



Clinical trial results: Bone Study Bone Healing During Ninlaro Exposure. An open label phase 2 single centre clinical trial

Summary

EudraCT number	2018-003258-25
Trial protocol	DK
Global end of trial date	10 January 2024

Results information

Result version number	v1 (current)
This version publication date	11 June 2025
First version publication date	11 June 2025
Summary attachment (see zip file)	Published article with 3 months results form the trial (Diaz delCastillo 23 - Increased Bone Volume by Ixazomib in Multiple Myeloma 3Month Results.pdf)

Trial information

Trial identification

Sponsor protocol code	X16120
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04028115
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Department of Hematology
Sponsor organisation address	Kløvervænget 6, Odense C, Denmark, 5000
Public contact	Odense University Hospital, Odense University Hospital, +45 65411156, birgitte.wolf.lundholm@rsyd.dk
Scientific contact	Odense University Hospital, Odense University Hospital, +45 65411156, birgitte.wolf.lundholm@rsyd.dk

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	02 December 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to investigate if treatment with ixazomib can cause healing of preexisting osteolytic bone lesions in Multiple Myeloma.

Protection of trial subjects:

In this trial, we did not give the study drug at first relapse but in a phase of temporary disease remission. Because of this, we did a full registration of adverse events observed during the trial. Registration of adverse events started upon inclusion in the trial and ended 3 months after last dose of Ixazomib. Adverse events were graded according to National Cancer Institute Common Toxicity Criteria (NCI CTC) Version 4.0 with an indication of starting date and end date, relation to investigational drug, outcome and severity. All grade 3 and 4 adverse events, considered related to Ixazomib were followed until resolution of the event or the event improves to a grade 2 or better. The unresolved aforementioned events were followed for a maximum of 6 months. In case of side effects, Ixazomib dosing was reduced or discontinued according to protocol directions. Further the protocol described actions to better AEs such as symptom relieving actions or medications. To avoid overdose of ixazomib patients were informed only to take ixazomib as prescribed and only one dose of ixazomib at a time.

Background therapy:

Ixazomib was given together with acyclovir 400 mg x 2 per day to avoid reactivation of herpes zoster infection.

Evidence for comparator: -

Actual start date of recruitment	24 October 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	17
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient were recruited at the Department of Hematology at Odense University Hospital from October 2019 to April 1 2024. Patients were recruited in the outpatient clinic during follow up appointments with their physician.

Pre-assignment

Screening details:

Patients screened to see if they conformed to the inclusion and exclusion criteria were patients with multiple myeloma in a stable remission with measurable bone disease on CT scan.
Four patients were excluded during screening, due to low kidney function, not sufficient bone disease on scan, or due to infection.

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	Intervention
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Arm description:

Treatment with Ixazomib 4 mg on day 1, 8, and 15 in a 28-day cycle for up to 24 cycles.

Arm type	Experimental
Investigational medicinal product name	ixazomib
Investigational medicinal product code	MLN9708
Other name	Ninlaro
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

4 mg on day 1, 8, and 15 in 28-day cycles.

Number of subjects in period 1	Intervention
Started	30
Completed	13
Not completed	17
Progressive multiple myeloma	13
Adverse event, non-fatal	4

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	30	30	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	58		
full range (min-max)	38 to 76	-	
Gender categorical			
Units: Subjects			
Female	16	16	
Male	14	14	

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description:	
Treatment with Ixazomib 4 mg on day 1, 8, and 15 in a 28-day cycle for up to 24 cycles.	

Primary: Healing of osteolytic bone lesions on low dose CT

End point title	Healing of osteolytic bone lesions on low dose CT ^[1]
End point description:	
lesions on low dose CT. Healing of osteolytic bone lesions on low dose CT. Healing will be evaluated based on the preexisting lesion on low dose CT required upon inclusion. All lesions will be evaluated individually using the inclusion scanning as reference. Healing will be defined as $\geq 25\%$ reduction in the size of osteolytic lesions (a reduction of at least 2 mm in the longest dimension is required), increased sclerosis in the edge of existing lesions, or healing of existing lesions.	
End point type	Primary
End point timeframe:	
from the inclusion in the protocol until the patient has been in the protocol for 24 months or until the patient leaves the protocol if that happens before 24 months	

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: For this primary end point there is no statistical analysis, as it is a count in the total group of patient treated. there is no control group. It is counts of lesion where healing is observed relative to baseline.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: incidents of healing	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from inclusion to 3 months after the last dose of ixazomib.

Adverse event reporting additional description:

Patients were evaluated by a physician every 4 weeks in regards to multiple myeloma status, ECOG performance status, side effects, renal function, liver function, hematology, neuropathy etc. Adverse events were graded and recorded according to NCI CTC v. 4.0.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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Reporting groups

Reporting group title	Intervention
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Reporting group description:

All patient included and treated in the trial.

Serious adverse events	Intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 30 (30.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Lung infection			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations, other	Additional description: 1 case of salmonella and 1 case of influenza		
subjects affected / exposed	2 / 30 (6.67%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		

Non-serious adverse events	Intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	5		
Creatinine increase			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	9		
Neutrophil count decreased			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Lymphocyte count decreased			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	6		
Vascular disorders			
Hot flashes			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	11 / 30 (36.67%)		
occurrences (all)	14		
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	11		
Platelet count decreased			

subjects affected / exposed occurrences (all)	17 / 30 (56.67%) 34		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Edema limbs subjects affected / exposed occurrences (all)	8 / 30 (26.67%) 11 4 / 30 (13.33%) 5		
Eye disorders Dry eyes subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Anal hemorrhage subjects affected / exposed occurrences (all) Diarrhea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 4 3 / 30 (10.00%) 3 4 / 30 (13.33%) 5 9 / 30 (30.00%) 14 3 / 30 (10.00%) 3 2 / 30 (6.67%) 2		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 5		

Pruritis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3		
Musculoskeletal and connective tissue disorders Atralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Muscle cramp subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3 3 / 30 (10.00%) 7 7 / 30 (23.33%) 21		
Infections and infestations Lung infection subjects affected / exposed occurrences (all) Upper respiratory infection subjects affected / exposed occurrences (all)	6 / 30 (20.00%) 6 6 / 30 (20.00%) 6		
Infections and infestations, other subjects affected / exposed occurrences (all) Abdominal infections subjects affected / exposed occurrences (all)	Additional description: COVID19 or unknown infection 6 / 30 (20.00%) 6 2 / 30 (6.67%) 2		
Metabolism and nutrition disorders Hypercalcemia subjects affected / exposed occurrences (all) Hyperkalemia subjects affected / exposed occurrences (all) Hypocalcemia subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 3 3 / 30 (10.00%) 4 2 / 30 (6.67%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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/36970780>