Clinical trial results:
Phase II study on the feasibility and efficacy of consolidation with 90Y-ibritumomab tiuxetan in patients with relapsed or refractory aggressive B-cell non-Hodgkin's lymphoma having achieved partial or complete remission after induction with R-PECC chemotherapy.

Summary

EudraCT number	2006-007083-28
Trial protocol	NL
Global end of trial date	11 July 2019
Results information	
Result version number	v1 (current)
This version publication date	26 January 2023
First version publication date	26 January 2023

Trial information

Trial identification	
Sponsor protocol code	HOVON85NHL
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Dutch Cochrane Centre: NTR1380

Notes:

Sponsors	
Sponsor organisation name	HOVON
Sponsor organisation address	De Boelelaan 1117, Amsterdam, Netherlands,
Public contact	HOVON Data Center, HOVON, +31 107041560, hdc@erasmusmc.nl
Scientific contact	HOVON Data Center, HOVON, +31 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	04 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2016
Global end of trial reached?	Yes
Global end of trial date	11 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the feasibility and efficacy of 90Y-ibritumomab tiuxetan consolidation treatment after R-PECC chemotherapy as second or third line treatment in patients with refractory or relapsed aggressive B-cell NHL, after or not eligible for autologous stem cell transplantation.

Primary objective:
Assessment of the feasibility of this treatment approach. Measured primarily by the percentage of patients that reach CR or PR after R-PECC and proceed to 90Y-ibritumomab tiuxetan treatment, and by the fraction of patients that endure the 90Y-ibritumomab tiuxetan treatment without major problems, i.e. the safety and tolerability of 90Y-ibritumomab tiuxetan after R-PECC chemotherapy.

Protection of trial subjects:

Monitoring and insurance.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	14

From 65 to 84 years	50
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	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 (max 750mg), day 1 or at day 0, cycle 1-4	
Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 40mg/m2, days 1-5, cycle 1-4	
Investigational medicinal product name	Chlorambucil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 8mg/m2, days 1-5, cycle 1-4	
Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 100mg.m2, days 1-5, cycle 1-4	
Investigational medicinal product name	Lomustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use
Dosage and administration details: 80mg/m2, day 1, cycle 1-4	
Investigational medicinal product name	90Y-ibritumomab tiuxetan
Investigational medicinal product code	
Other name	Zevalin
Pharmaceutical forms	Kit for radiopharmaceutical preparation
Routes of administration	Intravenous use
Dosage and administration details: 14.8 MBq/kg, single dose in consolidation	

Number of subjects in period 1	Experimental Group
Started	64
Completed	29
Not completed	35
Other	17
Lack of efficacy	18

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	64	64	
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)	14	14	
From 65-84 years	50	50	
85 years and over	0	0	
Age continuous Units: years			
median	70		
full range (min-max)	45 to 82	-	
Gender categorical Units: Subjects			
Female	21	21	
Male	43	43	

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	62			
Units: Whole	62			

Attachments (see zip file)	Statistical data section from publication/HO85 Statistical data List of reported SAE's/saedata85-10Jan2023.pdf List of reported non-SAE's/nonsaedata85-10Jan2023.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs of grade 2 or higher, with the exception of progression of disease, will be reported from the first study-related procedure until 30 days following the last dose of study drug or until the start of subsequent systemic therapy, if earlier.

Adverse event reporting additional description:

Resolution information after 30 days should also be provided. 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	Experimental Group

Reporting group description: -

Serious adverse events	Experimental Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 62 (38.71%)		
number of deaths (all causes)	53		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 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	2 / 62 (3.23%)		
occurrences causally related to treatment / all	1 / 2		
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 / 62 (3.23%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Blood and lymphatic disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	8 / 62 (12.90%)		
occurrences causally related to treatment / all	10 / 11		
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	7 / 62 (11.29%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	1 / 4		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	4 / 62 (6.45%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 62 (1.61%)		
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	2 / 62 (3.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see SAE chart for details.		
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	1 / 1		
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	7 / 62 (11.29%)		
occurrences causally related to treatment / all	6 / 9		
deaths causally related to treatment / all	2 / 2		

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	50 / 62 (80.65%)		
Vascular disorders			
Vascular	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
General disorders and administration site conditions			
Coagulation	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Constitutional symptoms	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	21 / 62 (33.87%)		
occurrences (all)	28		
Pain	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	10 / 62 (16.13%)		
occurrences (all)	13		
Immune system disorders			
Allergy/immunology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Pulmonary/upper respiratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	10 / 62 (16.13%)		
occurrences (all)	12		
Cardiac disorders			
Cardiac arrythmia	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	3		
Cardiac general	Additional description: All combined, see non-SAE chart for details.		

subjects affected / exposed	4 / 62 (6.45%)		
occurrences (all)	5		
Nervous system disorders			
Neurology	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	6 / 62 (9.68%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Blood/bone marrow	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	34 / 62 (54.84%)		
occurrences (all)	198		
Hemorrhage/bleeding	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	4 / 62 (6.45%)		
occurrences (all)	4		
Lymphatics	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	3		
Eye disorders			
Ocular/visual	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	3		
Gastrointestinal disorders			
Gastrointestinal	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	15 / 62 (24.19%)		
occurrences (all)	23		
Skin and subcutaneous tissue disorders			
Dermatology/skin	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 62 (14.52%)		
occurrences (all)	12		
Renal and urinary disorders			
Renal/genitourinary	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Musculoskeletal/soft tissue	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	5		
Infections and infestations			

Infection	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	12 / 62 (19.35%)		
occurrences (all)	16		
Metabolism and nutrition disorders			
Metabolic/laboratory	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 62 (14.52%)		
occurrences (all)	24		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2012	Lay-out and administrative changes Change of PET review address Change of supplier Zevalin FU duration specified conform HOVON guidelines Update of safety paragraph to current guidelines Revision appendix B to avoid contradiction with paragraph 11 Revision and update appendix H due to change of supplier

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported