Clinical trial results:
HOVON 124 WM study: A prospective phase I/II trial of the combination of ixazomib citrate, rituximab and dexamethasone in patients with relapsed or progressive Waldenström's macroglobulinemia.

Summary

EudraCT number	2013-002711-94
Trial protocol	NL BE GR
Global end of trial date	05 February 2024

Results information

Result version number	v1 (current)
This version publication date	29 November 2025
First version publication date	29 November 2025

Trial information

Trial identification

Sponsor protocol code	HO124WM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	Dr. Molenwaterplein 40, Rotterdam, Netherlands,
Public contact	HOVON, HOVON, +31 (0)107041560, hovon@erasmusmc.nl
Scientific contact	HOVON, HOVON, +31 (0)107041560, hovon@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 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2019
Global end of trial reached?	Yes
Global end of trial date	05 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

For the phase I part: to establish the recommended phase II dose for the combination of oral ixazomib citrate and dexamethasone in patients with WM.
For the phase II part: To assess the efficacy (overall response rate) of oral ixazomib citrate in combination with rituximab and dexamethasone

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2014
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: 36
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Greece: 14
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)	23
From 65 to 84 years	36

85 years and over	1

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	Ixazomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

(3.0 or 4.0 mg fixed dose) o.d. p.o. Day 1,8,15 cycle 1-8

Number of subjects in period 1	Experimental group
Started	60
Completed	22
Not completed	38
Adverse events, all combined	4
Other	3
At patients request	3
Lack of efficacy	28

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			
Adults			
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)	23	23	
From 65-84 years	36	36	
85 years and over	1	1	
Age continuous			
Units: years			
median	68		
full range (min-max)	46 to 91	-	
Gender categorical			
Units: Subjects			
Female	19	19	
Male	41	41	

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	60			
Units: Whole	60			

Attachments (see zip file)	HO124_Statistical data section from nonsaedata124-5Aug2025/nonsaedata124-5Aug2025.pdf saedata124-5Aug2025/saedata124-5Aug2025.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.

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	22 / 60 (36.67%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined		
subjects affected / exposed	10 / 60 (16.67%)		
occurrences causally related to treatment / all	1 / 11		
deaths causally related to treatment / all	0 / 2		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All Combined		
subjects affected / exposed	3 / 60 (5.00%)		
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		
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

General disorders and administration site conditions	Additional description: All Combined		
subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 2		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined		
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infectios and infestations	Additional description: All Combined		
subjects affected / exposed	6 / 60 (10.00%)		
occurrences causally related to treatment / all	7 / 8		
deaths causally related to treatment / all	1 / 1		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All Combined		
subjects affected / exposed	1 / 60 (1.67%)		
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 / 60 (86.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Additional description: All combined		
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Vascular disorders			
Vascular disorders	Additional description: All combined		
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Surgical and medical procedures			

Surgical and medical procedures	Additional description: All combined		
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined		
subjects affected / exposed	19 / 60 (31.67%)		
occurrences (all)	40		
Immune system disorders			
Immune system disorders	Additional description: All combined		
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	7		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined		
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	14		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined		
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	11		
Investigations			
Investigations	Additional description: All combined		
subjects affected / exposed	18 / 60 (30.00%)		
occurrences (all)	51		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined		
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Cardiac disorders			
Cardiac disorders	Additional description: All combined		
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Nervous system disorders			
Nervous system disorders	Additional description: All combined		
subjects affected / exposed	29 / 60 (48.33%)		
occurrences (all)	47		
Blood and lymphatic system disorders			

Blood and lymphatic system disorders	Additional description: All combined		
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	23		
Eye disorders			
Eye disorders	Additional description: All combined		
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined		
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All combined		
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	17		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined		
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined		
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	15		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined		
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2015	Amendment 1 Research Protocol Patient population: patients aged 18 years or older with recurrent WM, with ≥1 line of prior systemic treatment instead of 1–3 lines of prior systemic treatment. Clarification of inclusion and exclusion criteria. Adjustment of contraception requirements for women using rituximab. Adjustment and clarification of timing for clinical evaluations. Subject Information Sheet and Consent Form 5. Adjustment of contraception requirements for women using rituximab. 6. Adjustment and clarification of timing for clinical evaluations. Participating Hospitals 7. Addition of LUMC, Tergooi hospitals, and IJsselland hospital. 8. Change of local investigator at Erasmus MC.
28 June 2016	Amendment 2 The labeling of the study medication ixazomib citrate will be taken over by the central pharmacy at the Academic Medical Center, Amsterdam.
25 January 2017	Amendment 3 Other changes: In the updated ixazomib citrate Investigator's Brochure (IB, version 10), a fatal case of progressive multifocal leukoencephalopathy (PML) was reported in a patient treated with ixazomib citrate. It is not known whether ixazomib citrate contributed to the development of this condition in the patient. This information has been added to the patient information. Additional changes: Administrative correction of text regarding urine tests that was incorrect in the patient information. For already included patients, a summary of the patient information has been prepared. A new version of the Investigator's Brochure for ixazomib dated June 27, 2016 (version 10) and NLN9708 risk language April 20, 2016, along with the statement from the principal investigator, Prof. Dr. M. J. Kersten, indicating that the new IB has implications for the HOVON 124 study. Annual progress and safety reporting.

27 November 2017	Amendment 4 Reason for this change: Clarification of trial-specific procedures: Warm measurement of serum IgM in case of cryoglobulinemia. This is crucial for correct response assessment. The method of response assessment based on CT images. Although reference was made to the article by Cheson et al., these criteria were not clearly incorporated into the protocol. The time points when response evaluation should be performed. SAE (Serious Adverse Events) can now be reported by email. The inclusion period has been extended by 2 years due to delayed enrollment of patients. The KWF (Dutch Cancer Society) has agreed to a cost-neutral extension.
21 December 2018	Amendment 5 Reason for this change: Protocol: Textual, non-substantial adjustments. Patient Information: Update regarding privacy legislation, non-substantial. Change of local investigator: Dr. Koene replaces Dr. Vos at St. Antonius Hospital in Nieuwegein.
04 November 2019	Amendment 6 Reason for this change: Dr. Silbermann replaces Dr. Deenik at Tergooi Hospital in Hilversum.

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/34388022