



Clinical trial results:

A Phase 3 Study of Duvelisib (IPI-145) vs Ofatumumab in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2013-002405-61 |
| Trial protocol | ES HU IT GB BE AT DE LV GR |
| Global end of trial date | 23 December 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 15 December 2022 |
| First version publication date | 15 December 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | IPI-145-07 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02004522 |
| WHO universal trial number (UTN) | U1111-1138-8603 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Secura Bio |
| Sponsor organisation address | 1995 Village Center Circle, Suite 128, Las Vegas, NV, United States, 89134 |
| Public contact | NgocDiep Le, Verastem, Inc., 001 7812924200, dle@verastem.com |
| Scientific contact | NgocDiep Le, Verastem, Inc., 001 7812924200, dle@verastem.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 25 June 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 May 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 December 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

A phase 3 clinical trial to examine the efficacy of duvelisib monotherapy versus ofatumumab monotherapy in subjects with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

Protection of trial subjects:

This study was conducted in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 November 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Spain: 40 |
| Country: Number of subjects enrolled | United Kingdom: 17 |
| Country: Number of subjects enrolled | Austria: 11 |
| Country: Number of subjects enrolled | Belgium: 27 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 4 |
| Country: Number of subjects enrolled | Hungary: 65 |
| Country: Number of subjects enrolled | Italy: 41 |
| Country: Number of subjects enrolled | Australia: 21 |
| Country: Number of subjects enrolled | New Zealand: 12 |
| Country: Number of subjects enrolled | United States: 51 |
| Worldwide total number of subjects | 319 |
| EEA total number of subjects | 218 |

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) | 102 |
| From 65 to 84 years | 211 |
| 85 years and over | 6 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was performed at least 30 days prior to dosing (Cycle 1 Day 1).

Period 1

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

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | No |
| Arm title | Duvelisib |

Arm description:

Duvelisib is administered orally and supplied as 5 mg and 25 mg formulated capsules.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Duvelisib |
| Investigational medicinal product code | |
| Other name | Copiktra, IPI-145, PI3K Inhibitor |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received starting dose of 25 mg duvelisib twice a day initially over the course of 21-day treatment cycle followed by 28-day treatment cycles for up to 18 cycles or until disease progression or unacceptable toxicity (whichever comes first).

| | |
|------------------|------------|
| Arm title | Ofatumumab |
|------------------|------------|

Arm description:

Ofatumumab is administered as an intravenous (IV) infusion and is supplied in single-use vials at two strengths, 100 mg/5 mL and 1000 mg/50 mL.

| | |
|--|---------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Ofatumumab |
| Investigational medicinal product code | |
| Other name | Arzerra |
| Pharmaceutical forms | Solution for injection/infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received ofatumumab at the dose and schedule outlined in the approved product labelling for monotherapy in relapsed CLL at the time the study was initiated.

| Number of subjects in period 1 | Duvelisib | Ofatumumab |
|---|-----------|------------|
| Started | 160 | 159 |
| Completed | 34 | 0 |
| Not completed | 126 | 159 |
| Consent withdrawn by subject | 13 | 7 |
| Physician decision | 3 | 4 |
| Disease progression | 35 | 31 |
| Adverse event, non-fatal | 55 | 6 |
| Death | 12 | 3 |
| Other reason listed by PI | 4 | 1 |
| Completed treatment cycles per protocol | 1 | 103 |
| Never dosed | 2 | 4 |
| Protocol deviation | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Duvelisib |
|-----------------------|-----------|

Reporting group description:

Duvelisib is administered orally and supplied as 5 mg and 25 mg formulated capsules.

| | |
|-----------------------|------------|
| Reporting group title | Ofatumumab |
|-----------------------|------------|

Reporting group description:

Ofatumumab is administered as an intravenous (IV) infusion and is supplied in single-use vials at two strengths, 100 mg/5 mL and 1000 mg/50 mL.

| Reporting group values | Duvelisib | Ofatumumab | Total |
|--|-----------|------------|-------|
| Number of subjects | 160 | 159 | 319 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 48 | 54 | 102 |
| From 65-84 years | 109 | 102 | 211 |
| 85 years and over | 3 | 3 | 6 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 64 | 64 | 128 |
| Male | 96 | 95 | 191 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Duvelisib |
| Reporting group description: Duvelisib is administered orally and supplied as 5 mg and 25 mg formulated capsules. | |
| Reporting group title | Ofatumumab |
| Reporting group description: Ofatumumab is administered as an intravenous (IV) infusion and is supplied in single-use vials at two strengths, 100 mg/5 mL and 1000 mg/50 mL. | |
| Subject analysis set title | Intent to Treat |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: All randomized subjects with treatment group designated according to randomization. | |
| Subject analysis set title | Subjects With Abnormal Hematologic Values at Baseline |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects with abnormally high values for neutrophil count, haemoglobin, or platelet count at Baseline. | |

Primary: Progression-free Survival (PFS)

| | |
|---|--|
| End point title | Progression-free Survival (PFS) ^[1] |
| End point description: The primary efficacy endpoint for the study was PFS, defined as time from randomization to the first documentation of PD as determined by blinded independent review or death due to any cause. | |
| End point type | Primary |
| End point timeframe: From date of randomization until the date of first documented progression or date of death from any cause, whichever came first, assessed up to 3 years | |
| 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: Only descriptive statistics (median plus confidence interval) are reported for PFS. | |

| End point values | Duvelisib | Ofatumumab | | |
|----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[2] | 159 ^[3] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 13.3 (12.1 to 16.8) | 9.9 (9.2 to 11.3) | | |

Notes:

[2] - Intent to Treat

[3] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

| | |
|--|-----------------------------|
| End point title | Overall Response Rate (ORR) |
| End point description: ORR is a key secondary efficacy endpoint with overall response defined as best response of CR, CRi, PR, or PRwL, according to the modified IWCLL/IWG Response Criteria, with modification for treatment- | |

related lymphocytosis as defined in the protocol.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Until disease progression or unacceptable toxicity assessed up to 6 years | |

| End point values | Duvelisib | Ofatumumab | | |
|------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[4] | 159 ^[5] | | |
| Units: Count of participants | 118 | 72 | | |

Notes:

[4] - Intent to Treat

[5] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Hematologic Improvements

| | |
|-----------------|--|
| End point title | Number of Subjects With Hematologic Improvements |
|-----------------|--|

End point description:

Subjects with hematologic improvement included those subjects with abnormally high values for neutrophil count, haemoglobin, or platelet count at Baseline determined to have consistently met the criteria of an improvement for those parameters for a period of at least 60 days during which the subject did not have a transfusion or exogenous cytokines.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 3 years | |

| End point values | Duvelisib | Ofatumumab | | |
|------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 94 ^[6] | 95 ^[7] | | |
| Units: Count of participants | 56 | 51 | | |

Notes:

[6] - Subjects With Abnormal Hematologic Values at Baseline

[7] - Subjects With Abnormal Hematologic Values at Baseline

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

| | |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

A stratified Cox regression analysis was used to test for any treatment effect. 9999 = Upper limit not estimable due to an insufficient number of events at the time of analysis.

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

End point timeframe:

Every 6 months for up to 3 years after first dose

| End point values | Duvelisib | Ofatumumab | | |
|----------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[8] | 159 ^[9] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 54.94 (43.00 to 67.99) | 63.25 (44.15 to 9999) | | |

Notes:

[8] - Intent to Treat

[9] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Lymph Node Response Rate

| | |
|--|--------------------------|
| End point title | Lymph Node Response Rate |
| End point description: Lymph node response defined as greater than or equal to 50% decrease in the SPD of target lymph nodes. | |
| End point type | Secondary |
| End point timeframe: 3 years | |

| End point values | Duvelisib | Ofatumumab | | |
|------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[10] | 159 ^[11] | | |
| Units: Count of participants | 136 | 25 | | |

Notes:

[10] - Intent to Treat

[11] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

| | |
|--|----------------------------|
| End point title | Duration of Response (DOR) |
| End point description: Duration of response is defined only for subjects demonstrating a response (eg, CR, CRi, PR, PRwL), with the response and progression statuses both determined by the blinded, central independent review. The analysis will be descriptive for each treatment group only. | |
| End point type | Secondary |
| End point timeframe: Time from the first documentation of response to first documentation of progressive disease or death | |

| End point values | Duvelisib | Ofatumumab | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[12] | 159 ^[13] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 11.1 (9.2 to 18.3) | 9.3 (7.7 to 11.0) | | |

Notes:

[12] - Intent to Treat

[13] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment-Emergent Adverse Events (TEAEs) and Changes in Safety Laboratory Values

| | |
|-----------------|---|
| End point title | Treatment-Emergent Adverse Events (TEAEs) and Changes in Safety Laboratory Values |
|-----------------|---|

End point description:

An analysis of TEAEs with an onset within the first 24 weeks of treatment was performed to examine and compare the incidence of events across an equal period for each treatment arm. Twenty-four weeks was anticipated to be the median exposure to ofatumumab.

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

End point timeframe:

From 04 Feb 2014 until 19 June 2018

| End point values | Duvelisib | Ofatumumab | | |
|------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 160 ^[14] | 159 ^[15] | | |
| Units: Count of participants | 150 | 143 | | |

Notes:

[14] - Intent to Treat

[15] - Intent to Treat

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Samples Available for Duvelisib Pharmacokinetics (PK)

| | |
|-----------------|---|
| End point title | Number of Subjects With Samples Available for Duvelisib Pharmacokinetics (PK) ^[16] |
|-----------------|---|

End point description:

Number of subjects with samples available for duvelisib Pharmacokinetics (PK).

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

End point timeframe:

Cycle 2, Cycle 3, and Cycle 7

Notes:

[16] - 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 PK samples were collected for ofatumumab subjects.

| | | | | |
|-------------------------------|-----------------|--|--|--|
| End point values | Duvelisib | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 160 | | | |
| Units: Number of participants | 158 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

39 months

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Duvelisib |
|-----------------------|-----------|

Reporting group description:

Duvelisib is administered orally and supplied as 5 mg and 25 mg formulated capsules.

| | |
|-----------------------|------------|
| Reporting group title | Ofatumumab |
|-----------------------|------------|

Reporting group description:

Ofatumumab is administered as an IV infusion and is supplied in single-use vials at two strengths, 100 mg/5 mL and 1000 mg/50 mL.

| Serious adverse events | Duvelisib | Ofatumumab | |
|---|--------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 124 / 158 (78.48%) | 50 / 155 (32.26%) | |
| number of deaths (all causes) | 78 | 70 | |
| number of deaths resulting from adverse events | 24 | 7 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Glioblastoma multiforme | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Intestinal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant pleural effusion | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine carcinoma of the skin | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine tumour | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Richter's syndrome | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral embolism | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Disease progression | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 4 / 158 (2.53%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multi-organ failure | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 158 (4.43%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 3 / 9 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal stenosis | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung disorder | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural haemorrhage | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 6 / 158 (3.80%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 6 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 3 / 155 (1.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic rupture | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic haematoma | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 158 (1.27%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (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 | | | |
| Brain stem haemorrhage | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental impairment | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 10 / 158 (6.33%) | 3 / 155 (1.94%) | |
| occurrences causally related to treatment / all | 6 / 12 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic anaemia | | | |

| | | | |
|---|-------------------|-----------------|--|
| subjects affected / exposed | 2 / 158 (1.27%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 20 / 158 (12.66%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 20 / 21 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |

| | | | |
|---|-------------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (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 | 18 / 158 (11.39%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 17 / 20 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileal ulcer | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mallory-Weiss syndrome | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Portal hypertensive gastropathy | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis exfoliative | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash erythematous | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 4 / 158 (2.53%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 4 / 158 (2.53%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal failure chronic | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Aspergillus infection | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 5 / 158 (3.16%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Bronchitis viral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Bronchopulmonary aspergillosis subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Campylobacter gastroenteritis subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic sinusitis subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus colitis subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterococcal infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterococcal sepsis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 3 / 155 (1.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fungal infection | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 158 (2.53%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemophilus infection | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes virus infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion site cellulitis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lobar pneumonia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |

| | | | |
|---|-------------------|-----------------|--|
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 25 / 158 (15.82%) | 5 / 155 (3.23%) | |
| occurrences causally related to treatment / all | 13 / 28 | 3 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumonia bordetella | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia escherichia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia klebsiella | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia mycoplasmal | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia pseudomonas aeruginosa | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pseudomonas bronchitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 158 (0.63%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 158 (1.90%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 158 (1.27%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypervolaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 158 (0.00%) | 2 / 155 (1.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 1 / 155 (0.65%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 158 (0.63%) | 0 / 155 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Duvelisib | Ofatumumab | |
|--|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 149 / 158 (94.30%) | 130 / 155 (83.87%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 13 / 158 (8.23%) | 4 / 155 (2.58%) | |
| occurrences (all) | 18 | 4 | |
| Hypotension | | | |
| subjects affected / exposed | 4 / 158 (2.53%) | 8 / 155 (5.16%) | |
| occurrences (all) | 5 | 8 | |
| General disorders and administration site conditions | | | |

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|---|-------------------|-------------------|--|
| Asthenia subjects affected / exposed occurrences (all) | 20 / 158 (12.66%) | 17 / 155 (10.97%) | |
| | 37 | 19 | |
| | | | |
| | | | |
| Fatigue subjects affected / exposed occurrences (all) | 25 / 158 (15.82%) | 18 / 155 (11.61%) | |
| | 38 | 21 | |
| | | | |
| | | | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 16 / 158 (10.13%) | 7 / 155 (4.52%) | |
| | 22 | 7 | |
| | | | |
| | | | |
| Pyrexia subjects affected / exposed occurrences (all) | 46 / 158 (29.11%) | 15 / 155 (9.68%) | |
| | 76 | 18 | |
| | | | |
| | | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 36 / 158 (22.78%) | 22 / 155 (14.19%) | |
| | 69 | 28 | |
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| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 14 / 158 (8.86%) | 9 / 155 (5.81%) | |
| | 15 | 11 | |
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| Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all) | 8 / 158 (5.06%) | 2 / 155 (1.29%) | |
| | 8 | 2 | |
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| Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) | 9 / 158 (5.70%) | 3 / 155 (1.94%) | |
| | 10 | 3 | |
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| | | | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 8 / 158 (5.06%) | 9 / 155 (5.81%) | |
| | 9 | 10 | |
| | | | |
| | | | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 13 / 158 (8.23%) | 3 / 155 (1.94%) | |
| | 25 | 3 | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| Investigations Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 15 / 158 (9.49%) | 3 / 155 (1.94%) | |
| | 26 | 3 | |
| | | | |
| | | | |

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|--|--|---|--|
| Weight decreased subjects affected / exposed occurrences (all) | 21 / 158 (13.29%) 22 | 3 / 155 (1.94%) 3 | |
| Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) | 2 / 158 (1.27%) 2 | 28 / 155 (18.06%) 35 | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) | 13 / 158 (8.23%) 14 13 / 158 (8.23%) 17 7 / 158 (4.43%) 7 | 5 / 155 (3.23%) 6 13 / 155 (8.39%) 14 15 / 155 (9.68%) 20 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) | 39 / 158 (24.68%) 89 53 / 158 (33.54%) 177 27 / 158 (17.09%) 45 | 16 / 155 (10.32%) 30 32 / 155 (20.65%) 68 9 / 155 (5.81%) 12 | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Colitis | 17 / 158 (10.76%) 19 9 / 158 (5.70%) 9 | 3 / 155 (1.94%) 3 5 / 155 (3.23%) 6 | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 8 / 158 (5.06%) | 1 / 155 (0.65%) | |
| occurrences (all) | 8 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 27 / 158 (17.09%) | 12 / 155 (7.74%) | |
| occurrences (all) | 36 | 12 | |
| Diarrhoea | | | |
| subjects affected / exposed | 79 / 158 (50.00%) | 19 / 155 (12.26%) | |
| occurrences (all) | 196 | 24 | |
| Dry mouth | | | |
| subjects affected / exposed | 8 / 158 (5.06%) | 1 / 155 (0.65%) | |
| occurrences (all) | 8 | 1 | |
| Dyspepsia | | | |
| subjects affected / exposed | 9 / 158 (5.70%) | 4 / 155 (2.58%) | |
| occurrences (all) | 10 | 5 | |
| Nausea | | | |
| subjects affected / exposed | 38 / 158 (24.05%) | 17 / 155 (10.97%) | |
| occurrences (all) | 49 | 20 | |
| Paraesthesia oral | | | |
| subjects affected / exposed | 0 / 158 (0.00%) | 10 / 155 (6.45%) | |
| occurrences (all) | 0 | 11 | |
| Vomiting | | | |
| subjects affected / exposed | 23 / 158 (14.56%) | 10 / 155 (6.45%) | |
| occurrences (all) | 29 | 12 | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 11 / 158 (6.96%) | 9 / 155 (5.81%) | |
| occurrences (all) | 14 | 11 | |
| Rash | | | |
| subjects affected / exposed | 17 / 158 (10.76%) | 18 / 155 (11.61%) | |
| occurrences (all) | 22 | 23 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 9 / 158 (5.70%) | 2 / 155 (1.29%) | |
| occurrences (all) | 14 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|------------------------------------|-------------------|------------------|--|
| Arthralgia | | | |
| subjects affected / exposed | 11 / 158 (6.96%) | 5 / 155 (3.23%) | |
| occurrences (all) | 14 | 5 | |
| Back pain | | | |
| subjects affected / exposed | 12 / 158 (7.59%) | 8 / 155 (5.16%) | |
| occurrences (all) | 16 | 10 | |
| Muscle spasms | | | |
| subjects affected / exposed | 7 / 158 (4.43%) | 8 / 155 (5.16%) | |
| occurrences (all) | 7 | 10 | |
| Pain in extremity | | | |
| subjects affected / exposed | 9 / 158 (5.70%) | 3 / 155 (1.94%) | |
| occurrences (all) | 11 | 3 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 20 / 158 (12.66%) | 12 / 155 (7.74%) | |
| occurrences (all) | 29 | 16 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 158 (8.23%) | 4 / 155 (2.58%) | |
| occurrences (all) | 17 | 4 | |
| Pneumonia | | | |
| subjects affected / exposed | 8 / 158 (5.06%) | 4 / 155 (2.58%) | |
| occurrences (all) | 8 | 5 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 11 / 158 (6.96%) | 3 / 155 (1.94%) | |
| occurrences (all) | 18 | 4 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 22 / 158 (13.92%) | 12 / 155 (7.74%) | |
| occurrences (all) | 29 | 13 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 24 / 158 (15.19%) | 5 / 155 (3.23%) | |
| occurrences (all) | 37 | 5 | |
| Dehydration | | | |
| subjects affected / exposed | 8 / 158 (5.06%) | 1 / 155 (0.65%) | |
| occurrences (all) | 10 | 1 | |
| Hyperkalaemia | | | |

| | | | |
|-----------------------------|-------------------|-----------------|--|
| subjects affected / exposed | 11 / 158 (6.96%) | 5 / 155 (3.23%) | |
| occurrences (all) | 12 | 5 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 16 / 158 (10.13%) | 3 / 155 (1.94%) | |
| occurrences (all) | 32 | 3 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 02 April 2014 | <ul style="list-style-type: none">• Modified Inclusion criterion #3 to more clearly define eligibility around previous purine-analogue therapy. This change included the addition of a timeframe regarding relapse following previous therapy.• Revised exclusions for use of medications or procedures within a specified timeframe to add the use of live or live attenuated vaccines within 30 days prior to randomization. Other investigational therapy was also modified to remove the following:<ul style="list-style-type: none">– “subjects who have received investigational agents with a half-life > 3 days or of unknown length may be allowed on a case by case basis after discussion with the medical monitor”.• Changed Baseline QTcF exclusion criterion from > 480 ms to > 500 ms.• Updated treatment modifications (ie, dose interruptions/holds) with treatment interruption for duvelisib-treated subjects now based on new Grade 3 QTc > 20 ms from Baseline.• Added an additional secondary endpoint of lymph node response rate.• Reordered secondary endpoints based on re-examination of statistical assumptions.• Changed the statistical sections to improve the overall design of the trial:<ul style="list-style-type: none">- Changed the efficacy boundaries for testing the primary endpoint of PFS from Pocock type to O’Brien-Fleming type for the following reasons:<ul style="list-style-type: none">• The superiority of duvelisib compared to ofatumumab in PFS will not be declared by an independent data monitoring committee at an interim analysis unless very convincing evidence for efficacy is presented.• After this change, the criterion of stopping for efficacy was a one-sided p-value of 0.0015 (corresponding approximately to a HR of 0.540). Assuming the median PFS for ofatumumab arm is 9 months, the stopping rule will not be met unless the median PFS for duvelisib arm is approximately 16.7 months.• For the same number of events as the previous design (185 events), the overall power is greater than the previous design (93% vs 87%). |
| 02 March 2015 | <ul style="list-style-type: none">• Changed the QTcF exclusion criteria from QTcF > 500 ms to > 480 ms; revised the “Dose Interruption/Hold/Modification Guidelines” to interrupt treatment for all QTcF prolongation ≥ Grade 3 (≥ 500 ms).• Extended the length of survival follow-up from 3 to 6 years from randomization. |
| 09 February 2017 | <ul style="list-style-type: none">• The Sponsor of Study IPI-145-07 was changed from Infinity to Verastem.• The maximum number of duvelisib treatment cycles (39 cycles) was removed to permit subjects experiencing clinical benefit after 39 cycles to continue duvelisib treatment until disease progression or unacceptable toxicity.• The criteria for receiving additional duvelisib beyond Cycle 19 was modified to reflect potential clinical benefit of a stable disease (SD) response. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported