Clinical trial results:
Efficacy and tolerability of ixazomib, daratumumab and low dose dexamethasone (IDd) followed by ixazomib and daratumumab maintenance therapy until progression for a maximum of 2 years in unfit and frail newly diagnosed multiple myeloma patients; an open-label phase II trial

Summary

EudraCT number	2016-002600-90
Trial protocol	NL BE
Global end of trial date	08 July 2024

Results information

Result version number	v1 (current)
This version publication date	03 December 2025
First version publication date	03 December 2025

Trial information

Trial identification

Sponsor protocol code	HO143

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. Molewaterplein 40, Rotterdam, 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	01 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To determine the efficacy, defined as overall response rate (ORR), of 9 cycles of ixazomib, daratumumab and low dose dexamethasone
(overall response will be defined as (stringent) complete response ((s)CR), very good partial (VGPR) response and partial response (PR))

Protection of trial subjects:

Monitoring and insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2017
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: 120
Country: Number of subjects enrolled	Belgium: 13
Worldwide total number of subjects	133
EEA total number of subjects	133

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)	0
From 65 to 84 years	122
85 years and over	11

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	Not applicable
Blinding used	Not blinded

Arms

Arm title	Experimental

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Daratumumab
Investigational medicinal product code	JNJ-54767414
Other name	
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

16 mg/kg or 1800 mg On the following days of the 28 day cycle:

Cycle 1-2: 1, 8, 15 and 22 Cycle 3-6: 1 and 15 Cycle 7-9: 1

Investigational medicinal product name	Ixazomib
Investigational medicinal product code	MLN2238
Other name	NINLARO
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

4 mg* On day 1,8 and 15 of 28 day cycle

* adapt the dose to 3 mg in case of creatine clearance 20-30 ml/min or in case total bilirubin ≥ 1.5 - < 3 x ULN or transaminases ≥ 2 and < 5 times normal level.

Number of subjects in period 1	Experimental
Started	133
Completed	27
Not completed	106
Consent withdrawn by subject	10
Adverse events, all combined	15
Other	16

Lack of efficacy	65

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	133	133	
Age categorical Units: Subjects			
From 65-84 years	122	122	
85 years and over	11	11	
Age continuous Units: years			
median	78		
full range (min-max)	65 to 92	-	
Gender categorical Units: Subjects			
Female	55	55	
Male	78	78	

End points

End points reporting groups

Reporting group title	Experimental

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			
Subject group type	Reporting group			
Number of subjects analysed	133			
Units: Whole	133			

Attachments (see zip file)	nonsaedata143-5Aug2025/nonsaedata143-5Aug2025.pdf saedata143-5Aug2025/saedata143-5Aug2025.pdf Statistical data section from publication/Statistical data section

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

Reporting group description: -

Serious adverse events	Experimental		
Total subjects affected by serious adverse events			
subjects affected / exposed	98 / 130 (75.38%)		
number of deaths (all causes)	72		
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	22 / 130 (16.92%)		
occurrences causally related to treatment / all	5 / 28		
deaths causally related to treatment / all	2 / 4		
Vascular disorders			
Vascular disorders	Additional description: All combined		
subjects affected / exposed	3 / 130 (2.31%)		
occurrences causally related to treatment / all	1 / 3		
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	11 / 130 (8.46%)		
occurrences causally related to treatment / all	11 / 17		
deaths causally related to treatment / all	1 / 3		
Immune system disorders			

Immune system disorders	Additional description: All combined		
subjects affected / exposed	1 / 130 (0.77%)		
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		
subjects affected / exposed	5 / 130 (3.85%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined		
subjects affected / exposed	3 / 130 (2.31%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Product issues			
Product issues	Additional description: All combined		
subjects affected / exposed	1 / 130 (0.77%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined		
subjects affected / exposed	12 / 130 (9.23%)		
occurrences causally related to treatment / all	5 / 17		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders	Additional description: All combined		
subjects affected / exposed	11 / 130 (8.46%)		
occurrences causally related to treatment / all	8 / 13		
deaths causally related to treatment / all	1 / 2		
Nervous system disorders			
Nervous system disorders	Additional description: All combined		
subjects affected / exposed	13 / 130 (10.00%)		
occurrences causally related to treatment / all	4 / 16		
deaths causally related to treatment / all	0 / 1		

Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All combined		
subjects affected / exposed	3 / 130 (2.31%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 1		

Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All combined		
subjects affected / exposed	20 / 130 (15.38%)		
occurrences causally related to treatment / all	17 / 23		
deaths causally related to treatment / all	1 / 1		

Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All combined		
subjects affected / exposed	2 / 130 (1.54%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		

Skin and subcutaneous tissue disorders			
Skin and subcutaneous disorders	Additional description: All combined		
subjects affected / exposed	3 / 130 (2.31%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders			
Renal and urinary disorders	Additional description: All combined		
subjects affected / exposed	7 / 130 (5.38%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All combined		
subjects affected / exposed	7 / 130 (5.38%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Infections and infestations	Additional description: All combined		
subjects affected / exposed	41 / 130 (31.54%)		
occurrences causally related to treatment / all	21 / 50		
deaths causally related to treatment / all	0 / 5		

Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All combined		
subjects affected / exposed	7 / 130 (5.38%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	120 / 130 (92.31%)		
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	1 / 130 (0.77%)		
occurrences (all)	2		
Vascular disorders			
Vascular disorders	Additional description: All Combined		
subjects affected / exposed	17 / 130 (13.08%)		
occurrences (all)	19		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All Combined		
subjects affected / exposed	54 / 130 (41.54%)		
occurrences (all)	88		
Immune system disorders			
Immune system disorders	Additional description: All Combined		
subjects affected / exposed	6 / 130 (4.62%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All Combined		
subjects affected / exposed	13 / 130 (10.00%)		
occurrences (all)	15		
Psychiatric disorders			
Psychiatric disorders	Additional description: All Combined		
subjects affected / exposed	16 / 130 (12.31%)		
occurrences (all)	17		

Investigations			
Investigations	Additional description: All Combined		
subjects affected / exposed	59 / 130 (45.38%)		
occurrences (all)	161		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All Combined		
subjects affected / exposed	4 / 130 (3.08%)		
occurrences (all)	5		
Cardiac disorders			
Cardiac disorders	Additional description: All Combined		
subjects affected / exposed	9 / 130 (6.92%)		
occurrences (all)	9		
Nervous system disorders			
Nervous system disorders	Additional description: All Combined		
subjects affected / exposed	65 / 130 (50.00%)		
occurrences (all)	121		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All Combined		
subjects affected / exposed	22 / 130 (16.92%)		
occurrences (all)	31		
Ear and labyrinth disorders			
Ear and labyrinth disorders	Additional description: All Combined		
subjects affected / exposed	4 / 130 (3.08%)		
occurrences (all)	4		
Eye disorders			
Eye disorders	Additional description: All Combined		
subjects affected / exposed	5 / 130 (3.85%)		
occurrences (all)	7		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All Combined		
subjects affected / exposed	46 / 130 (35.38%)		
occurrences (all)	89		
Hepatobiliary disorders			
Hepatobiliary disorders	Additional description: All Combined		
subjects affected / exposed	1 / 130 (0.77%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			

Skin and subcutaneous tissue disorders	Additional description: All Combined		
subjects affected / exposed	27 / 130 (20.77%)		
occurrences (all)	35		
Renal and urinary disorders			
Renal and urinary disorders	Additional description: All Combined		
subjects affected / exposed	22 / 130 (16.92%)		
occurrences (all)	25		
Endocrine disorders			
Endocrine disorders	Additional description: All Combined		
subjects affected / exposed	3 / 130 (2.31%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All Combined		
subjects affected / exposed	42 / 130 (32.31%)		
occurrences (all)	75		
Infections and infestations			
Infections and infestations	Additional description: All Combined		
subjects affected / exposed	38 / 130 (29.23%)		
occurrences (all)	47		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All Combined		
subjects affected / exposed	29 / 130 (22.31%)		
occurrences (all)	39		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 August 2017	Amendment 1 Protocol Update of the current approved protocol regarding incorrect dexamethasone dosages. Instruction texts added and/or adjusted. ABR form Changes in local investigators and/or independent physicians.
12 October 2017	Amendment 2 The reason for this amendment is: Daratumumab labels: Adjustment of Daratumumab text labels from 100 mg/5 ml injection vial to 400 mg/20 ml injection vial. Patient information: Examples of patient information available at www.kanker.nl. Test subjects There are no consequences of this amendment for the test subjects. The number of test subjects has not changed. Summary of changes: Daratumumab text label data has been adjusted. Patient information available at www.kanker.nl has been updated.
05 December 2017	Amendment 4 Adjustment of ICF and Pre-ICF The number of evaluations during treatment now matches the protocol. Text paragraph “Additional imaging research” has been adjusted. The amount of extra blood for scientific research has been adjusted (now matches the protocol). Paragraph on patient data access has been adjusted. Treatment schedule has been adjusted (now matches the protocol). Risk language for Daratumumab and Ixazomib possible side effects has been adjusted. Changes in local investigator and/or independent physician Haga Hospital: independent physician [Name] replaces [Name]. Tergooi Hospital Hilversum: local investigator [Name] replaces [Name].

15 December 2017	Amendment 3 Reason for the amendment The reason for this amendment is a change in participating hospitals: Red Cross Hospital in Beverwijk; Local investigator [Name] replaces Capelle aan de IJssel; Local investigator [Name] Test subjects There are no consequences of this amendment for the test subjects. The number of test subjects has not changed compared to the original number. Summary of changes A hospital has been added: Red Cross Hospital in Beverwijk; Local investigator [Name] and independent physician [Name] A hospital has been removed: IJsselland Hospital in Capelle aan de IJssel; Local investigator [Name] and independent physician [Name] The amendment also includes changes in the ABR form: Section C9: Red Cross Hospital added
21 February 2018	Amendment 5 Reason for the amendment The reason for this amendment is a change in participating hospitals: Deventer Hospital in Deventer; Local investigator [Name] replaces UMCG in Groningen; Local investigator [Name] Test subjects There are no consequences of this amendment for the test subjects. The number of test subjects has not changed compared to the original number. Summary of changes A hospital has been added: Deventer Hospital in Deventer; Local investigator [Name] and independent physician [Name] A hospital has been removed: UMCG in Groningen; Local investigator [Name] and independent physician [Name] The amendment also includes changes in the ABR form: Section C9: Deventer Hospital replaces UMCG

06 June 2018	Amendment 6 Protocol Summary of changes: Inclusion criteria “Absolute neutrophil count (ANC) ≥ 1.0 x10/l and platelet count ≥ 75x10/l” adjusted. Time points for certain lab samples in PET-CT have been changed to (s)CR instead of “VGPR or better”. Table 10.2 and legend adjusted. Text in protocol clarified in several places. ABR / EudraCT Summary of changes: Riverland Hospital: independent physician [Name] replaces [Name]. Treat Zorggroep: independent physician [Name] replaces [Name]. Streekziekenhuis Koningin Beatrix: independent physician [Name] replaces [Name]. Groene Hart Hospital: local investigator [Name] replaces [Name]. Inclusion criteria “Absolute neutrophil count (ANC) ≥ 1.0 x10/l and platelet count ≥ 75x10/l” adjusted. Time points for certain lab samples in PET-CT have been changed to (s)CR instead of “VGPR or better”.
13 November 2018	Amendment 7 Summary of changes Treant Zorggroep: Local investigator [Name] replaces [Name].
13 February 2019	Amendment 8 Summary of changes Deventer Hospital: Local investigator [Name] replaces [Name].

12 June 2019	Amendment 9 Reason for the amendment Submission of Daratumumab Investigator's Brochure version 15 and Addendum 1 ICF addendum: possible side effects of daratumumab; storage conditions for ixazomib Changes in protocol: Update of exclusion criteria Mandatory HBV test during screening and follow-up Instruction on HBV reactivation policy Storage conditions for ixazomib Additional clarification in some protocol sections Changes in sponsor contact details Changes in ixazomib and daratumumab labels Summary of changes New version of Daratumumab Investigator's Brochure and addendum: IB Daratumumab Ed 15 dated 14 Dec 2018 and Addendum 1 dated 24 Jan 2019 Changes / ICF addendum Ixazomib storage temperature between 2–30°C Update Appendix 5 possible side effects of daratumumab: Very common side effects: high blood pressure Common side effects: herpes zoster and ingrown toenail Uncommon side effects: HBV reactivation in patients with prior hepatitis B infection; interference with pre-transfusion blood tests Changes in protocol Exclusion criteria (section 8.1.2): Patients seropositive for hepatitis B Patients seropositive for hepatitis C (except in cases of persistent virological response) HBV test during screening and follow-up (section 10.2) Screening: HBV test mandatory for all patients Follow-up: HBV test mandatory for patients with active or serological evidence of past HBV infection Instruction HBV reactivation policy (Appendix J5) Antiviral therapy must be started for patients with active HBV infection Storage conditions and label for ixazomib Ixazomib capsules must be stored at room temperature, between 2–30°C Changes in sponsor contact details [Name] is the current contact person for the HOVON Foundation The HOVON Data Center has moved; address updated accordingly Changes in ixazomib and daratumumab labels Ixazomib labels: storage temperature updated to 2–30°C

29 August 2019	Amendment 10 Reason for the amendment Submission of Daratumumab IB Ed15 Addendum 02 dated 01 May 2019 Submission of ICF Addendum version 02 dated 23 July 2019 Summary of changes Changes / ICF Addendum Entire Appendix 5 (possible side effects of daratumumab) added to the Addendum. Appendix 5 rewritten for better clarity and readability for patients. Newly observed side effects added: Very common side effects: bronchitis, constipation, back pain Common side effects: dizziness, high blood glucose levels, low calcium levels in blood, fluid loss (dehydration), chills
10 February 2020	Amendment 11 Reason for the amendment Addition of TMA as a newly identified ixazomib safety risk via ICF Addendum version 03 Submission of new IB ixazomib Ed 12 dated 19 June 2019 Submission of correction to IB Ed 12 SCO Table dated 25 June 2019 Test subjects The consequences of this amendment for the test subjects are as follows: Patients still being treated with ixazomib must be informed about the newly identified safety risk TMA and re-sign for voluntary participation in the study. Summary of changes TMA added as a newly identified safety risk to Appendix 5 of HO143 ICF (ixazomib citrate side effects).
23 April 2020	Amendment 12 Reason for the amendment Addendum ICF version 04 Adjustment of possible side effects of daratumumab via ICF Addendum Submission of new IB Daratumumab Ed16 dated 20 December 2019 Test subjects The consequences of this amendment for the test subjects are as follows: Patients still being treated with daratumumab must be informed about the newly identified possible side effects and re-sign for voluntary participation in the study. With this submission, I declare that all relevant documents from the aforementioned research file have been signed by the authorized persons. The signed documents are/will be submitted for review to the ethics committee as stated in question 11 of the ABR form.

05 November 2020	Amendment 13 Reason for the amendment Addendum ICF version 05 and protocol version 5.1 Submission of protocol v5.1 dated 16 July 2020 Submission of Addendum ICF v05 Submission of updated labels for Daratumumab Subcutaneous Submission of Cross Reference Letter for IMPD Daratumumab SQ dated Dec 2019 Submission of patient questionnaire survey Dara SC versus Dara IV Test subjects The consequences of this amendment for the test subjects are as follows: Patients currently treated with Daratumumab can switch from intravenous administration to subcutaneous injection. Additionally: Daratumumab will now be administered as a standard injection instead of infusion. These changes significantly reduce the time patients spend in the hospital for study treatment. All patients must re-sign the addendum for voluntary participation in the study. Patients switching from intravenous to subcutaneous Daratumumab must complete three time points and an additional questionnaire (patient preference survey).
21 June 2021	Amendment 14 Reason for the amendment IB Daratumumab JNJ-54767414 Ed17 dated 17 Dec 2020 IB Ixazomib Ed13 dated 27 May 2020 ICF Addendum version 06
17 February 2022	Amendment 15 Summary of changes Streekziekenhuis Koningin Beatrix Winterswijk: Local investigator [Name] replaces [Name]. Treant Zorggroep: Local investigator [Name] replaces [Name].
06 September 2022	Amendment 16 Summary of changes Elisabeth-TweeSteden Hospital: Local investigator [Name] replaces [Name].
25 February 2023	Amendment 17 Summary of changes Maasstad Hospital: Local investigator [Name] replaces [Name].
05 July 2024	Amendment 18 Summary and motivation for the changes Treant Zorggroep: Local investigator [Name] replaces [Name]. The EudraCT application form (Annex I) has been updated. This amendment also includes changes in the ABR form.

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/40845265