



Clinical trial results:

A Phase II, Multi-Center, Single-Arm Study of MPDL3280A in Patients With PD-L1-Positive Locally Advanced or Metastatic Non-Small Cell Lung Cancer

Summary

EudraCT number	2013-000177-69
Trial protocol	BE GB NL FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	20 November 2018
First version publication date	04 November 2016

Trial information

Trial identification

Sponsor protocol code	GO28625
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01846416
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG., +41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG., +41 61 6878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	07 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 January 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This is Phase II, global, multicenter, single-arm trial designed to evaluate the efficacy and safety of atezolizumab (MPDL3280A) [TECENTRIQ], an engineered anti-programmed death-ligand 1 (PD-L1) antibody in PD-L1-selected participants with locally advanced or metastatic non-small cell lung cancer (NSCLC). The primary objective for this study was to evaluate the efficacy of atezolizumab in participants with PD-L1-positive locally advanced or metastatic NSCLC, as measured by investigator-assessed objective response rate (ORR) according to modified Response Evaluation Criteria in Solid Tumors (RECIST).

Protection of trial subjects:

The study was conducted in accordance with the principles of the "Declaration of Helsinki" and Good Clinical Practice (GCP) according to the regulations and procedures described in the protocol. All the investigators were trained according to the applicable Sponsor standard operating procedures, and strictly adhered to the stated provisions. This was documented by investigator's signature on the protocol agreeing to carry out all of its terms in accordance with the applicable regulations and to follow International Conference on Harmonization (ICH) GCP guidelines. Approval from Institutional Review Boards (IRBs) and Ethics Committee (EC) was obtained before study start and was documented in a letter to investigator specifying the date the committee met, and granted approval. Approval from relevant competent authority was also obtained prior to starting the study. Protocol amendments were prepared by the Sponsor, and were submitted to IRB/EC and to Regulatory Authorities in accordance with the local regulatory requirements. Audits were performed by the Sponsor Quality Assurance group in compliance with GCP.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	20 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United States: 109
Worldwide total number of subjects	138
EEA total number of subjects	29

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)	60
From 65 to 84 years	76
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall 201 participants (pts) were screened for clinical eligibility, out of which 63 participants were screen failures, and hence 138 participants were enrolled, and 137 participants received treatment. Analysis was performed until primary analysis cut-off date 7 January 2015 (approximately 20 months duration).

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	Atezolizumab (MPDL3280A) : 1L Participants

Arm description:

Participants with no prior chemotherapy for advanced NSCLC disease received atezolizumab intravenously (IV) as a fixed dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until disease progression.

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

Dosage and administration details:

Atezolizumab as a fixed dose of 1200-mg IV infusion on Day 1 of each 21-day cycle. The initial dose of atezolizumab was delivered over 60 ($\pm$ 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 ($\pm$ 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 ($\pm$ 10) minutes.

Arm title	Atezolizumab (MPDL3280A) : 2L+ Participants
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Arm description:

Participants who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to maximum number of prior therapies received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.

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

Dosage and administration details:

Atezolizumab as a fixed dose of 1200-mg IV infusion on Day 1 of each 21-day cycle. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 ($\pm$ 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 ($\pm$ 10) minutes.

Arm title	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
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Arm description:

Participants with previously treated brain metastases and who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to the maximum number of prior therapies, received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.

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

Dosage and administration details:

Atezolizumab as a fixed dose of 1200-mg IV infusion on Day 1 of each 21-day cycle. The initial dose of atezolizumab was delivered over 60 ($\pm$ 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 ($\pm$ 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 ($\pm$ 10) minutes.

Number of subjects in period 1^[1]	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Started	31	93	13
Completed	0	0	0
Not completed	31	93	13
Consent withdrawn by subject	1	7	-
Ongoing as of 7 January 2015	21	41	3
Death	8	43	9
Unspecified	1	-	-
Lost to follow-up	-	2	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of the 138 participants enrolled into the study, 1 participant in the 2L+ participant arm, was withdrawn from the study prior to treatment, resulting in a total of 137 participants receiving study drug. The baseline period reported a summary of only treated participants.

Baseline characteristics

Reporting groups

Reporting group title	Atezolizumab (MPDL3280A) : 1L Participants
Reporting group description: Participants with no prior chemotherapy for advanced NSCLC disease received atezolizumab intravenously (IV) as a fixed dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until disease progression.	
Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Participants
Reporting group description: Participants who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to maximum number of prior therapies received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.	
Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Reporting group description: Participants with previously treated brain metastases and who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to the maximum number of prior therapies, received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.	

Reporting group values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Number of subjects	31	93	13
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	68 ± 10.8	65.2 ± 9.3	63.8 ± 7.7
Gender categorical Units: Subjects			
Female	17	34	7
Male	14	59	6

Reporting group values	Total		
Number of subjects	137		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	58		
Male	79		

End points

End points reporting groups

Reporting group title	Atezolizumab (MPDL3280A) : 1L Participants
Reporting group description: Participants with no prior chemotherapy for advanced NSCLC disease received atezolizumab intravenously (IV) as a fixed dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until disease progression.	
Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Participants
Reporting group description: Participants who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to maximum number of prior therapies received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.	
Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Reporting group description: Participants with previously treated brain metastases and who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to the maximum number of prior therapies, received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.	
Subject analysis set title	Atezolizumab (MPDL3280A): All Arms
Subject analysis set type	Intention-to-treat
Subject analysis set description: This analysis set included all the participants in the study.	

Primary: Percentage of Participants with Objective Response According to Modified RECIST

End point title	Percentage of Participants with Objective Response According to Modified RECIST ^[1]
End point description: Objective response was defined as a complete response (CR) or partial response (PR), as determined by investigator according to modified RECIST criteria. Modified RECIST was derived from RECIST v1.1 conventions and immune related response criteria. CR was defined as disappearance of all tumor lesions (target lesion [TL] and non-target lesion [non-TL]) and no new measurable or unmeasurable lesions, all lymph node short axes must be less than 10 millimeter, and PR was defined as at least 30 percent (%) decrease in sum of diameter of TLs, and all new measurable lesions to baseline in absence of CR, and both confirmed by consecutive assessment greater than or equal to 4 weeks from date first documented. Participants not meeting this criteria, including participants without at least 1 post-baseline response assessment were considered as non-responders. Analysis population: Efficacy-evaluable population; all treated participants who received at least 1 dose of atezolizumab during study.	
End point type	Primary
End point timeframe: Baseline, and Day 1 of Cycle 1 (21-day cycle), then every 6 weeks for the first 12 months and then every 9 weeks thereafter until disease progression (up to 20 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: The study was of an explorative nature; therefore only descriptive statistical methods were applied, and no formal statistical hypothesis testing was planned.

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (confidence interval 95%)	29 (14.22 to 48.04)	17.2 (10.17 to 26.43)	23.1 (5.04 to 53.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Objective Response According to RECIST Version 1.1 (v1.1)

End point title	Percentage of Participants with Objective Response According to RECIST Version 1.1 (v1.1)
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End point description:

Objective response was defined as a CR or PR, as determined by the investigator according to RECIST v1.1. For TLs, CR was defined as disappearance of all TLs. Any pathological lymph nodes, whether target or non-target, must had reduction in short axis to less than 10 mm. PR was defined as at least a 30% decrease in the sum of diameter of TLs, taking as reference the baseline sum of diameters, in absence of CR. For non-TLs, CR was defined as disappearance of all non-TLs and if applicable, normalization of tumor marker level. Participants not meeting these criteria, including participants without at least one post-baseline response assessment were considered as non-responders.

Analysis population: Efficacy-evaluable population.

End point type	Secondary
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End point timeframe:

Baseline, and Day 1 of Cycle 1 (21-day cycle), then every 6 weeks for the first 12 months and then every 9 weeks thereafter until disease progression (up to 20 months)

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (confidence interval 95%)	25.8 (11.86 to 44.61)	16.1 (9.32 to 25.2)	23.1 (5.04 to 53.81)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response According to RECIST v1.1

End point title	Duration of Objective Response According to RECIST v1.1
End point description:	
Duration of objective response was defined as time from initial occurrence of documented CR or PR until documented disease progression (using RECIST v1.1 as determined by investigator) or death, whichever occurred first. For TLs, CR was defined as disappearance of all TLs. Any pathological lymph nodes, whether target or non-target, must had reduction in short axis to less than 10 mm. PR was defined as at least a 30% decrease in sum of diameter of TLs, taking as reference baseline sum of diameters, in absence of CR. Progressive disease was at least a 20% increase in sum of diameters of TLs , taking as reference smallest sum on study (nadir). Participants were censored at the date of last tumor assessment.	
Analysis population: Efficacy-evaluable population with a confirmed objective response. '99999' signifies that median and upper limit of 95% confidence interval could not be calculated as the data was immature at the time of data cut-off (7 January 2015).	
End point type	Secondary
End point timeframe:	
Baseline, and Day 1 of Cycle 1 (21-day cycle), then every 6 weeks for the first 12 months and then every 9 weeks thereafter until disease progression (up to 20 months)	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	15	3	
Units: months				
median (confidence interval 95%)	99999 (2.858 to 99999)	99999 (10.382 to 99999)	99999 (4.172 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with 6-Month Duration of Objective Response

End point title	Percentage of Participants with 6-Month Duration of Objective Response
End point description:	
Duration of objective response at 6 months was defined as time from initial occurrence of documented CR or PR until Month 6. For TLs, CR was defined as disappearance of all TLs. Any pathological lymph nodes, whether target or non-target, must had reduction in short axis to less than 10 mm. PR was defined as at least a 30% decrease in sum of diameter of TLs, taking as reference baseline sum of diameters, in absence of CR. Progressive disease was at least a 20% increase in sum of diameters of TLs, taking as reference smallest sum on study (nadir). For non-TLs, CR was defined as disappearance of all non-TLs and if applicable, normalization of tumor marker level. Progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-TLs. Participants were censored at the date of last tumor assessment.	
Analysis population: Efficacy-evaluable population with a confirmed objective response.	
End point type	Secondary
End point timeframe:	
Month 6	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	8	15	3	
Units: percentage of participants				
number (not applicable)	75	91.7	66.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Disease Progression or Death According to RECIST v1.1

End point title	Percentage of Participants with Disease Progression or Death According to RECIST v1.1
End point description: For TLs, progressive disease was defined as at least a 20% increase in the sum of diameters of TLs, taking as reference the smallest sum on study (nadir). For non-TLs, progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-TLs. Analysis population: Efficacy-evaluable population.	
End point type	Secondary
End point timeframe: Baseline to the first occurrence of progression or death, whichever occurs earlier (up to 20 months)	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (not applicable)	67.7	74.2	84.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) According to RECIST v1.1

End point title	Progression-Free Survival (PFS) According to RECIST v1.1
End point description: PFS was defined as time from randomization to first occurrence of documented disease progression (based on RECIST v1.1 criteria) or death due to any cause within 30 days of the last treatment, whichever occurs earlier as determined by investigator. For TLs, progressive disease was defined as at least a 20% increase in the sum of diameter of TLs, taking as reference the smallest sum on the study	

(nadir). For non-TLs, progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-TLs. In event of no disease progression or documented death, PFS was censored at date of last evaluable tumor assessment. Participants with no post-baseline tumor assessments were censored at the time of first dose plus 1 day.

Analysis population: Efficacy-evaluable population.

End point type	Secondary
End point timeframe:	
Baseline to the first occurrence of progression or death, whichever occurs earlier (up to 20 months)	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: months				
median (confidence interval 95%)	4.468 (3.253 to 8.312)	2.727 (1.478 to 3.45)	2.497 (1.183 to 4.172)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at Month 6 and Month 12 According to RECIST v1.1

End point title	Percentage of Participants with PFS at Month 6 and Month 12 According to RECIST v1.1
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End point description:

Percentage of participants who were progression free at Month 6 and 12 (as per RECIST v1.1) was reported. For TLs, progressive disease was defined as at least a 20% increase in the sum of LD TLs, taking as reference the smallest sum on the study (nadir). For non-TLs, progressive disease was defined as the appearance of 1 or more new lesions and/or unequivocal progression of existing non-TLs. Analysis population: Efficacy-evaluable population. '99999' signifies that analysis could not be done as the data was immature at the time of data-cutoff (7 January 2015).

