Clinical trial results:
A Phase II, Multicenter, Single-Arm Study of Atezolizumab (MPDL3280A) in Patients with PD-L1Positive 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	18 December 2017

Results information

Result version number	v2 (current)
This version publication date	02 January 2019
First version publication date	04 November 2016
Version creation reason	• New data added to full data set Final CSR updates

Trial information

Trial identification

Sponsor protocol code	GO28625

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	Final
Date of interim/final analysis	18 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2017
Was the trial ended prematurely?	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	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	United States: 108
Worldwide total number of subjects	137
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)	59
From 65 to 84 years	76
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall 201 participants were screened for clinical eligibility, out of which 63 participants were screen failures, and hence 138 participants were enrolled, and 137 participants received treatment as one US subject was withdrawn from the study prior to study treatment.

Period 1

Period 1 title	Treatment Phase (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 (MPDL3280) : 1L Participants

Arm 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.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
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 (± 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 (± 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (± 10) minutes.

Arm title	Atezolizumab (MPDL3280): 2L+ Participants

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, Tecentriq
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 (± 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (± 10) minutes.

Arm title	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants

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, Tecentriq
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 (± 15) minutes. If the first infusion was tolerated without infusion-associated adverse events, the second infusion could be delivered over 30 (± 10) minutes. If the 30-minute infusion was well tolerated, all subsequent infusions could be delivered over 30 (± 10) minutes.

Number of subjects in period 1	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants
Started	31	93	13
Completed	0	0	0
Not completed	31	93	13
Physician decision	1	2	-
Consent withdrawn by subject	2	4	2
Adverse event, non-fatal	3	4	-
Death	2	9	1
Progressive Disease	21	63	9
Non-compliance	-	2	-
Unspecified	1	5	1
Study Terminated by Sponsor	1	4	-

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab (MPDL3280) : 1L Participants
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 (MPDL3280): 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 (MPDL3280): 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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants
Number of subjects	31	93	13
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: years			
arithmetic mean	68.0	65.2	63.8
standard deviation	± 10.8	± 9.3	± 7.7
Gender, Male/Female Units: Subjects			
Female	17	34	7
Male	14	59	6
Age Continuous Units: Years			
arithmetic mean	68.0	65.2	63.8
standard deviation	± 10.8	± 9.3	±

Reporting group values	Total		
Number of subjects	137		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Subjects			
Female	58		
Male	79		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		

Subject analysis sets

Subject analysis set title	Atezolizumab (MPDL3280) : All Arms
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PK-evaluable population was defined as patients who received any dose of atezolizumab treatment and had PK data at timepoints that were sufficient to determine PK parameters.

Reporting group values	Atezolizumab (MPDL3280) : All Arms		
Number of subjects	135		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age Continuous Units: years arithmetic mean standard deviation	 ±		
Gender, Male/Female Units: Subjects			
Female Male			
Age Continuous Units: Years arithmetic mean standard deviation	 65.7 ± 9.6		

End points

End points reporting groups

Reporting group title	Atezolizumab (MPDL3280) : 1L Participants

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 (MPDL3280): 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 (MPDL3280): 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 (MPDL3280) : All Arms
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The PK-evaluable population was defined as patients who received any dose of atezolizumab treatment and had PK data at timepoints that were sufficient to determine PK parameters.

Primary: Percentage of Participants with Objective Response According to Modified Response Evaluation Criteria in Solid Tumors (RECIST)

End point title	Percentage of Participants with Objective Response According to Modified Response Evaluation Criteria in Solid Tumors (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 millimeters (mm), 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 these criteria, including participants without at least one post-baseline response assessment were considered as non-responders.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	92	13	
Units: percentage of participants				

number (confidence interval 95%)	32 (17 to 51)	21 (13 to 30)	23 (5 to 54)	

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)

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 1 post-baseline response assessment were considered as non-responders.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	92	13	
Units: percentage of participants				
number (confidence interval 95%)	29 (14 to 48)	19 (11 to 28)	23 (5 to 54)	

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 (PD) 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. PD 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. '3.33333' signifies that the median was not evaluable.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	17	3	
Units: months				
median (full range (min-max))	9.2 (2.3 to 30.4)	17.0 (2.8 to 44.2)	3.33333 (2.8 to 9.9)	

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 have 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. For non-TLs, CR was defined as disappearance of all non-TLs and if applicable, normalization of tumor marker level. Participants were censored at the date of last tumor assessment.

End point type	Secondary

End point timeframe:

Month 6

End point values	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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)	75.0	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.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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)	75.0	91.7	66.7	

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 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.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: months				
median (full range (min-max))	4.5 (0.9 to 37.9)	2.7 (0.0 to 45.5)	2.5 (1.0 to 11.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at Month 6, Month 12 and Month 30 According to RECIST v1.1

End point title	Percentage of Participants with PFS at Month 6, Month 12 and Month 30 According to RECIST v1.1

End point description:

Percentage of participants who were progression free at Month 6 and 12 (based on RECIST v1.1) was reported. 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 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. '99999' signifies that the value was not estimable.

End point type	Secondary

End point timeframe:

Months 6, 12 and 30

End point values	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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	33.50	32.29	15.38	
Month 12	20	23	99999	
Month 30	13	10	99999	

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

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.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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: PFS According to Modified RECIST

End point title	PFS According to Modified RECIST

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.

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 (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 2L+ Brain Metastases Participants	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	93	13	
Units: months				
median (full range (min-max))	5.5 (0.9 to 37.9)	3.7 (0.0 to 45.5)	4.3 (1.1 to 16.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS at Month 6, Month 12 and Month 30 According to Modified RECIST

End point title	Percentage of Participants with PFS at Month 6, Month 12 and Month 30 According to Modified RECIST

End point description:

Percentage of participants who were progression free at Months 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. '99999' signifies a value that was not estimable.

End point type	Secondary

End point timeframe:

Months 6, 12 and 30

End point values	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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	39.10	44.87	
Month 12	31	29	24	
Month 30	12	10	99999	

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.

End point type	Secondary

End point timeframe:

Baseline till death or up to 20 months, whichever occurred first

End point values	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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)	74.2	76.3	76.9	

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.

End point type	Secondary

End point timeframe:

Baseline till death or up to 20 months, whichever occurred first

End point values	Atezolizumab (MPDL3280) : 1L Participants	Atezolizumab (MPDL3280): 2L+ Participants	Atezolizumab (MPDL3280): 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%)	14.4 (12.8 to 22.1)	9.3 (5.8 to 17.6)	6.8 (3.2 to 19.5)	

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

End point description:

Pharmacokinetic- evaluable population: All treated participants with pharmacokinetic data at specified time points. Here, Number of participants analyzed = number of participants with available data for this outcome. Per planned analysis, pharmacokinetic data were not analyzed separately for each cohort.

End point type	Secondary

End point timeframe:

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

End point values	Atezolizumab (MPDL3280) : All Arms			
Subject group type	Subject analysis set			
Number of subjects analysed	135			
Units: micrograms per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)	405 (± 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

End point description:

Pharmacokinetic- evaluable population. Here, Number of participants analyzed = number of participants with available data for this outcome, and n= number of participants with available data at the specified time point. Per planned analysis, pharmacokinetic data were not analyzed separately for each cohort. '99999' signifies a value that was not evaluable.

End point type	Secondary

End point timeframe:

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

End point values	Atezolizumab (MPDL3280) : All Arms			
Subject group type	Subject analysis set			
Number of subjects analysed	125			
Units: mcg/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

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Atezolizumab (MPDL3280A) : 1L Participants

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+ 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 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.

Serious adverse events	Atezolizumab (MPDL3280A) : 1L Participants	Atezolizumab (MPDL3280A) : 2L+ Brain Metastases Participants	Atezolizumab (MPDL3280A) : 2L+ Participants
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 31 (54.84%)	6 / 13 (46.15%)	46 / 93 (49.46%)
number of deaths (all causes)	23	10	71
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Embolism			

subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	2 / 13 (15.38%)	2 / 93 (2.15%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (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, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	3 / 31 (9.68%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

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

subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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 / 13 (0.00%)	0 / 93 (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			
Cardiac tamponade			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Pericardial effusion			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Coronary artery disease			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Pericarditis constrictive			

subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PALPITATIONS			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Guillain-Barre Syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (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
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photopsia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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			
Diarrhoea			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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 gastrointestinal haemorrhage			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
AUTOIMMUNE COLITIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	1 / 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 / 13 (0.00%)	0 / 93 (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%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis acute			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	3 / 93 (3.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			

subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 31 (9.68%)	0 / 13 (0.00%)	8 / 93 (8.60%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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 / 13 (0.00%)	0 / 93 (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%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	0 / 93 (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
Sepsis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERKALAEMIA			

subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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+ Brain Metastases Participants	Atezolizumab (MPDL3280A) : 2L+ Participants
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	13 / 13 (100.00%)	88 / 93 (94.62%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 13 (15.38%)	4 / 93 (4.30%)
occurrences (all)	0	4	6
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 31 (9.68%)	0 / 13 (0.00%)	9 / 93 (9.68%)
occurrences (all)	4	0	10
Hypertension			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	3	1	3
Hot flush			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	2 / 93 (2.15%)
occurrences (all)	0	1	3
Haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 31 (51.61%)	5 / 13 (38.46%)	38 / 93 (40.86%)
occurrences (all)	21	6	52

Pyrexia			
subjects affected / exposed	7 / 31 (22.58%)	1 / 13 (7.69%)	21 / 93 (22.58%)
occurrences (all)	8	1	23
Oedema peripheral			
subjects affected / exposed	3 / 31 (9.68%)	2 / 13 (15.38%)	14 / 93 (15.05%)
occurrences (all)	4	4	15
Chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	9 / 93 (9.68%)
occurrences (all)	1	0	9
Pain			
subjects affected / exposed	3 / 31 (9.68%)	2 / 13 (15.38%)	2 / 93 (2.15%)
occurrences (all)	5	2	2
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	9 / 93 (9.68%)
occurrences (all)	1	0	11
Chills			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	5 / 93 (5.38%)
occurrences (all)	1	1	5
Influenza like illness			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	4 / 93 (4.30%)
occurrences (all)	6	1	4
Malaise			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences (all)	0	0	6
Gait disturbance			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	2	0
General physical health deterioration			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			

Breast swelling			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 31 (16.13%)	3 / 13 (23.08%)	33 / 93 (35.48%)
occurrences (all)	6	5	47
Dyspnoea			
subjects affected / exposed	8 / 31 (25.81%)	3 / 13 (23.08%)	30 / 93 (32.26%)
occurrences (all)	9	4	35
Productive cough			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	13 / 93 (13.98%)
occurrences (all)	2	0	14
Wheezing			
subjects affected / exposed	3 / 31 (9.68%)	2 / 13 (15.38%)	7 / 93 (7.53%)
occurrences (all)	3	2	10
Dysphonia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	6 / 93 (6.45%)
occurrences (all)	1	1	7
Haemoptysis			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	6 / 93 (6.45%)
occurrences (all)	3	1	7
Nasal congestion			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences (all)	3	0	9
Pleural effusion			
subjects affected / exposed	2 / 31 (6.45%)	2 / 13 (15.38%)	5 / 93 (5.38%)
occurrences (all)	2	2	5
Pulmonary embolism			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	5 / 93 (5.38%)
occurrences (all)	1	0	5
Dyspnoea exertional			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			

subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	5 / 93 (5.38%)
occurrences (all)	3	0	5
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 31 (12.90%)	1 / 13 (7.69%)	11 / 93 (11.83%)
occurrences (all)	4	1	12
Anxiety			
subjects affected / exposed	0 / 31 (0.00%)	2 / 13 (15.38%)	11 / 93 (11.83%)
occurrences (all)	0	2	14
Depression			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	9 / 93 (9.68%)
occurrences (all)	4	1	17
Confusional state			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	4 / 93 (4.30%)
occurrences (all)	1	1	5
Hallucination			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	2 / 93 (2.15%)
occurrences (all)	0	1	2
Investigations			
Weight decreased			
subjects affected / exposed	6 / 31 (19.35%)	1 / 13 (7.69%)	9 / 93 (9.68%)
occurrences (all)	7	1	9
Alanine aminotransferase increased			
subjects affected / exposed	2 / 31 (6.45%)	2 / 13 (15.38%)	2 / 93 (2.15%)
occurrences (all)	2	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 31 (6.45%)	2 / 13 (15.38%)	3 / 93 (3.23%)
occurrences (all)	2	2	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Haemoglobin decreased			

subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	3 / 93 (3.23%)
occurrences (all)	4	0	9
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences (all)	1	0	9
JAW FRACTURE			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
LACERATION			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
LIMB INJURY			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	0	1	3
Atrial fibrillation			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences (all)	2	0	2
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	2 / 93 (2.15%)
occurrences (all)	0	1	2
Aortic valve thickening			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			

Headache			
subjects affected / exposed	5 / 31 (16.13%)	3 / 13 (23.08%)	10 / 93 (10.75%)
occurrences (all)	6	3	15
Dizziness			
subjects affected / exposed	4 / 31 (12.90%)	1 / 13 (7.69%)	8 / 93 (8.60%)
occurrences (all)	4	2	12
Dysgeusia			
subjects affected / exposed	4 / 31 (12.90%)	0 / 13 (0.00%)	4 / 93 (4.30%)
occurrences (all)	4	0	6
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Cognitive disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Hemiparesis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
Nystagmus			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
PARAESTHESIA			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	4 / 93 (4.30%)
occurrences (all)	2	0	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 31 (19.35%)	1 / 13 (7.69%)	19 / 93 (20.43%)
occurrences (all)	7	2	29
Neutropenia			

subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences (all)	4	0	2
Thrombocytopenia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	1	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	1	1	1
Deafness bilateral			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Vestibular disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
EXCESSIVE CERUMEN PRODUCTION			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	2 / 93 (2.15%)
occurrences (all)	0	1	3
Lacrimation increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	2 / 93 (2.15%)
occurrences (all)	0	1	2
Vision blurred			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	3	1	1
Periorbital oedema			

subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	2	0
CONJUNCTIVAL HYPERAEMIA			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	1	1	2
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 31 (35.48%)	4 / 13 (30.77%)	27 / 93 (29.03%)
occurrences (all)	14	4	30
Constipation			
subjects affected / exposed	8 / 31 (25.81%)	6 / 13 (46.15%)	16 / 93 (17.20%)
occurrences (all)	10	9	22
Diarrhoea			
subjects affected / exposed	8 / 31 (25.81%)	4 / 13 (30.77%)	17 / 93 (18.28%)
occurrences (all)	12	6	23
Vomiting			
subjects affected / exposed	4 / 31 (12.90%)	3 / 13 (23.08%)	14 / 93 (15.05%)
occurrences (all)	4	3	25
Dysphagia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	8 / 93 (8.60%)
occurrences (all)	2	1	9
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	7 / 93 (7.53%)
occurrences (all)	2	0	9
Abdominal pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	7 / 93 (7.53%)
occurrences (all)	2	0	7
Dyspepsia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	0	1	3
Abdominal pain upper			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	5 / 93 (5.38%)
occurrences (all)	2	1	6
Mouth swelling			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0

ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	0	1	3
STOMATITIS			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	3 / 93 (3.23%)
occurrences (all)	2	0	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 31 (16.13%)	1 / 13 (7.69%)	9 / 93 (9.68%)
occurrences (all)	8	1	13
Dry skin			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	12 / 93 (12.90%)
occurrences (all)	1	0	13
Night sweats			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	7 / 93 (7.53%)
occurrences (all)	2	1	9
Rash			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	9 / 93 (9.68%)
occurrences (all)	8	1	15
Decubitus ulcer			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0
Acne			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
RASH MACULO-PAPULAR			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	3 / 93 (3.23%)
occurrences (all)	2	0	5
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	1	1	3
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	6 / 31 (19.35%)	2 / 13 (15.38%)	18 / 93 (19.35%)
occurrences (all)	8	2	23
Back pain			
subjects affected / exposed	4 / 31 (12.90%)	2 / 13 (15.38%)	19 / 93 (20.43%)
occurrences (all)	5	2	20
Pain in extremity			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	8 / 93 (8.60%)
occurrences (all)	3	2	8
Musculoskeletal pain			
subjects affected / exposed	4 / 31 (12.90%)	1 / 13 (7.69%)	9 / 93 (9.68%)
occurrences (all)	4	1	9
Musculoskeletal chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	8 / 93 (8.60%)
occurrences (all)	2	0	8
Myalgia			
subjects affected / exposed	3 / 31 (9.68%)	1 / 13 (7.69%)	5 / 93 (5.38%)
occurrences (all)	5	1	5
Neck pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	5 / 93 (5.38%)
occurrences (all)	2	0	7
Bone pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	3 / 93 (3.23%)
occurrences (all)	0	1	3
Muscle spasms			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	4 / 93 (4.30%)
occurrences (all)	0	1	4
FLANK PAIN			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	5 / 93 (5.38%)
occurrences (all)	0	0	6
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	4 / 93 (4.30%)
occurrences (all)	2	0	4
Infections and infestations			
Upper respiratory tract infection			

subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	17 / 93 (18.28%)
occurrences (all)	3	0	23
Pneumonia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	8 / 93 (8.60%)
occurrences (all)	1	0	8
Urinary tract infection			
subjects affected / exposed	7 / 31 (22.58%)	2 / 13 (15.38%)	3 / 93 (3.23%)
occurrences (all)	12	2	5
Candida infection			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	1 / 93 (1.08%)
occurrences (all)	2	0	5
Cystitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	0 / 93 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	1	1	1
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	0 / 93 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 13 (7.69%)	1 / 93 (1.08%)
occurrences (all)	0	1	1
SINUSITIS			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	2 / 93 (2.15%)
occurrences (all)	2	0	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 31 (19.35%)	2 / 13 (15.38%)	22 / 93 (23.66%)
occurrences (all)	7	2	28
Hypokalaemia			
subjects affected / exposed	2 / 31 (6.45%)	4 / 13 (30.77%)	12 / 93 (12.90%)
occurrences (all)	4	5	24
Hyponatraemia			
subjects affected / exposed	3 / 31 (9.68%)	0 / 13 (0.00%)	12 / 93 (12.90%)
occurrences (all)	7	0	20

Dehydration			
subjects affected / exposed	2 / 31 (6.45%)	1 / 13 (7.69%)	7 / 93 (7.53%)
occurrences (all)	4	1	8
Hypomagnesaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 13 (0.00%)	8 / 93 (8.60%)
occurrences (all)	0	0	13
Hypercalcaemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences (all)	3	0	6
Hypoalbuminaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 13 (0.00%)	6 / 93 (6.45%)
occurrences (all)	1	0	7

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.
04 November 2015	- The Atezolizumab Investigator’s Brochure (IB), Version 7 outlined the defined guidelines for the management of immune-mediated toxicity. Given this, the management of gastrointestinal dermatologic, endocrine, pulmonary toxicity, hepatotoxicity, potential pancreatic or eye toxicity and other immune-mediated adverse events were removed from the protocol and reference was made to the IB; - Systemic immune activation (SIA) was 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 were added.

31 October 2016	- If the Sponsor decided to terminate Study GO28625, patients were offered the option of enrollment in an extension study in order to allow them continued access to atezolizumab treatment. The definition of the End of Study and post-trial access to atezolizumab were revised to reflect this information; - On the basis of updated clinical data regarding the atezolizumab half-life of 27 days, the following changes were implemented: The period during which female patients must remain abstinent or use contraception and the length of follow up of pregnancy reporting, were revised to 5 months after the last dose of study drug; and the period during which patients must agree not to receive live, attenuated vaccine was revised from 90 days to 5 months after the last dose of study drug; - The contraception requirements for male patients and the pregnancy reporting requirements for female partners of male patients were removed to align with the updated safety information for atezolizumab; - The 1-hour post-dose vital sign measurement was removed for infusions that occurred subsequent to the initial infusion. Vital signs for these infusions were to occur within 60 minutes before the infusion and during the infusion if clinically indicated; - Traditional herbal medicines were removed from prohibited therapies, and language was added to state that concomitant use of herbal therapies is not recommended because the pharmacokinetics, safety profile, and potential drug-drug interactions were generally unknown. Use of herbal therapies for patients in the study was allowed only at the discretion of the investigator, provided that there were no known interactions with any study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not specified.

Notes: