Clinical trial results:
Magnolia Study
Prolonged Protection from Bone Disease in Multiple Myeloma.
An open label phase 4 multicenter international randomised trial

Summary

EudraCT number	2014-002494-12
Trial protocol	DK SE NO
Global end of trial date	15 March 2023

Results information

Result version number	v1 (current)
This version publication date	30 November 2024
First version publication date	30 November 2024
Summary attachment (see zip file)	summary magnolia (Summary magnolia.docx)

Trial information

Trial identification

Sponsor protocol code	NMSG22/14

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02286830
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OdenseOUH
Sponsor organisation address	J. B. Winsløws Vej 4, Odense, Denmark, 5000
Public contact	Thomas Lund, Odense University Hospital, +45 21450256, Thomas.lund2@rsyd.dk
Scientific contact	Thomas Lund, Odense University Hospital, +45 21450256, Thomas.lund2@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	13 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2023
Global end of trial reached?	Yes
Global end of trial date	15 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the time to PBD from year 2 to year 4 in patients treated with monthly zoledronic acid in two consecutive years compared to patients treated with monthly zoledronic acid in four consecutive years.

Protection of trial subjects:

done according to the ethical committee approval

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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	Norway: 82
Country: Number of subjects enrolled	Denmark: 111
Worldwide total number of subjects	193
EEA total number of subjects	193

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)	81
From 65 to 84 years	112
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

recruited either at diagnosis or after 2 years of zoledronic acid treatment

Pre-assignment

Screening details:

Patients with MM in recruiting hospitals

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	2 years treatment

Arm description:

2 years of treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	4 years treatment

Arm description:

4 years of treatment

Arm type	Experimental
Investigational medicinal product name	zoledronic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Injection

Dosage and administration details:

4-3 mg ever fouth week

Number of subjects in period 1	2 years treatment	4 years treatment
Started	94	99
Completed	94	99

Baseline characteristics

Reporting groups	
Reporting group title	2 years treatment
Reporting group description: 2 years of treatment	
Reporting group title	4 years treatment
Reporting group description: 4 years of treatment	

Reporting group values	2 years treatment	4 years treatment	Total
Number of subjects	94	99	193
Age categorical Units: Subjects			
Adults (18-64 years)	46	35	81
From 65-84 years	48	64	112
Gender categorical Units: Subjects			
Female	39	39	78
Male	55	60	115

Subject analysis sets	
Subject analysis set title	number of osteolysis in each group
Subject analysis set type	Full analysis
Subject analysis set description: 9 in the intervention arm 21 in the control arm	

Reporting group values	number of osteolysis in each group		
Number of subjects	193		
Age categorical Units: Subjects			
Adults (18-64 years)	81		
From 65-84 years	112		
Gender categorical Units: Subjects			
Female	78		
Male	115		

End points

End points reporting groups

Reporting group title	2 years treatment
Reporting group description: 2 years of treatment	
Reporting group title	4 years treatment
Reporting group description: 4 years of treatment	
Subject analysis set title	number of osteolysis in each group
Subject analysis set type	Full analysis
Subject analysis set description: 9 in the intervention arm 21 in the control arm	

Primary: Bone disease

End point title	Bone disease
End point description:	
End point type	Primary
End point timeframe: LPLV	

End point values	2 years treatment	4 years treatment	number of osteolysis in each group	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	94	99	193	
Units: Number				
Number	21	9	30	

Statistical analyses

Statistical analysis title	Cox regression analysis of PBD
Comparison groups	4 years treatment v 2 years treatment
Number of subjects included in analysis	193
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Regression, Cox

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from start of trial til end of trial	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23
Reporting groups	
Reporting group title	2 years treatment
Reporting group description: 2 years of treatment	
Reporting group title	4 years treatment
Reporting group description: 4 years of treatment	

Serious adverse events	2 years treatment	4 years treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 94 (2.13%)	6 / 99 (6.06%)	
number of deaths (all causes)	3	2	
number of deaths resulting from adverse events			
Renal and urinary disorders			
Creatinine increase			
subjects affected / exposed	0 / 94 (0.00%)	2 / 99 (2.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypercalcaemia			
subjects affected / exposed	2 / 94 (2.13%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteonecrosis of jaw			
subjects affected / exposed	0 / 94 (0.00%)	4 / 99 (4.04%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	2 years treatment	4 years treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 94 (78.72%)	83 / 99 (83.84%)	
Renal and urinary disorders			
Creatinine increase			
subjects affected / exposed	24 / 94 (25.53%)	39 / 99 (39.39%)	
occurrences (all)	24	39	
Endocrine disorders			
Hypercalcaemia			
subjects affected / exposed	10 / 94 (10.64%)	15 / 99 (15.15%)	
occurrences (all)	10	15	
Hypocalcaemia			
subjects affected / exposed	39 / 94 (41.49%)	47 / 99 (47.47%)	
occurrences (all)	39	47	
Musculoskeletal and connective tissue disorders			
Osteonecrosis of jaw			
subjects affected / exposed	1 / 94 (1.06%)	2 / 99 (2.02%)	
occurrences (all)	1	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