Clinical trial results:
A phase II study to assess engraftment and engraftment kinetics after double cord blood transplantation with a reduced-intensity conditioning regimen in patients eligible for allogeneic stem cell transplantation lacking a matched unrelated donor

Summary

EudraCT number	2008-000053-35
Trial protocol	NL
Global end of trial date	04 July 2017

Results information

Result version number	v1 (current)
This version publication date	10 March 2022
First version publication date	10 March 2022

Trial information

Trial identification

Sponsor protocol code	HO106

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, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, 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	04 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 March 2012
Global end of trial reached?	Yes
Global end of trial date	04 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of engraftment and disease-free survival following double cord blood transplantation after a reduced intensity conditioning regimen in adult patients. In addition to description of clinical parameters biological studies will be performed in order to evaluate whether parameters can be identified that predict which graft ultimately prevails.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 July 2008
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: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
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 period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Experimental group
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	UCB
Investigational medicinal product code	
Other name	CBU
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Depending on the existence of major ABO-incompatibility between CBU and recipient and the number of prefreeze RBC CBU’s will undergo a careful washing procedure after thawing or will be infused immediately after a direct-thaw procedure.
Major ABO-incompatible CBU’s will undergo a post-thaw washing procedure if the total prefreeze RBC count exceeds 150 x 109 . Minor ABO-incompatible or ABO-compatible CBU’s will undergo a post-thaw washing procedure if the total prefreeze RBC count exceeds 300 x 109. In all other cases CBU´s will be infused immediately after a direct-thaw procedure. Grafts will be infused on two consecutive days (day 0 and day +1). An ABO compatible graft will be given first.

Number of subjects in period 1	Experimental group
Started	60
Completed	54
Not completed	6
Protocol deviation	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	60	60	
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)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Adults (18-65 years)	60	60	
Age continuous Units: years			
median	51		
full range (min-max)	20 to 65	-	
Gender categorical Units: Subjects			
Female	28	28	
Male	32	32	

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/document for results.

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Whole	60			

Attachments (see zip file)	Statistical data section from publication/HO106_Statistical data List of reported SAE's/sae106-11Jan2022.pdf List of reported non-SAE's/nonsae106-22Feb2022.pdf

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	3

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	42 / 54 (77.78%)		
number of deaths (all causes)	37		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia refractory			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
secondary malignancy			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disease progression			

subjects affected / exposed	5 / 54 (9.26%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
Body temperature increased				
subjects affected / exposed	2 / 54 (3.70%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Disease recurrence				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Upper respiratory tract infection				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Acute graft versus host disease				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Graft versus host disease				
subjects affected / exposed	6 / 54 (11.11%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Graft versus host disease in gastrointestinal tract				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Graft versus host disease in skin				

subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hypoxia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
respiratory insufficiency			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 1		
Investigations			
creatinine			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

creatinine increased			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Graft failure			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
head wound			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pericardial effusion			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Leukoencephalopathy			

subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Neuropathy sensory			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Personality disorder			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal detachment			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 54 (16.67%)		
occurrences causally related to treatment / all	1 / 9		
deaths causally related to treatment / all	0 / 1		

Body temperature increased			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin infection			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
renal insufficiency			
subjects affected / exposed	5 / 54 (9.26%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 1		
Endocrine disorders			
Thyroiditis			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus infection reactivation			

subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epstein-Barr virus infection reactivation				
subjects affected / exposed	3 / 54 (5.56%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Hepatic infection				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 54 (9.26%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	1 / 3			
Sepsis				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin infection				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 54 (1.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				

subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
metabolic disturbance			
subjects affected / exposed	2 / 54 (3.70%)		
occurrences causally related to treatment / all	0 / 2		
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	52 / 54 (96.30%)		
Vascular disorders			
Vascular	Additional description: All combined, see AE chart for details		
subjects affected / exposed	5 / 54 (9.26%)		
occurrences (all)	5		
General disorders and administration site conditions			
Constitutional			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Pain	Additional description: All combined, see AE chart for details		
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Hemorrhage/bleeding	Additional description: All combined, see AE chart for details		
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Cardiac disorders			
Cardiac arrhythmia	Additional description: All combined, see AE chart for details		

subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	4		
Cardiac general	Additional description: All combined, see AE chart for details		
subjects affected / exposed	9 / 54 (16.67%)		
occurrences (all)	9		
Nervous system disorders			
Neurology	Additional description: All combined, see AE chart for details		
subjects affected / exposed	4 / 54 (7.41%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Blood/BM	Additional description: All combined, see AE chart for details		
subjects affected / exposed	33 / 54 (61.11%)		
occurrences (all)	108		
Coagulation	Additional description: All combined, see AE chart for details		
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	4		
Eye disorders			
Ocular/visual	Additional description: All combined, see AE chart for details		
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	3		
Gastrointestinal disorders			
Gastrointestinal	Additional description: All combined, see AE chart for details		
subjects affected / exposed	12 / 54 (22.22%)		
occurrences (all)	13		
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see AE chart for details		
subjects affected / exposed	2 / 54 (3.70%)		
occurrences (all)	2		
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see AE chart for details		
subjects affected / exposed	1 / 54 (1.85%)		
occurrences (all)	1		
Endocrine disorders			
Endocrine			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Infections and infestations			

Infection	Additional description: All combined, see AE chart for details		
subjects affected / exposed	43 / 54 (79.63%)		
occurrences (all)	95		
Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see AE chart for details		
subjects affected / exposed	12 / 54 (22.22%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2009	Change of sponsor
02 March 2010	Addition of extra site
01 July 2010	Amendment of product information and PIF/ICF
30 November 2010	Change of safety reporting procedures and addition of extra site
30 May 2011	Addition of extra site

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25107890