Clinical trial results:
Zoledronic Acid to Maintain Bone Mass After Denosumab Discontinuation: AfterDmab

Summary

EudraCT number	2016-000852-91
Trial protocol	NL
Global end of trial date	01 February 2020

Results information

Result version number	v1 (current)
This version publication date	14 February 2021
First version publication date	14 February 2021
Summary attachment (see zip file)	summary (AfterdmabEurDracCT.docx)

Trial information

Trial identification

Sponsor protocol code	W15.032

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02499237
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LUMC
Sponsor organisation address	albinusdreef 2, leiden, Netherlands,
Public contact	Clinical Research Internal Medicine, Leiden University Medical Center, research_interne@Lumc.nl
Scientific contact	Clinical Research Internal Medicine, Leiden University Medical Center, research_interne@Lumc.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	05 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2020
Global end of trial reached?	Yes
Global end of trial date	01 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate changes in BMD of the lumbar spine (LS) one year after treatment discontinuation in denosumab-treated women and in denosumab-treated women who received a single infusion of zoledronic acid one year before treatment discontinuation

Protection of trial subjects:

NR

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Greece: 60
Worldwide total number of subjects	75
EEA total number of subjects	75

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)	45
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

recruitment at the FLS from the Leiden University Medical Center from 25/10/2016 till 01-02-2018

Pre-assignment

Screening details:

as stated in summary

Period 1

Period 1 title	25/10/2016 till 01-02-2018 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Zoledronate

Arm description: -

Arm type	Experimental
Investigational medicinal product name	zoledronate
Investigational medicinal product code	PR1
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg iv

Arm title	none

Arm description:

no active treatment

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1[1]	Zoledronate	none
Started	30	30
Completed	27	30
Not completed	3	0
Consent withdrawn by subject	3	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: query not clear

Baseline characteristics

Reporting groups

Reporting group title	25/10/2016 till 01-02-2018

Reporting group description: -

Reporting group values	25/10/2016 till 01-02-2018	Total	
Number of subjects	60	60	
Age categorical			
age			
Units: Subjects			
Adults (18-64 years)	30	30	
From 65-84 years	29	29	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	60	60	
Male	0	0	

Subject analysis sets

Subject analysis set title	zol
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The trial required 56 patients to have a power of 95% to detect a 6% difference in LS-BMD between the two treatment groups with a two-sided error α probability of 0.05. Data for continuous variables are presented as mean ± standard error of the mean (SEM). Data for categorical variables are presented as number and/or frequencies. Kolmogorov-Smirnov test was used to test the normality of distribution of continuous variables. Within group comparisons of continuous variables were performed with repeated measures analysis of variance (ANOVA) or Friedman test. In case of statistically significant trend, multiple pairwise comparisons were performed with Bonferroni post-hoc adjustment. Independent T-test or Mann-Whitney test were used to compare continuous variables between groups. Chi-square or Fischer's exact test were used for comparisons of categorical variables between groups. Spearman's (rs) coefficient of correlation was used for bivariate correlations between continuous variables. A

Subject analysis set title	no
Subject analysis set type	Intention-to-treat

Subject analysis set description:

see protocol

Reporting group values	zol	no	
Number of subjects	27	30	
Age categorical			
age			
Units: Subjects			
Adults (18-64 years)	30		
From 65-84 years	26		
85 years and over	1		
Gender categorical Units: Subjects			
Female	57		
Male	0		

End points

End points reporting groups

Reporting group title	Zoledronate
Reporting group description: -	
Reporting group title	none
Reporting group description: no active treatment	
Subject analysis set title	zol
Subject analysis set type	Intention-to-treat
Subject analysis set description: The trial required 56 patients to have a power of 95% to detect a 6% difference in LS-BMD between the two treatment groups with a two-sided error α probability of 0.05. Data for continuous variables are presented as mean ± standard error of the mean (SEM). Data for categorical variables are presented as number and/or frequencies. Kolmogorov-Smirnov test was used to test the normality of distribution of continuous variables. Within group comparisons of continuous variables were performed with repeated measures analysis of variance (ANOVA) or Friedman test. In case of statistically significant trend, multiple pairwise comparisons were performed with Bonferroni post-hoc adjustment. Independent T-test or Mann-Whitney test were used to compare continuous variables between groups. Chi-square or Fischer's exact test were used for comparisons of categorical variables between groups. Spearman's (rs) coefficient of correlation was used for bivariate correlations between continuous variables. A	
Subject analysis set title	no
Subject analysis set type	Intention-to-treat
Subject analysis set description: see protocol	

Primary: lumbale spine

End point title	lumbale spine
End point description: see summary	
End point type	Primary
End point timeframe: 24 months	

End point values	Zoledronate	none	zol	no
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	27	30
Units: g/cm				
number (not applicable)				
BMD	30	30	27	30

Statistical analyses

Statistical analysis title	analyses
Statistical analysis description: see protocol	
Comparison groups	Zoledronate v none v zol v no

Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1
Variability estimate	Standard deviation
Dispersion value	2

Adverse events

Adverse events information	
Timeframe for reporting adverse events: during the trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	SNOMED CT
Dictionary version	2
Reporting groups	
Reporting group title	patients

Reporting group description: -

Serious adverse events	patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 27 (66.67%)		
General disorders and administration site conditions			
flue like reaction	Additional description: Eighteen (66.7%) of the 27 women in the ZOL group developed symptoms compatible with a transient acute phase reaction that was treated with paracetamol. No adverse events were recorded in the Dmab group of women. No cases of osteonecrosis of the jaw		
subjects affected / exposed	18 / 27 (66.67%)		
occurrences (all)	18		

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