



Clinical trial results: A Multicenter, Open-Label Trial of Belinostat in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2008-005843-40 |
| Trial protocol | DK FR IT NL BE DE ES HU SK PL GB |
| Global end of trial date | 27 October 2014 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 27 January 2017 |
| First version publication date | 11 November 2016 |
| Version creation reason | <ul style="list-style-type: none">• Changes to summary attachments Replacing draft results provided in attachments (Study report and Investigator's Brochure) by final consolidated results (Full Data Set). Deleting the investigator's brochure and study report attachments from version 1. |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | PXD101-CLN-19 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00865969 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Spectrum Pharmaceuticals |
| Sponsor organisation address | 157 Technology Drive, Irvine, United States, 92618 |
| Public contact | Clinical Operations, Spectrum Pharmaceuticals, clinicaltrialinquiries@sppirx.com |
| Scientific contact | Clinical Operations, Spectrum Pharmaceuticals, clinicaltrialinquiries@sppirx.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 | 13 December 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 October 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the objective response rate in patients with peripheral T cell lymphoma who are treated with belinostat monotherapy.

Protection of trial subjects:

Informed Consent Form was used to ensure all participation is voluntary and study subjects are aware of their right, including personal health information privacy. Clinical monitoring visits were conducted throughout the life of study to ensure study patient safety are continuously monitored and protected. The assigned medical monitor also reviewed the data on frequent basis to ensure that all safety data are adequately monitored and issues addressed timely.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 December 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Netherlands: 10 |
| Country: Number of subjects enrolled | Israel: 4 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | United States: 37 |
| Country: Number of subjects enrolled | Croatia: 4 |
| Country: Number of subjects enrolled | South Africa: 3 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Slovakia: 2 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Belgium: 11 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Germany: 16 |
| Country: Number of subjects enrolled | Hungary: 11 |
| Country: Number of subjects enrolled | Italy: 3 |
| Worldwide total number of subjects | 129 |
| EEA total number of subjects | 78 |

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) | 67 |
| From 65 to 84 years | 62 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with relapsed or refractory T-Cell lymphoma must sign consent and meet all Inclusion/Exclusion criteria

Period 1

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

Arms

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

Dosage and administration details:

1000 mg/m² of Belinostat administered as a 30 minutes IV infusion on days 1-5 of every 3-week cycle

| Number of subjects in period 1 | Belinostat |
|---------------------------------------|------------|
| Started | 129 |
| Completed | 129 |

Baseline characteristics

Reporting groups

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

| Reporting group values | Overall Trial | Total | |
|---|---------------|-------|--|
| Number of subjects | 129 | 129 | |
| 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 | 63 | | |
| full range (min-max) | 29 to 81 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 60 | 60 | |
| Male | 69 | 69 | |
| Disease Stage at Entry | | | |
| Units: Subjects | | | |
| Stage IA | 6 | 6 | |
| Stage IIA | 8 | 8 | |
| Stage IIIA | 26 | 26 | |
| Stage IVA | 38 | 38 | |
| Stage IIB | 4 | 4 | |
| Stage IIIB | 19 | 19 | |
| Stage IVB | 26 | 26 | |
| Unknown | 2 | 2 | |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 167.6 | | |
| standard deviation | ± 10.1 | - | |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 74.9 | | |
| standard deviation | ± 18.6 | - | |

End points

End points reporting groups

| | |
|--------------------------------|------------|
| Reporting group title | Belinostat |
| Reporting group description: - | |

Primary: Objective Response Rate

| | |
|-----------------|--|
| End point title | Objective Response Rate ^[1] |
|-----------------|--|

End point description:

Overall study duration from first dose until 2 years after the first dose. Objective response rate was defined as the percentage of patients with a complete response or a partial response according to IWG criteria. Response was assessed on the basis of clinical and radiological criteria. In addition to the primary analysis of response by central radiographic and clinical review by the IRC, the response assessment was also determined by the local Investigators. As pre-defined, the primary endpoint analysis for this study was based on the IRC assessment of response.

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

End point timeframe:

24 months

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: Descriptive statistics for these endpoints

| End point values | Belinostat | | | |
|----------------------------------|---------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[2] | | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 25.8 (18.3 to 34.6) | | | |

Notes:

[2] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

| | |
|-----------------|------------------|
| End point title | Time to Response |
|-----------------|------------------|

End point description:

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

End point timeframe:

24 months

| | | | | |
|-------------------------------|--------------------|--|--|--|
| End point values | Belinostat | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[3] | | | |
| Units: Weeks | | | | |
| median (full range (min-max)) | 5.6 (4.3 to 50.4) | | | |

Notes:

[3] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

| | |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

The Duration of Response was assessed by IWG criteria per the IRC and estimated by the Kaplan-Meier method. The median Duration of Response for the Efficacy Analysis Dataset, was assessed by IRC using IWG criteria and based on 31 responding patients.

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

End point timeframe:

24 months

| | | | | |
|----------------------------------|--------------------|--|--|--|
| End point values | Belinostat | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[4] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 13.6 (4.5 to 29.4) | | | |

Notes:

[4] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

| | |
|-----------------|---------------------|
| End point title | Time to Progression |
|-----------------|---------------------|

End point description:

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

End point timeframe:

24 months

| | | | | |
|----------------------------------|--------------------|--|--|--|
| End point values | Belinostat | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[5] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2 (1.5 to 2.8) | | | |

Notes:

[5] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

| | |
|-----------------|---------------------------|
| End point title | Progression Free Survival |
|-----------------|---------------------------|

End point description:

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

End point timeframe:

24 months

| | | | | |
|----------------------------------|--------------------|--|--|--|
| End point values | Belinostat | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[6] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 1.6 (1.4 to 2.7) | | | |

Notes:

[6] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

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

End point description:

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

End point timeframe:

24 months

| | | | | |
|----------------------------------|--------------------|--|--|--|
| End point values | Belinostat | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 ^[7] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 7.9 (6.1 to 13.9) | | | |

Notes:

[7] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

25 months. Patients must be carefully monitored for all adverse events that occur from the time Informed Consent is obtained until 30 days after the last study drug administration.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

Reporting groups

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|-----------------------|-------------------------|
| Reporting group title | Full Patient Population |
|-----------------------|-------------------------|

Reporting group description:

Overall description of adverse events in CLN-19 trial.

| Serious adverse events | Full Patient Population | | |
|---|-------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 61 / 129 (47.29%) | | |
| number of deaths (all causes) | 14 | | |
| number of deaths resulting from adverse events | 14 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour associated fever | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 2 / 129 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Extremity necrosis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Iliac artery occlusion | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shock | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vasculitis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Central venous catheterisation | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 129 (4.65%) | | |
| occurrences causally related to treatment / all | 4 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Multi-organ disorder | | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 3 | | | |
| Fatigue | | | | |
| subjects affected / exposed | 2 / 129 (1.55%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthenia | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chills | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disease progression | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Euthanasia | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| General physical health deterioration | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malaise | | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain | | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alveolitis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chylothorax | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| hypoxia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |

| | | | |
|---|-----------------|--|--|
| Anxiety | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Impaired self-care | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Injury, poisoning and procedural complications | | | |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple fractures | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 129 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 129 (1.55%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Splenomegaly | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Toxic cataract | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Hepatobiliary disorders | | | |

| | | | |
|---|-----------------|--|--|
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain of skin | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthralgia | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 10 / 129 (7.75%) | | |
| occurrences causally related to treatment / all | 2 / 10 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Infection | | | |
| subjects affected / exposed | 4 / 129 (3.10%) | | |
| occurrences causally related to treatment / all | 2 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 129 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 129 (1.55%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumopathy | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related infection | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocarditis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal fungal infection | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infection | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 2 / 129 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decreased appetite | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 129 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Full Patient Population | | |
|---|-------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 125 / 129 (96.90%) | | |
| Investigations | | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 20 / 129 (15.50%) | | |
| occurrences (all) | 45 | | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 15 / 129 (11.63%) | | |
| occurrences (all) | 46 | | |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|-------------------------|--|--|
| subjects affected / exposed occurrences (all) | 11 / 129 (8.53%) 20 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 29 | | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 16 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 16 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 8 | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 12 | | |
| Vascular disorders | | | |
| Hypotension subjects affected / exposed occurrences (all) | 13 / 129 (10.08%) 26 | | |
| Phlebitis subjects affected / exposed occurrences (all) | 12 / 129 (9.30%) 23 | | |
| Flushing subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 11 | | |
| Hypertension subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 8 | | |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 19 / 129 (14.73%) 20 | | |
| Dizziness | | | |

| | | | |
|---|--------------------------|--|--|
| subjects affected / exposed occurrences (all) | 13 / 129 (10.08%) 26 | | |
| Neuropathy peripheral subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 9 | | |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 47 / 129 (36.43%) 76 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 45 / 129 (34.88%) 98 | | |
| Oedema Peripheral subjects affected / exposed occurrences (all) | 27 / 129 (20.93%) 34 | | |
| Chills subjects affected / exposed occurrences (all) | 21 / 129 (16.28%) 23 | | |
| Infusion site pain subjects affected / exposed occurrences (all) | 18 / 129 (13.95%) 31 | | |
| Asthenia subjects affected / exposed occurrences (all) | 12 / 129 (9.30%) 14 | | |
| Pain subjects affected / exposed occurrences (all) | 12 / 129 (9.30%) 12 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 41 / 129 (31.78%) 132 | | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 21 / 129 (16.28%) 73 | | |
| Leukopenia | | | |

| | | | |
|--|--------------------------|--|--|
| subjects affected / exposed occurrences (all) | 13 / 129 (10.08%) 36 | | |
| Neutropenia subjects affected / exposed occurrences (all) | 13 / 129 (10.08%) 39 | | |
| Lymphopenia subjects affected / exposed occurrences (all) | 11 / 129 (8.53%) 91 | | |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 55 / 129 (42.64%) 130 | | |
| Vomiting subjects affected / exposed occurrences (all) | 37 / 129 (28.68%) 95 | | |
| Constipation subjects affected / exposed occurrences (all) | 29 / 129 (22.48%) 37 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 28 / 129 (21.71%) 44 | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 14 / 129 (10.85%) 17 | | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 9 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea subjects affected / exposed occurrences (all) | 29 / 129 (22.48%) 34 | | |
| Cough subjects affected / exposed occurrences (all) | 25 / 129 (19.38%) 27 | | |
| Oropharyngeal pain | | | |

| | | | |
|--|-------------------------|--|--|
| subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 10 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 26 / 129 (20.16%) 36 | | |
| Pruritus | | | |
| subjects affected / exposed occurrences (all) | 21 / 129 (16.28%) 39 | | |
| Night sweats | | | |
| subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 11 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 8 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 11 | | |
| Anxiety | | | |
| subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 8 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed occurrences (all) | 11 / 129 (8.53%) 20 | | |
| Muscle spasms | | | |
| subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 13 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed occurrences (all) | 10 / 129 (7.75%) 12 | | |
| Bronchitis | | | |
| subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 15 | | |

| | | | |
|--|-------------------------|--|--|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 8 | | |
| Sinusitis subjects affected / exposed occurrences (all) | 7 / 129 (5.43%) 8 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 19 / 129 (14.73%) 23 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 17 / 129 (13.18%) 45 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 12 / 129 (9.30%) 36 | | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 10 / 129 (7.75%) 16 | | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 9 / 129 (6.98%) 18 | | |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 8 / 129 (6.20%) 37 | | |

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