



Clinical trial results:

A Phase III, Randomized, Multi-Centre, Open-Label, Fixed Dose, Neulasta Active-Controlled Clinical Trial of F-627 in Women with Breast Cancer Receiving Myelotoxic Chemotherapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-003553-15 |
| Trial protocol | LV HU BG |
| Global end of trial date | 18 March 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 16 February 2024 |
| First version publication date | 16 February 2024 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | GC-627-05 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03252431 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Evive Biotechnology (Shanghai) Ltd |
| Sponsor organisation address | Building 2-B, 797 Puxing HWY, Shanghai, China, 201114 |
| Public contact | GCR, Evive Biotechnology (Shanghai) Ltd, pr@evivebiotech.com |
| Scientific contact | GCR, Evive Biotechnology (Shanghai) Ltd, pr@evivebiotech.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 | 18 December 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 March 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 March 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of F-627 given as a single fixed dose (20 mg) pre-filled syringe as compared to Neulasta® standard dosing (6 mg) in the first chemotherapy cycle.

Protection of trial subjects:

This study was conducted in accordance with ICH GCP regulations/guidelines. The protocol, informed consent form and other subject information were approved by the Independent Ethics Committee / Institutional Review Board.

Background therapy:

75 mg/m² docetaxel + 600 mg/m² cyclophosphamide

Evidence for comparator:

Neulasta® standard dosing (6 mg)

| | |
|---|---------------|
| Actual start date of recruitment | 12 April 2018 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Russian Federation: 145 |
| Country: Number of subjects enrolled | Ukraine: 166 |
| Country: Number of subjects enrolled | United States: 1 |
| Country: Number of subjects enrolled | Bulgaria: 36 |
| Country: Number of subjects enrolled | Hungary: 45 |
| Worldwide total number of subjects | 393 |
| EEA total number of subjects | 81 |

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) | 332 |
| From 65 to 84 years | 61 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This study was conducted between 12 Apr 2018 and 05 Mar 2020 at 41 study sites across five countries, including Bulgaria, Hungary, Russia, Ukraine, and the United States.

Pre-assignment

Screening details:

A total of 416 subjects were screened and 393 were randomized to the study (197 randomized to F-627 and 196 randomized to Neulasta®). Overall, 373 (94.9%) subjects completed the treatment program, and 363 subjects (92.4%) who completed the 6 month follow-up.

Period 1

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

Arms

| | |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes |
| Arm title | F-627 |

Arm description:

F-627, 20mg fixed dose prefilled syringe, dosed on Day 2 of each of 4 chemotherapy cycles

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | efbemalenograstim alfa |
| Investigational medicinal product code | L03AA18 |
| Other name | Ryzneuta, F-627 |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Solution for injection , Subcutaneous use |

Dosage and administration details:

F-627, prefilled syringe administered on Day 2 of each of the 4 chemotherapy cycles

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

Arm description:

Neulasta, 6mg fixed dose prefilled syringe, dosed on Day 2 of each of the 4 chemotherapy cycles

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Neulasta (pegfilgrastim) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Subcutaneous use, Solution for injection |

Dosage and administration details:

Neulasta, 6mg fixed dose prefilled syringe, dosed by subcutaneous injection on Day 2 of each of the 4 chemotherapy cycles

| Number of subjects in period 1 | F-627 | Neulasta |
|---------------------------------------|-------|----------|
| Started | 197 | 196 |
| Completed | 186 | 187 |
| Not completed | 11 | 9 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 2 | 1 |
| Physician decision | 2 | 2 |
| Adverse event, non-fatal | 5 | 5 |
| Protocol deviation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|---|----------|
| Reporting group title | F-627 |
| Reporting group description: | |
| F-627, 20mg fixed dose prefilled syringe, dosed on Day 2 of each of 4 chemotherapy cycles | |
| Reporting group title | Neulasta |
| Reporting group description: | |
| Neulasta, 6mg fixed dose prefilled syringe, dosed on Day 2 of each of the 4 chemotherapy cycles | |

| Reporting group values | F-627 | Neulasta | Total |
|--|---------|----------|-------|
| Number of subjects | 197 | 196 | 393 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 171 | 161 | 332 |
| From 65-84 years | 26 | 35 | 61 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 51.4 | 53.4 | |
| standard deviation | ± 11.82 | ± 11.11 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 197 | 196 | 393 |
| Male | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| White | 197 | 196 | 393 |
| Black or African American | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Native Hawaiian or other Pacific Islander | 0 | 0 | 0 |
| Other | 0 | 0 | 0 |
| Reproductive Status | | | |
| Units: Subjects | | | |
| Childbearing potential | 86 | 70 | 156 |
| Post-menopausal | 100 | 116 | 216 |
| Surgically sterile | 11 | 10 | 21 |
| Baseline ECOG performance Status | | | |
| Units: Subjects | | | |
| EOCG 0 | 153 | 146 | 299 |

| | | | |
|--|---------|---------|----|
| EOCG 1 | 44 | 50 | 94 |
| EOCG 2 | 0 | 0 | 0 |
| EOCG 3 | 0 | 0 | 0 |
| EOCG 4 | 0 | 0 | 0 |
| EOCG 5 | 0 | 0 | 0 |
| Weight Units: Kg | | | |
| arithmetic mean | 75.84 | 74.93 | |
| standard deviation | ± 16.88 | ± 16.87 | - |
| BMI Units: Weight(kg) / [Height(m)^2] | | | |
| arithmetic mean | 28.72 | 28.51 | |
| standard deviation | ± 6.36 | ± 6.20 | - |
| Height Units: cm | | | |
| arithmetic mean | 162.6 | 162.2 | |
| standard deviation | ± 6.27 | ± 6.67 | - |
| BSA Units: [Height(cm) X Weight(kg)] / 3600] ^1/2 | | | |
| arithmetic mean | 1.84 | 1.83 | |
| standard deviation | ± 0.21 | ± 0.21 | - |

Subject analysis sets

| | |
|---|--------------------|
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Intent-to-treat analysis set (ITT) included all randomized subjects | |

| Reporting group values | ITT | | |
|--|---------|--|--|
| Number of subjects | 393 | | |
| 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) | 332 | | |
| From 65-84 years | 61 | | |
| 85 years and over | 0 | | |
| Age continuous Units: years | | | |
| arithmetic mean | 52.4 | | |
| standard deviation | ± 11.50 | | |
| Gender categorical Units: Subjects | | | |
| Female | 393 | | |

| | | | |
|------|---|--|--|
| Male | 0 | | |
|------|---|--|--|

| | | | |
|---|---------|--|--|
| Race | | | |
| Units: Subjects | | | |
| White | 393 | | |
| Black or African American | 0 | | |
| Asian | 0 | | |
| American Indian or Alaska Native | 0 | | |
| Native Hawaiian or other Pacific Islander | 0 | | |
| Other | 0 | | |
| Reproductive Status | | | |
| Units: Subjects | | | |
| Childbearing potential | 156 | | |
| Post-menopausal | 216 | | |
| Surgically sterile | 21 | | |
| Baseline ECOG performance Status | | | |
| Units: Subjects | | | |
| EOCG 0 | 299 | | |
| EOCG 1 | 94 | | |
| EOCG 2 | 0 | | |
| EOCG 3 | 0 | | |
| EOCG 4 | 0 | | |
| EOCG 5 | 0 | | |
| Weight | | | |
| Units: Kg | | | |
| arithmetic mean | 75.39 | | |
| standard deviation | ± 16.86 | | |
| BMI | | | |
| Units: Weight(kg) / [Height(m)^2] | | | |
| arithmetic mean | 28.62 | | |
| standard deviation | ± 6.27 | | |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 162.4 | | |
| standard deviation | ± 6.47 | | |
| BSA | | | |
| Units: [Height(cm) X Weight(kg)] / 3600] ^1/2 | | | |
| arithmetic mean | 1.83 | | |
| standard deviation | ± 0.21 | | |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | F-627 |
| Reporting group description: F-627, 20mg fixed dose prefilled syringe, dosed on Day 2 of each of 4 chemotherapy cycles | |
| Reporting group title | Neulasta |
| Reporting group description: Neulasta, 6mg fixed dose prefilled syringe, dosed on Day 2 of each of the 4 chemotherapy cycles | |
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: Intention-to-treat analysis set (ITT) included all randomized subjects | |

Primary: Duration of severe neutropenia (DSN) in Cycle 1

| | |
|--|---|
| End point title | Duration of severe neutropenia (DSN) in Cycle 1 |
| End point description: | |
| End point type | Primary |
| End point timeframe: Chemotherapy cycle 1 | |

| End point values | F-627 | Neulasta | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 197 | 196 | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | 0.2 (± 0.51) | 0.2 (± 0.45) | | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | FAS |
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.7074 ^[1] |
| Method | t-test, 2-sided |

Notes:

[1] - p-value was for the testing of mean (F-627) = mean (Neulasta®)

Secondary: Number of Days of Intravenous Antibiotic Use

| | |
|------------------------|--|
| End point title | Number of Days of Intravenous Antibiotic Use |
| End point description: | |

| | |
|----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Across all 4 chemotherapy cycles | |

| End point values | F-627 | Neulasta | ITT | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: Days | | | | |
| arithmetic mean (standard deviation) | 0.3 (± 1.36) | 0.1 (± 0.70) | 0.2 (± 1.09) | |

Statistical analyses

| Statistical analysis title | FAS |
|---|-------------------------|
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0538 ^[2] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[2] - p-value was based on the two-sided exact test from a Wilcoxon Rank Sum test

Secondary: Number of Days of Hospitalization for Infection

| | |
|------------------------|---|
| End point title | Number of Days of Hospitalization for Infection |
| End point description: | |

| | |
|----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Across all 4 chemotherapy cycles | |

| End point values | F-627 | Neulasta | ITT | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: Days | | | | |
| arithmetic mean (standard deviation) | 0.1 (± 0.78) | 0.0 (± 0.57) | 0.0 (± 0.69) | |

Statistical analyses

| Statistical analysis title | FAS |
|----------------------------|------------------|
| Comparison groups | F-627 v Neulasta |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 ^[3] |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[3] - p-value was based on the two-sided exact test from a Wilcoxon Rank Sum test

Secondary: Incidence of Febrile Neutropenia

| | |
|----------------------------------|----------------------------------|
| End point title | Incidence of Febrile Neutropenia |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Across all 4 chemotherapy cycles | |

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: event | 6 | 1 | 7 | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | FAS |
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1217 ^[4] |
| Method | Fisher exact |

Notes:

[4] - p-value was for the proportion difference between F-627and Neulasta® using Fisher's Exact Test

Secondary: Incidence of Severe Neutropenia for Chemotherapy Cycle 1

| | |
|------------------------|--|
| End point title | Incidence of Severe Neutropenia for Chemotherapy Cycle 1 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Chemotherapy cycle 1 | |

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: event | 23 | 23 | 46 | |

Statistical analyses

| Statistical analysis title | FAS |
|---|-------------------------|
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9853 ^[5] |
| Method | Chi-squared |

Notes:

[5] - p-value was for the proportion difference between F-627 and Neulasta® using Chi-Square Test

Secondary: Incidence of Use of Intravenous Antibiotics

| | |
|-----------------|---|
| End point title | Incidence of Use of Intravenous Antibiotics |
|-----------------|---|

End point description:

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

End point timeframe:

Across all 4 chemotherapy cycles

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: event | 9 | 2 | 11 | |

Statistical analyses

| Statistical analysis title | FAS |
|---|-------------------------|
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0618 ^[6] |
| Method | Fisher exact |

Notes:

[6] - p-value was for the proportion difference between F-627 and Neulasta® using Fisher's Exact Test

Secondary: Incidence of Hospitalization for Infection

| | |
|-----------------|--|
| End point title | Incidence of Hospitalization for Infection |
|-----------------|--|

End point description:

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

End point timeframe:

Across all 4 chemotherapy cycles

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: event | 1 | 1 | 2 | |

Statistical analyses

| | |
|---|------------------|
| Statistical analysis title | FAS |
| Comparison groups | F-627 v Neulasta |
| Number of subjects included in analysis | 393 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 1 [7] |
| Method | Fisher exact |

Notes:

[7] - p-value was for the proportion difference between F-627 and Neulasta® using Fisher's Exact Test

Other pre-specified: Incidence of Severe Neutropenia in Cycle 3

| | |
|-----------------|--|
| End point title | Incidence of Severe Neutropenia in Cycle 3 |
|-----------------|--|

End point description:

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

End point timeframe:

Chemotherapy Cycle 3

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 193 | 191 | 384 | |
| Units: Event | | | | |
| Severe Neutropenia | 5 | 12 | 17 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of Severe Neutropenia in Cycle 4

End point title Incidence of Severe Neutropenia in Cycle 4

End point description:

End point type Other pre-specified

End point timeframe:

Cycle 4

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 186 | 188 | 374 | |
| Units: event | | | | |
| Severe Neutropenia | 3 | 10 | 13 | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Incidence of Severe Neutropenia in Cycle 2

End point title Incidence of Severe Neutropenia in Cycle 2

End point description:

End point type Other pre-specified

End point timeframe:

Cycle 2

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 194 | 196 | 390 | |
| Units: event | | | | |
| Severe Neutropenia | 9 | 10 | 19 | |

Statistical analyses

No statistical analyses for this end point

Post-hoc: Incidence of Protocol-defined Febrile Neutropenia

| | |
|-----------------|---|
| End point title | Incidence of Protocol-defined Febrile Neutropenia |
|-----------------|---|

End point description:

| | |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

End point timeframe:

All cycles

| End point values | F-627 | Neulasta | ITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 197 | 196 | 393 | |
| Units: events | | | | |
| Febrile Neutropenia | 3 | 1 | 4 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 12 weeks (4 treatment cycles)

Adverse event reporting additional description:

All subjects who received at least 1 dose of F-627 or Neulasta were included in the safety analysis set.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | F-627 |
|-----------------------|-------|

Reporting group description:

F-627, 20mg fixed dose prefilled syringe, dosed on Day 2 of each of 4 chemotherapy cycles

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

Reporting group description:

Neulasta, 6mg fixed dose prefilled syringe, dosed on Day 2 of each of the 4 chemotherapy cycles

| Serious adverse events | F-627 | Neulasta | |
|---|------------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 197 (6.09%) | 5 / 196 (2.55%) | |
| number of deaths (all causes) | 1 | 2 | |
| number of deaths resulting from adverse events | 1 | 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 197 (0.00%) | 1 / 196 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (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 | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 197 (1.02%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anemia | | | |
| subjects affected / exposed | 0 / 197 (0.00%) | 1 / 196 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 197 (0.00%) | 1 / 196 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 197 (0.00%) | 1 / 196 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urticaria | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 197 (1.02%) | 1 / 196 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 197 (0.51%) | 0 / 196 (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 | F-627 | Neulasta | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 178 / 197 (90.36%) | 169 / 196 (86.22%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 19 / 197 (9.64%) | 13 / 196 (6.63%) | |
| occurrences (all) | 22 | 13 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 15 / 197 (7.61%) | 6 / 196 (3.06%) | |
| occurrences (all) | 23 | 9 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 11 / 197 (5.58%) | 10 / 196 (5.10%) | |
| occurrences (all) | 14 | 10 | |
| Nervous system disorders | | | |

| | | | |
|--|--------------------------|--------------------------|--|
| Headache subjects affected / exposed occurrences (all) | 18 / 197 (9.14%) 23 | 10 / 196 (5.10%) 12 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia subjects affected / exposed occurrences (all) | 40 / 197 (20.30%) 87 | 50 / 196 (25.51%) 110 | |
| Anaemia subjects affected / exposed occurrences (all) | 47 / 197 (23.86%) 75 | 38 / 196 (19.39%) 73 | |
| Leukopenia subjects affected / exposed occurrences (all) | 39 / 197 (19.80%) 98 | 44 / 196 (22.45%) 104 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 20 / 197 (10.15%) 39 | 20 / 196 (10.20%) 39 | |
| Leukocytosis subjects affected / exposed occurrences (all) | 14 / 197 (7.11%) 59 | 10 / 196 (5.10%) 41 | |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 58 / 197 (29.44%) 153 | 46 / 196 (23.47%) 132 | |
| Fatigue subjects affected / exposed occurrences (all) | 24 / 197 (12.18%) 53 | 17 / 196 (8.67%) 28 | |
| Pyrexia subjects affected / exposed occurrences (all) | 18 / 197 (9.14%) 25 | 9 / 196 (4.59%) 14 | |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 71 / 197 (36.04%) 143 | 58 / 196 (29.59%) 115 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 32 / 197 (16.24%) 48 | 27 / 196 (13.78%) 37 | |

| | | | |
|--|---------------------------|---------------------------|--|
| Stomatitis subjects affected / exposed occurrences (all) | 13 / 197 (6.60%) 26 | 12 / 196 (6.12%) 23 | |
| Vomiting subjects affected / exposed occurrences (all) | 12 / 197 (6.09%) 14 | 7 / 196 (3.57%) 10 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 103 / 197 (52.28%) 108 | 100 / 196 (51.02%) 101 | |
| Erythema subjects affected / exposed occurrences (all) | 17 / 197 (8.63%) 35 | 17 / 196 (8.67%) 40 | |
| Musculoskeletal and connective tissue disorders | | | |
| Bone pain subjects affected / exposed occurrences (all) | 41 / 197 (20.81%) 77 | 34 / 196 (17.35%) 63 | |
| Arthralgia subjects affected / exposed occurrences (all) | 30 / 197 (15.23%) 70 | 22 / 196 (11.22%) 46 | |
| Myalgia subjects affected / exposed occurrences (all) | 21 / 197 (10.66%) 31 | 18 / 196 (9.18%) 29 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 11 / 197 (5.58%) 13 | 7 / 196 (3.57%) 11 | |

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