



Clinical trial results:

A Randomised, Multi-Centre, Assessor-Blinded, Active-Controlled, Parallel Group, Equivalence Phase III Study Comparing the Safety and Efficacy of USV Pegfilgrastim and Neulasta® in Breast Cancer Patients Undergoing Myelosuppressive Chemotherapy

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-000266-64 |
| Trial protocol | HU BG |
| Global end of trial date | 21 February 2017 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 08 March 2018 |
| First version publication date | 08 March 2018 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | PEGF/USV/P3/003 |
|-----------------------|-----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | USV PRIVATE LIMITED |
| Sponsor organisation address | ARVIND VITHAL GANDHI CHOWK, BSD MARG, GOVANDI, MUMBAI, India, 400088 |
| Public contact | Dr. Esmail Samiwala, USV Private Limited, Arvind Vithal Gandhi Chowk, BSD Marg, Govandi, Mumbai 400088, India, +91 22 25561197, esmail.samiwala@usv.in |
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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 | 21 February 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 February 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 February 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of USV Pegfilgrastim compared to Neulasta® with respect to the mean duration of severe neutropenia (DSN) defined as the mean number of days with Grade 4 neutropenia [absolute neutrophil count (ANC) less than $0.5 \times 10^9/L$], during Cycle 1 of the chemotherapy treatment.

Protection of trial subjects:

Before initiating this clinical study, the investigator/institution obtained the written and dated approval/favourable opinion from the appropriately constituted Institutional Review Board/Independent Ethics Committee (IRB/IEC) for the Clinical Study Protocol, Investigational Drug Brochure, written Informed Consent Form, and any other written information provided to subjects.

The study was carried out in compliance with the Clinical Study Protocol and the principles of Good Clinical Practice (GCP), as per standard operating procedures (SOP) and in accordance with the International Council for Harmonisation (ICH) ICH E6 GCP, the EU Clinical Trials Directive 2001/20/EC, the principles of the accepted version of the World Medical Association Declaration of Helsinki and/or all relevant federal regulations, as set forth in Parts 50, 56, 312, Subpart D, of Title 21 of the Code of Federal Regulations (CFR) and as per all applicable local regulatory guidelines.

Background therapy:

All eligible subjects received a maximum of 6 cycles of TAC chemotherapy (docetaxel 75 mg/m², doxorubicin 50 mg/m², cyclophosphamide 500 mg/m²) during the treatment period.

Evidence for comparator:

Selected reference product (comparator) for this study was EU-licensed Neulasta®. Neulasta® is a colourless solution intended for s.c. injection commercially available as prefilled syringes.

| | |
|---|-----------------|
| Actual start date of recruitment | 21 October 2015 |
| 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 | Romania: 15 |
| Country: Number of subjects enrolled | Bulgaria: 1 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Georgia: 133 |
| Country: Number of subjects enrolled | Serbia: 23 |
| Country: Number of subjects enrolled | Ukraine: 46 |
| Country: Number of subjects enrolled | Russian Federation: 20 |
| Worldwide total number of subjects | 248 |
| EEA total number of subjects | 26 |

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) | 216 |
| From 65 to 84 years | 32 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Total 254 subjects were enrolled (172 in USV Pegfilgrastim and 82 in Neulasta arm). Subjects were randomised in a ratio of 2:1 to receive either USV Pegfilgrastim or EU-licensed Neulasta® (active control treatment) in a country stratified manner. A total of 6 subjects, discontinued the study before receipt of first dose of IMP.

Pre-assignment

Screening details:

A total of 296 subjects from 31 centres were screened for inclusion into the study of which 42 subjects were classified as screen failures. Forty-two subjects (16.5%) were considered as screen failures.

Period 1

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

Blinding implementation details:

This was assessor blinded trial. The allocated treatment was disclosed only to the unblinded study staff. There were separate blinded and unblinded study teams in each study site. The unblinded team member(s) were responsible for the receipt, accountability, preparation, and administration of the study treatment (pegfilgrastim treatment). The assessor(s) –the principal investigator and other co-investigators participating in the subject assessments were blinded to the treatment allocation.

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | USV PEGFILGRASTIM |

Arm description:

The subjects who met eligibility criteria were randomized to one of the two arms. Subjects randomized to USV Pegfilgrastim were to receive USV Pegfilgrastim in all 6 chemotherapy cycles. Out of 248 subjects who received at least one dose of Pegfilgrastim, 166 were in USVPegfilgrastim group, 152 completed treatment period and 147 completed follow up period.

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | USV Pegfilgrastim |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

USV Pegfilgrastim is a clear colourless sterile solution supplied in a single-dose pre-filled sterile syringe, each containing 6 mg (based on protein content) of pegfilgrastim in 0.6 mL solution for subcutaneous injection. The treatment with USV Pegfilgrastim was administered by the unblinded team member on Day 2 of each chemotherapy cycle (at least 24 hour after administration of chemotherapy) and consisted of a single 6 mg subcutaneous (s.c.) injection per cycle.

| | |
|------------------|----------|
| Arm title | Neulasta |
|------------------|----------|

Arm description:

82 subjects were randomized and received at least one dose of EU-licensed Neulasta®. 78 subjects in this arm completed the treatment period and 77 subjects completed the follow up period. The treatment with Neulasta® (EU-licensed comparator) was administered by the unblinded team member on Day 2 (D2) of each chemotherapy cycle (at least 24h after administration of chemotherapy) and consisted of a single 6 mg subcutaneous (s.c.) injection per cycle.

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

| | |
|--|----------------------|
| Investigational medicinal product name | EU-licensed Neulasta |
| Investigational medicinal product code | |
| Other name | Pegfilgrastim |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

A single dose 6mg/mL pre-filled syringe of EU-licensed Neulasta® was administered for each chemotherapy cycle, as a subcutaneous injection on day 2 of each chemotherapy cycle (at least 24h after chemotherapy).

| Number of subjects in period 1 | USV PEGFILGRASTIM | Neulasta |
|---------------------------------------|----------------------|----------|
| Started | 166 | 82 |
| Completed | 147 | 77 |
| Not completed | 19 | 5 |
| Physician decision | 1 | 1 |
| Consent withdrawn by subject | 15 | 4 |
| Adverse event, non-fatal | 3 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | USV PEGFILGRASTIM |
|-----------------------|-------------------|

Reporting group description:

The subjects who met eligibility criteria were randomized to one of the two arms. Subjects randomized to USV Pegfilgrastim were to receive USV Pegfilgrastim in all 6 chemotherapy cycles. Out of 248 subjects who received at least one dose of Pegfilgrastim, 166 were in USVPegfilgrastim group, 152 completed treatment period and 147 completed follow up period.

| | |
|-----------------------|----------|
| Reporting group title | Neulasta |
|-----------------------|----------|

Reporting group description:

82 subjects were randomized and received at least one dose of EU-licensed Neulasta®. 78 subjects in this arm completed the treatment period and 77 subjects completed the follow up period. The treatment with Neulasta® (EU-licensed comparator) was administered by the unblinded team member on Day 2 (D2) of each chemotherapy cycle (at least 24h after administration of chemotherapy) and consisted of a single 6 mg subcutaneous (s.c.) injection per cycle.

| Reporting group values | USV PEGFILGRASTIM | Neulasta | Total |
|---|----------------------|----------|-------|
| Number of subjects | 166 | 82 | 248 |
| 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 | | | |
| Age in years | | | |
| Units: years | | | |
| arithmetic mean | 52.4 | 53.4 | |
| standard deviation | ± 11.26 | ± 11.02 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 166 | 82 | 248 |
| Male | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | USV PEGFILGRASTIM |
| Reporting group description: The subjects who met eligibility criteria were randomized to one of the two arms. Subjects randomized to USV Pegfilgrastim were to receive USV Pegfilgrastim in all 6 chemotherapy cycles. Out of 248 subjects who received at least one dose of Pegfilgrastim, 166 were in USVPegfilgrastim group, 152 completed treatment period and 147 completed follow up period. | |
| Reporting group title | Neulasta |
| Reporting group description: 82 subjects were randomized and received at least one dose of EU-licensed Neulasta®. 78 subjects in this arm completed the treatment period and 77 subjects completed the follow up period. The treatment with Neulasta® (EU-licensed comparator) was administered by the unblinded team member on Day 2 (D2) of each chemotherapy cycle (at least 24h after administration of chemotherapy) and consisted of a single 6 mg subcutaneous (s.c.) injection per cycle. | |

Primary: Mean duration of severe neutropenia (Grade 4), defined as the number of days in which the subject had an ANC < $0.5 \times 10^9/L$ during Cycle 1 of chemotherapy.

| | |
|--|--|
| End point title | Mean duration of severe neutropenia (Grade 4), defined as the number of days in which the subject had an ANC < $0.5 \times 10^9/L$ during Cycle 1 of chemotherapy. |
| End point description: The main efficacy endpoint was defined as the mean number of days of Grade 4 neutropenia (ANC below $0.5 \times 10^9/L$) during the first treatment cycle. The primary analysis of the duration of severe neutropenia in Cycle 1 consisted in testing equivalence of USV Pegfilgrastim and Neulasta®. The Least-square means (LSMeans) were estimated within a general linear model framework (using proc genmod in SAS), accounting for treatment arm, and applying a log link. LS Mean difference and 95% Confidence Interval (CI) between the two treatment arms was then back-transformed by exponentiation, resulting in a ratio of means and its 95% CI. Equivalence was concluded if the 95% CI of the ratio of means was entirely contained in the interval [0.65, 1.55]. | |
| End point type | Primary |
| End point timeframe: First Chemotherapy cycle | |

| End point values | USV PEGFILGRASTIM | Neulasta | | |
|---|-------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: LSM | | | | |
| least squares mean (standard deviation) | 1.58 (± 1.207) | 1.65 (± 1.231) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Statistical Analysis of Primary endpoint |
| Statistical analysis description: The DSN in Cycle 1 was the primary endpoint for the comparative assessment of efficacy of USV | |

Pegfilgrastim to Neulasta®. Severe neutropenia was defined as occurrence of ANC below $0.5 \times 10^9/L$. Equivalence was concluded if the 95% CI of the ratio of least-square means of DSN for the two treatment arms was entirely contained in the interval [0.65-1.55].

| | |
|---|------------------------------|
| Comparison groups | USV PEGFILGRASTIM v Neulasta |
| Number of subjects included in analysis | 248 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence ^[1] |
| Parameter estimate | LSM Ratio |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.18 |

Notes:

[1] - Equivalence was concluded if the 95% CI of the ratio of least-square means of DSN for the two treatment arms was entirely contained in the interval [0.65-1.55].

Secondary: Mean duration of severe neutropenia (DSN) during Cycles 2

| | |
|---|---|
| End point title | Mean duration of severe neutropenia (DSN) during Cycles 2 |
| End point description: | |
| Duration of Severe Neutropenia (Days) in Cycle 2-6 was analyzed. For each cycle, least square Means (95% CI) of Treatment Arms and their Ratio, Estimated within a Generalized Linear Model Accounting for the Treatment Effect (FAS) | |
| End point type | Secondary |
| End point timeframe: | |
| Cycle 2 | |

| End point values | USV PEGFILGRASTIM | Neulasta | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: LSM of Duration of severe Neutropenia | | | | |
| least squares mean (confidence interval 95%) | 0.96 (0.79 to 1.17) | 0.99 (0.76 to 1.29) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Duration of severe neutropenia Cycle 4

| | |
|--|---|
| End point title | Mean Duration of severe neutropenia Cycle 4 |
| End point description: | |
| Duration of Severe Neutropenia (Days) in Cycle 4: Least-Square Means (95% CI) of Treatment Arms and their Ratio, Estimated within a Generalized Linear Model Accounting for the Treatment Effect (FAS) | |
| End point type | Secondary |

End point timeframe:

Cycle 4

| End point values | USV PEGFILGRASTI M | Neulasta | | |
|--|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: Least Square Mean | | | | |
| least squares mean (confidence interval 95%) | 1.03 (0.84 to 1.26) | 0.98 (0.73 to 1.30) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Duration of severe neutropenia Cycle 3

| | |
|-----------------|---|
| End point title | Mean Duration of severe neutropenia Cycle 3 |
|-----------------|---|

End point description:

Duration of Severe Neutropenia (Days) in Cycle 3: Least-Square Means (95% CI) of Treatment Arms and their Ratio, Estimated within a Generalized Linear Model Accounting for the Treatment Effect (FAS)

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

End point timeframe:

Cycle 4

| End point values | USV PEGFILGRASTI M | Neulasta | | |
|--|--------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: Least Square Mean | | | | |
| least squares mean (confidence interval 95%) | 0.89 (0.73 to 1.07) | 1.01 (0.79 to 1.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean duration of severe neutropenia Cycle 5

| | |
|-----------------|---|
| End point title | Mean duration of severe neutropenia Cycle 5 |
|-----------------|---|

End point description:

Duration of Severe Neutropenia (Days) in Cycle 5: Least-Square Means (95% CI) of Treatment Arms and their Ratio, Estimated within a Generalized Linear Model Accounting for the Treatment Effect (FAS)

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 5 | |

| End point values | USV PEGFILGRASTI M | Neulasta | | |
|--|--------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: Least square Mean | | | | |
| least squares mean (confidence interval 95%) | 0.92 (0.75 to 1.12) | 1.0 (0.76 to 1.32) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean duration of severe neutropenia cycle 6

| | |
|--|---|
| End point title | Mean duration of severe neutropenia cycle 6 |
| End point description: | |
| Duration of Severe Neutropenia (Days) in Cycle 6: Least-Square Means (95% CI) of Treatment Arms and their Ratio, Estimated within a Generalized Linear Model Accounting for the Treatment Effect (FAS) | |
| End point type | Secondary |
| End point timeframe: | |
| Cycle 6 | |

| End point values | USV PEGFILGRASTI M | Neulasta | | |
|--|--------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 166 | 82 | | |
| Units: Least Square Mean | | | | |
| least squares mean (confidence interval 95%) | 1.12 (0.9 to 1.38) | 1.09 (0.81 to 1.47) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were assessed from randomization to end of study period

Adverse event reporting additional description:

Adverse events were reported by the subjects

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 18 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | USV PEGFILGRASTIM |
|-----------------------|-------------------|

Reporting group description:

The subjects who met eligibility criteria were randomized to one of the two arms. Subjects randomized to USV Pegfilgrastim were to receive USV Pegfilgrastim in all 6 chemotherapy cycles. Out of 248 subjects who received at least one dose of Pegfilgrastim, 166 were in USVPegfilgrastim group, 152 completed treatment period and 147 completed follow up period.

| | |
|-----------------------|----------|
| Reporting group title | Neulasta |
|-----------------------|----------|

Reporting group description:

82 subjects were randomized and received at least one dose of EU-licensed Neulasta®. 78 subjects in this arm completed the treatment period and 77 subjects completed the follow up period. The treatment with Neulasta® (EU-licensed comparator) was administered by the unblinded team member on Day 2 (D2) of each chemotherapy cycle (at least 24h after administration of chemotherapy) and consisted of a single 6 mg subcutaneous (s.c.) injection per cycle.

| Serious adverse events | USV PEGFILGRASTIM | Neulasta | |
|---|---|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 166 (5.42%) | 3 / 82 (3.66%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 1 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastasis to central nervous system | Additional description: Serious Adverse Event during Follow up period | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral T-cell lymphoma unspecified | Additional description: SAE during follow up period | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |

| | | | |
|--|-----------------|----------------|--|
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 166 (3.61%) | 2 / 82 (2.44%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 1 / 82 (1.22%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Infections and infestations | | | |
| Breast abscess | | | |
| subjects affected / exposed | 1 / 166 (0.60%) | 0 / 82 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | USV PEGFILGRASTIM | Neulasta | |
|---|---|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 164 / 166 (98.80%) | 82 / 82 (100.00%) | |
| Nervous system disorders | | | |
| Dizziness | Additional description: AE during treatment period | | |
| subjects affected / exposed | 36 / 166 (21.69%) | 15 / 82 (18.29%) | |
| occurrences (all) | 54 | 46 | |
| Headache | Additional description: AE during treatment period | | |
| subjects affected / exposed | 46 / 166 (27.71%) | 18 / 82 (21.95%) | |
| occurrences (all) | 80 | 25 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | Additional description: AEs in Treatment Period) | | |
| subjects affected / exposed | 15 / 166 (9.04%) | 9 / 82 (10.98%) | |
| occurrences (all) | 47 | 30 | |
| Febrile neutropenia | Additional description: AEs during treatment period | | |
| subjects affected / exposed | 9 / 166 (5.42%) | 2 / 82 (2.44%) | |
| occurrences (all) | 9 | 2 | |
| Leukocytosis | Additional description: AE during treatment period | | |
| subjects affected / exposed | 6 / 166 (3.61%) | 5 / 82 (6.10%) | |
| occurrences (all) | 34 | 28 | |
| leukopenia | Additional description: AE during treatment period | | |
| subjects affected / exposed | 74 / 166 (44.58%) | 36 / 82 (43.90%) | |
| occurrences (all) | 364 | 184 | |
| Neutropenia | Additional description: AE during treatment period | | |
| subjects affected / exposed | 130 / 166 (78.31%) | 63 / 82 (76.83%) | |
| occurrences (all) | 788 | 427 | |
| Thrombocytopenia | Additional description: AE during treatment period | | |
| subjects affected / exposed | 25 / 166 (15.06%) | 8 / 82 (9.76%) | |
| occurrences (all) | 93 | 31 | |
| General disorders and administration site conditions | | | |
| Asthenia | Additional description: AE during treatment period | | |
| subjects affected / exposed | 35 / 166 (21.08%) | 18 / 82 (21.95%) | |
| occurrences (all) | 65 | 30 | |
| Fatigue | Additional description: AE during treatment period | | |

| | | | |
|--|--|-------------------------|--|
| subjects affected / exposed occurrences (all) | 21 / 166 (12.65%) 31 | 12 / 82 (14.63%) 32 | |
| Injection site reaction | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 16 / 166 (9.64%) 72 | 8 / 82 (9.76%) 32 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 9 / 166 (5.42%) 11 | 2 / 82 (2.44%) 2 | |
| Abdominal pain upper | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 12 / 166 (7.23%) 12 | 9 / 82 (10.98%) 14 | |
| Diarrhoea | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 33 / 166 (19.88%) 38 | 20 / 82 (24.39%) 24 | |
| Nausea | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 79 / 166 (47.59%) 206 | 38 / 82 (46.34%) 158 | |
| Vomiting | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 17 / 166 (10.24%) 21 | 7 / 82 (8.54%) 11 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 62 / 166 (37.35%) 69 | 30 / 82 (36.59%) 32 | |
| Musculoskeletal and connective tissue disorders | | | |
| Bone pain | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 54 / 166 (32.53%) 473 | 27 / 82 (32.93%) 165 | |
| Spinal pain | Additional description: AE during treatment period | | |
| subjects affected / exposed occurrences (all) | 13 / 166 (7.83%) 24 | 8 / 82 (9.76%) 40 | |

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