Clinical trial results:
Allogeneic Stem Cell Transplantation after Reduced Intensity Conditioning for High-risk Relapsed or Refractory CLL

Summary

EudraCT number	2007-005487-28
Trial protocol	NL BE
Global end of trial date	18 November 2016

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	HOVON88CLL

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 (0)107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, +31 (0)107041560, 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	12 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 December 2014
Global end of trial reached?	Yes
Global end of trial date	18 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess, on an intention-to-treat basis, the efficacy and safety of a treatment protocol including salvage chemoimmunotherapy (R-DHAP) followed, in the absence of progression, by RIC alloSCT from sibling or unrelated donors, in high-risk CLL patients as measured by the progression free survival

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 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: 46
Country: Number of subjects enrolled	Belgium: 4
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	34
From 65 to 84 years	16
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	Arm 1

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	Mabthera
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

375 mg/m2 course 1 only on day 1
500 mg/m2 course 2 - 6 on day 1

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

40mg per day on days 1, 2, 3, 4

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

100mg/m2 per day on day 1 (24 hrs continuous)

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

4g/m2 per day (2 doses of 2g/m2) on day 2 (3 hrs infusion for every administration of 2 g/m2)

Number of subjects in period 1	Arm 1
Started	50
Completed	16
Not completed	34
Adverse reactions	9
Other	10
Lack of efficacy	15

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	50	50	
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)	34	34	
From 65-84 years	16	16	
85 years and over	0	0	
Age continuous Units: years			
median	60		
full range (min-max)	43 to 69	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	37	37	

End points

End points reporting groups

Reporting group title	Arm 1

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	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	46			
Units: Whole	46			

Attachments (see zip file)	Statistical data section from publication/HO88 Statistical data List of reported non-SAE's/nonsaedata88-25Nov2022.pdf List of reported SAE's/saedata88-25Nov2022.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Until 30 days, and after 30 days if related to IMP, see additional description for all details and exceptions.

Adverse event reporting additional description:

All adverse events, with the exception of disease progression, will be reported from the first study related procedure until 30 days after going off protocol treatment or until the start of subsequent systemic anti-CLL therapy, if earlier. Adverse events occurring after 30 days should also be reported if considered related to study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3

Reporting groups

Reporting group title	Arm 1

Reporting group description: -

Serious adverse events	Arm 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	37 / 45 (82.22%)		
number of deaths (all causes)	30		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm benign, malignant and unspecif. (inc. cysts/polyp)	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Vascular disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	5 / 45 (11.11%)		
occurrences causally related to treatment / all	5 / 7		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Immune system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	7 / 45 (15.56%)		
occurrences causally related to treatment / all	4 / 8		
deaths causally related to treatment / all	2 / 3		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Investigations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorder	Additional description: All combined, see SAE chart for details		

subjects affected / exposed	5 / 45 (11.11%)		
occurrences causally related to treatment / all	5 / 7		
deaths causally related to treatment / all	2 / 2		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	15 / 45 (33.33%)		
occurrences causally related to treatment / all	21 / 21		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eye disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 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 / 45 (11.11%)		
occurrences causally related to treatment / all	7 / 7		
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	2 / 45 (4.44%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	21 / 45 (46.67%)		
occurrences causally related to treatment / all	21 / 32		
deaths causally related to treatment / all	2 / 4		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 45 (86.67%)		
Vascular disorders			
Vascular	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	4		
Surgical and medical procedures			
Surgery/intra-operative injury	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
General disorders and administration site conditions			
Constitutional symptoms	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	12 / 45 (26.67%)		
occurrences (all)	15		
Pain	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Immune system disorders			
Allergy/immunology	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	6		
Cardiac disorders			
Cardiac arrythmia	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	4		
Cardiac general	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	12 / 45 (26.67%)		
occurrences (all)	17		
Nervous system disorders			

Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	7		
Neurology	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	14		
Lymphatics	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Auditory/ear	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	6 / 45 (13.33%)		
occurrences (all)	8		
Eye disorders			
Ocular/visual	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	5		
Gastrointestinal disorders			
Gastrointestinal	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	20 / 45 (44.44%)		
occurrences (all)	36		
Syndromes	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	9 / 45 (20.00%)		
occurrences (all)	9		
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	5		
Endocrine disorders			

Endocrine	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Hepatobiliary/pancreas	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Musculoskeletal/soft tissue	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Infections and infestations			
Infection	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	28 / 45 (62.22%)		
occurrences (all)	49		
Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	15 / 45 (33.33%)		
occurrences (all)	44		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 August 2011	- addition of prophylactic antibiotics during chemotherapy - addition of exclusion criterion 'Unwillingness or not capable to use effective means of anticonception (all men and pre-menopausal women)' - evaluations in follow up period specified - AE's hematotoxicity and GVHD do not have to be reported on AE form, because they are already reported on other forms - extension of inclusion period

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported