Clinical trial results:
EFFICACY AND SAFETY ASSESSMENT OF ZOLEDRONATE IN HIV-INFECTED PATIENTS WITH LOW BONE MINERAL DENSITY

Summary

EudraCT number	2008-005051-18
Trial protocol	ES
Global end of trial date	10 November 2011

Results information

Result version number	v1 (current)
This version publication date	29 March 2019
First version publication date	29 March 2019

Trial information

Trial identification

Sponsor protocol code	VIH-ZOL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00795483
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundació Lluita contra la SIDA
Sponsor organisation address	Crta de Canyet s/n, Badalona, Spain, 08916
Public contact	Fundació Lluita contra la SIDA, Fundació Lluita contra la SIDA, 34 93 497 84 14,
Scientific contact	Fundació Lluita contra la SIDA, Fundació Lluita contra la SIDA, 34 93 497 84 14,

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	30 April 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 November 2011
Global end of trial reached?	Yes
Global end of trial date	10 November 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and tolerability of two doses of zoledronate, by comparing three groups of patients: those with annual administration, those with biennial administration (one dose in 2 years) and a control group with no administration of zoledronate.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 2008
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	Spain: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	31
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We invited patients with chronic HIV-1 infection and low bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) in lumbar spine or hip to participate in the study.

Pre-assignment

Screening details:

At week 48, patients from the zoledronate group were randomized again (1:1) to receive a second dose of zoledronate (5 mg) 1 year after the first dose (two doses in 2 years) or to continue with diet counselling only (no second dose of zoledronate). Patients in the control group continued to receive diet counselling only until week 96.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description:

diet counselling (to assure appropriate vitamin D and calcium intake (1200–1500 mg of calcium and 800 mg of vitamin D per day)

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	One year zoledronate group

Arm description:

zoledronate (intravenous infusion; 5 mg/year) combined with diet counselling

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

Dosage and administration details:

5 mg/year (single dose)

Arm title	Two-year zoledronate group

Arm description:

zoledronate (intravenous infusion; 5 mg/year during two years) combined with diet counselling

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

Dosage and administration details:

5 mg/year

Number of subjects in period 1	Control group	One year zoledronate group	Two-year zoledronate group
Started	10	9	12
Completed	8	9	12
Not completed	2	0	0
Lost to follow-up	2	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Control group
Reporting group description:	
diet counselling (to assure appropriate vitamin D and calcium intake (1200–1500 mg of calcium and 800 mg of vitamin D per day)	
Reporting group title	One year zoledronate group
Reporting group description:	
zoledronate (intravenous infusion; 5 mg/year) combined with diet counselling	
Reporting group title	Two-year zoledronate group
Reporting group description:	
zoledronate (intravenous infusion; 5 mg/year during two years) combined with diet counselling	

Reporting group values	Control group	One year zoledronate group	Two-year zoledronate group
Number of subjects	10	9	12
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	9	12
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
median	48.6	46.4	49.4
inter-quartile range (Q1-Q3)	41.6 to 58.8	44.4 to 58.3	45.6 to 57.0
Gender categorical			
Units: Subjects			
Female	1	2	1
Male	9	7	11

Reporting group values	Total		
Number of subjects	31		
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)	31		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
median			
inter-quartile range (Q1-Q3)	-		
Gender categorical Units: Subjects			
Female	4		
Male	27		

End points

End points reporting groups

Reporting group title	Control group
Reporting group description:	
diet counselling (to assure appropriate vitamin D and calcium intake (1200–1500 mg of calcium and 800 mg of vitamin D per day)	
Reporting group title	One year zoledronate group
Reporting group description:	
zoledronate (intravenous infusion; 5 mg/year) combined with diet counselling	
Reporting group title	Two-year zoledronate group
Reporting group description:	
zoledronate (intravenous infusion; 5 mg/year during two years) combined with diet counselling	

Primary: Changes in lumbar spine L1−L4 BMD

End point title	Changes in lumbar spine L1−L4 BMD
End point description:	

End point type	Primary
End point timeframe:	
From baseline to week 96	

End point values	Control group	One year zoledronate group	Two-year zoledronate group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	12	
Units: (g/cm2)				
median (inter-quartile range (Q1-Q3))				
baseline	1.01 (0.95 to 1.10)	0.93 (0.92 to 1.02)	0.94 (0.89 to 1.06)	
week 48	0.98 (0.91 to 1.10)	0.99 (0.96 to 1.07)	0.99 (0.95 to 1.10)	
week 96	1.01 (0.95 to 1.09)	0.98 (0.96 to 1.06)	1.04 (0.96 to 1.10)	

Statistical analyses

Statistical analysis title	Comparing Medians
Statistical analysis description:	
Comparin Baseline	
Comparison groups	Control group v One year zoledronate group

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.39
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians
Statistical analysis description: Comparing Baseline	
Comparison groups	Control group v Two-year zoledronate group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.22
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians
Statistical analysis description: Comparing Baseline	
Comparison groups	One year zoledronate group v Two-year zoledronate group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.97
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week 48	
Comparison groups	Control group v One year zoledronate group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week48	
Comparison groups	Control group v Two-year zoledronate group

Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.56
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week 48	
Comparison groups	One year zoledronate group v Two-year zoledronate group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: Week 96	
Comparison groups	Control group v One year zoledronate group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.22
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: Week 96	
Comparison groups	Control group v Two-year zoledronate group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.79
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: Week 96	
Comparison groups	One year zoledronate group v Two-year zoledronate group

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.25
Method	Wilcoxon (Mann-Whitney)

Primary: Changes in total hip BMD

End point title	Changes in total hip BMD

End point description:

End point type	Primary

End point timeframe:
from baseline to week 96

End point values	Control group	One year zoledronate group	Two-year zoledronate group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	9	12	
Units: g/cm2				
median (inter-quartile range (Q1-Q3))				
Baseline	0.84 (0.82 to 0.88)	0.82 (0.74 to 0.89)	0.80 (0.78 to 0.89)	
week 48	0.84 (0.80 to 0.90)	0.85 (0.78 to 0.87)	0.83 (0.81 to 0.91)	
week 96	0.84 (0.83 to 0.90)	0.84 (0.76 to 0.89)	0.84 (0.82 to 0.95)	

Statistical analyses

Statistical analysis title	Comparing Medians Bl

Statistical analysis description:
Baseline

Comparison groups	Control group v One year zoledronate group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.49
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians Bl

Statistical analysis description:
Baseline

Comparison groups	Control group v Two-year zoledronate group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.21
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians Bl
Statistical analysis description: Baseline	
Comparison groups	One year zoledronate group v Two-year zoledronate group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.67
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week 48	
Comparison groups	Control group v One year zoledronate group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.88
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week 48	
Comparison groups	Control group v Two-year zoledronate group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w48
Statistical analysis description: Week 48	
Comparison groups	One year zoledronate group v Two-year zoledronate group

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.83
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: Week 96	
Comparison groups	Control group v One year zoledronate group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.96
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: Week96	
Comparison groups	Control group v Two-year zoledronate group
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.67
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Comparing Medians w96
Statistical analysis description: eek 96	
Comparison groups	One year zoledronate group v Two-year zoledronate group
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.52
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from baseline to 48 week follow up	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	DAIDS AE GRADING TAB
Dictionary version	1.0
Reporting groups	
Reporting group title	One year zoledronate group

Reporting group description: -

Serious adverse events	One year zoledronate group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	One year zoledronate group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)		
Nervous system disorders			
asthenia			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Infections and infestations			
Fever			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2008	Number of patients enrolled decreased and randomization ratio changed
12 April 2010	Study design changed

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported