



Clinical trial results:

Autologous-Allogeneic Tandem Stem Cell Transplantation and Maintenance Therapy with Thalidomide / DLI for patients with Multiple Myeloma (MM) and age ≤ 60 years: A phase II-study

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-004928-21 |
| Trial protocol | DE |
| Global end of trial date | 17 April 2018 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 22 October 2022 |
| First version publication date | 22 October 2022 |
| Summary attachment (see zip file) | Auto-Allo TSCT in MM_Integrated Study Report - Synopsis V1.0 2020-04-07, signed (Auto-Allo TSCT in MM_Integrated Study Report - Synopsis V1.0 2020-04-07, signed.pdf) |

Trial information

Trial identification

| | |
|-----------------------|----------------------|
| Sponsor protocol code | Auto-Allo-TSCT in MM |
|-----------------------|----------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00777998 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Department of Stem Cell Transplantation, University Medical Center Hamburg-Eppendorf |
| Sponsor organisation address | Martinistrasse 52, Hamburg, Germany, 20246 |
| Public contact | Coordinating Principal Investigator, Prof. Dr. Nicolaus Kröger, Department of Stem Cell Transplantation, University Medical Center Eppendorf, +49 40741054850, nkroeger@uke.uni-hamburg.de |
| Scientific contact | Coordinating Principal Investigator, Prof. Dr. Nicolaus Kröger, Department of Stem Cell Transplantation, University Medical Center Eppendorf, +49 40741054850, nkroeger@uke.uni-hamburg.de |

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 | 15 April 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 April 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Event-free survival four years after auto-allo tandem-transplantation and maintenance therapy with thalidomide in comparison to those patients without a suitable donor, who will receive tandem autologous stem cell transplantation followed by thalidomide maintenance therapy.

Any of the following occurrences will be considered an endpoint event:

- recurrence or progression of the primary disease,
- disease related mortality, or
- treatment related mortality.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, the general principles indicated in the Declaration of Helsinki, and all applicable regulatory requirements. Prior to study initiation the study protocol was reviewed and approved by an Independent Ethics Committee (IEC). The study, all study procedures and the risks and benefits were explained to the subjects by responsible and authorized investigators and written informed consent were collected prior to any study related examinations. The patients were assured maximum confidentiality of their data. The information was guided by the Patient Information Form and the Declaration of Consent provided in German language. The patients were to be given sufficient time for decision-making. Patient's participation in the study was entirely voluntary and could be revoked at any time without having to specify a reason and without adversely affecting their further therapy.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 25 August 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Germany: 217 |
| Worldwide total number of subjects | 217 |
| EEA total number of subjects | 217 |

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) | 217 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was performed in 20 active hospital sites in Germany (3 additional centers participated but did not enroll any patients).

Recruitment period: May 2008 - May 2013

Pre-assignment

Screening details:

Inclusion: myeloma stage II or III according to Salmon and Durie, age between 18 and 60 years, and a maximum of 8 cycles chemotherapy prior to registration independently of the response

Exclusion: more than 8 cycles chemotherapy, severe irreversible renal, hepatic, pulmonary, or cardiac diseases, positive serology for HIV, and prior transplant

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 178 ^[1] |
| Number of subjects completed | 178 |

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Enrolled were total of 217 patients before first autologous transplant. Before first autograft, 3 patients died, 1 experienced screening failure, 4 patients were excluded due to patient or investigator decision, and 1 patient because of missing data.

Period 1

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

Arms

| | |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm 1 |

Arm description:

Tandem autologous

| | |
|--|-------------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Autologous hematopoietic stem cells |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Infusion |

Dosage and administration details:

Infusion of autologous hematopoietic stem cells, dosage depends of amount of cells collected from the patient

| | |
|------------------|-------|
| Arm title | Arm 2 |
|------------------|-------|

Arm description:

tandem autologous-allogeneic

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|-------------------------------------|
| Investigational medicinal product name | Allogeneic hematopoietic stem cells |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Infusion |

Dosage and administration details:

Infusion of allogeneic hematopoietic stem cells, dosage depends on amount of donated stem cells

| Number of subjects in period 1^[2] | Arm 1 | Arm 2 |
|---|-------|-------|
| Started | 46 | 132 |
| Completed | 46 | 132 |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: From 217 initially included patients 208 received first autograft, of whom then 132 received second allogeneic transplant and 46 a second autograft. Before second transplant, 30 patients withdrew, of whom 3 died, 5 withdrew from consent, 4 had progressive disease, 12 re excluded due to patient or investigator decision, 2 were lost to follow-up, and 4 patients were excluded due to unknown reasons.

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Arm 1 |
|-----------------------|-------|

Reporting group description:

Tandem autologous

| | |
|-----------------------|-------|
| Reporting group title | Arm 2 |
|-----------------------|-------|

Reporting group description:

tandem autologous-allogeneic

| Reporting group values | Arm 1 | Arm 2 | Total |
|---|----------|----------|-------|
| Number of subjects | 46 | 132 | 178 |
| 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 | 53 | 51 | |
| full range (min-max) | 34 to 61 | 26 to 61 | - |
| Gender categorical Units: Subjects | | | |
| Female | 19 | 74 | 93 |
| Male | 27 | 58 | 85 |

End points

End points reporting groups

| | |
|--|---------------|
| Reporting group title | Arm 1 |
| Reporting group description: | |
| Tandem autologous | |
| Reporting group title | Arm 2 |
| Reporting group description: | |
| tandem autologous-allogeneic | |
| Subject analysis set title | Full analysis |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The Full Analysis data set (FAS) include all patients who were included in the safety analysis. However, a blinded analysis meeting was authorized to decide whether any study participants had to be excluded from the FAS in cases of very severe protocol violations that prevented a valid assessment of treatment efficacy. | |

Primary: Progression-free survival

| | |
|------------------------|---------------------------|
| End point title | Progression-free survival |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| 4-years | |

| End point values | Arm 1 | Arm 2 | Full analysis | |
|----------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 46 | 132 | 0 ^[1] | |
| Units: year | | | | |
| number (confidence interval 95%) | 35 (21 to 49) | 47 (38 to 55) | (to) | |

Notes:

[1] - only results for comparators reported

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | PFS |
| Comparison groups | Arm 1 v Arm 2 |
| Number of subjects included in analysis | 178 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.26 |
| Method | Logrank |
| Parameter estimate | Median difference (final values) |
| Point estimate | 12 |

| | |
|----------------------|--------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6 |
| upper limit | 17 |
| Variability estimate | Standard deviation |
| Dispersion value | 6 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from the time of informed consent until end of study.

Only SAEs that were observed in at least three patients are shown in this report.

Adverse event reporting additional description:

A total of 12 SAEs reported by 12 patients in the Auto-Allo group (12.0% of 100 who received thalidomide after the second SCT) and four SAEs reported by three patients in the Auto-Auto group (7.9% of 28 who received thalidomide) were assessed to be potentially related to thalidomide by the local investigators.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18 |

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | Auto-Allo TCST group |
|-----------------------|----------------------|

Reporting group description: -

| | |
|-----------------------|----------------------|
| Reporting group title | Auto-Auto TSCT group |
|-----------------------|----------------------|

Reporting group description: -

| Serious adverse events | Auto-Allo TCST group | Auto-Auto TSCT group | |
|---|---|----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 103 / 132 (78.03%) | 32 / 46 (69.57%) | |
| number of deaths (all causes) | 45 | 15 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Recurrence or persistence of primary disease | Additional description: Plasma Cell Myeloma | | |
| subjects affected / exposed | 17 / 132 (12.88%) | 8 / 46 (17.39%) | |
| occurrences causally related to treatment / all | 0 / 17 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 12 | 0 / 8 | |
| Surgical and medical procedures | | | |
| Surgery | | | |
| subjects affected / exposed | 2 / 132 (1.52%) | 2 / 46 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |

| | | | |
|--|-------------------|----------------|--|
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 5 / 132 (3.79%) | 2 / 46 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 132 (3.79%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 24 / 132 (18.18%) | 3 / 46 (6.52%) | |
| occurrences causally related to treatment / all | 0 / 26 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 132 (1.52%) | 2 / 46 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Graft versus host disease | | | |
| subjects affected / exposed | 10 / 132 (7.58%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 10 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 7 | 0 / 0 | |
| Graft versus host disease in gastrointestinal tract | | | |

| | | | |
|--|------------------|----------------|--|
| subjects affected / exposed | 4 / 132 (3.03%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 132 (7.58%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 132 (0.76%) | 2 / 46 (4.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteolysis | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 9 / 132 (6.82%) | 4 / 46 (8.70%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 8 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 12 / 132 (9.09%) | 8 / 46 (17.39%) | |
| occurrences causally related to treatment / all | 0 / 16 | 1 / 8 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 9 / 132 (6.82%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 8 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 4 / 132 (3.03%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 0 / 46 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 4 / 132 (3.03%) | 1 / 46 (2.17%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 2 / 132 (1.52%) | 1 / 46 (2.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 132 (1.52%) | 1 / 46 (2.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Auto-Allo TCST group | Auto-Auto TSCT group | |
|---|--|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 130 / 132 (98.48%) | 46 / 46 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Plasma cell myeloma | Additional description: Recurrence or persistence of primary disease | | |
| subjects affected / exposed | 26 / 132 (19.70%) | 9 / 46 (19.57%) | |
| occurrences (all) | 28 | 11 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 17 / 132 (12.88%) | 2 / 46 (4.35%) | |
| occurrences (all) | 28 | 2 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 13 / 132 (9.85%) | 6 / 46 (13.04%) | |
| occurrences (all) | 16 | 8 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 47 / 132 (35.61%) | 25 / 46 (54.35%) | |
| occurrences (all) | 68 | 35 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 19 / 132 (14.39%) | 6 / 46 (13.04%) | |
| occurrences (all) | 29 | 6 | |
| Pyrexia | | | |
| subjects affected / exposed | 49 / 132 (37.12%) | 15 / 46 (32.61%) | |
| occurrences (all) | 78 | 17 | |
| Pain | | | |

| | | | |
|---|-------------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 5 / 132 (3.79%) 5 | 3 / 46 (6.52%) 3 | |
| Immune system disorders | | | |
| Graft versus host disease subjects affected / exposed occurrences (all) | 9 / 132 (6.82%) 10 | 1 / 46 (2.17%) 1 | |
| Hypersensitivity subjects affected / exposed occurrences (all) | 7 / 132 (5.30%) 7 | 1 / 46 (2.17%) 1 | |
| Graft versus host disease in skin subjects affected / exposed occurrences (all) | 11 / 132 (8.33%) 12 | 0 / 46 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 14 / 132 (10.61%) 16 | 1 / 46 (2.17%) 1 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 9 / 132 (6.82%) 11 | 1 / 46 (2.17%) 1 | |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 4 / 132 (3.03%) 5 | 3 / 46 (6.52%) 3 | |
| Psychiatric disorders | | | |
| Insomnia subjects affected / exposed occurrences (all) | 8 / 132 (6.06%) 9 | 2 / 46 (4.35%) 2 | |
| Investigations | | | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 13 / 132 (9.85%) 14 | 0 / 46 (0.00%) 0 | |
| Blood potassium decreased subjects affected / exposed occurrences (all) | 3 / 132 (2.27%) 5 | 3 / 46 (6.52%) 3 | |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 5 / 132 (3.79%) 6 | 4 / 46 (8.70%) 4 | |

| | | | |
|--------------------------------------|-------------------|------------------|--|
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 9 / 132 (6.82%) | 1 / 46 (2.17%) | |
| occurrences (all) | 11 | 1 | |
| Weight increased | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 3 / 46 (6.52%) | |
| occurrences (all) | 4 | 3 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 3 / 46 (6.52%) | |
| occurrences (all) | 4 | 3 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 23 / 132 (17.42%) | 7 / 46 (15.22%) | |
| occurrences (all) | 25 | 9 | |
| Paraesthesia | | | |
| subjects affected / exposed | 7 / 132 (5.30%) | 4 / 46 (8.70%) | |
| occurrences (all) | 12 | 5 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 9 / 132 (6.82%) | 5 / 46 (10.87%) | |
| occurrences (all) | 10 | 6 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 36 / 132 (27.27%) | 13 / 46 (28.26%) | |
| occurrences (all) | 54 | 22 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 4 / 46 (8.70%) | |
| occurrences (all) | 3 | 4 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 2 / 132 (1.52%) | 4 / 46 (8.70%) | |
| occurrences (all) | 2 | 4 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 17 / 132 (12.88%) | 3 / 46 (6.52%) | |
| occurrences (all) | 25 | 6 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 30 / 132 (22.73%) | 12 / 46 (26.09%) | |
| occurrences (all) | 45 | 20 | |

| | | | |
|-----------------------------|-------------------|------------------|--|
| Neutropenia | | | |
| subjects affected / exposed | 12 / 132 (9.09%) | 2 / 46 (4.35%) | |
| occurrences (all) | 16 | 2 | |
| Pancytopenia | | | |
| subjects affected / exposed | 7 / 132 (5.30%) | 0 / 46 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 17 / 132 (12.88%) | 6 / 46 (13.04%) | |
| occurrences (all) | 24 | 8 | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 19 / 132 (14.39%) | 11 / 46 (23.91%) | |
| occurrences (all) | 29 | 18 | |
| Leukopenia | | | |
| subjects affected / exposed | 6 / 132 (4.55%) | 4 / 46 (8.70%) | |
| occurrences (all) | 6 | 7 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 13 / 132 (9.85%) | 4 / 46 (8.70%) | |
| occurrences (all) | 15 | 6 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 8 / 132 (6.06%) | 2 / 46 (4.35%) | |
| occurrences (all) | 8 | 2 | |
| Constipation | | | |
| subjects affected / exposed | 16 / 132 (12.12%) | 14 / 46 (30.43%) | |
| occurrences (all) | 21 | 16 | |
| Diarrhoea | | | |
| subjects affected / exposed | 55 / 132 (41.67%) | 25 / 46 (54.35%) | |
| occurrences (all) | 80 | 34 | |
| Gastritis | | | |
| subjects affected / exposed | 7 / 132 (5.30%) | 3 / 46 (6.52%) | |
| occurrences (all) | 7 | 3 | |
| Nausea | | | |
| subjects affected / exposed | 26 / 132 (19.70%) | 5 / 46 (10.87%) | |
| occurrences (all) | 35 | 7 | |
| Stomatitis | | | |

| | | | |
|---|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 8 / 132 (6.06%) 9 | 1 / 46 (2.17%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 9 / 132 (6.82%) 14 | 3 / 46 (6.52%) 4 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema subjects affected / exposed occurrences (all) | 7 / 132 (5.30%) 8 | 4 / 46 (8.70%) 6 | |
| Pruritus subjects affected / exposed occurrences (all) | 7 / 132 (5.30%) 8 | 1 / 46 (2.17%) 1 | |
| Rash subjects affected / exposed occurrences (all) | 28 / 132 (21.21%) 42 | 12 / 46 (26.09%) 17 | |
| Drug eruption subjects affected / exposed occurrences (all) | 0 / 132 (0.00%) 0 | 3 / 46 (6.52%) 3 | |
| Renal and urinary disorders | | | |
| Acute kidney injury subjects affected / exposed occurrences (all) | 7 / 132 (5.30%) 7 | 1 / 46 (2.17%) 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 15 / 132 (11.36%) 16 | 3 / 46 (6.52%) 3 | |
| Back pain subjects affected / exposed occurrences (all) | 15 / 132 (11.36%) 16 | 9 / 46 (19.57%) 11 | |
| Bone pain subjects affected / exposed occurrences (all) | 8 / 132 (6.06%) 8 | 2 / 46 (4.35%) 2 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 13 / 132 (9.85%) 15 | 4 / 46 (8.70%) 6 | |
| Pain in extremity | | | |

| | | | |
|------------------------------|-------------------|------------------|--|
| subjects affected / exposed | 9 / 132 (6.82%) | 5 / 46 (10.87%) | |
| occurrences (all) | 10 | 6 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 132 (0.76%) | 3 / 46 (6.52%) | |
| occurrences (all) | 1 | 3 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 15 / 132 (11.36%) | 5 / 46 (10.87%) | |
| occurrences (all) | 21 | 5 | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 28 / 132 (21.21%) | 0 / 46 (0.00%) | |
| occurrences (all) | 34 | 0 | |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 11 / 132 (8.33%) | 1 / 46 (2.17%) | |
| occurrences (all) | 13 | 1 | |
| Herpes zoster | | | |
| subjects affected / exposed | 20 / 132 (15.15%) | 6 / 46 (13.04%) | |
| occurrences (all) | 22 | 6 | |
| Infection | | | |
| subjects affected / exposed | 17 / 132 (12.88%) | 11 / 46 (23.91%) | |
| occurrences (all) | 21 | 15 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 40 / 132 (30.30%) | 9 / 46 (19.57%) | |
| occurrences (all) | 50 | 10 | |
| Pneumonia | | | |
| subjects affected / exposed | 23 / 132 (17.42%) | 15 / 46 (32.61%) | |
| occurrences (all) | 34 | 15 | |
| Sepsis | | | |
| subjects affected / exposed | 14 / 132 (10.61%) | 2 / 46 (4.35%) | |
| occurrences (all) | 15 | 2 | |
| Sinusitis | | | |
| subjects affected / exposed | 7 / 132 (5.30%) | 1 / 46 (2.17%) | |
| occurrences (all) | 7 | 1 | |
| Cystitis | | | |
| subjects affected / exposed | 5 / 132 (3.79%) | 3 / 46 (6.52%) | |
| occurrences (all) | 5 | 4 | |

| | | | |
|------------------------------------|------------------|-----------------|--|
| Oral candidiasis | | | |
| subjects affected / exposed | 6 / 132 (4.55%) | 3 / 46 (6.52%) | |
| occurrences (all) | 6 | 4 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 132 (2.27%) | 3 / 46 (6.52%) | |
| occurrences (all) | 3 | 3 | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 11 / 132 (8.33%) | 5 / 46 (10.87%) | |
| occurrences (all) | 14 | 7 | |

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