# Clinical trial results:
# AN OPEN-LABEL, RANDOMIZED, PHASE 3 STUDY OF INOTUZUMAB OZOGAMICIN ADMINISTERED IN COMBINATION WITH RITUXIMAB COMPARED TO DEFINED INVESTIGATORS CHOICE THERAPY IN SUBJECTS WITH RELAPSED OR REFRACTORY CD22-POSITIVE AGGRESSIVE NON HODGKIN LYMPHOMA WHO ARE NOT CANDIDATES FOR INTENSIVE HIGH-DOSE CHEMOTHERAPY

## Summary

| | |
|---|---|
| EudraCT number | 2010-020147-12 |
| Trial protocol | CZ SE ES DE GB HU LT BG BE GR NL SK |
| Global end of trial date | 28 March 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 30 May 2016 |
| First version publication date | 15 August 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | B1931008 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01232556 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Alias: 3129K5-3303 |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 01 June 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 28 March 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate efficacy as measured by overall survival (OS), with a goal of demonstrating the superiority of inotuzumab ozogamicin when administered in combination with rituximab, compared with an active comparator arm.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 April 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 54 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Spain: 22 |
| Country: Number of subjects enrolled | Sweden: 12 |
| Country: Number of subjects enrolled | United Kingdom: 15 |
| Country: Number of subjects enrolled | Belgium: 12 |
| Country: Number of subjects enrolled | Bulgaria: 4 |
| Country: Number of subjects enrolled | Czech Republic: 5 |
| Country: Number of subjects enrolled | France: 30 |
| Country: Number of subjects enrolled | Germany: 18 |
| Country: Number of subjects enrolled | Hungary: 8 |
| Country: Number of subjects enrolled | Ireland: 2 |
| Country: Number of subjects enrolled | Lithuania: 2 |
| Country: Number of subjects enrolled | Canada: 22 |
| Country: Number of subjects enrolled | Croatia: 4 |
| Country: Number of subjects enrolled | India: 1 |
| Country: Number of subjects enrolled | Japan: 73 |
| Country: Number of subjects enrolled | Mexico: 1 |
| Country: Number of subjects enrolled | Russian Federation: 7 |

| | |
|---|---|
| Country: Number of subjects enrolled | Singapore: 3 |
| Country: Number of subjects enrolled | Taiwan: 7 |
| Country: Number of subjects enrolled | Thailand: 2 |
| Country: Number of subjects enrolled | Ukraine: 17 |
| Country: Number of subjects enrolled | United States: 71 |
| Worldwide total number of subjects | 338 |
| EEA total number of subjects | 134 |

Notes:

**Subjects enrolled per age group**

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 109 |
| From 65 to 84 years | 222 |
| 85 years and over | 7 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Overall study summary and the baseline characteristics summary were calculated using the ITT population. Adverse events were calculated using the safety population.

### 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** | Inotuzumab ozogamicin plus (+) rituximab |

Arm description:

Subjects received rituximab and inotuzumab ozogamicin via intravenous (IV) infusion.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Inotuzumab ozogamicin |
| Investigational medicinal product code | PF-05208773 |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Inotuzumab ozogamicin 1.8 milligram per square meter (mg/m^2) via IV infusion on Day 2 of each 28-day cycle for a maximum of 6 cycles.

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

Dosage and administration details:

Rituximab 375 mg/m^2 via IV infusion on Day 1 of each 28-day cycle for a maximum of 6 cycles.

| | |
|---|---|
| **Arm title** | Rituximab+gemcitabine or rituximab+bendamustine |

Arm description:

Subjects received either R-bendamustine (rituximab via IV infusion and bendamustine via IV infusion) or R-gemcitabine (rituximab via IV infusion and gemcitabine via IV infusion. Choice of therapy was at the discretion of the investigator.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Rituximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Rituximab 375 mg/m^2 via IV infusion on Day 1 in 28-day cycles for a maximum of 6 cycles when given in combination with bendamustine and rituximab 375 mg/m^2 via IV infusion on Days 1, 8, 15 and 22 of Cycle 1 and on Day 1 for all other cycles when given in combination with gemcitabine.

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

Dosage and administration details:

Bendamustine 120 mg/m^2 via IV infusion on Days 1 and 2 in 28-day cycles for a maximum of 6 cycles.

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

Dosage and administration details:

Gemcitabine 1000 mg/m^2 via IV infusion on Days 1, 8 and 15 of each 28-day cycle for a maximum of 6 cycles.

| **Number of subjects in period 1** | Inotuzumab ozogamicin plus (+) rituximab | Rituximab+gemcitabine or rituximab+bendamustine |
|---|---|---|
| Started | 166 | 172 |
| Completed | 7 | 1 |
| Not completed | 159 | 171 |
| Lost to follow-up | - | 2 |
| Study terminated by sponsor | 35 | 51 |
| Subject died | 97 | 97 |
| Unspecified | 6 | 4 |
| Subject refused further follow-up | 21 | 17 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Inotuzumab ozogamicin plus (+) rituximab |
| Reporting group description: | |
| Subjects received rituximab and inotuzumab ozogamicin via intravenous (IV) infusion. | |
| Reporting group title | Rituximab+gemcitabine or rituximab+bendamustine |
| Reporting group description: | |
| Subjects received either R-bendamustine (rituximab via IV infusion and bendamustine via IV infusion) or R-gemcitabine (rituximab via IV infusion and gemcitabine via IV infusion. Choice of therapy was at the discretion of the investigator. | |

| Reporting group values | Inotuzumab ozogamicin plus (+) rituximab | Rituximab+gemcitabine or rituximab+bendamustine | Total |
|---|---|---|---|
| Number of subjects | 166 | 172 | 338 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 68.6 | 66.9 | |
| standard deviation | ± 12.29 | ± 11.4 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 75 | 75 | 150 |
| Male | 91 | 97 | 188 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Inotuzumab ozogamicin plus (+) rituximab |
| Reporting group description: | |
| Subjects received rituximab and inotuzumab ozogamicin via intravenous (IV) infusion. | |
| Reporting group title | Rituximab+gemcitabine or rituximab+bendamustine |
| Reporting group description: | |
| Subjects received either R-bendamustine (rituximab via IV infusion and bendamustine via IV infusion) or R-gemcitabine (rituximab via IV infusion and gemcitabine via IV infusion. Choice of therapy was at the discretion of the investigator. | |
| Subject analysis set title | Inotuzumab ozogamicin+rituximab |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received rituximab 375 mg/m^2 via IV infusion on Day 1 and inotuzumab ozogamicin 1.8 mg/m^2 via IV infusion on Day 2 of each 28-day cycle for a maximum of 6 cycles. | |
| Subject analysis set title | Rituximab+gemcitabine or rituximab+bendamustine |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received either R-bendamustine (rituximab 375 mg/m^2 via IV infusion on Day 1 and bendamustine 120 mg/m^2 via IV infusion on Days 1 and 2 in 28-day cycles for a maximum of 6 cycles) or R-gemcitabine (rituximab 375 mg/m^2 via IV infusion on Days 1, 8, 15 and 22 of Cycle 1 and on Day 1 for all other cycles, and gemcitabine 1000 mg/m^2 via IV infusion on Days 1, 8 and 15 of each 28-day cycle for a maximum of 6 cycles). Choice of therapy was at the discretion of the investigator. | |

### Primary: Overall Survival (OS)

| | |
|---|---|
| End point title | Overall Survival (OS) |
| End point description: | |
| OS was defined as the time from randomization to death due to any cause, censoring at the date of last contact or the end of the study. The Kaplan-Meier method was used to determine OS. The hazard ratio and corresponding 95 per cent (%) 2-sided confidence interval were calculated using stratified Cox proportional hazard regression. Intent-to-treat (ITT) Population. | |
| End point type | Primary |
| End point timeframe: | |
| From randomization up to 5 years after last dose or up to final study visit, whichever occurs first | |

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 166 | 172 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 9.5 (7 to 14.5) | 9.5 (7.7 to 14.1) | | |

### Statistical analyses

| Statistical analysis title | Analysis for Overall Survival |
|---|---|

Statistical analysis description:

Primary null hypothesis: Equality of survival distributions. Sample size sufficient to have power 0.96 for an experimental/control hazard ratio of 0.6. Hazard's Ratio from stratified Cox proportional hazards model. The stratification factors are are pre-randomization investigator choice, baseline Secondary International Prognostic Index (sIPI), and best response to most recent chemo therapy. One sided stratified log-rank test was used.

| | |
|---|---|
| Comparison groups | Inotuzumab ozogamicin+rituximab v Rituximab+gemcitabine or rituximab+bendamustine |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.708 [1] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.083 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.44 |

Notes:

[1] - A one sided 0.025 level testing plan was specified with two interim analyses and final testing level at one-sided 0.023.

## Secondary: Progression-Free Survival (PFS)

| End point title | Progression-Free Survival (PFS) |
|---|---|

End point description:

PFS is defined as time from date of randomization to date of progressive disease (PD), (including investigator's claim of clinical progression)date of death from any cause, or initiation of a new treatment for the lymphoma due to persistent/refractory disease. The Kaplan-Meier method was used to determine PFS. The hazard ratio and corresponding 95 % 2-sided confidence interval were calculated using stratified Cox proportional hazard regression. PD requires the following: a. Appearance of any new lesion more than 1.5 centimeters (cm) in any axis during or at the end of treatment, even if other lesions are decreasing in size. b. At least a 50% increase from nadir in the sum of the product diameters of any previously involved nodes, or in a single involved node, or the size of other lesions. c. At least a 50% increase in the longest diameter of any single previously identified node more than 1 cm in its short axis. ITT Population.

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

End point timeframe:

From randomization up to 2 years or final study visit, whichever occurs first, including but not limited to planned assessments scheduled approximately every 12 weeks

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 166 | 172 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.7 (2.9 to 5) | 3.5 (2.8 to 4.9) | | |

## Statistical analyses

| **Statistical analysis title** | Analysis for Progression-Free Survival (PFS) |
|---|---|

Statistical analysis description:

Second comparison in hierarchical testing strategy was used for power calculation. HR from stratified Cox proportional hazards model. The stratification factors are are pre-randomization investigator choice, baseline sIPI, and best response to most recent chemo therapy. From one sided stratified log-rank test.

| | |
|---|---|
| Comparison groups | Rituximab+gemcitabine or rituximab+bendamustine v Inotuzumab ozogamicin+rituximab |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.271 [2] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.924 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 1.19 |

Notes:

[2] - A hierarchical testing strategy was specified for OS, PFS and response. PFS could be tested at the 0.023 level if the OS test result were positive. Response could be tested if both the OS and PFS test results were positive.

## Secondary: Percentage of Subjects With A Best Overall Response of Complete Response (CR) or Partial Response (PR) per National Cancer Institute (NCI) International Response Criteria for Non Hodgkin Lymphoma (NHL)

| End point title | Percentage of Subjects With A Best Overall Response of Complete Response (CR) or Partial Response (PR) per National Cancer Institute (NCI) International Response Criteria for Non Hodgkin Lymphoma (NHL) |
|---|---|

End point description:

CR is defined as disappearance of all detectable clinical evidence of disease (including cleared infiltrate on repeat bone marrow aspirate/biopsy if lymphoma involvement of bone marrow before treatment). Partial Response (PR) requires the following: a. Greater than or equal to (≥)50 % decrease in SPD of the six largest dominant nodes or nodal masses. b. No increase in the size of other nodes, liver, or spleen. c. Splenic and hepatic nodules must regress by ≥50% in the SPD, or for single nodules, in the greatest transverse diameter. d. With the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. e. No new sites of disease. The 95% CI was determined using the exact method based on binomial distribution. ITT Population.

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

End point timeframe:

Up to 2 years from first study drug dose or up to final study visit, whichever occurs first, including but not limited to planned assessments scheduled approximately every 12 weeks

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 166 | 172 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 29.5 (22.7 to 37.08) | 29.7 (22.94 to 37.08) | | |

### Statistical analyses

| Statistical analysis title | Analysis for Best overall response of CR or PR |
|---|---|

Statistical analysis description:

Third comparison in hierarchical testing strategy was used for power calculation. Third comparison in hierarchical testing strategy was used for power calculation. The stratification factors are pre-randomization investigator choice, baseline sIPI, and best response to most recent chemo therapy.

| | |
|---|---|
| Comparison groups | Inotuzumab ozogamicin+rituximab v Rituximab+gemcitabine or rituximab+bendamustine |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.843 [3] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[3] - A hierarchical testing strategy was specified for OS, PFS and response. PFS could be tested at the 0.023 level if the OS test result were positive. Response could be tested if both the OS and PFS test results were positive.

### Secondary: Percentage of Subjects With a Best Overall Response of CR, Unconfirmed CR (unCR), PR, or Unconfirmed PR (unPR) per NCI International Response Criteria for NHL

| End point title | Percentage of Subjects With a Best Overall Response of CR, Unconfirmed CR (unCR), PR, or Unconfirmed PR (unPR) per NCI International Response Criteria for NHL |
|---|---|

End point description:

CR is defined as disappearance of all detectable clinical evidence of disease (including cleared infiltrate on repeat bone marrow aspirate/biopsy if lymphoma involvement of bone marrow before treatment). Partial Response (PR) requires the following: a. ≥50 % decrease in SPD of the six largest dominant nodes or nodal masses. b. No increase in the size of other nodes, liver, or spleen. c. Splenic and hepatic nodules must regress by ≥50% in the SPD, or for single nodules, in the greatest transverse diameter. d. With the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. e. No new sites of disease. unCR and unPR means didn't have confirmatory assessment (including bone marrow assessment for CR). The 95% CI was determined using the exact method based on binomial distribution. ITT Population.

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

End point timeframe:

Up to 2 years from first study drug dose or up to final study visit, whichever occurs first, including but not limited to planned assessments scheduled approximately every 12 weeks

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 166 | 172 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 41 (33.4 to 48.85) | 43.6 (36.07 to 51.36) | | |

## Statistical analyses

| Statistical analysis title | Analysis for CR, unCR, PR and unPR |
|---|---|

Statistical analysis description:

Third comparison in hierarchical testing strategy was used for power calculation. The stratification factors are pre-randomization investigator choice, baseline sIPI, and best response to most recent chemo therapy.

| | |
|---|---|
| Comparison groups | Inotuzumab ozogamicin+rituximab v Rituximab+gemcitabine or rituximab+bendamustine |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.714 [4] |
| Method | Cochran-Mantel-Haenszel |

Notes:

[4] - A hierarchical testing strategy was specified for OS, PFS and response. PFS could be tested at the 0.023 level if the OS test result were positive. Response could be tested if both the OS and PFS test results were positive.

## Secondary: Duration of Response (DOR)

| End point title | Duration of Response (DOR) |
|---|---|

End point description:

The duration of overall response is measured from the time measurement criteria are met for CR or PR (whichever status is recorded first) until the first date that recurrence or progressive disease is objectively documented, taking as reference for progressive disease the smallest measurements recorded since the treatment started. ITT population; only subjects with a CR, unCR, PR, or unPR were included in the analysis. Here, "99999" in confidence interval signifies "not estimable". The upper limit of the 95 percent (%) confidence interval could not be determined due to the large number of censored events.

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

End point timeframe:

Up to 2 years from first study drug dose or up to final study visit, whichever occurs first, including but not limited to planned assessments scheduled approximately every 12 weeks

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 166 | 172 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 11.56 (7.8 to 99999) | 6.93 (5.5 to 10.8) | | |

### Statistical analyses

| Statistical analysis title | Analysis for Duration of Response |
|---|---|
| Statistical analysis description: | |
| DOR was not part of the formal hypothesis testing strategy. HR from stratified Cox proportional hazards model. The stratification factors are pre-randomization investigator choice, baseline sIPI, and best response to most recent chemo therapy. One sided stratified log-rank test was used. | |
| Comparison groups | Inotuzumab ozogamicin+rituximab v Rituximab+gemcitabine or rituximab+bendamustine |
| Number of subjects included in analysis | 338 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.142 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.25 |

## Secondary: Health Status as Assessed by the European Quality of Life 5 Dimension (EQ-5D) Questionnaire

| End point title | Health Status as Assessed by the European Quality of Life 5 Dimension (EQ-5D) Questionnaire |
|---|---|
| End point description: | |
| EQ-5D consists of a descriptive system and an EQ visual analogue scale. The descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 3 levels: no problems, some problems, extreme problems. The scale, the best state is marked 100 and the worst state is marked 0, is to help the subject to say how good or bad a health state is. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 1 of each cycle and 6-9 weeks after the last dose | |

| End point values | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0[5] | 0[6] | | |
| Units: score on a scale | | | | |

| | | | | |
|---|---|---|---|---|
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[5] - Analysis was not performed since data was insufficient due to early termination of the study.

[6] - Analysis was not performed since data was insufficient due to early termination of the study.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Health Related Quality of Life (HRQOL) as Assessed by the Functional Assessment of Cancer Therapy for Lymphoma (FACT-Lym) Questionnaire

| End point title | Health Related Quality of Life (HRQOL) as Assessed by the Functional Assessment of Cancer Therapy for Lymphoma (FACT-Lym) Questionnaire |
|---|---|

End point description:

FACT-Lym is a questionnaire to record the physical well-being, social/family well-being, emotional well-being, and functional well-being. It contains 42 items (questions) covering HRQOL and common lymphoma symptoms and treatment side-effects. The questionnaire begins with 27 items covering four core HRQOL subscales: Physical Well-being (7 items), Social/Family Well-being (7), Emotional Well-being (6), and Functional Well-being (7). The FACT-Lym also includes an Additional Concerns subscale (15 items). It also asks subjects about their concerns about lumps and swelling, fevers, infections, weight, appetite, emotional stability and treatment. The subjects were requested to circle one number on a 0 to 4 points scale per line to indicate how true each statement has been for him/her during the past 7 days.

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

End point timeframe:

Day 1 of each cycle and 6-9 weeks after the last dose

| **End point values** | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0[7] | 0[8] | | |
| Units: score on a scale | | | | |
| arithmetic mean (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[7] - Analysis was not performed since data was insufficient due to early termination of the study.

[8] - Analysis was not performed since data was insufficient due to early termination of the study.

### Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs)

| End point title | Percentage of Subjects With Treatment-Emergent Adverse Events (AEs) or Serious Adverse Events (SAEs) |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-

threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-Emergent Adverse Events (TEAEs) were defined as those starting on the first study drug dose date and within 56 days after the last study drug dose date. Summaries are based on safety population (subjects who received study drug). One subject in the rituximab+ inotuzumab ozogamicin arm received rituximab only, and was excluded from the safety population analysis.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

First dose date up to 56 days after last dose of study drug

| **End point values** | Inotuzumab ozogamicin plus (+) rituximab | Rituximab+gemcitabine or rituximab+bendamustine | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 164 | 167 | | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Subjects With AEs | 98.8 | 100 | | |
| Subjects With SAEs | 37.2 | 37.7 | | |
| Subjects With Grade 3 or 4 AEs | 79.9 | 79.6 | | |
| Subjects With Grade 5 AEs | 14.6 | 13.8 | | |
| Subjects Discontinued Due to AEs | 25 | 18 | | |
| Subjects With Dose Reduced Due to AEs | 27.4 | 29.3 | | |
| Subjects With Temporary Discontinuation Due to AEs | 31.1 | 46.1 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs: from informed consent through and including end of treatment (EOT) visit. NonSAEs: from first dose through and including EOT visit. EOT visit = at least 42 days post last dose. Summaries include SAE/AEs from first dose up to 56 days post last dose

Adverse event reporting additional description:

AEs use safety population.1 subject in rituximab+inotuzumab arm received rituximab only(excluded from safety population).Source for SAEs, deaths is project database(PDB), safety database (SDB),respectively.Death(all causes)=fatal SAEs within 56 days post last dose;deaths resulting from AEs=fatal treatment related SAEs within 56 days post last dose.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Inotuzumab ozogamicin+rituximab |

Reporting group description:

Subjects received rituximab 375 mg/m^2 via IV infusion on Day 1 and inotuzumab ozogamicin 1.8 mg/m^2 via IV infusion on Day 2 of each 28-day cycle for a maximum of 6 cycles.

| | |
|---|---|
| Reporting group title | Rituximab+gemcitabine or rituximab+bendamustine |

Reporting group description:

Subjects received either R-bendamustine (rituximab 375 mg/m^2 via IV infusion on Day 1 and bendamustine 120 mg/m^2 via IV infusion on Days 1 and 2 in 28-day cycles for a maximum of 6 cycles) or R-gemcitabine (rituximab 375 mg/m^2 via IV infusion on Days 1, 8, 15 and 22 of Cycle 1 and on Day 1 for all other cycles, and gemcitabine 1000 mg/m^2 via IV infusion on Days 1, 8 and 15 of each 28-day cycle for a maximum of 6 cycles). Choice of therapy was at the discretion of the investigator.

| **Serious adverse events** | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 61 / 164 (37.20%) | 63 / 167 (37.72%) | |
| number of deaths (all causes) | 22 | 23 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lymphoma | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome transformation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 3 / 167 (1.80%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 164 (1.83%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disease progression | Additional description: 1 inotuzumab subject,disease progression(DP) reported as fatal event in SDB,but as Lymphoma in PDB(death and event displayed under DP and lymphoma, respectively). 2 control subjects had fatal event of DP (1related) in SDB only;not counted at PT level. | | |
| subjects affected / exposed | 15 / 164 (9.15%) | 20 / 167 (11.98%) | |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 21 | |
| deaths causally related to treatment / all | 0 / 16 | 1 / 22 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema due to hepatic disease | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 164 (3.05%) | 4 / 167 (2.40%) | |
| occurrences causally related to treatment / all | 1 / 5 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 3 / 167 (1.80%) | |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium febrile | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transfusion reaction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraplegia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 5 / 164 (3.05%) | 7 / 167 (4.19%) | |
| occurrences causally related to treatment / all | 2 / 6 | 4 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 2 / 2 | 8 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal wall haematoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis acute | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venoocclusive liver disease | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Haematuria | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Groin pain | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus viraemia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | Additional description: Lung infection reported as fatal event for 1 subject in SDP but as fatal SAE of 'Respiratory tract infection' in PDB. In this table, death and event displayed under lung and respiratory tract infection, respectively. | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Meningitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 8 / 164 (4.88%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 9 / 12 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonella sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal skin infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 164 (1.22%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 164 (1.83%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 164 (1.83%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Inotuzumab ozogamicin+rituximab | Rituximab+gemcitabine or rituximab+bendamustine | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 155 / 164 (94.51%) | 158 / 167 (94.61%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 28 / 164 (17.07%) | 17 / 167 (10.18%) | |
| occurrences (all) | 60 | 48 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 44 / 164 (26.83%) | 18 / 167 (10.78%) | |
| occurrences (all) | 93 | 54 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 24 / 164 (14.63%) | 16 / 167 (9.58%) | |
| occurrences (all) | 57 | 18 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 4 / 167 (2.40%) | |
| occurrences (all) | 20 | 5 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 5 / 164 (3.05%) | 13 / 167 (7.78%) | |
| occurrences (all) | 18 | 15 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 4 / 167 (2.40%) | |
| occurrences (all) | 20 | 10 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 38 / 164 (23.17%) | 16 / 167 (9.58%) | |
| occurrences (all) | 90 | 23 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 4 / 164 (2.44%) | 10 / 167 (5.99%) | |
| occurrences (all) | 7 | 23 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 7 / 167 (4.19%) | |
| occurrences (all) | 28 | 17 | |

| | | | |
|---|---|---|---|
| Weight decreased | | | |
| subjects affected / exposed | 4 / 164 (2.44%) | 11 / 167 (6.59%) | |
| occurrences (all) | 4 | 16 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 4 / 164 (2.44%) | 12 / 167 (7.19%) | |
| occurrences (all) | 25 | 80 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 8 / 164 (4.88%) | 13 / 167 (7.78%) | |
| occurrences (all) | 11 | 16 | |
| Dysgeusia | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 8 / 167 (4.79%) | |
| occurrences (all) | 10 | 8 | |
| Headache | | | |
| subjects affected / exposed | 8 / 164 (4.88%) | 11 / 167 (6.59%) | |
| occurrences (all) | 21 | 11 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 24 / 164 (14.63%) | 43 / 167 (25.75%) | |
| occurrences (all) | 50 | 123 | |
| Leukopenia | | | |
| subjects affected / exposed | 37 / 164 (22.56%) | 54 / 167 (32.34%) | |
| occurrences (all) | 167 | 285 | |
| Lymphopenia | | | |
| subjects affected / exposed | 28 / 164 (17.07%) | 39 / 167 (23.35%) | |
| occurrences (all) | 137 | 255 | |
| Neutropenia | | | |
| subjects affected / exposed | 57 / 164 (34.76%) | 81 / 167 (48.50%) | |
| occurrences (all) | 216 | 302 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 101 / 164 (61.59%) | 64 / 167 (38.32%) | |
| occurrences (all) | 506 | 189 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 13 / 164 (7.93%) | 14 / 167 (8.38%) | |
| occurrences (all) | 14 | 19 | |

| | | | |
|---|---|---|---|
| Chills | | | |
| subjects affected / exposed | 5 / 164 (3.05%) | 9 / 167 (5.39%) | |
| occurrences (all) | 5 | 9 | |
| Fatigue | | | |
| subjects affected / exposed | 55 / 164 (33.54%) | 42 / 167 (25.15%) | |
| occurrences (all) | 75 | 59 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 17 / 164 (10.37%) | 15 / 167 (8.98%) | |
| occurrences (all) | 21 | 22 | |
| Pyrexia | | | |
| subjects affected / exposed | 37 / 164 (22.56%) | 35 / 167 (20.96%) | |
| occurrences (all) | 44 | 47 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 14 / 164 (8.54%) | 13 / 167 (7.78%) | |
| occurrences (all) | 18 | 18 | |
| Constipation | | | |
| subjects affected / exposed | 38 / 164 (23.17%) | 33 / 167 (19.76%) | |
| occurrences (all) | 52 | 54 | |
| Diarrhoea | | | |
| subjects affected / exposed | 22 / 164 (13.41%) | 31 / 167 (18.56%) | |
| occurrences (all) | 34 | 38 | |
| Nausea | | | |
| subjects affected / exposed | 50 / 164 (30.49%) | 54 / 167 (32.34%) | |
| occurrences (all) | 73 | 89 | |
| Vomiting | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 32 / 167 (19.16%) | |
| occurrences (all) | 34 | 46 | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 12 / 164 (7.32%) | 3 / 167 (1.80%) | |
| occurrences (all) | 29 | 5 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 24 / 164 (14.63%) | 13 / 167 (7.78%) | |
| occurrences (all) | 27 | 17 | |

| | | | |
|---|---|---|---|
| Dyspnoea | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 14 / 167 (8.38%) | |
| occurrences (all) | 10 | 19 | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 6 / 164 (3.66%) | 10 / 167 (5.99%) | |
| occurrences (all) | 6 | 15 | |
| Rash | | | |
| subjects affected / exposed | 8 / 164 (4.88%) | 13 / 167 (7.78%) | |
| occurrences (all) | 9 | 20 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 7 / 164 (4.27%) | 9 / 167 (5.39%) | |
| occurrences (all) | 12 | 10 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 4 / 167 (2.40%) | |
| occurrences (all) | 10 | 4 | |
| Back pain | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 17 / 167 (10.18%) | |
| occurrences (all) | 12 | 20 | |
| Pain in extremity | | | |
| subjects affected / exposed | 6 / 164 (3.66%) | 10 / 167 (5.99%) | |
| occurrences (all) | 6 | 12 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 6 / 167 (3.59%) | |
| occurrences (all) | 10 | 7 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 9 / 164 (5.49%) | 12 / 167 (7.19%) | |
| occurrences (all) | 9 | 14 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 28 / 164 (17.07%) | 31 / 167 (18.56%) | |
| occurrences (all) | 37 | 47 | |
| Hypercalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 164 (5.49%) | 6 / 167 (3.59%) | |
| occurrences (all) | 19 | 6 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 11 / 164 (6.71%) | 14 / 167 (8.38%) | |
| occurrences (all) | 15 | 19 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 12 / 164 (7.32%) | 12 / 167 (7.19%) | |
| occurrences (all) | 24 | 23 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Interpretation of the results is limited by total enrollment being less than the planned total enrollment, discontinuation of some protocol activities, and shortened follow-up period which were all due to the early termination of the study.

Notes: