%)	40 / 310 (12.90%)	
occurrences (all)	22	53	
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	6 / 119 (5.04%)	12 / 310 (3.87%)	
occurrences (all)	6	12	
HAEMATURIA			
subjects affected / exposed	12 / 119 (10.08%)	49 / 310 (15.81%)	
occurrences (all)	15	76	
PROTEINURIA			
subjects affected / exposed	6 / 119 (5.04%)	3 / 310 (0.97%)	
occurrences (all)	8	4	
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	10 / 119 (8.40%)	11 / 310 (3.55%)	
occurrences (all)	10	11	
Musculoskeletal and connective tissue disorders			

MUSCULAR WEAKNESS			
subjects affected / exposed	6 / 119 (5.04%)	31 / 310 (10.00%)	
occurrences (all)	7	44	
MUSCLE SPASMS			
subjects affected / exposed	6 / 119 (5.04%)	10 / 310 (3.23%)	
occurrences (all)	6	12	
PAIN IN EXTREMITY			
subjects affected / exposed	11 / 119 (9.24%)	40 / 310 (12.90%)	
occurrences (all)	17	55	
MYALGIA			
subjects affected / exposed	5 / 119 (4.20%)	17 / 310 (5.48%)	
occurrences (all)	5	20	
ARTHRALGIA			
subjects affected / exposed	27 / 119 (22.69%)	65 / 310 (20.97%)	
occurrences (all)	45	98	
BACK PAIN			
subjects affected / exposed	19 / 119 (15.97%)	57 / 310 (18.39%)	
occurrences (all)	21	83	
FLANK PAIN			
subjects affected / exposed	5 / 119 (4.20%)	23 / 310 (7.42%)	
occurrences (all)	9	30	
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	21 / 119 (17.65%)	62 / 310 (20.00%)	
occurrences (all)	30	94	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	9 / 119 (7.56%)	23 / 310 (7.42%)	
occurrences (all)	13	28	
NASOPHARYNGITIS			
subjects affected / exposed	3 / 119 (2.52%)	19 / 310 (6.13%)	
occurrences (all)	3	25	
Metabolism and nutrition disorders			
HYPOMAGNESAEMIA			
subjects affected / exposed	3 / 119 (2.52%)	16 / 310 (5.16%)	
occurrences (all)	4	18	
HYPOKALAEMIA			

subjects affected / exposed	3 / 119 (2.52%)	19 / 310 (6.13%)	
occurrences (all)	4	24	
DEHYDRATION			
subjects affected / exposed	10 / 119 (8.40%)	15 / 310 (4.84%)	
occurrences (all)	10	25	
HYPERGLYCAEMIA			
subjects affected / exposed	11 / 119 (9.24%)	17 / 310 (5.48%)	
occurrences (all)	21	30	
HYPONATRAEMIA			
subjects affected / exposed	12 / 119 (10.08%)	20 / 310 (6.45%)	
occurrences (all)	26	25	
DECREASED APPETITE			
subjects affected / exposed	37 / 119 (31.09%)	89 / 310 (28.71%)	
occurrences (all)	46	110	
HYPERKALAEMIA			
subjects affected / exposed	11 / 119 (9.24%)	10 / 310 (3.23%)	
occurrences (all)	19	14	
HYPOALBUMINAEMIA			
subjects affected / exposed	4 / 119 (3.36%)	20 / 310 (6.45%)	
occurrences (all)	5	26	

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.
26 September 2015	The protocol was amended with the referral to the Atezolizumab Investigator's Brochure for management guidelines for gastrointestinal, dermatologic, endocrine, pulmonary toxicity, hepatotoxicity, potential pancreatic or eye toxicity, and other immune-mediated adverse events. Systemic immune activation (SIA) has been identified as a potential risk of atezolizumab when given in combination with other immunomodulating agents. The management recommendations regarding early identification and management of SIA have been added. Additional thyroid-function testing has been added every three cycles to monitor the known risk of hyperthyroidism and hypothyroidism. The use of any live vaccine has been updated to be prohibited within 90 days following the administration of the last dose of study drug in addition to 28 days prior to and during study treatment.
31 October 2016	The protocol was amended include the period during which female patients must remain abstinent or use contraception and the length of follow up of pregnancy reporting, have been revised to 5 months after the last dose of study drug. The period during which patients must agree not to receive live, attenuated vaccine has been revised to 5 months after the last dose of study drug. Management of systemic immune activation has been revised to be consistent with the atezolizumab program.
17 October 2018	The protocol was amended to include revised guidelines for managing patients who experience atezolizumab-associated adverse events for hypophysitis, myocarditis, and nephritis and have been provided in an appendix.

10 February 2020	The protocol has been amended with the clarification that the Sponsor may terminate an individual cohort at any time. The list of atezolizumab risks has been updated to include myositis. Systemic immune activation has been replaced by hemophagocytic lymphohistiocytosis and macrophage activation syndrome in the list of potential risks for atezolizumab and the management guidelines for systemic immune activation have been replaced with management guidelines for hemophagocytic lymphohistiocytosis and macrophage activation syndrome. The atezolizumab adverse event management guidelines have been revised to add laboratory and cardiac imaging abnormalities as signs or symptoms that are suggestive of myocarditis. Guidelines for managing patients who experience atezolizumab-associated adverse events have been revised to include myositis. The management guidelines for infusion-related reactions associated with atezolizumab have been updated to include guidelines for cytokine-release syndrome (CRS).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported