



Clinical trial results:

TARGETED INTENSIFICATION BY A PREPARATIVE REGIMEN FOR PATIENTS WITH HIGH-GRADE B-CELL LYMPHOMA UTILIZING STANDARD-DOSE YTTRIUM-90 IBRITUMOMAB TIUXETAN (ZEVALIN) RADIOIMMUNOTHERAPY (RIT) COMBINED WITH HIGH-DOSE BEAM FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT):Z BEAM 2

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2007-000270-23 |
| Trial protocol | BE |
| Global end of trial date | 29 January 2014 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 14 October 2017 |
| First version publication date | 14 October 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | Z BEAM 2 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00689169 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | LYSA |
| Sponsor organisation address | CH Lyon Sud - Service d'Hématologie - Bâtiment 1F - 3ème étage , Pierre-Bénite Cedex, France, 69495 |
| Public contact | Christine Stephan, LYSARC, +33 4 72 66 93 33, |
| Scientific contact | Christophe Fruchart, LYSA, fruchart-c@chu-caen.fr |

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 | 28 June 2012 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy and the safety of a preparative regimen utilizing standard-dose Yttrium-90 Ibritumomab Tiuxetan (Zevalin) radioimmunotherapy combined with high-dose BEAM followed by ASCT after first line treatment in patients aged from 18 to 65 years CD20 positive Diffuse Large B-Cell lymphoma with poor prognosis

PRIMARY ENDPOINT:

Event free survival (EFS) at 2 years: events being death from any cause, relapse for complete responders and unconfirmed complete responders, progression during and after treatment and changes of therapy.

Protection of trial subjects:

Supportive treatments administered according to the standard use of each center.
Treatment for progression/relapse administered at the discretion of treating physician.

Background therapy:

No background therapy.

Evidence for comparator:

No comparator.

| | |
|---|---------------------|
| Actual start date of recruitment | 21 August 2007 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Scientific research |
| Long term follow-up duration | 10 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------|
| Country: Number of subjects enrolled | Belgium: 7 |
| Country: Number of subjects enrolled | France: 66 |
| Country: Number of subjects enrolled | Switzerland: 2 |
| Worldwide total number of subjects | 75 |
| EEA total number of subjects | 73 |

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) | 75 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment period : from 21/08/2007 to 18/12/2008.

Patients recruited in France, Belgium and Switzerland.

Pre-assignment

Screening details:

pathologically proven large B-Cell lymphoma CD20 positive (without transformation from low grade), in CR or PR after induction treatment (R CHOP like or R ACVBP), eligible for autologous stem cell transplantation

75 patient included

Period 1

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

Arms

| | |
|-----------|---------------|
| Arm title | Z-BEAM + ASCT |
|-----------|---------------|

Arm description:

Conditioning regiment rituximab + ZBEAM followed by ASCT

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

Dosage and administration details:

250 mg/m² administered at D-21 and D-14 before ASCT

| | |
|--|---|
| Investigational medicinal product name | 90Y ibritumomab tiuxetan |
| Investigational medicinal product code | |
| Other name | Zevalin |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

0,4 mCi/kg administered at D-14 before ASCT

| | |
|--|---|
| Investigational medicinal product name | Carmustine |
| Investigational medicinal product code | |
| Other name | BCNU |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

300 mg/m² administered at D-6 before ASCT

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

| | |
|---|---|
| Dosage and administration details: | |
| 100 mg/m ² /12h administered from D-6 to D-3 before ASCT | |
| Investigational medicinal product name | cytarabine |
| Investigational medicinal product code | |
| Other name | aracytine |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| 200 mg/m ² /12h administered from D-6 to D-3 before ASCT | |
| Investigational medicinal product name | melphalan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| 140 mg/m ² administered at D-2 before ASCT | |

| Number of subjects in period 1 | Z-BEAM + ASCT |
|---------------------------------------|----------------------|
| Started | 75 |
| Enrollment of patient | 75 |
| Study treatment | 73 |
| ASCT | 71 |
| Completed | 71 |
| Not completed | 4 |
| No study treatment received | 2 |
| Lack of efficacy | 2 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall trial |
| Reporting group description: - | |

| Reporting group values | Overall trial | Total | |
|--|---------------|-------|--|
| Number of subjects | 75 | 75 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 49 | | |
| full range (min-max) | 19 to 64 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 43 | 43 | |
| Male | 32 | 32 | |
| Performance status (ECOG) at baseline | | | |
| Units: Subjects | | | |
| 00 | 24 | 24 | |
| 01 | 27 | 27 | |
| 02 | 16 | 16 | |
| 03 | 7 | 7 | |
| 04 | 1 | 1 | |
| Age | | | |
| Units: Subjects | | | |
| <= 60 | 68 | 68 | |
| > 60 | 7 | 7 | |
| Ann Arbor Stage | | | |
| Units: Subjects | | | |
| Stage 1 | 1 | 1 | |
| Stage 2 | 4 | 4 | |
| Stage 3 | 12 | 12 | |
| Stage 4 | 58 | 58 | |
| B symptoms | | | |
| Units: Subjects | | | |
| No | 35 | 35 | |

| | | | |
|---|----|----|--|
| Yes | 40 | 40 | |
| LDH | | | |
| Units: Subjects | | | |
| <= 1N | 7 | 7 | |
| > 1N | 68 | 68 | |
| Age-adjusted IPI | | | |
| Units: Subjects | | | |
| 00 | 0 | 0 | |
| 01 | 5 | 5 | |
| 02 | 53 | 53 | |
| 03 | 17 | 17 | |
| Number of extranodal sites involved | | | |
| Units: Subjects | | | |
| <= 1 | 31 | 31 | |
| >1 | 44 | 44 | |
| IPI | | | |
| Units: Subjects | | | |
| 01 | 1 | 1 | |
| 02 | 27 | 27 | |
| 03 | 31 | 31 | |
| 04 | 15 | 15 | |
| 05 | 1 | 1 | |
| Bone Marrow biopsy at diagnosis | | | |
| Units: Subjects | | | |
| Not involved | 56 | 56 | |
| Involved | 15 | 15 | |
| Not done | 4 | 4 | |
| PET Scan at diagnosis | | | |
| Units: Subjects | | | |
| Positive | 53 | 53 | |
| Not done | 22 | 22 | |
| Performance Status (ECOG) at registration | | | |
| Units: Subjects | | | |
| 00 | 50 | 50 | |
| 01 | 24 | 24 | |
| 02 | 1 | 1 | |
| Response after induction treatment | | | |
| Units: Subjects | | | |
| COMPLETE RESPONSE | 30 | 30 | |
| UNCONFIRMED COMPLETE RESPONSE | 33 | 33 | |
| PARTIAL RESPONSE | 12 | 12 | |
| Bone marrow biopsy after induction | | | |
| Units: Subjects | | | |
| Not involved | 25 | 25 | |
| Not done | 50 | 50 | |
| PET scan after induction | | | |
| Units: Subjects | | | |
| Negative | 54 | 54 | |
| Positive | 21 | 21 | |
| Induction treatment - type of | | | |

| | | | |
|--|--------------|----|--|
| chemotherapy | | | |
| Units: Subjects | | | |
| R-CHOP like | 36 | 36 | |
| R-ACVBP like | 39 | 39 | |
| Weight | | | |
| Units: kg | | | |
| median | 63 | | |
| full range (min-max) | 45 to 100 | - | |
| Height | | | |
| Units: cm | | | |
| median | 170 | | |
| full range (min-max) | 140 to 195 | - | |
| Body area | | | |
| Units: m ² | | | |
| median | 1.74 | | |
| full range (min-max) | 1.44 to 2.29 | - | |
| Number of extranodal sites at diagnosis | | | |
| Units: number | | | |
| median | 2 | | |
| full range (min-max) | 0 to 9 | - | |
| Number of sites used for response evaluation at diagnosis | | | |
| Units: number | | | |
| median | 2 | | |
| full range (min-max) | 1 to 6 | - | |
| Number of sites used for response evaluation at registration | | | |
| Units: number | | | |
| median | 2 | | |
| full range (min-max) | 1 to 6 | - | |

End points

End points reporting groups

| | |
|--|------------------------------|
| Reporting group title | Z-BEAM + ASCT |
| Reporting group description: | |
| Conditioning regiment rituximab + ZBEAM followed by ASCT | |
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| The safety population comprises all patients registered and having received the dose of study treatment (Zevalin). | |
| Subject analysis set title | Patient with transplantation |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All patients registered and having received ZBEAM and transplantation. | |

Primary: Event Free survival from ASCT

| | |
|--|--|
| End point title | Event Free survival from ASCT ^[1] |
| End point description: | |
| Event free survival (EFS) at 2 years: events being death from any cause, relapse for complete responders and unconfirmed complete responders, progression during and after treatment and changes of therapy. | |
| Event-Free survival is measured both from date of inclusion and from date of transplantation to date of first event. | |
| End point type | Primary |
| End point timeframe: | |
| 24 months after ASCT | |
| Notes: | |
| [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. | |
| Justification: Since there is only one treatment arm, it is not possible to indicate comparative statistical analysis as required by EudraCT system. | |

| End point values | Patient with transplantation | | | |
|---------------------------------|------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 71 | | | |
| Units: percent | | | | |
| number (confidence interval 5%) | 78.8 (67.4 to 86.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate

| | |
|---|-----------------------|
| End point title | Overall Response Rate |
| End point description: | |
| Overall response rate (ORR) (complete response CR and partial response PR) at day 100 after ASCT. | |
| Overall response rate (ORR) will be defined as defined according to Cheson 1999 criteria. | |
| Patients without response assessment are considered as non-responder. | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Overall Response rate at D100 after ASCT or at withdrawal. | |

| End point values | Safety population | | | |
|---------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 73 | | | |
| Units: percent | | | | |
| number (confidence interval 5%) | 83.6 (73 to 91.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

| | |
|--|------------------|
| End point title | Overall survival |
| End point description: | |
| Overall survival is measured from the date of inclusion or from evaluation at month 3 post-transplant to the date of death, irrespective of the cause. Patients who have not died at the time of analysis will be censored at the most recent date they were known to be alive or at the stopping date if the most recent date is later. | |
| End point type | Secondary |
| End point timeframe: | |
| Overall survival 24 months after ASCT. | |

| End point values | Patient with transplantation | | | |
|---------------------------------|------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 71 | | | |
| Units: percent | | | | |
| number (confidence interval 5%) | 83.1 (72.1 to 90) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) occurring during the treatment period will be recorded until 100 days after the end of the last dose of treatment

Adverse event reporting additional description:

Due to the expected toxicity of these treatments, only grade 3,4 and 5 toxicities (Common Terminology Criteria for Adverse Events (CTCAE) v3.0) or grade 2 for infections, and toxicities (grade 1 to 5) related to a Serious Adverse Event, must be reported as "Adverse Event".

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 10.0 |

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Safety population |
|-----------------------|-------------------|

Reporting group description:

The safety population comprises all patients registered and having received the dose of study treatment (Zevalin).

| Serious adverse events | Safety population | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 73 (24.66%) | | |
| number of deaths (all causes) | 14 | | |
| number of deaths resulting from adverse events | 1 | | |
| Cardiac disorders | | | |
| Myopericarditis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|----------------|--|--|
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Lung disorder | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |

| | | | | |
|---|----------------|--|--|--|
| Septic shock | | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Arthritis bacterial | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes virus infection | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes oesophagitis | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis fungal | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchopulmonary aspergillosis | | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders | | | | |

| | | | |
|---|----------------|--|--|
| Dehydration | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Safety population | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 68 / 73 (93.15%) | | |
| General disorders and administration site conditions | | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 35 / 73 (47.95%) | | |
| occurrences (all) | 35 | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences (all) | 3 | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Lung disorder | | | |
| subjects affected / exposed | 4 / 73 (5.48%) | | |
| occurrences (all) | 4 | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Psychiatric disorders | | | |

| | | | |
|--|---|--|--|
| Depression subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | | |
| Investigations Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) Liver function test abnormal subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 73 (2.74%) 2 1 / 73 (1.37%) 1 1 / 73 (1.37%) 1 | | |
| Cardiac disorders Myopericarditis subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | | |
| Blood and lymphatic system disorders Febrile neutropenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) | 39 / 73 (53.42%) 39 1 / 73 (1.37%) 1 1 / 73 (1.37%) 1 1 / 73 (1.37%) 1 | | |
| Eye disorders Keratitis subjects affected / exposed occurrences (all) Diplopia | 1 / 73 (1.37%) 1 | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 73 (6.85%) | | |
| occurrences (all) | 5 | | |
| Anal inflammation | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| renal failure acute | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 8 / 73 (10.96%) | | |
| occurrences (all) | 8 | | |
| Neutropenic infection | | | |

| | | | |
|-------------------------------------|----------------|--|--|
| subjects affected / exposed | 5 / 73 (6.85%) | | |
| occurrences (all) | 5 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 5 / 73 (6.85%) | | |
| occurrences (all) | 5 | | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 4 / 73 (5.48%) | | |
| occurrences (all) | 4 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences (all) | 3 | | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences (all) | 3 | | |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences (all) | 3 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 3 / 73 (4.11%) | | |
| occurrences (all) | 3 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Escherichia infection | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Bronchitis | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Herpes oesophagitis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Cystitis | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Enterococcal infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Genital infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Oral fungal infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Klebsiella infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Proteus infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Herpes virus infection | | | |

| | | | |
|----------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Enterocolitis fungal | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Candidiasis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Bacteremia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Fungal infection | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 73 (1.37%) 1 | | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 73 (2.74%) | | |
| occurrences (all) | 2 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 73 (1.37%) | | |
| occurrences (all) | 1 | | |

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

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25072780>