Clinical trial results:
Double umbilical cord blood transplantation in high-risk hematological patients.
A phase II study focussing on the mechanism of graft predominance

Summary

EudraCT number	2012-001188-55
Trial protocol	NL BE
Global end of trial date	28 January 2020

Results information

Result version number	v1 (current)
This version publication date	28 March 2023
First version publication date	28 March 2023

Trial information

Trial identification

Sponsor protocol code	HOVON115

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON , +31 0107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON , +31 0107041560, hdc@erasmusmc.nl

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	15 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 May 2017
Global end of trial reached?	Yes
Global end of trial date	28 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To study the presence of an alloreactive immune response of CD4+ T-cells of the predominant CBU, directed against the non-engrafting CBU as a causative mechanism in CBU predominance.

Protection of trial subjects:

Monitoring and Insurance.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2012
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	Netherlands: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	62
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria.

Period 1

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

Arms

Arm title	Experimental Group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Cord blood unit
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous use

Dosage and administration details:

minimum TNC dose of 4x10^7/kg recipient body weight

Number of subjects in period 1	Experimental Group
Started	70
Completed	45
Not completed	25
Other	5
Lack of efficacy	20

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	70	70	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	62	62	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous Units: years			
median	56		
full range (min-max)	20 to 69	-	
Gender categorical Units: Subjects			
Female	34	34	
Male	36	36	

End points

End points reporting groups

Reporting group title	Experimental Group

Reporting group description: -

Primary: Primary Endpoint

End point title	Primary Endpoint[1]

End point description:

End point type	Primary

End point timeframe:

See publication.

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: See attached chart/documents for results.

End point values	Experimental Group			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Whole	70			

Attachments (see zip file)	List of reported non-SAE's/nonsaedata115-13Jan2023.pdf List of reported SAE's/saedata115-13Jan2023.pdf Statistical data section from publication/Statistical data section

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be reported from the first study-related procedure until 30 days following the last dose of any drug from the protocol treatment schedule or until the start of subsequent systemic therapy for the disease under study, if earlier.

Adverse event reporting additional description:

Adverse events occurring after 30 days should also be reported if considered at least possibly related to the investigational medicinal product by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Experimental Group

Reporting group description: -

Serious adverse events	Experimental Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 68 (50.00%)		
number of deaths (all causes)	33		
number of deaths resulting from adverse events			
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 68 (2.94%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Immune system disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	9 / 68 (13.24%)		
occurrences causally related to treatment / all	10 / 10		
deaths causally related to treatment / all	5 / 5		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	4 / 68 (5.88%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	3 / 4		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 68 (2.94%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	3 / 68 (4.41%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	2 / 68 (2.94%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	5 / 68 (7.35%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined, see SAE chart for details.		

subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	7 / 68 (10.29%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	1 / 1		
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	10 / 68 (14.71%)		
occurrences causally related to treatment / all	4 / 10		
deaths causally related to treatment / all	1 / 2		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 68 (1.47%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Experimental Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 68 (94.12%)		
Vascular disorders			
Vascular disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	18 / 68 (26.47%)		
occurrences (all)	19		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	5		
Reproductive system and breast disorders			

Reproductive system and breast disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 68 (4.41%)		
occurrences (all)	3		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 68 (2.94%)		
occurrences (all)	2		
Investigations			
Investigations	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	26 / 68 (38.24%)		
occurrences (all)	47		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	7 / 68 (10.29%)		
occurrences (all)	7		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 68 (13.24%)		
occurrences (all)	9		
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	29 / 68 (42.65%)		
occurrences (all)	38		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	20 / 68 (29.41%)		
occurrences (all)	23		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	8 / 68 (11.76%)		
occurrences (all)	8		
Renal and urinary disorders			

Renal and urinary disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 68 (13.24%)		
occurrences (all)	9		
Endocrine disorders			
Endocrine disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 68 (1.47%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	4 / 68 (5.88%)		
occurrences (all)	4		
Infections and infestations			
Infections and infestations	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	41 / 68 (60.29%)		
occurrences (all)	94		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	24 / 68 (35.29%)		
occurrences (all)	37		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 October 2013	adjusted age to ≤ 70 years, secondary end point 'transplant related mortality' as primary end point.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported