



## 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
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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, 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 68783333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 68783333, 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
<b>Arm title</b>	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.

<b>Arm title</b>	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.

<b>Number of subjects in period 1</b>	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
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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 standard deviation	71.8 ± 8.9	65.6 ± 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) <sup>[1]</sup>		
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) <sup>[2][3]</sup>
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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  $\geq 4$  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 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.

<b>End point values</b>	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
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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  $\geq 30\%$  decrease in sum of LD of target lesions in reference to Baseline sum LD. Response was to be confirmed  $\geq 4$  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
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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
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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  $\geq 30\%$  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
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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)

<b>End point values</b>	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) <sup>[4]</sup>
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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  $\geq 30\%$  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
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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.

<b>End point values</b>	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
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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 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: 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 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)

<b>End point values</b>	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: 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 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)

<b>End point values</b>	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: 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 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) <sup>[5]</sup>
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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 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.

<b>End point values</b>	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: 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) <sup>[6]</sup>			
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			
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.

<b>End point values</b>	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			
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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  $\geq 4$  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 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: 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: 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

<b>End point values</b>	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: 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)	

<b>End point values</b>	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)	

<b>End point values</b>	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)

<b>End point values</b>	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

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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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### Reporting groups

Reporting group title	MPDL3280A COHORT1 INFUSION
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Reporting group description:

Participants with advanced disease who are treatment-naïve 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
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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.

<b>Serious adverse events</b>	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	
<b>Vascular disorders</b>			
<b>HYPOTENSION</b>			
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	
<b>HAEMATOMA</b>			
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	
<b>DEEP VEIN THROMBOSIS</b>			
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	
<b>EMBOLISM</b>			
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	
<b>Surgical and medical procedures</b>			
<b>URETERAL STENT INSERTION</b>			
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	
<b>RENAL STONE REMOVAL</b>			
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	
<b>General disorders and administration site conditions</b>			
<b>NON-CARDIAC CHEST PAIN</b>			
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	
<b>GAIT DISTURBANCE</b>			
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	
<b>Immune system disorders</b>			
<b>HYPERSENSITIVITY</b>			
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	
<b>Social circumstances</b>			
<b>IMMOBILE</b>			
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	
<b>Reproductive system and breast disorders</b>			
<b>VAGINAL HAEMORRHAGE</b>			
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	
<b>PELVIC PAIN</b>			
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	
<b>PENILE PAIN</b>			
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	
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>RESPIRATORY DISTRESS</b>			

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
<b>HICCUPS</b>		
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
<b>PLEURAL EFFUSION</b>		
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
<b>DYSPNOEA</b>		
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
<b>PNEUMONITIS</b>		
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
<b>HAEMOPTYSIS</b>		
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
<b>HYPOXIA</b>		
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
<b>PULMONARY ARTERY THROMBOSIS</b>		
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
<b>RESPIRATORY FAILURE</b>		

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	
<b>PNEUMOTHORAX</b>			
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	
<b>PULMONARY EMBOLISM</b>			
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	
<b>Psychiatric disorders</b>			
<b>HALLUCINATION</b>			
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	
<b>CONFUSIONAL STATE</b>			
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	
<b>DELIRIUM</b>			
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	
<b>MENTAL STATUS CHANGES</b>			
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	
<b>Product issues</b>			
<b>THROMBOSIS IN DEVICE</b>			
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	
<b>Investigations</b>			

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	
<b>Injury, poisoning and procedural complications</b>			
<b>STOMA SITE HAEMORRHAGE</b>			
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	
<b>VASCULAR PSEUDOANEURYSM RUPTURED</b>			
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	
<b>HIP FRACTURE</b>			
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	
<b>FRACTURE</b>			
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	
<b>SPINAL COMPRESSION FRACTURE</b>			
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	
<b>ILIUM FRACTURE</b>			
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	
<b>JOINT INJURY</b>			
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	
<b>POST PROCEDURAL HAEMORRHAGE</b>			

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	
<b>LOWER LIMB FRACTURE</b>			
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	
<b>FALL</b>			
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	
<b>TOXICITY TO VARIOUS AGENTS</b>			
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	
<b>Cardiac disorders</b>			
<b>CARDIAC FAILURE</b>			
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	
<b>CARDIAC ARREST</b>			
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	
<b>ATRIAL FIBRILLATION</b>			
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	
<b>CORONARY ARTERY DISEASE</b>			
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	
<b>PERICARDIAL EFFUSION</b>			