End point type	Secondary
End point timeframe:	
Months 6 and 12	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (not applicable)				

Month 6	33.5	32.29	15.38	
Month 12	99999	21.45	99999	

Statistical analyses

No statistical analyses for this end point

Secondary: PFS According to Modified RECIST

End point title	PFS According to Modified RECIST
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End point description:

PFS according to modified RECIST was defined as time from first dose of atezolizumab to first occurrence of documented disease progression or death due to any cause, as determined by investigator for participants who discontinued at first documented radiographic progression. For participants who continued beyond first documented progression and had follow-up tumor assessment or death, PFS was defined as time from first dose of atezolizumab to subsequent radiographic progression or death. For TLs, progressive disease was defined as at least a 20% increase in the sum of diameters of TLs and new measurable lesions, taking as reference the smallest sum recorded since treatment started. In event of no disease progression or documented death, PFS was censored at date of last evaluable tumor assessment.

Analysis population: Efficacy-evaluable population.

End point type	Secondary
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End point timeframe:

Baseline to the first occurrence of progression or death, whichever occurs earlier (up to 20 months)

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: months				
median (confidence interval 95%)	5.52 (4.107 to 10.283)	3.45 (2.727 to 5.947)	4.337 (2.168 to 16.197)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Disease Progression or Death According to Modified RECIST

End point title	Percentage of Participants with Disease Progression or Death According to Modified RECIST
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End point description:

For TLs, progressive disease was defined as at least a 20% increase in the sum of diameters of TLs and new measurable lesions, taking as reference the smallest sum recorded since treatment started.

Analysis population: Efficacy-evaluable population.

End point type	Secondary
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End point timeframe:

Baseline to the first occurrence of progression or death, whichever occurs earlier (up to 20 months)

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (not applicable)	58.1	66.7	69.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at Month 6 and Month 12 According to Modified RECIST

End point title	Percentage of Participants with PFS at Month 6 and Month 12 According to Modified RECIST
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End point description:

Percentage of participants who were progression free at Month 6 and 12 (according to modified RECIST). For TLs, progressive disease was defined as at least a 20% increase in the sum of diameters of TLs and new measurable lesions, taking as reference the smallest sum recorded since treatment started. Analysis population: Efficacy-evaluable population. '99999' signifies that analysis could not be done as the data was immature at the time of data cut-off (7 January 2015).

End point type	Secondary
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End point timeframe:

Months 6 and 12

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				
number (not applicable)				
Month 6	43.12	39.1	44.87	
Month 12	99999	28.82	35.9	

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 first dose of the study drug to the time of death from any cause of the study. Participants who were still alive at the time of analysis were censored at the time of their last study assessment (for active participants) or at the last date known alive (for participants in follow-up). If no post-baseline data were available, OS was censored at the date of first treatment plus 1 day. Analysis population: Efficacy-evaluable population. '-99999 and 99999' signifies that analysis could not be done as the data was immature at the time of data cut-off (7 January 2015)	
End point type	Secondary
End point timeframe: Baseline till death or up to 20 months, whichever occurred first	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: months				
median (confidence interval 95%)	99999 (-99999 to 99999)	10.612 (5.749 to 99999)	6.834 (3.154 to 16.197)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Death

End point title	Percentage of Participants with Death
End point description: Participants were followed for survival throughout the study. Analysis population: Efficacy-evaluable population.	
End point type	Secondary
End point timeframe: Baseline till death or up to 20 months, whichever occurred first	

End point values	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: percentage of participants				

number (not applicable)	25.8	46.2	69.2	
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Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) for Atezolizumab

End point title	Maximum Plasma Concentration (Cmax) for Atezolizumab
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End point description:

Analysis population: Pharmacokinetic- evaluable population - All treated participants with pharmacokinetic data at specified time points.

Here, 'Number of subjects analysed' = 'number of participants with available data for this endpoint'. Per planned analysis, pharmacokinetic data were not analyzed separately for each arm.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour) and 30 minutes after infusion on Day 1 of Cycle 1

End point values	Atezolizumab (MPDL3280A): All Arms			
Subject group type	Subject analysis set			
Number of subjects analysed	135			
Units: micrograms per mL				
geometric mean (geometric coefficient of variation)	405 ($\pm$ 31.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) for Atezolizumab

End point title	Minimum Plasma Concentration (Cmin) for Atezolizumab
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End point description:

Analysis population: Pharmacokinetic- evaluable population.

Here, 'Number of subjects analysed' = number of participants with available data for this endpoint and n= number of participants with available data at the specified time point. "99999" signifies that geometric co-efficient of variation was not calculated as only 1 participant was analyzed at the specified time point. Per planned analysis, pharmacokinetic data were not analyzed separately for each arm.

End point type	Secondary
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End point timeframe:

Pre-dose (0 hour) on Day 1 of Cycles 2, 3, 4, 8, and 16

End point values	Atezolizumab (MPDL3280A): All Arms			
Subject group type	Subject analysis set			
Number of subjects analysed	125			
Units: micrograms per mL				
geometric mean (geometric coefficient of variation)				
Pre-dose Cycle 2 (Day 1) (n= 125)	68.8 (± 55.3)			
Pre-dose Cycle 3 (Day 1) (n= 100)	90.6 (± 136.6)			
Pre-dose Cycle 4 (Day 1) (n= 92)	123 (± 136.9)			
Pre-dose Cycle 8 (Day 1) (n= 51)	206 (± 45.9)			
Pre-dose Cycle 16 (Day 1) (n= 1)	135 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline until 20 months

Adverse event reporting additional description:

All participants who received at least one dose of atezolizumab were included in analysis.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Atezolizumab (MPDL3280A) : 1L Participants
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Reporting group description:

Participants with no prior chemotherapy for advanced NSCLC disease received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until disease progression.

Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Participants
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Reporting group description:

Participants who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to maximum number of prior therapies received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.

Reporting group title	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
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Reporting group description:

Participants with previously treated brain metastases and who had progressed during or following a prior platinum-based chemotherapy regimen without restriction to the maximum number of prior therapies, received atezolizumab IV as a fixed dose of 1200-mg on Day 1 of each 21-day cycle until no longer deemed to be experiencing clinical benefit as assessed by the investigator.

Serious adverse events	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 31 (51.61%)	43 / 93 (46.24%)	6 / 13 (46.15%)
number of deaths (all causes)	2	10	2
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	2 / 13 (15.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 93 (2.15%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)	5 / 93 (5.38%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	2 / 31 (6.45%)	2 / 93 (2.15%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pleural effusion				
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pulmonary embolism				
subjects affected / exposed	0 / 31 (0.00%)	2 / 93 (2.15%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pulmonary haemorrhage				
subjects affected / exposed	0 / 31 (0.00%)	2 / 93 (2.15%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Bronchial obstruction				
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Bronchostenosis				
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pneumonitis				
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pulmonary hypertension				
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Pulmonary oedema				
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Respiratory disorder				

subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis constrictive			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Nervous system disorders			

Guillain-Barre syndrome			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Febrile neutropenia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photopsia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	2 / 31 (6.45%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nausea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis acute			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	1 / 31 (3.23%)	3 / 93 (3.23%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess neck			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	2 / 93 (2.15%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 31 (6.45%)	5 / 93 (5.38%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			

subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	87 / 93 (93.55%)	13 / 13 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 31 (0.00%)	4 / 93 (4.30%)	2 / 13 (15.38%)
occurrences (all)	0	4	4
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	1 / 31 (3.23%)	3 / 93 (3.23%)	1 / 13 (7.69%)
occurrences (all)	1	3	1
Hypotension			
subjects affected / exposed	3 / 31 (9.68%)	8 / 93 (8.60%)	0 / 13 (0.00%)
occurrences (all)	3	9	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)	7 / 93 (7.53%)	0 / 13 (0.00%)
occurrences (all)	1	8	0
Chest pain			
subjects affected / exposed	1 / 31 (3.23%)	8 / 93 (8.60%)	0 / 13 (0.00%)
occurrences (all)	1	8	0
Chills			

subjects affected / exposed	1 / 31 (3.23%)	5 / 93 (5.38%)	1 / 13 (7.69%)
occurrences (all)	1	5	1
Fatigue			
subjects affected / exposed	15 / 31 (48.39%)	36 / 93 (38.71%)	5 / 13 (38.46%)
occurrences (all)	16	44	5
Gait disturbance			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
General physical health deterioration			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	3 / 31 (9.68%)	2 / 93 (2.15%)	1 / 13 (7.69%)
occurrences (all)	6	2	1
Malaise			
subjects affected / exposed	0 / 31 (0.00%)	6 / 93 (6.45%)	0 / 13 (0.00%)
occurrences (all)	0	6	0
Oedema peripheral			
subjects affected / exposed	3 / 31 (9.68%)	7 / 93 (7.53%)	2 / 13 (15.38%)
occurrences (all)	3	9	4
Pain			
subjects affected / exposed	5 / 31 (16.13%)	2 / 93 (2.15%)	2 / 13 (15.38%)
occurrences (all)	7	2	2
Pyrexia			
subjects affected / exposed	6 / 31 (19.35%)	17 / 93 (18.28%)	1 / 13 (7.69%)
occurrences (all)	6	18	1
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Breast swelling			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	4 / 31 (12.90%)	31 / 93 (33.33%)	2 / 13 (15.38%)
occurrences (all)	4	39	4
Dysphonia			
subjects affected / exposed	1 / 31 (3.23%)	6 / 93 (6.45%)	1 / 13 (7.69%)
occurrences (all)	1	7	1
Dyspnoea			
subjects affected / exposed	7 / 31 (22.58%)	24 / 93 (25.81%)	2 / 13 (15.38%)
occurrences (all)	9	27	3
Dyspnoea exertional			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Haemoptysis			
subjects affected / exposed	3 / 31 (9.68%)	4 / 93 (4.30%)	1 / 13 (7.69%)
occurrences (all)	3	7	1
Nasal congestion			
subjects affected / exposed	1 / 31 (3.23%)	6 / 93 (6.45%)	0 / 13 (0.00%)
occurrences (all)	1	7	0
Pleural effusion			
subjects affected / exposed	1 / 31 (3.23%)	4 / 93 (4.30%)	1 / 13 (7.69%)
occurrences (all)	1	4	1
Productive cough			
subjects affected / exposed	1 / 31 (3.23%)	10 / 93 (10.75%)	0 / 13 (0.00%)
occurrences (all)	1	10	0
Pulmonary embolism			
subjects affected / exposed	0 / 31 (0.00%)	5 / 93 (5.38%)	0 / 13 (0.00%)
occurrences (all)	0	5	0
Wheezing			
subjects affected / exposed	1 / 31 (3.23%)	7 / 93 (7.53%)	1 / 13 (7.69%)
occurrences (all)	1	9	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 31 (0.00%)	9 / 93 (9.68%)	2 / 13 (15.38%)
occurrences (all)	0	10	2
Confusional state			

subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	1	1	1
Depression			
subjects affected / exposed	1 / 31 (3.23%)	7 / 93 (7.53%)	1 / 13 (7.69%)
occurrences (all)	1	10	1
Hallucination			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	3 / 31 (9.68%)	9 / 93 (9.68%)	1 / 13 (7.69%)
occurrences (all)	3	9	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 93 (1.08%)	2 / 13 (15.38%)
occurrences (all)	1	1	2
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	1 / 31 (3.23%)	2 / 93 (2.15%)	1 / 13 (7.69%)
occurrences (all)	1	2	1
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Haemoglobin decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	6 / 31 (19.35%)	8 / 93 (8.60%)	1 / 13 (7.69%)
occurrences (all)	7	8	1
Injury, poisoning and procedural complications			

Facial bones fracture subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Laceration subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Wound subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Cardiac disorders			
Aortic valve disease subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Atrial fibrillation subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 93 (1.08%) 1	0 / 13 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 93 (1.08%) 1	1 / 13 (7.69%) 1
Tachycardia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	3 / 93 (3.23%) 3	1 / 13 (7.69%) 1
Nervous system disorders			
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Dizziness subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	6 / 93 (6.45%) 8	1 / 13 (7.69%) 2
Dysgeusia subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	4 / 93 (4.30%) 4	0 / 13 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	8 / 93 (8.60%) 12	3 / 13 (23.08%) 3
Hemiparesis			

subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Memory impairment			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nystagmus			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 93 (1.08%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 31 (19.35%)	17 / 93 (18.28%)	1 / 13 (7.69%)
occurrences (all)	6	19	2
Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	2 / 31 (6.45%)	2 / 93 (2.15%)	0 / 13 (0.00%)
occurrences (all)	3	2	0
Thrombocytopenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Deafness bilateral			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ear pain			

subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Vertigo subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 93 (1.08%) 1	1 / 13 (7.69%) 1
Vestibular disorder subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 1
Eye disorders			
Diplopia subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 93 (2.15%) 3	1 / 13 (7.69%) 1
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 93 (2.15%) 2	1 / 13 (7.69%) 1
Periorbital oedema subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 93 (0.00%) 0	1 / 13 (7.69%) 2
Vision blurred subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	1 / 93 (1.08%) 1	1 / 13 (7.69%) 1
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	7 / 93 (7.53%) 7	0 / 13 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 93 (2.15%) 3	1 / 13 (7.69%) 1
Constipation subjects affected / exposed occurrences (all)	7 / 31 (22.58%) 8	14 / 93 (15.05%) 18	4 / 13 (30.77%) 7
Diarrhoea subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 7	15 / 93 (16.13%) 19	4 / 13 (30.77%) 6
Dyspepsia			

subjects affected / exposed	0 / 31 (0.00%)	3 / 93 (3.23%)	1 / 13 (7.69%)
occurrences (all)	0	3	1
Dysphagia			
subjects affected / exposed	1 / 31 (3.23%)	8 / 93 (8.60%)	1 / 13 (7.69%)
occurrences (all)	1	8	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 31 (3.23%)	7 / 93 (7.53%)	0 / 13 (0.00%)
occurrences (all)	1	7	0
Mouth swelling			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	8 / 31 (25.81%)	23 / 93 (24.73%)	4 / 13 (30.77%)
occurrences (all)	9	25	5
Vomiting			
subjects affected / exposed	3 / 31 (9.68%)	13 / 93 (13.98%)	3 / 13 (23.08%)
occurrences (all)	3	16	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	2 / 31 (6.45%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Dermatitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 31 (3.23%)	10 / 93 (10.75%)	0 / 13 (0.00%)
occurrences (all)	1	11	0
Night sweats			
subjects affected / exposed	2 / 31 (6.45%)	7 / 93 (7.53%)	1 / 13 (7.69%)
occurrences (all)	2	8	1
Pruritus			
subjects affected / exposed	4 / 31 (12.90%)	7 / 93 (7.53%)	1 / 13 (7.69%)
occurrences (all)	5	9	1

Rash subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	8 / 93 (8.60%) 9	1 / 13 (7.69%) 1
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 93 (1.08%) 1	1 / 13 (7.69%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	6 / 31 (19.35%) 8	17 / 93 (18.28%) 19	2 / 13 (15.38%) 2
Back pain subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	16 / 93 (17.20%) 16	2 / 13 (15.38%) 2
Bone pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	3 / 93 (3.23%) 3	1 / 13 (7.69%) 1
Muscle spasms subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 93 (2.15%) 2	1 / 13 (7.69%) 1
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	8 / 93 (8.60%) 8	0 / 13 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 5	4 / 93 (4.30%) 4	1 / 13 (7.69%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	6 / 93 (6.45%) 7	1 / 13 (7.69%) 1
Neck pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	5 / 93 (5.38%) 5	0 / 13 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	8 / 93 (8.60%) 8	1 / 13 (7.69%) 2
Infections and infestations			

Candida infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 93 (1.08%)	0 / 13 (0.00%)
occurrences (all)	2	2	0
Cystitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 93 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)	7 / 93 (7.53%)	0 / 13 (0.00%)
occurrences (all)	1	7	0
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 93 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	13 / 93 (13.98%)	0 / 13 (0.00%)
occurrences (all)	3	18	0
Urinary tract infection			
subjects affected / exposed	3 / 31 (9.68%)	2 / 93 (2.15%)	2 / 13 (15.38%)
occurrences (all)	5	2	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 31 (19.35%)	20 / 93 (21.51%)	2 / 13 (15.38%)
occurrences (all)	7	23	2
Dehydration			
subjects affected / exposed	2 / 31 (6.45%)	6 / 93 (6.45%)	1 / 13 (7.69%)
occurrences (all)	4	7	1
Hypercalcaemia			
subjects affected / exposed	1 / 31 (3.23%)	5 / 93 (5.38%)	0 / 13 (0.00%)
occurrences (all)	2	5	0
Hypoalbuminaemia			

subjects affected / exposed	1 / 31 (3.23%)	5 / 93 (5.38%)	0 / 13 (0.00%)
occurrences (all)	1	7	0
Hypokalaemia			
subjects affected / exposed	2 / 31 (6.45%)	12 / 93 (12.90%)	4 / 13 (30.77%)
occurrences (all)	2	21	5
Hypomagnesaemia			
subjects affected / exposed	0 / 31 (0.00%)	7 / 93 (7.53%)	0 / 13 (0.00%)
occurrences (all)	0	8	0
Hyponatraemia			
subjects affected / exposed	1 / 31 (3.23%)	10 / 93 (10.75%)	0 / 13 (0.00%)
occurrences (all)	3	14	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 May 2013	- The enrolled first-line participants could not continue treatment with atezolizumab beyond PD per RECIST v1.1; - The exclusion criterion for hepatitis B was clarified to exclude participants with active hepatitis B but permit enrollment to participants with a past hepatitis B virus infection or resolved hepatitis B virus infection; - The total number of participants to be enrolled was increased to allow for a total of 75 participants in the 2L+ arm and 130 participants in the study; - Statistical considerations section was clarified that there was no plan to perform a formal statistical comparison of the response rates between the three arms; - Minor changes were made to improve clarity and consistency.
16 August 2013	- Clarifications made to the inclusion criterion unique to 2L+ Brain Metastases Participants arm specifying that brain metastases had to be treated and asymptomatic at screening for participants to be eligible; - A new exclusion criterion for participants with prior allogeneic bone marrow transplantation or prior solid organ transplantation was added. Clarifications were made on exclusion criteria for participants with known hypersensitivity with Chinese hamster ovary cell products, positive human immunovirus test, and past or resolved hepatitis B virus infection; - Clarifications were made to assessment of vital signs, observation time for infusions, and reporting of delayed post-infusion symptoms; - Guidelines were added to specify the importance of continued monitoring of participants for signs or symptoms of new or worsening brain involvement; - The window for prior treatment with immunostimulatory agents was adjusted; - Additional minor changes were made to improve clarity and consistency.
21 May 2014	- Updated the protocol with more recent efficacy and safety information for atezolizumab; - The duration of treatment was modified to allow participants to be treated until no longer experiencing clinical benefit; accordingly the 1-year initial treatment, follow-up, and re-treatment periods were not applicable; - The frequency of tumor assessments was reduced after 1 year of treatment and the safety follow-up period was changed from 90 to 30 days; - The clinical safety experience and dose modification guidelines for duration of treatment suspension and treatment of specific toxicities were updated; - Additional minor changes were made to improve clarity and consistency.
19 September 2014	- The safety follow-up was reverted to original 90 days from 30 days implemented in the protocol amendment 3 (dated 21 May 2014) to allow further evaluation of safety after treatment discontinuation and to maintain consistency within the study across all sites; - The clinical experience section of the protocol was updated to align with the Investigator's Brochure and to maintain consistency across active atezolizumab protocols with respect to description of risks and adverse event management guidelines; - Additional minor changes were made to improve clarity and consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported