



## Clinical trial results:

**Clinical Phase II Trial to evaluate efficacy and safety of CD34+ cells mobilization and collection after treatment with plerixafor and filgrastim in patients with Fanconi anemia for subsequent transduction with a lentiviral vector carrying FANCA gene and reinfusion in the patient**

### Summary

EudraCT number	2011-006197-88
Trial protocol	ES
Global end of trial date	30 November 2018

### Results information

Result version number	v1 (current)
This version publication date	04 October 2021
First version publication date	04 October 2021

### Trial information

#### Trial identification

Sponsor protocol code	FANCOSTEM-1
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02931071
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez Soriano, VHIR, 0034 934894865, joaquin.lopez.soriano@vhir.org
Scientific contact	Cristina Díaz de Heredia Rubio, VHIR, 0034 934893093, crdiaz@vhebron.net

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:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	30 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2018
Global end of trial reached?	Yes
Global end of trial date	30 November 2018
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

The main objective is to assess the safety of cell mobilization after treatment with filgrastim and plerixafor in patients with Fanconi Anemia.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Spain: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

Notes:

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**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)	9
Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	11
Number of subjects completed	11

### Period 1

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

### Arms

<b>Arm title</b>	CD34+ cells mobilization, collection and immunoselection
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Filgrastim
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use
Dosage and administration details:	
12 microgram/Kg/12 hours, subcutaneous days 0 to 5	
Investigational medicinal product name	Plerixafor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Subcutaneous use

Dosage and administration details:

240 microgram/kg/day subcutaneous at days 5 to 8

<b>Number of subjects in period 1</b>	CD34+ cells mobilization, collection and immunoselection
Started	11
Mobilization of CD34+ cells	11
Collection of CD34+ cells	11
Immunoselection of PB HSPCs	11

Completed	11
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## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	11	11	
Age categorical			
Units: Subjects			
Children	9	9	
Adolescent	2	2	
Age continuous			
Units: years			
median	5		
full range (min-max)	2 to 16	-	
Gender categorical			
Units: Subjects			
Female	1	1	
Male	10	10	
Chromosome fragility test			
Test with diepoxybutane or mitomycin C to confirm chromosome fragility for Fanconi anemia, discarding mosaicism			
Units: Subjects			
Yes	11	11	
Neutrophils			
> or = $0.75 \times 10^9$ cells/L			
Units: cell/L			
median	1.26		
full range (min-max)	0.76 to 2.4	-	
Platelet			
> or = to $30 \times 10^9$ cell/L			
Units: cells/L			
median	76		
full range (min-max)	27 to 191	-	
Haemoglobin levels			
> or = to 8g/dL			
Units: g/dL			
median	11.3		
full range (min-max)	10.4 to 12.8	-	

### Subject analysis sets

Subject analysis set title	Efficacy and safety of cell yield
Subject analysis set type	Full analysis

Subject analysis set description:

After screening, 11 patients were treated with filgrastim and plerixafor for mobilization of CD34+ cells. 9 patients satisfactorily mobilized cells and underwent cell collection. After collection, cells were sorted

Reporting group values	Efficacy and safety of cell yield		
Number of subjects	11		
Age categorical			
Units: Subjects			
Children	9		
Adolescent	2		
Age continuous			
Units: years			
median	5		
full range (min-max)	2 to 16		
Gender categorical			
Units: Subjects			
Female	1		
Male	10		
Chromosome fragility test			
Test with diepoxybutane or mitomycin C to confirm chromosome fragility for Fanconi anemia, discarding mosaicism			
Units: Subjects			
Yes	11		
Neutrophils			
> or = $0.75 \times 10^9$ cells/L			
Units: cell/L			
median	1.26		
full range (min-max)	0.76 to 2.4		
Platelet			
> or = to $30 \times 10^9$ cell/L			
Units: cells/L			
median	76		
full range (min-max)	27 to 191		
Haemoglobin levels			
> or = to 8g/dL			
Units: g/dL			
median	11.3		
full range (min-max)	10.4 to 12.8		

## End points

### End points reporting groups

Reporting group title	CD34+ cells mobilization, collection and immunoselection
Reporting group description: -	
Subject analysis set title	Efficacy and safety of cell yield
Subject analysis set type	Full analysis
Subject analysis set description:	
After screening, 11 patients were treated with filgrastim and plerixafor for mobilization of CD34+ cells. 9 patients satisfactorily mobilized cells and underwent cell collection. After collection, cells were sorted	

### Primary: Safety

End point title	Safety <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe:	
12 months follow-up after cell mobilization	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Goal of the study was to evaluate the safety of the procedure for mobilizing and collecting CD34 cells. There were no treatments in separate arms or periods to justify an statistical analysis. No procedure-associated serious adverse events were observed. Safety of the procedure is included in the adverse events section

<b>End point values</b>	CD34+ cells mobilization, collection and immunoselection			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Lack of severe adverse effects	11			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Patients with CD34 cell threshold mobilized

End point title	Patients with CD34 cell threshold mobilized
End point description:	
> or = to 5 CD34 cell/microliter	
End point type	Secondary
End point timeframe:	
After treatment with filgrastim and plerixafor	

<b>End point values</b>	CD34+ cells mobilization, collection and immunoselection			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: cells/microL				
Yes	9			

### Statistical analyses

No statistical analyses for this end point

### Secondary: CD34 cell collected

End point title	CD34 cell collected
End point description: Number of patients with efficient collection of cells after apheresis, > or = to $4 \times 10^6$ cells/kg body weight (projections of body weight after 5 years)	
End point type	Secondary
End point timeframe: After apheresis collection	

<b>End point values</b>	CD34+ cells mobilization, collection and immunoselection			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Cells/Kg				
Yes	4			

### Statistical analyses

No statistical analyses for this end point

### Secondary: CD34 cell immunoselected

End point title	CD34 cell immunoselected
End point description: Recovery of CD34 cells after immunoselection has to be > or = to 50%	
End point type	Secondary
End point timeframe: After mobilisation, collection, and immunoselection	



<b>End point values</b>	CD34+ cells mobilization, collection and immunoselection			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percentage of cells				
Yes	0			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Global efficacy of the procedure

End point title	Global efficacy of the procedure
End point description:	
Patients achieving $\geq 4 \times 10^6$ CD34 cells/kg, projecting body weight at 5 years	
End point type	Secondary
End point timeframe:	
After completing the procedure	

<b>End point values</b>	CD34+ cells mobilization, collection and immunoselection			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Cells/Kg				
Yes	0			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The whole study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	2
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### Reporting groups

Reporting group title	Drug-related
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Reporting group description: -

Reporting group title	Total adverse events
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Reporting group description: -

Serious adverse events	Drug-related	Total adverse events	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	4 / 11 (36.36%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Fever of unknown origin			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
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			
Interstitial lung disease			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Varicella			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory infection			

subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
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 %

<b>Non-serious adverse events</b>	Drug-related	Total adverse events	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	9 / 11 (81.82%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Fever			
subjects affected / exposed	2 / 11 (18.18%)	4 / 11 (36.36%)	
occurrences (all)	2	4	
Pain at administration site			
subjects affected / exposed	1 / 11 (9.09%)	1 / 11 (9.09%)	
occurrences (all)	1	1	
Pain at central venous line access			
subjects affected / exposed	0 / 11 (0.00%)	3 / 11 (27.27%)	
occurrences (all)	0	3	
Bleeding at central venous line access			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Throat pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Headache			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	
Blood and lymphatic system disorders Anemia subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2	3 / 11 (27.27%) 3	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2  2 / 11 (18.18%) 2  1 / 11 (9.09%) 1	5 / 11 (45.45%) 5  4 / 11 (36.36%) 4  2 / 11 (18.18%) 2	
Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	1 / 11 (9.09%) 1	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	2 / 11 (18.18%) 2	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2015	Change of sponsor from Cristina Díaz de Heredia to VHIR Change of CRO from Quantum to Sermes Modification of hour of administration of plerixafor, closer to the apheresis procedure Modification of consent forms Modification in pharmaceutical form of filgrastim to vials for injection Filgrastim datasheet was added to documentation
06 September 2017	Sample size and recruitment period were expanded

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Although the threshold of CD34 immunoselected cells was not achieved, enough number of cells were obtained for gene correction and engraftment.

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34485595>