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	
<b>ARRHYTHMIA</b>			
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	
<b>MYOCARDIAL INFARCTION</b>			
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	
<b>Nervous system disorders</b>			
<b>CEREBROVASCULAR ACCIDENT</b>			
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	
<b>ATAXIA</b>			
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	
<b>PARAPLEGIA</b>			
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	
<b>CEREBRAL HAEMORRHAGE</b>			
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	
<b>SYNCOPE</b>			
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	
<b>TRANSIENT ISCHAEMIC ATTACK</b>			

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	
<b>DIPLEGIA</b>			
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	
<b>ENCEPHALOPATHY</b>			
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	
<b>Blood and lymphatic system disorders</b>			
<b>ANAEMIA</b>			
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	
<b>LYMPH NODE PAIN</b>			
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	
<b>LEUKOCYTOSIS</b>			
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	
<b>Ear and labyrinth disorders</b>			
<b>VERTIGO</b>			
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	
<b>Gastrointestinal disorders</b>			
<b>VOMITING</b>			
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
<b>RECTAL HAEMORRHAGE</b>		
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
<b>ABDOMINAL HERNIA</b>		
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
<b>ABDOMINAL PAIN LOWER</b>		
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
<b>INTESTINAL PERFORATION</b>		
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
<b>COLITIS</b>		
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
<b>DIARRHOEA</b>		
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
<b>SMALL INTESTINAL OBSTRUCTION</b>		
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
<b>NAUSEA</b>		

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	
<b>Hepatobiliary disorders</b>			
<b>HEPATITIS</b>			
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	
<b>HYPERBILIRUBINAEMIA</b>			
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	
<b>CHOLECYSTITIS</b>			
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	
<b>LIVER DISORDER</b>			
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	
<b>Skin and subcutaneous tissue disorders</b>			
<b>RASH MACULO-PAPULAR</b>			
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	
<b>ERYTHEMA</b>			
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	
<b>DERMATITIS PSORIASIFORM</b>			
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	
<b>Renal and urinary disorders</b>			

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	
<b>URETERIC OBSTRUCTION</b>			
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	
<b>Endocrine disorders</b>			
<b>HYPOTHYROIDISM</b>			
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	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>MUSCULAR WEAKNESS</b>			
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	
<b>FLANK PAIN</b>			
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	
<b>OSTEOPOROSIS</b>			
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	
<b>RHABDOMYOLYSIS</b>			
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	
<b>BONE PAIN</b>			
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	

<b>BACK PAIN</b>			
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	
<b>PATHOLOGICAL FRACTURE</b>			
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	
<b>ARTHRALGIA</b>			
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	
<b>Infections and infestations</b>			
<b>BRONCHITIS</b>			
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	
<b>POST PROCEDURAL INFECTION</b>			
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	
<b>ABDOMINAL INFECTION</b>			
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	
<b>INFLUENZA</b>			
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	
<b>DEVICE RELATED INFECTION</b>			
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	
<b>URINARY TRACT INFECTION</b>			

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
<b>PULMONARY SEPSIS</b>		
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
<b>PYELONEPHRITIS</b>		
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
<b>BACTERAEMIA</b>		
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
<b>GASTROENTERITIS</b>		
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
<b>BILIARY SEPSIS</b>		
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
<b>MENINGOENCEPHALITIS HERPETIC</b>		
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
<b>STAPHYLOCOCCAL INFECTION</b>		
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
<b>CELLULITIS OF MALE EXTERNAL GENITAL ORGAN</b>		

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	
<b>RETROPERITONEAL INFECTION</b>			
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	
<b>CELLULITIS</b>			
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	
<b>KIDNEY INFECTION</b>			
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	
<b>Metabolism and nutrition disorders</b>			
<b>HYPONATRAEMIA</b>			
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	
<b>HYPERKALAEMIA</b>			
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	
<b>DEHYDRATION</b>			
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	
<b>FAILURE TO THRIVE</b>			
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	
<b>HYPERCALCAEMIA</b>			

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 %

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

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

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

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported