# Clinical trial results:
# A Phase II, Open-Label Study Evaluating the Safety and Efficacy of GDC-0199 (ABT-199) Plus Bendamustine Plus Rituximab (BR) in Comparison with BR Alone or GDC-0199 Plus Rituximab (R) in Patients with Relapsed and Refractory Follicular Non-Hodgkin's Lymphoma

## Summary

| | |
|---|---|
| EudraCT number | 2014-000576-26 |
| Trial protocol | GB IT DE BE FR |
| Global end of trial date | 16 March 2018 |

### Results information

| | |
|---|---|
| Result version number | v2 |
| This version publication date | 20 April 2018 |
| First version publication date | 14 October 2017 |
| Version creation reason | |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | BO29337 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02187861 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Interim |
| Date of interim/final analysis | 06 April 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 September 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 March 2018 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the efficacy of venetoclax plus BR compared with BR alone and venetoclax plus rituximab in participants with relapsed and refractory follicular lymphoma, as measured by the positron emission tomography (PET) defined complete metabolic response (CMR) at the time of primary response assessment as defined by an Independent Review Committee (IRC)

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 applicable local regulations and policies.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 13 November 2014 |
| 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 | Australia: 33 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Canada: 22 |
| Country: Number of subjects enrolled | France: 13 |
| Country: Number of subjects enrolled | United Kingdom: 18 |
| Country: Number of subjects enrolled | Germany: 17 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | United States: 34 |
| Worldwide total number of subjects | 164 |
| EEA total number of subjects | 75 |

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 | 0 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 86 |
| From 65 to 84 years | 78 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The clinical cut-off date for data included in this posting was 06 April 2017.

### 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** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) |

Arm description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Venetoclax |
| Investigational medicinal product code | GDC-0199 |
| Other name | ABT-199 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

| | |
|---|---|
| Investigational medicinal product name | Bendamustine |
| Investigational medicinal product code | |
| Other name | Levact |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bendamustine was administered as per the schedule specified under arm description.

| | |
|---|---|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | MabThera, Rituxan |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

| | |
|---|---|
| **Arm title** | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) |

Arm description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Venetoclax |
| Investigational medicinal product code | GDC-0199 |
| Other name | ABT-199 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

| | |
|---|---|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | MabThera, Rituxan |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

| | |
|---|---|
| **Arm title** | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |

Arm description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Venetoclax |
| Investigational medicinal product code | GDC-0199 |
| Other name | ABT-199 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Venetoclax was administered as per the schedule specified under arm description.

| | |
|---|---|
| Investigational medicinal product name | Bendamustine |
| Investigational medicinal product code | |
| Other name | Levact |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Bendamustine was administered as per the schedule specified under arm description.

| | |
|---|---|
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | MabThera, Rituxan |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Rituximab was administered as per the schedule specified under arm description.

| | |
|---|---|
| **Arm title** | Chemotherapy-Containing Cohort: Arm C (BR) |

Arm description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Bendamustine |
| Investigational medicinal product code | |
| Other name | Levact |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

| | |
|---|---|
| Dosage and administration details:<br>Bendamustine was administered as per the schedule specified under arm description. | |
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | MabThera, Rituxan |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details:<br>Rituximab was administered as per the schedule specified under arm description. | |

| **Number of subjects in period 1** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|---|---|
| Started | 9 | 53 | 51 |
| Treated | 9 | 52 | 49 |
| Completed | 0 | 0 | 0 |
| Not completed | 9 | 53 | 51 |
| Physician decision | - | 1 | - |
| Consent withdrawn by subject | - | - | 2 |
| Adverse Event | 2 | 1 | 3 |
| Death | - | 3 | 1 |
| Progressive Disease | 3 | 35 | 13 |
| Alive in Study Follow-Up | 4 | 10 | 26 |
| Unspecified | - | 2 | 6 |
| Lack of efficacy | - | 1 | - |

| **Number of subjects in period 1** | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Started | 51 |
| Treated | 50 |
| Completed | 0 |
| Not completed | 51 |
| Physician decision | 3 |
| Consent withdrawn by subject | 3 |
| Adverse Event | - |
| Death | 2 |
| Progressive Disease | 11 |
| Alive in Study Follow-Up | 31 |
| Unspecified | 1 |
| Lack of efficacy | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) |

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| Reporting group title | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) |
|---|---|

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

| Reporting group title | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| Reporting group title | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| Reporting group values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|---|---|
| Number of subjects | 9 | 53 | 51 |
| Age Categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 57.9 | 62.0 | 64.9 |
| standard deviation | ± 12.7 | ± 11.9 | ± 9.8 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 5 | 26 | 16 |
| Male | 4 | 27 | 35 |

| Reporting group values | Chemotherapy-Containing Cohort: Arm C (BR) | Total | |
|---|---|---|---|
| Number of subjects | 51 | 164 | |
| Age Categorical<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 61.0 | | |
| standard deviation | ± 11.6 | - | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 21 | 68 | |
| Male | 30 | 96 | |

## End points

### End points reporting groups

| Reporting group title | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) |
|---|---|

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| Reporting group title | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) |
|---|---|

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

| Reporting group title | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| Reporting group title | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

### Primary: Percentage of Participants with Complete Metabolic Response (CMR) According to Independent Review Committee (IRC) as per Lugano Classification, Using Positron Emission Tomography (PET) Scan at Primary Response Assessment (PRA)

| End point title | Percentage of Participants with Complete Metabolic Response (CMR) According to Independent Review Committee (IRC) as per Lugano Classification, Using Positron Emission Tomography (PET) Scan at Primary Response Assessment (PRA) |
|---|---|

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake less than or equal to [<=] mediastinum), or 3 (uptake less than [<] mediastinum but <=liver) with or without a residual mass on PET 5-point scale (5-PS), for lymph nodes and extralymphatic sites with no new lesions and no evidence of fluorodeoxyglucose (FDG)-avid disease in bone marrow. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% confidence interval (CI) for percentage of responders was calculated using Clopper-Pearson method. Intent-to-treat (ITT) population included all enrolled participants.

| End point type | Primary |
|---|---|

End point timeframe:

6-8 weeks after Cycle 6 Day 1 (PRA) (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 55.6 (21.20 to 86.30) | 11.3 (4.27 to 23.03) | 74.5 (60.37 to 85.67) | 70.6 (56.17 to 82.51) |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | 3.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.38 |
| upper limit | 21.23 |

**Secondary: Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at PRA**

| End point title | Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at PRA |
|---|---|

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

4-10 weeks after Cycle 6 Day 1 (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 55.6 (21.20 to 86.30) | 13.2 (5.48 to 25.34) | 68.6 (54.11 to 80.89) | 64.7 (50.07 to 77.57) |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | 3.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.36 |
| upper limit | 22.2 |

**Secondary: Percentage of Participants with CMR According to IRC as per Lugano Classification, Using PET Scan at Year 1**

| End point title | Percentage of Participants with CMR According to IRC as per Lugano Classification, Using PET Scan at Year 1 |
|---|---|

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (uptake <mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 55.6 (21.20 to 86.30) | 20.8 (10.84 to 34.11) | 41.2 (27.58 to 55.83) | 39.2 (25.84 to 53.89) |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | 1.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.07 |
| upper limit | 20.99 |

**Secondary: Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at Year 1**

| End point title | Percentage of Participants with CMR According to Investigator as per Lugano Classification, Using PET Scan at Year 1 |
|---|---|

End point description:

CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 55.6 (21.20 to 86.30) | 17.0 (8.07 to 29.80) | 41.2 (27.58 to 55.83) | 43.1 (29.35 to 57.75) |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | -1.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.12 |
| upper limit | 17.2 |

**Secondary: Percentage of Participants with Complete Response (CR) According to IRC as per Lugano Classification, Using Computed Tomography (CT) Scan**

| End point title | Percentage of Participants with Complete Response (CR) According to IRC as per Lugano Classification, Using Computed Tomography (CT) Scan |
|---|---|

End point description:

CR: defined as reduction of longest transverse diameter of lesion (LDi) of target nodes/nodal masses to <=1.5 centimeters (cm), and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/immunohistochemistry (IHC)-negative bone marrow morphology. Assessment was performed by an IRC according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 6−8 weeks after Cycle 6 Day 1 | 44.4 (13.70 to 78.80) | 5.7 (1.18 to 15.66) | 39.2 (25.84 to 53.89) | 25.5 (14.33 to 39.63) |
| Year 1 | 55.6 (21.20 to 86.30) | 13.2 (5.48 to 25.34) | 27.5 (15.89 to 41.74) | 23.5 (12.79 to 37.49) |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Statistical analysis description: | |
| At 6−8 weeks after Cycle 6 Day 1 | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | 13.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.24 |
| upper limit | 31.69 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| At Year 1 | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | 3.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.98 |
| upper limit | 20.82 |

## Secondary: Percentage of Participants with CR According to Investigator as per Lugano Classification, Using CT Scan

| End point title | Percentage of Participants with CR According to Investigator as per Lugano Classification, Using CT Scan |
|---|---|

End point description:

CR: defined as reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. Assessment was performed by Investigator according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 4-10 weeks after Cycle 6 Day 1 | 22.2 (2.81 to 60.01) | 5.7 (1.18 to 15.66) | 15.7 (7.02 to 28.59) | 31.4 (19.11 to 45.89) |
| Year 1 | 33.3 (7.49 to 70.07) | 5.7 (1.18 to 15.66) | 13.7 (5.70 to 26.26) | 21.6 (11.29 to 35.32) |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

At 4-10 weeks after Cycle 6 Day 1

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | -15.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -31.87 |
| upper limit | 0.49 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description:<br>At Year 1 | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Difference in response rates |
| Point estimate | -7.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.56 |
| upper limit | 6.87 |

## Secondary: Percentage of Participants with Objective Response (OR) According to IRC as per Lugano Classification, Using PET Scan

| End point title | Percentage of Participants with Objective Response (OR) According to IRC as per Lugano Classification, Using PET Scan |
|---|---|

End point description:

OR was defined as CMR or Partial Metabolic Response (PMR). CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. PMR: a score 4 (uptake moderately greater than [>] liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites with no new lesions and reduced residual uptake in bone marrow compared with baseline. Assessment was performed by an IRC according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 6−8 weeks after Cycle 6 Day 1 | 55.6 (21.20 to 86.30) | 20.8 (10.84 to 34.11) | 76.5 (62.51 to 87.21) | 74.5 (60.37 to 85.67) |
| Year 1 | 66.7 (29.93 to 92.51) | 32.1 (19.92 to 46.32) | 45.1 (31.13 to 59.66) | 51.0 (36.60 to 65.25) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET Scan

| End point title | Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET Scan |
|---|---|

End point description:

OR was defined as CMR or PMR. CMR: a score 1 (no uptake above background), 2 (uptake <=mediastinum), or 3 (<mediastinum but <=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites with no new lesions and no evidence of FDG-avid disease in bone marrow. PMR: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites with no new lesions and reduced residual uptake in bone marrow compared with baseline. Assessment was performed by Investigator according to Lugano classification using PET scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 4-10 weeks after Cycle 6 Day 1 | 55.6 (21.20 to 86.30) | 28.3 (16.79 to 42.35) | 76.5 (62.51 to 87.21) | 74.5 (60.37 to 85.67) |
| Year 1 | 55.6 (21.20 to 86.30) | 20.8 (10.84 to 34.11) | 41.2 (27.58 to 55.83) | 47.1 (32.93 to 61.54) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with OR According to IRC as per Lugano Classification, Using CT Scan

| End point title | Percentage of Participants with OR According to IRC as per Lugano Classification, Using CT Scan |
|---|---|

End point description:

OR was defined as CR or Partial Response (PR). CR: reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. PR: greater than or equal to (>=) 50 percent (%) decrease in sum of the product of the perpendicular diameters (SPD) of up to 6 target measurable nodes and extra-nodal sites; absence/reduction/no increase in size of non-measured lesions; reduction in length of spleen at least >50% beyond normal; and no new lesions. Assessment was performed by an IRC according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

6-8 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 6−8 weeks after Cycle 6 Day 1 | 66.7 (29.93 to 92.51) | 30.2 (18.34 to 44.34) | 80.4 (66.88 to 90.18) | 84.3 (71.41 to 92.98) |
| Year 1 | 66.7 (29.93 to 92.51) | 22.6 (12.28 to 36.21) | 41.2 (27.58 to 55.83) | 60.8 (46.11 to 74.16) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using CT Scan

| End point title | Percentage of Participants with OR According to Investigator as per Lugano Classification, Using CT Scan |
|---|---|

End point description:

OR was defined as CR or PR. CR: reduction of LDi of target nodes/nodal masses to <=1.5 cm, and no extralymphatic sites of disease; absence of non-measured lesions and new lesions; reduction of enlarged organs to normal; and normal/IHC-negative bone marrow morphology. PR: >=50% decrease in SPD of up to 6 target measurable nodes and extra-nodal sites; absence/reduction/no increase in size of non-measured lesions; reduction in length of spleen at least >50% beyond normal; and no new lesions. Assessment was performed by Investigator according to Lugano classification using CT scan. 95% CI for percentage of responders was calculated using Clopper-Pearson method. ITT population.

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

End point timeframe:

4-10 weeks after Cycle 6 Day 1 and 48-56 weeks after Cycle 1 Day 1 (Cycle length = 28 days)

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 4-10 weeks after Cycle 6 Day 1 | 55.6 (21.20 to 86.30) | 32.1 (19.92 to 46.32) | 74.5 (60.37 to 85.67) | 78.4 (64.68 to 88.71) |
| Year 1 | 55.6 (21.20 to 86.30) | 28.3 (16.79 to 42.35) | 47.1 (32.93 to 61.54) | 49.0 (34.75 to 63.40) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET or CT Scan up to Data Cut-off (06 April 2017)

| End point title | Percentage of Participants with OR According to Investigator as per Lugano Classification, Using PET or CT Scan up to Data Cut-off (06 April 2017) |
|---|---|

End point description:

OR was defined as CMR/CR or PMR/PR. CMR, CR, PMR, and PR have been defined in previous endpoints, and are not repeated here due to space constraint. Assessment was performed by Investigator according to Lugano classification using PET scan or CT scan (if PET is missing). ITT population. 'Number of subjects analysed'=those evaluable for this outcome measure.

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

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| End point values | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 25 | 47 | 47 |
| Units: percentage of participants | | | | |
| number (not applicable) | 33.3 | 56.0 | 27.7 | 31.9 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR) According to Investigator as per Lugano Classification, Using PET or CT Scan

| End point title | Duration of Response (DOR) According to Investigator as per Lugano Classification, Using PET or CT Scan |
|---|---|

End point description:

DOR was defined as time from CMR/CR or PMR/PR until progressive disease (PD) or death due to any cause. CMR, CR, PMR, and PR have been defined in previous endpoints, and are not repeated here due to space constraint. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET scan or CT scan (if PET is missing). DOR was calculated using Kaplan-Meier method. ITT population. 'Number of subjects analysed'=those evaluable for this outcome measure. '99999' indicates that upper limit of 95% confidence interval (CI) could not be calculated due to the low number of participants with event.

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

End point timeframe:

From CMR or PMR until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 25 | 47 | 47 |
| Units: months | | | | |
| median (confidence interval 95%) | 16.16 (9.46 to 99999) | 14.32 (10.15 to 21.45) | 15.18 (10.35 to 99999) | 10.61 (9.63 to 99999) |

### Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Stratified Analysis: Strata were disease burden and DOR of prior cancer therapy.

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 1.42 |

Notes:

[1] - Hazard ratio (HR) was calculated using Cox regression.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Unstratified Analysis | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 94 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 1.35 |

Notes:

[2] - HR was calculated using Cox regression.

## Secondary: Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan) or Death

| End point title | Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan) or Death |
|---|---|

End point description:

PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. ITT population.

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

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (not applicable) | 33.3 | 75.5 | 27.5 | 33.3 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

| End point title | Progression-Free Survival (PFS) According to Investigator as per Lugano Classification, Using PET or CT Scan |
|---|---|

End point description:

PFS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) until the date of disease progression, or death due to any cause. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. PFS was calculated using Kaplan-Meier method. ITT population. '99999' indicates that upper limit of 95% CI could not be calculated due to the low number of participants with event.

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

End point timeframe:

Baseline until disease progression or death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: months | | | | |
| median (confidence interval 95%) | 18.83 (12.78 to 99999) | 6.57 (6.18 to 12.02) | 17.77 (13.37 to 99999) | 13.34 (12.25 to 99999) |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Stratified Analysis: Strata were disease burden and PFS of prior cancer therapy.

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 1.31 |

Notes:

[3] - HR was calculated using Cox regression.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Unstratified Analysis | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.31 |
| upper limit | 1.3 |

Notes:

[4] - HR was calculated using Cox regression.

## Secondary: Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan), Death, or Start of a New Anti-lymphoma Therapy

| End point title | Percentage of Participants with Disease Progression (According to Investigator as per Lugano Classification, Using PET or CT Scan), Death, or Start of a New Anti-lymphoma Therapy |
|---|---|

End point description:

PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. ITT population.

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

End point timeframe:

Baseline until disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (not applicable) | 33.3 | 75.5 | 27.5 | 33.3 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Event-Free Survival (EFS) According to Investigator as per Lugano Classification, Using PET or CT Scan

| End point title | Event-Free Survival (EFS) According to Investigator as per Lugano Classification, Using PET or CT Scan |
|---|---|

End point description:

EFS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) to the date of disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first. PD: a score 4 (uptake moderately >liver) or 5 (uptake markedly >liver and/or new lesions) with increase in intensity of uptake from baseline on PET 5-PS for individual target nodes/nodal lesions; new FDG-avid foci for extranodal lesions; new FDG-avid foci consistent with lymphoma for new lesions; or new or recurrent FDG-avid foci for bone marrow. Assessment was performed by Investigator according to Lugano classification using PET or CT scan. EFS was calculated using Kaplan-Meier method. ITT population. '99999' indicates that upper limit of 95% CI could not be calculated due to the low number of participants with event.

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

End point timeframe:

Baseline until disease progression, death, or start of a new anti-lymphoma therapy whichever occurred first (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: months | | | | |
| median (confidence interval 95%) | 18.83 (12.78 to 99999) | 6.57 (6.18 to 12.02) | 17.77 (13.37 to 99999) | 13.34 (12.25 to 99999) |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Stratified Analysis: Strata were disease burden and EFS of prior cancer therapy.

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 1.31 |

Notes:

[5] - HR was calculated using Cox regression.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|
| Statistical analysis description: | |
| Unstratified Analysis | |
| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
| Number of subjects included in analysis | 102 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[6] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.31 |
| upper limit | 1.3 |

Notes:

[6] - HR was calculated using Cox regression.

## Secondary: Percentage of Participants who Died Due to Any Cause

| End point title | Percentage of Participants who Died Due to Any Cause |
|---|---|
| End point description: | |
| ITT population | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline until death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017]) | |

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 53 | 51 | 51 |
| Units: percentage of participants | | | | |
| number (not applicable) | 0 | 5.7 | 2.0 | 3.9 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

OS was defined as the period from the date of treatment initiation (Safety Run-in and Arm A) or randomization date (Arms B and C) to death due to any cause. For participants who are alive, OS was censored at the last contact. OS was calculated using Kaplan-Meier method. ITT population. '9999' indicates that median and corresponding 95% CI could not be estimated due to higher number of censored participants.

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

End point timeframe:

Baseline until death due to any cause (assessed up to approximately 2.5 years [cut-off date 06 April 2017])

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[7] | 3 | 1 | 2 |
| Units: months | | | | |
| median (confidence interval 95%) | ( to ) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | 9999 (9999 to 9999) |

Notes:

[7] - None of the participants were evaluable as all of them were alive at data cut-off.

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Stratified Analysis: Strata were disease burden and OS of prior cancer therapy.

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|
| Number of subjects included in analysis | 3 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[8] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.05 |
| upper limit | 5.91 |

Notes:

[8] - HR was calculated using Cox regression.

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

Unstratified Analysis

| Comparison groups | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) v Chemotherapy-Containing Cohort: Arm C (BR) |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 3 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[9] |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.05 |
| upper limit | 5.63 |

Notes:

[9] - HR was calculated using Cox regression.

## Secondary: Apparent Clearance (CL) of Venetoclax

| | |
|---|---|
| End point title | Apparent Clearance (CL) of Venetoclax[10] |

End point description:

CL is a quantitative measure of the rate at which a drug substance is removed from the body. The data could not be collected as the timepoints for pharmacokinetics collection and the daily dosing of venetoclax did not permit an assessment of CL.

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[10] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[11] | 0[12] | 0[13] | |
| Units: milliliters per hour (mL/hour) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

[11] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

[12] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

[13] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of CL.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent Volume of Distribution (Vd) of Venetoclax

| | |
|---|---|
| End point title | Apparent Volume of Distribution (Vd) of Venetoclax[14] |

End point description:

Vd was defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug. The data could not be collected as the timepoints for pharmacokinetics collection and the daily dosing of venetoclax did not permit an

assessment of Vd.

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[14] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[15] | 0[16] | 0[17] | |
| Units: milliliters (mL) | | | | |
| arithmetic mean (standard deviation) | () | () | () | |

Notes:

[15] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

[16] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

[17] - Pharmacokinetics timepoints and daily dosing of venetoclax did not permit an assessment of Vd.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Maximum Plasma Concentration (Tmax) of Venetoclax

| End point title | Time to Maximum Plasma Concentration (Tmax) of |
|---|---|

End point description:

Pharmacokinetic-evaluable population included all enrolled participants with available pharmacokinetic data for venetoclax.

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[18] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 51 | 46 | |
| Units: hours | | | | |
| median (full range (min-max)) | 8.00 (4.00 to | 6.00 (1.95 to | 6.21 (1.98 to | |

| | | |
|---|---|---|
| 8.08) | 8.18) | 9.22) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Plasma Concentration (Cmax) of Venetoclax

| End point title | Maximum Plasma Concentration (Cmax) of Venetoclax[19] |
|---|---|

End point description:

Pharmacokinetic-evaluable population

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[19] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 51 | 46 | |
| Units: nanograms per milliliter (ng/mL) | | | | |
| arithmetic mean (standard deviation) | 1350 (± 427) | 1220 (± 478) | 1340 (± 460) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Plasma Concentration-Time Curve from Time 0 to Last Observed Concentration (AUClast) of Venetoclax

| End point title | Area Under the Plasma Concentration-Time Curve from Time 0 to Last Observed Concentration (AUClast) of Venetoclax[20] |
|---|---|

End point description:

Area under the plasma concentration versus time curve from zero to the last measured concentration (AUClast). Pharmacokinetic-evaluable population.

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[20] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 51 | 46 | |
| Units: hours*ng/mL | | | | |
| arithmetic mean (standard deviation) | 5310 (± 1730) | 4950 (± 1950) | 5500 (± 2270) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Plasma Concentration-Time Curve from Time 0 to 8 Hours Post Dose (AUC0-8h) of Venetoclax

| End point title | Area Under the Plasma Concentration-Time Curve from Time 0 to 8 Hours Post Dose (AUC0-8h) of Venetoclax[21] |
|---|---|

End point description:

Area under the plasma concentration versus time curve from time 0 (pre-dose) to 8 hours post dose (AUC0-8h). Pharmacokinetic-evaluable population. 'Number of subjects analysed'=those evaluable for this outcome measure.

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

End point timeframe:

Pre-dose (within 30 minutes), and 2, 4, 6, 8 hours post-dose on Cycle 1 Day 1; pre-dose (within 30 minutes) on Cycle 1 Days 8, 15, 22; pre-dose (within 30 minutes) and 4 hours post-dose on Day 1 of Cycles 4 and 6 (Cycle length = 28 days)

Notes:

[21] - 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: This endpoint was only applicable for the arms containing venetoclax treatment

| **End point values** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 30 | 23 | |
| Units: hours*ng/mL | | | | |
| arithmetic mean (standard deviation) | 5240 (± 1860) | 4820 (± 1980) | 5330 (± 2270) | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 2.5 years (cut-off date 06 April 2017)

Adverse event reporting additional description:

Safety-evaluable population included participants who received at least one dose of any study treatment. 'Related' under this section refers to the adverse events related to venetoclax.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + BR) |

Reporting group description:

Participants received venetoclax no more than 600 milligrams (mg) orally once daily continuously along with rituximab 375 milligrams per square meter (mg/m^2) intravenous (IV) infusion on Day 1 of 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of the 28-day cycle. Safety run-in continued until first 9 participants completed the safety observation window of 28 days. After first 28 days of safety observation (Cycle 1), participants continued to receive venetoclax 600 mg orally once daily up to 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| | |
|---|---|
| Reporting group title | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) |

Reporting group description:

Participants received venetoclax 800 mg orally once daily for 1 year along with rituximab 375 mg/m^2 IV infusion on Days 1, 8, 15, 22 of Cycle 1 and Day 1 of Cycles 4, 6, 8, 10, and 12. Each cycle was of 28 days.

| | |
|---|---|
| Reporting group title | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |

Reporting group description:

Participants received venetoclax 800 mg orally once daily continuously for 1 year along with rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| | |
|---|---|
| Reporting group title | Chemotherapy-Containing Cohort: Arm C (BR) |

Reporting group description:

Participants received rituximab 375 mg/m^2 IV infusion on Day 1 of each 28-day cycle and bendamustine 90 mg/m^2 IV infusion on Days 1 and 2 of each 28-day cycle, for 6 cycles.

| **Serious adverse events** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 16 / 52 (30.77%) | 24 / 49 (48.98%) |
| number of deaths (all causes) | 0 | 3 | 1 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Renal stone removal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteral stent insertion | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration | | | |

| | | | |
|---|---|---|---|
| site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute left ventricular failure | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aplastic anaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 52 (0.00%) | 6 / 49 (12.24%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 4 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal colic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster disseminated | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 3 / 49 (6.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 2 / 49 (4.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Chemotherapy- | | |
|---|---|---|---|

| | Containing Cohort: Arm C (BR) | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 50 (20.00%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Renal stone removal | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ureteral stent insertion | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune system disorders | | | | |
| Cytokine release syndrome | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Chronic obstructive pulmonary disease | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoxia | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pleuritic pain | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute left ventricular failure | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial infarction | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| Dizziness | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood and lymphatic system disorders | | | | |
| Anaemia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aplastic anaemia | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile neutropenia | | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thrombocytopenia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Eye disorders | | | | |
| Diplopia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erosive oesophagitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vomiting | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Acute sinusitis | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atypical pneumonia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cystitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytomegalovirus infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster disseminated | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal candidiasis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia pseudomonal | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory syncytial virus infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders | | | | |
| Dehydration | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperkalaemia | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Chemotherapy-Containing Cohort:Safety Run-In (Venetoclax + | Chemotherapy-Free Cohort: Arm A (Venetoclax + Rituximab) | Chemotherapy-Containing Cohort: Arm B (Venetoclax + BR) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 9 (100.00%) | 49 / 52 (94.23%) | 49 / 49 (100.00%) |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 52 (5.77%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 3 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 2 / 52 (3.85%) | 3 / 49 (6.12%) |
| occurrences (all) | 3 | 2 | 5 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 52 (7.69%) | 5 / 49 (10.20%) |
| occurrences (all) | 1 | 4 | 8 |
| Catheter site pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 5 / 52 (9.62%) | 4 / 49 (8.16%) |
| occurrences (all) | 1 | 5 | 5 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 13 / 52 (25.00%) | 22 / 49 (44.90%) |
| occurrences (all) | 6 | 14 | 29 |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 52 (1.92%) | 2 / 49 (4.08%) |
| occurrences (all) | 2 | 1 | 3 |
| Malaise | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 1 | 4 |
| Mass | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 | 2 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 2 / 49 (4.08%) |
| occurrences (all) | 3 | 1 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 5 / 52 (9.62%) | 11 / 49 (22.45%) |
| occurrences (all) | 2 | 6 | 17 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 6 / 52 (11.54%) | 11 / 49 (22.45%) |
| occurrences (all) | 4 | 6 | 13 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 6 / 49 (12.24%) |
| occurrences (all) | 1 | 1 | 6 |
| Lung consolidation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal congestion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 1 | 3 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 1 | 3 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 52 (5.77%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 1 | 4 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 0 | 1 |
| Throat irritation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 1 | 1 |
| Hallucination | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 1 / 52 (1.92%) | 5 / 49 (10.20%) |
| occurrences (all) | 3 | 1 | 5 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 0 | 4 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 2 / 49 (4.08%) |
| occurrences (all) | 2 | 0 | 2 |
| Blood creatinine increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 52 (5.77%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 3 | 2 |
| Gamma−glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 8 | 4 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 52 (7.69%) | 8 / 49 (16.33%) |
| occurrences (all) | 1 | 4 | 8 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 52 (5.77%) | 2 / 49 (4.08%) |
| occurrences (all) | 0 | 3 | 2 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 1 | 7 |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 17 / 52 (32.69%) | 9 / 49 (18.37%) |
| occurrences (all) | 3 | 18 | 12 |
| Laceration | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 0 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 52 (3.85%) | 2 / 49 (4.08%) |
| occurrences (all) | 1 | 2 | 5 |
| Palpitations | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Sinus tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 2 | 4 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 1 | 3 |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 52 (7.69%) | 8 / 49 (16.33%) |
| occurrences (all) | 1 | 5 | 8 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 52 (5.77%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 3 | 3 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 5 / 52 (9.62%) | 8 / 49 (16.33%) |
| occurrences (all) | 4 | 7 | 11 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 3 / 52 (5.77%) | 18 / 49 (36.73%) |
| occurrences (all) | 3 | 3 | 25 |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 4 / 52 (7.69%) | 8 / 49 (16.33%) |
| occurrences (all) | 2 | 7 | 11 |
| Neutropenia | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | 12 / 52 (23.08%) | 30 / 49 (61.22%) |
| occurrences (all) | 12 | 34 | 94 |
| Thrombocytopenia | | | |

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|---|---|---|---|
| subjects affected / exposed | 3 / 9 (33.33%) | 7 / 52 (13.46%) | 28 / 49 (57.14%) |
| occurrences (all) | 15 | 9 | 70 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 1 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 52 (9.62%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 6 / 52 (11.54%) | 5 / 49 (10.20%) |
| occurrences (all) | 3 | 7 | 7 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 52 (3.85%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 2 | 3 |
| Constipation | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 5 / 52 (9.62%) | 10 / 49 (20.41%) |
| occurrences (all) | 4 | 5 | 10 |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | 21 / 52 (40.38%) | 24 / 49 (48.98%) |
| occurrences (all) | 14 | 27 | 47 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 52 (5.77%) | 0 / 49 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 52 (5.77%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 3 | 1 |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mouth ulceration | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 0 | 4 |
| Nausea | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 14 / 52 (26.92%) | 32 / 49 (65.31%) |
| occurrences (all) | 12 | 16 | 58 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 0 | 5 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 7 / 52 (13.46%) | 23 / 49 (46.94%) |
| occurrences (all) | 7 | 12 | 43 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 1 | 3 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 52 (5.77%) | 1 / 49 (2.04%) |
| occurrences (all) | 2 | 3 | 1 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 0 | 1 |
| Yellow skin | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 52 (0.00%) | 2 / 49 (4.08%) |
| occurrences (all) | 2 | 0 | 2 |
| Renal colic | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Arthralgia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 52 (5.77%) | 5 / 49 (10.20%) |
| occurrences (all) | 1 | 3 | 5 |
| Back pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 2 / 52 (3.85%) | 1 / 49 (2.04%) |
| occurrences (all) | 2 | 2 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 2 | 6 |
| Periarthritis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Aspergillus infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 2 | 4 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Conjunctivitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 2 / 49 (4.08%) |
| occurrences (all) | 1 | 1 | 2 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 52 (3.85%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 2 | 3 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 4 / 49 (8.16%) |
| occurrences (all) | 0 | 0 | 4 |
| Mycobacterium kansasii infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 52 (1.92%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 4 / 49 (8.16%) |
| occurrences (all) | 1 | 0 | 6 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 0 | 6 |
| Perineal abscess | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 52 (0.00%) | 0 / 49 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 52 (5.77%) | 3 / 49 (6.12%) |
| occurrences (all) | 1 | 3 | 5 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 6 / 52 (11.54%) | 6 / 49 (12.24%) |
| occurrences (all) | 2 | 9 | 8 |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 52 (7.69%) | 4 / 49 (8.16%) |
| occurrences (all) | 1 | 4 | 9 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 52 (5.77%) | 1 / 49 (2.04%) |
| occurrences (all) | 2 | 3 | 3 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 52 (9.62%) | 10 / 49 (20.41%) |
| occurrences (all) | 0 | 6 | 13 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 2 | 3 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 6 / 52 (11.54%) | 11 / 49 (22.45%) |
| occurrences (all) | 2 | 7 | 16 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 52 (1.92%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 1 | 5 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 52 (0.00%) | 3 / 49 (6.12%) |
| occurrences (all) | 0 | 0 | 3 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 52 (5.77%) | 5 / 49 (10.20%) |
| occurrences (all) | 0 | 4 | 6 |

| **Non-serious adverse events** | Chemotherapy-Containing Cohort: Arm C (BR) | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 48 / 50 (96.00%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 5 | | |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chills | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 3 | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 50 (28.00%) | | |
| occurrences (all) | 21 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mass | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 50 (16.00%) | | |
| occurrences (all) | 15 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 11 / 50 (22.00%) | | |
| occurrences (all) | 15 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 3 | | |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Productive cough | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| occurrences (all) | 8 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 5 | | |
| Throat irritation | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hallucination | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 3 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 6 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma−glutamyltransferase increased | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| occurrences (all) | 8 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight increased | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 12 | | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 6 / 50 (12.00%) | | |
| occurrences (all) | 6 | | |
| Laceration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 4 | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| occurrences (all) | 8 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 50 (10.00%) | | |
| occurrences (all) | 5 | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Neutropenia | | | |
| subjects affected / exposed | 17 / 50 (34.00%) | | |
| occurrences (all) | 57 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 8 / 50 (16.00%) | | |
| occurrences (all) | 15 | | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |
| Constipation | | | |
| subjects affected / exposed | 17 / 50 (34.00%) | | |
| occurrences (all) | 19 | | |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 13 / 50 (26.00%) | | |
| occurrences (all) | 18 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Nausea | | | |
| subjects affected / exposed | 22 / 50 (44.00%) | | |
| occurrences (all) | 34 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 13 / 50 (26.00%) | | |
| occurrences (all) | 18 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | |
| occurrences (all) | 6 | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin lesion | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | | |
| occurrences (all) | 3 | | |

| | | | |
|---|---|---|---|
| Yellow skin | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 2 | | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | |
| occurrences (all) | 3 | | |
| Back pain | | | |
| subjects affected / exposed | 7 / 50 (14.00%) | | |
| occurrences (all) | 8 | | |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | |
| occurrences (all) | 1 | | |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | | |
|---|---|---|---|---|
| Aspergillus infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences (all) | 1 | | | |
| Conjunctivitis | | | | |
| subjects affected / exposed | 4 / 50 (8.00%) | | | |
| occurrences (all) | 5 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences (all) | 1 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Mycobacterium kansasii infection | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |
| Oral candidiasis | | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | | | |
| occurrences (all) | 2 | | | |
| Oral herpes | | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | | | |
| occurrences (all) | 2 | | | |
| Perineal abscess | | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | | | |
| occurrences (all) | 0 | | | |

| | | | |
|---|---|---|---|
| Rhinitis<br>subjects affected / exposed<br>occurrences (all) | 4 / 50 (8.00%)<br>5 | | |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all) | 3 / 50 (6.00%)<br>3 | | |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 4 / 50 (8.00%)<br>4 | | |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 50 (4.00%)<br>4 | | |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 50 (0.00%)<br>0 | | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 6 / 50 (12.00%)<br>6 | | |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 50 (2.00%)<br>1 | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 4 / 50 (8.00%)<br>4 | | |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 50 (0.00%)<br>0 | | |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 50 (0.00%)<br>0 | | |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 50 (2.00%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 24 March 2014 | The protocol was amended to clarify instructions for detection and reporting of liver function abnormalities; and for addition of EudraCT number 2014-000576-26. |
| 25 April 2014 | The protocol was amended to allow investigator's choice of a Chemotherapy Free Cohort or a Chemotherapy-Containing Regimen. Participants assigned to the Chemotherapy-Containing Cohort were subsequently randomized to standard chemo-immunotherapy (bendamustine + rituximab, BR) versus BR + venetoclax. This change was made in response to concerns that participants who required a rapid response to treatment should not be randomized to an unproven Chemotherapy Free regimen; Rituximab dosing regimen in Arm A (Chemotherapy-Free cohort) was modified to align more closely with published data. The revised regimen was: Rituximab 375 mg/m^2 on Cycle 1 on Days 1, 8, 15, and 22, followed by 5 additional doses of rituximab administered every 8 weeks on Day 1 of Cycles 4, 6, 8, 10, and 12. |
| 06 January 2015 | The standard lymphoma response criteria were updated; Participants with prior exposure to hepatitis B, as manifest by hepatitis B virus (HBV) serologies showing hepatitis B core antibody−positive and hepatitis B surface antigen−negative were previously excluded from the study; It was clarified that non-vasectomized males must practice birth control and refrain from sperm donation for 6 months after the last dose of rituximab; The rationale for sample size determination was clarified; It was clarified how the tissue punch was to be obtained for tissue microarrays; The Year 1 assessment could now be performed up to 4 weeks, instead of 2 weeks, to allow flexibility on the timing. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported