Clinical trial results:
A Phase III, Randomized, Multi-Centre, Double-Blind, Placebo Controlled Clinical Trial of F-627 in Women with Breast Cancer Receiving Myelotoxic Chemotherapy

Summary

EudraCT number	2016-001930-93
Trial protocol	HU
Global end of trial date	18 December 2017

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-627-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02872103
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, prr@evivebiotech.com
Scientific contact	GCR, Evive Biotechnology (Shanghai) Ltd, prr@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	05 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2017
Global end of trial reached?	Yes
Global end of trial date	18 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Efficacy:
The objective of the study was to evaluate the efficacy and safety of F-627 given as a single 20 mg fixed dose pre-filled syringe (PFS) in the subject's first chemotherapy cycle in comparison to Placebo
Safety:
To assess safety in subjects treated with the 20 mg fixed dose of F-627 using the adverse event (AE)/serious adverse event (SAE) reporting, and other standard laboratory findings including hematology and blood chemistry, urinalysis, and symptoms including, but not limited to, bone and back pain.

Protection of trial subjects:

This study was conducted in accordance with ICH GCP regulations. The IEC/IRB approved the protocol and ICF.
Only 1/3 of the subjects enrolled were randomized to the placebo arm and received treatment only in chemotherapy cycle 1.
Short-acting G-CSF drugs were not permitted during the normal course of the study. However, a short-acting G-CSF may have been used if rescue therapy was needed due to the development of febrile neutropenia (FN) or prolonged severe neutropenia (>6 days).

Background therapy:

Chemotherapy: 75 mg/m2 docetaxel and 60 mg/m2 doxorubicin

Evidence for comparator:

No comparator used in this trial.

Actual start date of recruitment	17 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Russian Federation: 48
Country: Number of subjects enrolled	Ukraine: 68
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	122
EEA total number of subjects	5

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)	112
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted between 17 August 2016 and 28 November 2017 at 16 study centers in the United States, Ukraine, Russia, and Hungary.

Pre-assignment

Screening details:

A total of 135 subjects were screened and 122 (90.4%) subjects were randomized to the study, including 83 subjects randomized to F-627 and 39 subjects randomized to Placebo as their treatment in chemotherapy cycle 1. Overall, 118 subjects completed the study and 4 subjects discontinued prematurely.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	F-627

Arm description:

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

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

Dosage and administration details:

F-627, 20 mg fixed dose pre-filled syringe, dosed by subcutaneous injection on Day 2 of each of 4 chemotherapy cycles.

Arm title	Placebo

Arm description:

Placebo, pre-filled syringe administered on Day 2 of the first chemotherapy cycle; and F-627, 20 mg fixed dose pre-filled syringe administered on Day 2 of each of the following 3 chemotherapy cycles.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection , Subcutaneous use

Dosage and administration details:

Placebo, pre-filled syringe administered by subcutaneous injection on Day 2 of the first chemotherapy cycle. F-627, 20 mg fixed dose pre-filled syringe administered on Day 2 of each of the following 3 chemotherapy cycles.

Number of subjects in period 1	F-627	Placebo
Started	83	39
Completed	81	37
Not completed	2	2
Physician decision	-	1
Adverse event, non-fatal	-	1
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	F-627
Reporting group description:	
F-627, 20 mg fixed dose pre-filled syringe, dosed on Day 2 of each of 4 chemotherapy cycles	
Reporting group title	Placebo
Reporting group description:	
Placebo, pre-filled syringe administered on Day 2 of the first chemotherapy cycle; and F-627, 20 mg fixed dose pre-filled syringe administered on Day 2 of each of the following 3 chemotherapy cycles.	

Reporting group values	F-627	Placebo	Total
Number of subjects	83	39	122
Age categorical Units: Subjects			
Adults (18-64 years)	76	36	112
From 65-84 years	7	3	10
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	50.8	51.5	
standard deviation	± 9.25	± 9.00	-
Gender categorical Units: Subjects			
Female	83	39	122
Male	0	0	0

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	122		
Age categorical Units: Subjects			
Adults (18-64 years)	112		
From 65-84 years	10		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	51.0		
standard deviation	± 9.14		
Gender categorical Units: Subjects			
Female	122		
Male	0		

End points

End points reporting groups

Reporting group title	F-627
Reporting group description:	
F-627, 20 mg fixed dose pre-filled syringe, dosed on Day 2 of each of 4 chemotherapy cycles	
Reporting group title	Placebo
Reporting group description:	
Placebo, pre-filled syringe administered on Day 2 of the first chemotherapy cycle; and F-627, 20 mg fixed dose pre-filled syringe administered on Day 2 of each of the following 3 chemotherapy cycles.	
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	

Primary: Duration of Severe Neutropenia (DSN) in Cycle 1

End point title	Duration of Severe Neutropenia (DSN) in Cycle 1
End point description:	
DSN was calculated as the number of consecutive days from the first day when a patient’s ANC was <0.5 × 10^9/L until the patient reached an ANC ≥ 0.5 × 10^9/L.	
End point type	Primary
End point timeframe:	
Chemotherapy Cycle 1	

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	27		
Units: days				
arithmetic mean (standard deviation)	1.3 (± 1.2)	3.9 (± 1.4)		

Statistical analyses

Statistical analysis title	Cycle 1
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: Duration of Moderate Neutropenia in Cycle 1

End point title	Duration of Moderate Neutropenia in Cycle 1

End point description:

End point type	Secondary

End point timeframe:
Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	28		
Units: day				
arithmetic mean (standard deviation)	2.1 (± 1.51)	5.1 (± 1.90)		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: Duration of Mild Neutropenia in Cycle 1

End point title	Duration of Mild Neutropenia in Cycle 1

End point description:

End point type	Secondary

End point timeframe:
Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	28		
Units: day				
arithmetic mean (standard deviation)	2.6 (± 1.47)	6.8 (± 2.54)		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Secondary: Incidence Rate of Febrile Neutropenia in Cycle 1

End point title	Incidence Rate of Febrile Neutropenia in Cycle 1

End point description:

End point type	Secondary

End point timeframe:

Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: event	4	10		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0016
Method	Fisher exact

Secondary: Incidence Rate of Severe Neutropenia in Cycle 1

End point title	Incidence Rate of Severe Neutropenia in Cycle 1

End point description:

End point type	Secondary

End point timeframe:

Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: event	58	37		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0019
Method	Chi-squared

Secondary: Time to ANC Recovery Post Nadir in Cycle 1

End point title	Time to ANC Recovery Post Nadir in Cycle 1

End point description:

End point type	Secondary

End point timeframe:

Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	38		
Units: day				
arithmetic mean (standard deviation)	2.1 (± 1.09)	4.1 (± 2.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rate of Infection in Cycle 1

End point title	Incidence Rate of Infection in Cycle 1

End point description:

End point type	Secondary
End point timeframe: Chemotherapy cycle 1	

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: event	2	3		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3258
Method	Fisher exact

Secondary: Incidence Rate of Use of Antibiotic Medications in Cycle 1

End point title	Incidence Rate of Use of Antibiotic Medications in Cycle 1
End point description:	

End point type	Secondary
End point timeframe: Chemotherapy cycle 1	

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: event	9	13		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0047
Method	Chi-squared

Secondary: Incidence Rate of Use of Pain Medications in Cycle 1

End point title	Incidence Rate of Use of Pain Medications in Cycle 1

End point description:

End point type	Secondary

End point timeframe:

Chemotherapy cycle 1

End point values	F-627	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	39		
Units: event	8	9		

Statistical analyses

Statistical analysis title	FAS
Comparison groups	F-627 v Placebo
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0545
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from the time of randomization until 28 days after the completion of the trial (a total of 16 weeks) or 28 days after the premature withdrawal of a subject from the trial.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	F-627

Reporting group description:

Patients received F-627 all cycles

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	F-627	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 83 (4.82%)	11 / 39 (28.21%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 83 (1.20%)	0 / 39 (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	3 / 83 (3.61%)	11 / 39 (28.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 83 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

pneumonia			
subjects affected / exposed	0 / 83 (0.00%)	1 / 39 (2.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	F-627	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 83 (98.80%)	39 / 39 (100.00%)	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	7 / 83 (8.43%)	3 / 39 (7.69%)	
occurrences (all)	9	5	
Headache			
subjects affected / exposed	2 / 83 (2.41%)	2 / 39 (5.13%)	
occurrences (all)	3	3	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	82 / 83 (98.80%)	39 / 39 (100.00%)	
occurrences (all)	881	396	
Leukopenia			
subjects affected / exposed	42 / 83 (50.60%)	15 / 39 (38.46%)	
occurrences (all)	109	44	
Anaemia			
subjects affected / exposed	31 / 83 (37.35%)	7 / 39 (17.95%)	
occurrences (all)	45	17	
Thrombocytopenia			
subjects affected / exposed	17 / 83 (20.48%)	3 / 39 (7.69%)	
occurrences (all)	36	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 83 (26.51%)	11 / 39 (28.21%)	
occurrences (all)	41	19	
Asthenia			

subjects affected / exposed	17 / 83 (20.48%)	8 / 39 (20.51%)	
occurrences (all)	39	18	
Pyrexia			
subjects affected / exposed	2 / 83 (2.41%)	2 / 39 (5.13%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	51 / 83 (61.45%)	23 / 39 (58.97%)	
occurrences (all)	125	53	
Vomiting			
subjects affected / exposed	15 / 83 (18.07%)	8 / 39 (20.51%)	
occurrences (all)	21	17	
Stomatitis			
subjects affected / exposed	11 / 83 (13.25%)	5 / 39 (12.82%)	
occurrences (all)	15	7	
Constipation			
subjects affected / exposed	2 / 83 (2.41%)	2 / 39 (5.13%)	
occurrences (all)	2	2	
Gastritis			
subjects affected / exposed	0 / 83 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 83 (2.41%)	2 / 39 (5.13%)	
occurrences (all)	2	3	
Cough			
subjects affected / exposed	0 / 83 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	61 / 83 (73.49%)	26 / 39 (66.67%)	
occurrences (all)	65	26	
Erythema			
subjects affected / exposed	9 / 83 (10.84%)	5 / 39 (12.82%)	
occurrences (all)	20	6	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	14 / 83 (16.87%)	3 / 39 (7.69%)	
occurrences (all)	34	7	
Bone pain			
subjects affected / exposed	7 / 83 (8.43%)	6 / 39 (15.38%)	
occurrences (all)	13	6	
Pain in extremity			
subjects affected / exposed	0 / 83 (0.00%)	2 / 39 (5.13%)	
occurrences (all)	0	2	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	2 / 83 (2.41%)	3 / 39 (7.69%)	
occurrences (all)	2	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 83 (10.84%)	3 / 39 (7.69%)	
occurrences (all)	12	4	
Hypomagnesaemia			
subjects affected / exposed	2 / 83 (2.41%)	2 / 39 (5.13%)	
occurrences (all)	3	3	

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