



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/cm ²) | | | | |
| 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 BI |
| 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 BI |
| 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 BI |
| 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: 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 | = 0.52 |
| 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