



## 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 |
|-----------------------|---------|

##### 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:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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  |
| <b>Arm title</b>             | 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.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Atezolizumab (MPDL3280A) : 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             |
| 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.

|                  |  |
|------------------|--|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | 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  |

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**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:<br>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:<br>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:<br>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<br>Units: Subjects |  |   |  |

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

| Reporting group values             | Total |  |  |
|------------------------------------|-------|--|--|
| Number of subjects                 | 137   |  |  |
| Age categorical<br>Units: Subjects |       |  |  |

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



## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Atezolizumab (MPDL3280A) : 1L Participants                   |
| Reporting group description:<br>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:<br>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:<br>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:<br>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 <sup>[1]</sup> |
| End point description:<br>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.<br>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:<br>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) |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|-----------------|----------------------------------|

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 |
|----------------|-----------|

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 |
|-----------------|---|

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 |
|----------------|-----------|

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 |
|-----------------|--|

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 |
|----------------|-----------|

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:<br>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.<br>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:<br>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:<br>Participants were followed for survival throughout the study.<br>Analysis population: Efficacy-evaluable population. |                                       |
| End point type   | Secondary                             |
| End point timeframe:<br>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 |  |
|-------------------------|------|------|------|--|

## 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:

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 |
|----------------|-----------|

End point timeframe:

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

|   |                                    |  |  |  |
|---|------------------------------------|--|--|--|
| <b>End point values</b>                             | 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 |
|-----------------|--|

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 |
|----------------|-----------|

End point timeframe:

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



|   |                                    |  |  |  |
|---|------------------------------------|--|--|--|
| <b>End point values</b>                             | 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 |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

### 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+ 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.

| 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 %

| <b>Non-serious adverse events</b>                                   | 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<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0 | 0 / 93 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  |
| Laceration<br>subjects affected / exposed<br>occurrences (all)            | 0 / 31 (0.00%)<br>0 | 0 / 93 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  |
| Wound<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 31 (0.00%)<br>0 | 0 / 93 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  |
| Cardiac disorders   |                     |                      |                      |
| Aortic valve disease<br>subjects affected / exposed<br>occurrences (all)  | 0 / 31 (0.00%)<br>0 | 0 / 93 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)   | 2 / 31 (6.45%)<br>2 | 1 / 93 (1.08%)<br>1  | 0 / 13 (0.00%)<br>0  |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)  | 0 / 31 (0.00%)<br>0 | 1 / 93 (1.08%)<br>1  | 1 / 13 (7.69%)<br>1  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 31 (0.00%)<br>0 | 3 / 93 (3.23%)<br>3  | 1 / 13 (7.69%)<br>1  |
| Nervous system disorders  |                     |                      |                      |
| Cognitive disorder<br>subjects affected / exposed<br>occurrences (all)    | 0 / 31 (0.00%)<br>0 | 0 / 93 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)             | 1 / 31 (3.23%)<br>1 | 6 / 93 (6.45%)<br>8  | 1 / 13 (7.69%)<br>2  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)             | 3 / 31 (9.68%)<br>3 | 4 / 93 (4.30%)<br>4  | 0 / 13 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)              | 2 / 31 (6.45%)<br>2 | 8 / 93 (8.60%)<br>12 | 3 / 13 (23.08%)<br>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<br>occurrences (all)                          | 0 / 31 (0.00%)<br>0  | 0 / 93 (0.00%)<br>0    | 1 / 13 (7.69%)<br>1  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)               | 0 / 31 (0.00%)<br>0  | 1 / 93 (1.08%)<br>1    | 1 / 13 (7.69%)<br>1  |
| Vestibular disorder<br>subjects affected / exposed<br>occurrences (all)   | 0 / 31 (0.00%)<br>0  | 0 / 93 (0.00%)<br>0    | 1 / 13 (7.69%)<br>1  |
| Eye disorders   |                      |                        |                      |
| Diplopia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 31 (0.00%)<br>0  | 2 / 93 (2.15%)<br>3    | 1 / 13 (7.69%)<br>1  |
| Lacrimation increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 31 (0.00%)<br>0  | 2 / 93 (2.15%)<br>2    | 1 / 13 (7.69%)<br>1  |
| Periorbital oedema<br>subjects affected / exposed<br>occurrences (all)    | 0 / 31 (0.00%)<br>0  | 0 / 93 (0.00%)<br>0    | 1 / 13 (7.69%)<br>2  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)        | 1 / 31 (3.23%)<br>2  | 1 / 93 (1.08%)<br>1    | 1 / 13 (7.69%)<br>1  |
| Gastrointestinal disorders  |                      |                        |                      |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 31 (0.00%)<br>0  | 7 / 93 (7.53%)<br>7    | 0 / 13 (0.00%)<br>0  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)  | 0 / 31 (0.00%)<br>0  | 2 / 93 (2.15%)<br>3    | 1 / 13 (7.69%)<br>1  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)          | 7 / 31 (22.58%)<br>8 | 14 / 93 (15.05%)<br>18 | 4 / 13 (30.77%)<br>7 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)             | 6 / 31 (19.35%)<br>7 | 15 / 93 (16.13%)<br>19 | 4 / 13 (30.77%)<br>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<br>subjects affected / exposed<br>occurrences (all)  | 0 / 31 (0.00%)<br>0  | 8 / 93 (8.60%)<br>9    | 1 / 13 (7.69%)<br>1  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 31 (0.00%)<br>0  | 1 / 93 (1.08%)<br>1    | 1 / 13 (7.69%)<br>1  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 6 / 31 (19.35%)<br>8 | 17 / 93 (18.28%)<br>19 | 2 / 13 (15.38%)<br>2 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 4 / 31 (12.90%)<br>4 | 16 / 93 (17.20%)<br>16 | 2 / 13 (15.38%)<br>2 |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 31 (0.00%)<br>0  | 3 / 93 (3.23%)<br>3    | 1 / 13 (7.69%)<br>1  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 31 (0.00%)<br>0  | 2 / 93 (2.15%)<br>2    | 1 / 13 (7.69%)<br>1  |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 31 (0.00%)<br>0  | 8 / 93 (8.60%)<br>8    | 0 / 13 (0.00%)<br>0  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 3 / 31 (9.68%)<br>5  | 4 / 93 (4.30%)<br>4    | 1 / 13 (7.69%)<br>1  |
| Musculoskeletal pain<br>subjects affected / exposed<br>occurrences (all)  | 3 / 31 (9.68%)<br>3  | 6 / 93 (6.45%)<br>7    | 1 / 13 (7.69%)<br>1  |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 31 (3.23%)<br>1  | 5 / 93 (5.38%)<br>5    | 0 / 13 (0.00%)<br>0  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 2 / 31 (6.45%)<br>3  | 8 / 93 (8.60%)<br>8    | 1 / 13 (7.69%)<br>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       | <ul style="list-style-type: none"><li>- The enrolled first-line participants could not continue treatment with atezolizumab beyond PD per RECIST v1.1;</li><li>- 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;</li><li>- 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;</li><li>- Statistical considerations section was clarified that there was no plan to perform a formal statistical comparison of the response rates between the three arms;</li><li>- Minor changes were made to improve clarity and consistency.</li></ul>  |
| 16 August 2013    | <ul style="list-style-type: none"><li>- 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;</li><li>- 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;</li><li>- Clarifications were made to assessment of vital signs, observation time for infusions, and reporting of delayed post-infusion symptoms;</li><li>- Guidelines were added to specify the importance of continued monitoring of participants for signs or symptoms of new or worsening brain involvement;</li><li>- The window for prior treatment with immunostimulatory agents was adjusted;</li><li>- Additional minor changes were made to improve clarity and consistency.</li></ul> |
| 21 May 2014       | <ul style="list-style-type: none"><li>- Updated the protocol with more recent efficacy and safety information for atezolizumab;</li><li>- 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;</li><li>- 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;</li><li>- The clinical safety experience and dose modification guidelines for duration of treatment suspension and treatment of specific toxicities were updated;</li><li>- Additional minor changes were made to improve clarity and consistency.</li></ul>  |
| 19 September 2014 | <ul style="list-style-type: none"><li>- 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;</li><li>- 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;</li><li>- Additional minor changes were made to improve clarity and consistency.</li></ul>   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported