Clinical trial results:
A multicenter, phase II study of bortezomib and dexamethasone as induction treatment followed by high dose melphalan (HDM) and autologous stem cell transplantation (SCT) in patients with de novo amyloid light chain (AL) amyloidosis.

Summary

EudraCT number	2010-021445-42
Trial protocol	NL BE DE
Global end of trial date	29 January 2021

Results information

Result version number	v1 (current)
This version publication date	04 September 2022
First version publication date	04 September 2022

Trial information

Trial identification

Sponsor protocol code	HO104

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	14 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 June 2016
Global end of trial reached?	Yes
Global end of trial date	29 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of bortezomib plus dexamethasone followed by HDM and auto-SCT in patients with newly diagnosed AL amyloidosis who are 18-70 years inclusive.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 2012
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: 45
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	50
From 65 to 84 years	7
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	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will be treated with 4 cycles of bortezomib and dexamethasone (q 3 weeks). The recommended starting dose of bortezomib is 1.3 mg/m2 and it is given subcutaneously in the hospital on an outpatient basis.

Number of subjects in period 1	Experimental group
Started	57
Completed	38
Not completed	19
Consent withdrawn by subject	1
not eligible for ASCT or other causes	9
Adverse events	5
Lack of efficacy	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	57	57	
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 (18-70 years)	57	57	
Age continuous Units: years			
median	59		
full range (min-max)	26 to 70	-	
Gender categorical Units: Subjects			
Female	25	25	
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/documents for results

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Whole	57			

Attachments (see zip file)	Statistical data section from publication/HO104_statistical List of reported non-SAE's/nonsaedata104-7Jul2022.pdf List of reported SAE's/saedata104-7Jul2022.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	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	35 / 57 (61.40%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events			
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Symptomatic hypotension			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Oedema			

subjects affected / exposed	2 / 57 (3.51%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
General malaise				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnea/ bronchial hyperreactivity				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary bleeding				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 57 (3.51%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Sinusitis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiac arrest				
subjects affected / exposed	2 / 57 (3.51%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	2 / 2			
Heart failure				

subjects affected / exposed	5 / 57 (8.77%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
Cardiac right ventricular dysfunction			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Complete atrioventricular block			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intercranial hemorrhage			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Near syncope			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Poly neuropathy			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombopenia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Colitis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhea			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastro−intestinal necrosis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischemic colitis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepato−Renal sundrome			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Acute tubulus necrosis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Progress. of renal insufficiency				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal insufficiency				
subjects affected / exposed	2 / 57 (3.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Muscle weakness arms and legs				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Communitiy aquired pneumonia				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	2 / 57 (3.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	4 / 57 (7.02%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			

Pneumosepsis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	3 / 57 (5.26%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Fluid overflow				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Fluid retention				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycemia				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatremia				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences causally related to treatment / all	1 / 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	52 / 57 (91.23%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Vascular disorders			
Vascular disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	15 / 57 (26.32%)		
occurrences (all)	20		
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	32 / 57 (56.14%)		
occurrences (all)	53		
Immune system disorders			
Immune system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 57 (1.75%)		
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	17 / 57 (29.82%)		
occurrences (all)	20		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	12 / 57 (21.05%)		
occurrences (all)	14		
Investigations			

Investigations	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	25 / 57 (43.86%)		
occurrences (all)	50		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Cardiac disorders			
Cardiac disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	13 / 57 (22.81%)		
occurrences (all)	21		
Nervous system disorders			
Nervous system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	33 / 57 (57.89%)		
occurrences (all)	63		
Blood and lymphatic system disorders			
Blood and lymphatic disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	16 / 57 (28.07%)		
occurrences (all)	24		
Eye disorders			
Eye disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	5 / 57 (8.77%)		
occurrences (all)	8		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	33 / 57 (57.89%)		
occurrences (all)	78		
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	12 / 57 (21.05%)		
occurrences (all)	19		
Renal and urinary disorders			

Renal and urinary disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	6 / 57 (10.53%)		
occurrences (all)	8		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	11 / 57 (19.30%)		
occurrences (all)	11		
Infections and infestations			
Infections and infestations	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	25 / 57 (43.86%)		
occurrences (all)	40		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	27 / 57 (47.37%)		
occurrences (all)	63		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2011	AM1: change of administration route bortezomib (s.c. instead of i.v.). New version of protocol, ICF, bortezomib IB and bortezomib labels.
10 July 2012	AM2: addition of pre-study ICF, new version of protocol, ICF and bortezomib IB.
10 January 2013	AM3: new version of protocol, ICF and bortezomib IB.
27 March 2014	AM4: closure of dexa-only arm, new version of protocol, ICF and bortezomib IB
17 July 2015	AM5: new version of protocol, ICF and bortezomib IB.

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/30923094