



## 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,<br>pr@evivebiotech.com |
| Scientific contact           | GCR, Evive Biotechnology (Shanghai) Ltd,<br>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/m<sup>2</sup> docetaxel + 600 mg/m<sup>2</sup> 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   |
| <b>Arm title</b>             | 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

|                  |          |
|------------------|----------|
| <b>Arm title</b> | 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

| <b>Number of subjects in period 1</b> | 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<br>Units: Kg<br>arithmetic mean<br>standard deviation                                      | 75.84<br>± 16.88 | 74.93<br>± 16.87 | -  |
| BMI<br>Units: Weight(kg) / [Height(m)^2]<br>arithmetic mean<br>standard deviation                 | 28.72<br>± 6.36  | 28.51<br>± 6.20  | -  |
| Height<br>Units: cm<br>arithmetic mean<br>standard deviation                                      | 162.6<br>± 6.27  | 162.2<br>± 6.67  | -  |
| BSA<br>Units: [Height(cm) X Weight(kg)] /<br>3600]^(1/2)<br>arithmetic mean<br>standard deviation | 1.84<br>± 0.21   | 1.83<br>± 0.21   | -  |

### Subject analysis sets

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

| Reporting group values  | ITT             |  |  |
|---|-----------------|--|--|
| Number of subjects  | 393             |  |  |
| Age categorical<br>Units: Subjects                                      |                 |  |  |
| In utero  | 0               |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks)                   | 0               |  |  |
| Newborns (0-27 days)  | 0               |  |  |
| Infants and toddlers (28 days-23<br>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<br>Units: years<br>arithmetic mean<br>standard deviation | 52.4<br>± 11.50 |  |  |
| Gender categorical<br>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:<br>F-627, 20mg fixed dose prefilled syringe, dosed on Day 2 of each of 4 chemotherapy cycles       |                    |
| Reporting group title   | Neulasta           |
| Reporting group description:<br>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:<br>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:<br>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 <sup>[1]</sup> |
| 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 <sup>[2]</sup> |
| 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 <sup>[3]</sup>      |
| 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 <sup>[4]</sup> |
| 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 <sup>[5]</sup> |
| 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 <sup>[6]</sup> |
| 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**

|   |                  |
|---|------------------|
| <b>Statistical analysis title</b>       | 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

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**Post-hoc: Incidence of Protocol-defined Febrile Neutropenia**

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|                 |   |
|-----------------|---|
| 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                    |  |

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**Statistical analyses**

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

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

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported