



Clinical trial results:

A PHASE II, OPEN-LABEL, MULTICENTER, RANDOMIZED STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF MPDL3280A (ANTI-PD-L1 ANTIBODY) COMPARED WITH DOCETAXEL IN PATIENTS WITH NON-SMALL CELL LUNG CANCER AFTER PLATINUM FAILURE

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2013-001142-34 |
| Trial protocol | BE DE HU GB ES IT SE FR |
| Global end of trial date | 01 December 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v2 |
| This version publication date | 08 July 2017 |
| First version publication date | 22 May 2016 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GO28753 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|---------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01903993 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Alias: POPLAR |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, 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 May 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and safety of atezolizumab compared with docetaxel in subjects with locally advanced or metastatic non-small cell lung cancer (NSCLC) who have progressed during or following a platinum-containing regimen.

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.

Background therapy: -

Evidence for comparator:

Docetaxel is an approved standard 2nd line treatment with demonstrated survival benefit in Cancer.

| | |
|---|----------------|
| Actual start date of recruitment | 05 August 2013 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 3 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | France: 16 |
| Country: Number of subjects enrolled | Thailand: 15 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | Turkey: 7 |
| Country: Number of subjects enrolled | United States: 132 |
| Country: Number of subjects enrolled | Korea, Republic of: 16 |
| Country: Number of subjects enrolled | Poland: 27 |
| Country: Number of subjects enrolled | Spain: 18 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Belgium: 10 |
| Country: Number of subjects enrolled | Germany: 24 |
| Country: Number of subjects enrolled | Italy: 5 |
| Worldwide total number of subjects | 287 |
| EEA total number of subjects | 112 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 174 |
| From 65 to 84 years | 113 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 527 subjects were screened, of whom 287 subjects were randomised. 143 subjects to the docetaxel arm and 144 subjects to the atezolizumab arm. Overall, 10 subjects (8 in the docetaxel arm and 2 in the atezolizumab arm) did not receive any study treatment.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | Docetaxel |

Arm description:

Subjects received docetaxel 75 milligram per meter square (mg/m²) administered intravenously on Day 1 of each 21 day cycle until disease progression or unacceptable toxicity or death.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received starting dose of 75 mg/m² every three week (q3w) until disease progression, unacceptable toxicity or death. Dose modifications were according to the locally approved label. Subjects randomized to receive docetaxel had to be premedicated with corticosteroids according to local practice.

| | |
|------------------|--------------|
| Arm title | Atezolizumab |
|------------------|--------------|

Arm description:

Subjects were administered atezolizumab intravenously on Day 1 of each 21 day cycle at a fixed dose of 1200 mg. Atezolizumab treatment were to continued as long as subjects were experiencing clinical benefit as assessed by the investigator.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atezolizumab |
| Investigational medicinal product code | MPDL3280A |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received atezolizumab of 1200 mg (equivalent to an average body weight-based dose of 15 milligram per kilogram [mg/kg]) which was administered by IV infusion q3w on Day 1 of each 21 day cycle. Subject were allowed to continue treatment beyond progression per response evaluation criteria in solid tumors (RECIST) v1.1 if they were experiencing clinical benefit per investigator, did not have a decline in performance status, did not have signs or symptoms of unequivocal progression, did not have tumor progression at critical sites, and signed an informed consent signature page acknowledging deferment any standard treatment options that may exist in favor of continuing atezolizumab.

| Number of subjects in period 1 | Docetaxel | Atezolizumab |
|---------------------------------------|-----------|--------------|
| Started | 143 | 144 |
| Received Treatment | 135 | 142 |
| Completed | 20 | 49 |
| Not completed | 123 | 95 |
| Consent withdrawn by subject | 13 | 5 |
| Death | 108 | 89 |
| Lost to follow-up | 2 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Docetaxel |
|-----------------------|-----------|

Reporting group description:

Subjects received docetaxel 75 milligram per meter square (mg/m²) administered intravenously on Day 1 of each 21 day cycle until disease progression or unacceptable toxicity or death.

| | |
|-----------------------|--------------|
| Reporting group title | Atezolizumab |
|-----------------------|--------------|

Reporting group description:

Subjects were administered atezolizumab intravenously on Day 1 of each 21 day cycle at a fixed dose of 1200 mg. Atezolizumab treatment were to continued as long as subjects were experiencing clinical benefit as assessed by the investigator.

| Reporting group values | Docetaxel | Atezolizumab | Total |
|------------------------|-----------|--------------|-------|
| Number of subjects | 143 | 144 | 287 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 61.8 | 61.5 | |
| standard deviation | ± 9.4 | ± 9.2 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 67 | 51 | 118 |
| Male | 76 | 93 | 169 |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | Docetaxel |
| Reporting group description: Subjects received docetaxel 75 milligram per meter square (mg/m ²) administered intravenously on Day 1 of each 21 day cycle until disease progression or unacceptable toxicity or death. | |
| Reporting group title | Atezolizumab |
| Reporting group description: Subjects were administered atezolizumab intravenously on Day 1 of each 21 day cycle at a fixed dose of 1200 mg. Atezolizumab treatment were to continued as long as subjects were experiencing clinical benefit as assessed by the investigator. | |

Primary: Overall Survival (OS)

| | |
|--|-----------------------|
| End point title | Overall Survival (OS) |
| End point description: Overall Survival (OS) was defined as the time from the date of randomisation to the date of death due to any cause. Data for subjects who were not reported as dead at the time of analysis was censored at the date when they were last known to be alive. Intent-to-treat (ITT) population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned. | |
| End point type | Primary |
| End point timeframe: From the time of randomisation to the date of death due to any cause or up to data cut off date: 01 Dec 2015 (up to 28 months) | |

| End point values | Docetaxel | Atezolizumab | | |
|----------------------------------|-----------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 143 | 144 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.7 (8.6 to 12) | 12.6 (9.7 to 16) | | |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Overall Survival |
| Statistical analysis description: Hazard ratios (HR) were estimated by a Cox regression model. | |
| Comparison groups | Docetaxel v Atezolizumab |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 287 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0106 |
| Method | Log rank (stratified) |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.92 |

Secondary: Progression-Free Survival (PFS)

| | |
|---|---------------------------------|
| End point title | Progression-Free Survival (PFS) |
| End point description: | |
| <p>PFS was defined as the time (in months) between the date of randomization and the date of first documented disease progression or death, whichever occurs first. Disease progression was determined based on investigator assessment using response evaluation criteria In solid tumors (RECIST) v1.1. Progressive disease (PD): at least a 20% increase in the sum of diameters of target lesions including baseline In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered progression. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| From the time of randomisation to the date of death due to any cause or up to data cut off date: 01 Dec 2015 (up to 28 months) | |

| End point values | Docetaxel | Atezolizumab | | |
|----------------------------------|------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 143 | 144 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 3.4 (2.8 to 4.1) | 2.7 (2 to 4.1) | | |

Statistical analyses

| | |
|---|---------------------------|
| Statistical analysis title | Progression free survival |
| Statistical analysis description: | |
| <p>HR were estimated by a Cox regression model. The two treatment comparison was based on a stratified log-rank test.</p> | |
| Comparison groups | Docetaxel v Atezolizumab |

| | |
|---|-----------------------|
| Number of subjects included in analysis | 287 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5563 |
| Method | Log rank (stratified) |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 1.2 |

Secondary: Objective Response Rate (ORR)

| | |
|---|-------------------------------|
| End point title | Objective Response Rate (ORR) |
| End point description: | |
| <p>ORR was defined as the percentage of subjects with confirmed objective tumor response, complete response (CR) or partial response (PR), as determined by investigator using RECIST v1.1 criteria. CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline until date of death due to any cause or up to data cut off date: 01 Dec 2015 (up to 28 months) | |

| End point values | Docetaxel | Atezolizumab | | |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 143 | 144 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 15.3 (9.83 to 22.21) | 14.7 (9.33 to 21.57) | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Objective response rate |
| Comparison groups | Atezolizumab v Docetaxel |
| Number of subjects included in analysis | 287 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8884 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in Response Rates |
| Point estimate | 0.59 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.67 |
| upper limit | 8.85 |

Secondary: Duration of Response (DOR)

| | |
|---|----------------------------|
| End point title | Duration of Response (DOR) |
| End point description: | |
| DOR was defined as the duration from the first tumor assessment that supports the subject's objective response (CR or PR, whichever is first recorded) to disease progression or death due to any cause, whichever occurs first. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned. Here, 99999 indicates upper limit of confidence interval (CI) for Atezolizumab arm as the CI was not estimable. | |
| End point type | Secondary |
| End point timeframe: | |
| From the time of randomisation to the date of death due to any cause or up to data cut off date: 01 Dec 2015 (up to 28 months) | |

| End point values | Docetaxel | Atezolizumab | | |
|----------------------------------|-------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 21 ^[1] | 22 ^[2] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 7.2 (5.6 to 12.5) | 18.6 (11.6 to 99999) | | |

Notes:

[1] - Number of subjects who were evaluable for this endpoint.

[2] - Number of subjects who were evaluable for this endpoint.

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Duration of response |
| Statistical analysis description: | |
| HR were estimated by a unstratified Cox regression model. | |
| Comparison groups | Docetaxel v Atezolizumab |
| Number of subjects included in analysis | 43 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0028 |
| Method | Log rank (unstratified) |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.15 |
| upper limit | 0.7 |

Secondary: ORR (Modified RECIST)

| | |
|-----------------|--------------------------------------|
| End point title | ORR (Modified RECIST) ^[3] |
|-----------------|--------------------------------------|

End point description:

ORR was defined as the percentage of subjects with confirmed objective tumor response, CR or PR, as determined by investigator using modified RECIST criteria. CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to ≤ 10 mm. PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the time of randomisation to the date of death due to any cause or up to data cut off: 08 May 2015 (up to 21 months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analyses for this end point.

| | | | | |
|----------------------------------|-----------------------|--|--|--|
| End point values | Atezolizumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 144 | | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 16.7 (10.98 to 23.78) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS (Modified RECIST)

| | |
|-----------------|--------------------------------------|
| End point title | PFS (Modified RECIST) ^[4] |
|-----------------|--------------------------------------|

End point description:

PFS was defined as the time (in months) between the date of randomisation and the date of first documented disease progression or death, whichever occurs first. Disease progression was determined based on investigator assessment using modified RECIST criteria. PD: at least a 20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered progression. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the time of randomisation to the date of death due to any cause or up to data cut off: 08 May 2015 (up to 21 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analyses for this end point.

| End point values | Atezolizumab | | | |
|----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 144 | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 4.2 (3.9 to 6.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR (Modified RECIST)

| | |
|-----------------|--------------------------------------|
| End point title | DOR (Modified RECIST) ^[5] |
|-----------------|--------------------------------------|

End point description:

DOR was defined as the duration from the first tumor assessment that supports the subject's objective response (CR or PR, whichever is first recorded) to disease progression or death due to any cause, whichever occurs first. ITT population for efficacy analyses included all randomised subjects, regardless of whether they received any study drug. In the efficacy analyses, the ITT population, subjects were grouped according to the treatment arm to which they were assigned. Here, 99999 indicates upper limit of confidence interval (CI) for Atezolizumab arm as the CI was not estimable.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From the time of randomisation to the date of death due to any cause or up to data cut off: 08 May 2015 (up to 21 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analyses for this end point.

| End point values | Atezolizumab | | | |
|----------------------------------|----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 ^[6] | | | |
| Units: months | | | | |
| median (confidence interval 95%) | 14.9 (11.6 to 99999) | | | |

Notes:

[6] - Number of subjects who were evaluable for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug to the data cutoff date: 01 Dec 2015 (up to 28 months)

Adverse event reporting additional description:

Treatment-emergent adverse events are reported here and they include all adverse events that occurred on or after first dose of study drug until 30 days after last administration of study drug or initiation of another non-protocol anti-cancer therapy after the last administration of study drug, or clinical data cutoff date, whichever occurs first.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Docetaxel |
|-----------------------|-----------|

Reporting group description:

Subjects received docetaxel 75 milligram per meter square (mg/m²) administered intravenously on Day 1 of each 21 day cycle until disease progression or unacceptable toxicity.

| | |
|-----------------------|--------------|
| Reporting group title | Atezolizumab |
|-----------------------|--------------|

Reporting group description:

Subjects were administered atezolizumab intravenously on Day 1 of each 21 day cycle at a fixed dose of 1200 mg. Atezolizumab treatment were to continued as long as subjects were experiencing clinical benefit as assessed by the investigator.

| Serious adverse events | Docetaxel | Atezolizumab | |
|---|-------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 46 / 135 (34.07%) | 50 / 142 (35.21%) | |
| number of deaths (all causes) | 5 | 6 | |
| number of deaths resulting from adverse events | 3 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastatic pain | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour associated fever | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Embolism | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peripheral embolism | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous stenosis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 2 / 135 (1.48%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 1 | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 3 / 142 (2.11%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 135 (1.48%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 135 (0.74%) | 6 / 142 (4.23%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 3 / 135 (2.22%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 4 / 142 (2.82%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 6 / 135 (4.44%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Psychiatric disorders | | | |
| Confusional state | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urine output decreased | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Radiation pneumonitis | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 7 / 135 (5.19%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 7 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 135 (1.48%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids thrombosed | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 135 (0.00%) | 2 / 142 (1.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|------------------|--|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| H1N1 influenza | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 135 (2.22%) | 10 / 142 (7.04%) | |
| occurrences causally related to treatment / all | 2 / 3 | 3 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory tract infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 135 (2.22%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 135 (0.74%) | 0 / 142 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cachexia | | | |
| subjects affected / exposed | 0 / 135 (0.00%) | 1 / 142 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Docetaxel | Atezolizumab | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 124 / 135 (91.85%) | 126 / 142 (88.73%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 4 / 135 (2.96%) | 9 / 142 (6.34%) | |
| occurrences (all) | 4 | 9 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 21 / 135 (15.56%) | 15 / 142 (10.56%) | |
| occurrences (all) | 27 | 25 | |
| Chest pain | | | |
| subjects affected / exposed | 6 / 135 (4.44%) | 10 / 142 (7.04%) | |
| occurrences (all) | 8 | 11 | |
| Fatigue | | | |
| subjects affected / exposed | 53 / 135 (39.26%) | 55 / 142 (38.73%) | |
| occurrences (all) | 85 | 78 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 13 / 135 (9.63%) | 9 / 142 (6.34%) | |
| occurrences (all) | 18 | 11 | |
| Pain | | | |
| subjects affected / exposed | 10 / 135 (7.41%) | 5 / 142 (3.52%) | |
| occurrences (all) | 11 | 6 | |
| Pyrexia | | | |
| subjects affected / exposed | 15 / 135 (11.11%) | 22 / 142 (15.49%) | |
| occurrences (all) | 18 | 27 | |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 135 (1.48%) | 8 / 142 (5.63%) | |
| occurrences (all) | 2 | 10 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 33 / 135 (24.44%) | 40 / 142 (28.17%) | |
| occurrences (all) | 40 | 49 | |
| Dyspnoea | | | |
| subjects affected / exposed | 27 / 135 (20.00%) | 34 / 142 (23.94%) | |
| occurrences (all) | 32 | 38 | |

| | | | |
|---|-------------------------|-------------------------|--|
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 3 / 135 (2.22%) 3 | 10 / 142 (7.04%) 10 | |
| Haemoptysis subjects affected / exposed occurrences (all) | 6 / 135 (4.44%) 10 | 14 / 142 (9.86%) 19 | |
| Productive cough subjects affected / exposed occurrences (all) | 2 / 135 (1.48%) 2 | 8 / 142 (5.63%) 10 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 11 / 135 (8.15%) 12 | 22 / 142 (15.49%) 23 | |
| Investigations Weight decreased subjects affected / exposed occurrences (all) | 9 / 135 (6.67%) 9 | 16 / 142 (11.27%) 20 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 11 / 135 (8.15%) 12 | 10 / 142 (7.04%) 15 | |
| Dysgeusia subjects affected / exposed occurrences (all) | 7 / 135 (5.19%) 8 | 1 / 142 (0.70%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 10 / 135 (7.41%) 10 | 14 / 142 (9.86%) 17 | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 16 / 135 (11.85%) 20 | 3 / 142 (2.11%) 5 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 12 / 135 (8.89%) 21 | 1 / 142 (0.70%) 2 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 26 / 135 (19.26%) 37 | 25 / 142 (17.61%) 42 | |

| | | | |
|--|--|--|--|
| Neutropenia subjects affected / exposed occurrences (all) | 15 / 135 (11.11%) 23 | 2 / 142 (1.41%) 2 | |
| Eye disorders Lacrimation increased subjects affected / exposed occurrences (all) | 7 / 135 (5.19%) 9 | 1 / 142 (0.70%) 1 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 31 / 135 (22.96%) 33 37 / 135 (27.41%) 50 7 / 135 (5.19%) 7 7 / 135 (5.19%) 8 45 / 135 (33.33%) 63 9 / 135 (6.67%) 9 18 / 135 (13.33%) 20 | 31 / 142 (21.83%) 32 24 / 142 (16.90%) 32 3 / 142 (2.11%) 3 8 / 142 (5.63%) 9 31 / 142 (21.83%) 40 3 / 142 (2.11%) 3 20 / 142 (14.08%) 25 | |
| Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Nail disorder | 52 / 135 (38.52%) 57 10 / 135 (7.41%) 10 | 3 / 142 (2.11%) 3 3 / 142 (2.11%) 3 | |

| | | | |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 9 / 135 (6.67%) 9 | 1 / 142 (0.70%) 1 | |
| Pruritus subjects affected / exposed occurrences (all) | 5 / 135 (3.70%) 5 | 13 / 142 (9.15%) 21 | |
| Rash subjects affected / exposed occurrences (all) | 16 / 135 (11.85%) 19 | 15 / 142 (10.56%) 27 | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 135 (0.00%) 0 | 9 / 142 (6.34%) 9 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 12 / 135 (8.89%) 16 | 22 / 142 (15.49%) 26 | |
| Back pain subjects affected / exposed occurrences (all) | 10 / 135 (7.41%) 11 | 16 / 142 (11.27%) 17 | |
| Musculoskeletal chest pain subjects affected / exposed occurrences (all) | 4 / 135 (2.96%) 5 | 9 / 142 (6.34%) 10 | |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 7 / 135 (5.19%) 7 | 19 / 142 (13.38%) 19 | |
| Myalgia subjects affected / exposed occurrences (all) | 18 / 135 (13.33%) 24 | 8 / 142 (5.63%) 9 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 13 / 135 (9.63%) 18 | 9 / 142 (6.34%) 11 | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 3 / 135 (2.22%) 5 | 10 / 142 (7.04%) 14 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| Decreased appetite subjects affected / exposed occurrences (all) | 28 / 135 (20.74%) 35 | 49 / 142 (34.51%) 59 | |
| Dehydration subjects affected / exposed occurrences (all) | 11 / 135 (8.15%) 11 | 5 / 142 (3.52%) 7 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 4 / 135 (2.96%) 4 | 9 / 142 (6.34%) 12 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 4 / 135 (2.96%) 4 | 8 / 142 (5.63%) 12 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 5 / 135 (3.70%) 6 | 8 / 142 (5.63%) 10 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 28 July 2013 | 1. Inclusion Criteria: a) The window for prior treatment with immunostimulatory agents has been adjusted to be consistent with the exclusion criterion covering this prior therapy b) The criterion for liver function test results has been modified to be consistent with the docetaxel US Package Insert c) The formula for estimated glomerular filtration rate has been corrected with regard to numbers and variables that should be superscripted 2.Exclusion Criteria: a) Exclusion for subjects with known or untreated central nervous system (CNS) metastases clarified to indicate that subjects must not have active or untreated CNS metastases as determined by computerized tomography (CT) or magnetic resonance imaging (MRI) evaluation during screening and prior radiographic assessments. Additionally, subjects must not have had stereotactic radiation or whole-brain radiation within 28 days prior to Cycle 1, Day 1 b) Exclusion added for known hypersensitivity or allergy to Chinese hamster ovary cell products or any component of the MPDL3280A formulation as a safety precaution c) Exclusion added for subjects with prior allogeneic bone marrow transplantation or prior solid organ transplantation as a safety precaution d) Exclusion added for subjects having a positive Human immunodeficiency virus (HIV) test as a safety precaution e) Exclusion criterion for subjects with active hepatitis B clarified with respect to definitive serology results f) Exclusion criteria for subjects with active hepatitis C broken out into its own criterion for clarity |
| 30 January 2014 | Study design, determination of sample size, and administrative structure were revised to reflect the continuation of enrollment of subjects until a minimum of approximately 54 subjects Programmed death - ligand 1 (PD-L1) –positive. |
| 20 May 2014 | 1. Treatment duration for atezolizumab was modified to allow subjects to be treated until clinical benefit was no longer being experienced; accordingly, the 16-cycle or 12-month initial treatment, follow-up, and re-treatment periods no longer applied. 2. The frequency of tumor assessments after 36 weeks changed from every 12 weeks to every 9 weeks (± 1 week) to be more consistent with clinical practice in non–small cell lung cancer. 3. The timing of the interim safety and efficacy data evaluation by the Internal Monitoring Committee changed from when 30 and 60 deaths were observed to when approximately 30 and 100 deaths had occurred. The change to evaluate at 100 deaths was determined to be more appropriate than 60 with regard to estimating efficacy in both the PD-L1 IC2/IC3 and overall study populations. 4. The terms “PD-L1 positive” and “PD-L1 negative” were replaced with “PD-L1 (Tumor-infiltrating immune cell 2/Tumor-infiltrating immune cell 3 (IC2/IC3)” and “PD-L1 IC0/IC1,” respectively, to clarify that these categorizations did not necessarily reflect a final definition of positivity for PD-L1 expression using this diagnostic assay. 5. The AE/safety follow-up period changed from 90 to 30 days in order to harmonize safety data collection across the atezolizumab clinical development program. The follow-up period was shortened because of the low frequency of significant drugrelated AEs following treatment discontinuation across studies. 6. Statistical considerations and the analysis plan were changed to reflect the increase in study size that was put into place in Version 3 of this protocol. |
| 24 July 2014 | The safety follow-up period was changed back to the original 90 days to maintain a consistent follow-up period throughout the study and to allow further evaluation of safety after treatment discontinuation in this Phase II trial. |

| | |
|------------------|--|
| 24 February 2015 | 1. Adjusted the event threshold for the primary analysis to approximately 180 death events and converted the originally planned analysis at approximately 150 death events to an interim analysis. This change was made in order to allow for an improved evaluation of late events in the survival curves of atezolizumab compared with docetaxel. 2. Clarified that stratification by PD-L1 immunohistochemistry (IHC) status was based on PD-L1 expression on tumor-infiltrating immune cells. 3. In addition to the primary analyses on the ITT population and the subgroup of subjects with PD-L1 IHC 2 or IHC 3 expression status in ICs, the protocol was amended to allow for subgroup analyses based on other categories of PD-L1 expression (e.g., including expression on tumor cells [TCs]). |
|------------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported