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Trial record **1 of 1** for: CZOL446M2309

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Efficacy in Reducing Fractures and Safety of Zoledronic Acid in Men With Osteoporosis

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00439647

First received: February 22, 2007
Last updated: October 10, 2011
Last verified: October 2011
History of Changes

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Results First Received: October 10, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Male Osteoporosis
Interventions:	Drug: Zoledronic acid 5 mg iv Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Participant Flow: Overall Study

	Zoledronic Acid	**Placebo**

STARTED	**588** [1]	**611**
Modified Intent to Treat (mITT)	**553**	**574**
COMPLETED	**530**	**540**
NOT COMPLETED	**58**	**71**
Withdrawal by Subject	**25**	**22**
Death	**15**	**18**
Adverse Event	**11**	**11**
Lost to Follow-up	**4**	**12**
Protocol Violation	**3**	**4**
Lack of Efficacy	**0**	**4**

[1] "Started" indicates intent to treat (ITT) and safety set.

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Total	Total of all reporting groups

Baseline Measures

	Zoledronic Acid	**Placebo**	**Total**
Number of Participants [units: participants]	**588**	**611**	**1199**
Age [units: years] Mean (Standard Deviation)	**65.8 (8.3)**	**65.7 (8.6)**	**65.8 (8.5)**
Gender [units: participants]			
Female	**0**	**0**	**0**
Male	**588**	**611**	**1199**

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 24 Months [Time Frame: 24 Months]

Measure Type	Primary
Measure Title	Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 24 Months
Measure Description	Vertebral fracture (VF) was assessed based on morphometry. QM(quantitative morphometry) incident VF(QM positive) is defined by at least 20% decrease in vertebral height of at least 4mm. If participant had QM positive at any vertebrae at any visit, x-rays from visits for participants were evaluated using Genant semi-quantitative method for VF assessment: Grade1 Mild VF is defined as 20-24% decrease in anterior, middle, and/or posterior vertebral height. Grade2 moderate VF is defined as 25-40% decrease in vertebral height. Grade3 Severe VF is defined as more than 40% decrease in vertebral height
Time Frame	24 Months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. In this analysis, missing Month 24 fractures were imputed using LOCF.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 24 Months [units: Percentage of Participants]	**1.6**	**4.9**

No statistical analysis provided for Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 24 Months

2. Secondary: Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 12 Months [Time Frame: 12 Months]

Measure Type	Secondary
Measure Title	Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 12 Months
Measure Description	Vertebral fracture (VF) was assessed based on morphometry. QM(quantitative morphometry) incident VF(QM positive) is defined by at least 20% decrease in vertebral height of at least 4mm. If participant had QM positive at any vertebrae at any visit, x-rays from visits for participants were evaluated using Genant semi-quantitative method for VF assessment: Grade1 Mild VF is defined as 20-24% decrease in anterior, middle, and/or posterior vertebral height. Grade2 moderate VF is defined as 25-40% decrease in vertebral height. Grade3 Severe VF is defined as more than 40% decrease in vertebral height
Time Frame	12 Months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.

Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. Patients with a baseline x-ray and a 12M x-ray are included.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 12 Months [units: Percentage of participants]	**0.9**	**2.8**

No statistical analysis provided for Percentage of Participants With at Least One New Morphometric Vertebral Fracture Over 12 Months

3. Secondary: Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 12 Months [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 12 Months
Measure Description	Moderate or severe vertebral fracture (VF) was assessed based on morphometry. A QM (quantitative morphometry) incident VF(QM positive) was defined by at least a 20% decrease in any vertebral height (at least 4 mm). If a participant had a QM positive at any vertebrae at any visit,x-rays from all visits for participants were evaluated using Genant semi-quantitative (SQ) method for VF assessment. Grade 2 moderate VF was defined as a 25-40% reduction in any vertebral height.Grade 3 Severe: VF was defined as more than 40% reduction in any vertebral height.
Time Frame	12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. Patients with a baseline x-ray and a 12M x-ray are included.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 12 Months [units: Percentage of participants]	**0.4**	**1.9**

No statistical analysis provided for Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 12 Months

4. Secondary: Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 24 Months [Time Frame: 24 Months]

Measure Type	Secondary
Measure Title	Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 24 Months
Measure Description	Moderate or severe vertebral fracture (VF) was assessed based on morphometry. A QM (quantitative morphometry) incident VF(QM positive) was defined by at least a 20% decrease in any vertebral height (at least 4 mm). If a participant had a QM positive at any vertebrae at any visit,x-rays from all visits for participants were evaluated using Genant semi-quantitative (SQ) method for VF assessment. Grade 2 moderate VF was defined as a 25-40% reduction in any vertebral height.Grade 3 Severe: VF was defined as more than 40% reduction in any vertebral height.
Time Frame	24 Months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. Patients with a baseline x-ray and a 12M x-ray are included.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 24 Months [units: Percentage of participants]	**1.1**	**3.0**

No statistical analysis provided for Percentage of Participants With at Least One New Moderate or Severe Morphometric Vertebral Fracture Over 24 Months

5. Secondary: Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 12 Months [Time Frame: Baseline, 12 months]

Measure Type	Secondary
Measure Title	Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 12 Months
Measure Description	Worsening vertebral fracture (VF) was assessed based on morphometry. QM (quantitative morphometry) incident VF (QM positive) was defined by at least a 20% decrease in any vertebral height (at least 4 mm). If a participant had a QM positive at any vertebrae at any visit, x-rays from all visits for participants were evaluated using Genant semi-quantitative (SQ) method for VF assessment. A worsening fracture was defined as an SQ reading that was greater than the baseline SQ reading, which was at least 1 (prevalent fracture)
Time Frame	Baseline, 12 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. Patients with a baseline x-ray and a 12M x-ray are included.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 12 Months [units: Percentage of Participants]	**1.3**	**2.8**

No statistical analysis provided for Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 12 Months

6. Secondary: Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 24 Months [Time Frame: Baseline, Month 24]

Measure Type	Secondary
Measure Title	Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 24 Months
Measure Description	Worsening vertebral fracture (VF) was assessed based on morphometry. A QM (quantitative morphometry) incident VF (QM positive) was defined by at least a 20% decrease in any vertebral height (at least 4 mm). If a participant had a QM positive at any vertebrae at any visit,x-rays from all visits for participants were evaluated using Genant semi-quantitative (SQ) method for VF assessment. A worsening fracture was defined as an SQ reading that was greater than the baseline SQ reading, which was at least 1 (prevalent fracture)
Time Frame	Baseline, Month 24

Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. In this analysis, missing Month 24 fractures were imputed using LOCF.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**553**	**574**
Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 24 Months [units: Percentage of Participants]	**2.0**	**4.9**

No statistical analysis provided for Percentage of Participants With at Least One New or Worsening Morphometric Vertebral Fracture Over 24 Months

7. Secondary: Mean Change in Height From Baseline [Time Frame: from Baseline to 12 months and 24 months]

Measure Type	Secondary
Measure Title	Mean Change in Height From Baseline
Measure Description	Height was measured using a stadiometer. Two measurements were taken in millimeters (mm), and repeated if the two measurements differed by greater than 4 mm. The average of the two (or four) height measurements was used for analysis
Time Frame	from Baseline to 12 months and 24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Modified Intent-to-treat (mITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the primary efficacy variable. Patients with a baseline x-ray and a 12M x-ray are included.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	

	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**529**	**547**
Mean Change in Height From Baseline [units: mm] Mean (Standard Error)		
12 months	**-0.86 (0.333)**	**-2.50 (0.522)**
24 months	**-2.33 (0.389)**	**-4.61 (0.610)**

No statistical analysis provided for Mean Change in Height From Baseline

8. Secondary: Number of Participants With First Clinical Vertebral Fracture [Time Frame: 24 months]

Measure Type	Secondary
Measure Title	Number of Participants With First Clinical Vertebral Fracture
Measure Description	Clinical vertebral fracture is a painful vertebral fracture which came to clinical attention, e.g., with increased back pain, impairment of mobility or functional limitations. Subjects who did not experience a fracture event were censored at the end of study. End of study was defined as the last visit or date of death, whichever was earlier.
Time Frame	24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT (intent to treat) population consisted of all subjects as randomized.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**588**	**611**
Number of Participants With First Clinical Vertebral Fracture [units: Participants]	**1**	**3**

No statistical analysis provided for Number of Participants With First Clinical Vertebral Fracture

9. Secondary: Number of Participants With First Clinical Fracture [Time Frame: 24 months]

Measure Type	Secondary
Measure Title	Number of Participants With First Clinical Fracture
Measure Description	Clinical fracture is painful fracture in any site which came to clinical attention, e.g., with increased pain, impaired mobility or functional limitations. Subjects who did not experience fracture were censored at end of study. End of study was defined as the earlier of last visit or date of death.
Time Frame	24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT (intent to treat) population consisted of all subjects as randomized.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**588**	**611**
Number of Participants With First Clinical Fracture [units: Participants]	**6**	**11**

No statistical analysis provided for Number of Participants With First Clinical Fracture

10. Secondary: Number of Participants With First Non-vertebral Fracture [Time Frame: 24 months]

Measure Type	Secondary
Measure Title	Number of Participants With First Non-vertebral Fracture
Measure Description	Non-vertebral fracture is any fracture which was not of the vertebrae. Subjects who did not experience a fracture event were censored at the end of study. End of study was defined as the last visit or date of death, whichever was earlier.
Time Frame	24 months
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT (intent to treat) population consisted of all subjects as randomized.

Reporting Groups

	Description

Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**588**	**611**
Number of Participants With First Non-vertebral Fracture [units: Participants]	**5**	**8**

No statistical analysis provided for Number of Participants With First Non-vertebral Fracture

11. Secondary: Percentage Change From Baseline in Lumbar Spine Bone Mass Density (BMD) [Time Frame: Month 6, Month 12, Month 24]

Measure Type	Secondary
Measure Title	Percentage Change From Baseline in Lumbar Spine Bone Mass Density (BMD)
Measure Description	Dual energy x-ray absorptiometry (DXA) Least Square Means (LSM) were analyzed using an ANCOVA model with treatment and baseline value as explanatory variables. Percent change in BMD at lumbar spine at Months 6, 12, and 24 relative to baseline as measured by DXA in a subset of at least 100 evaluable subjects at selected sites. Percentage change from baseline = 100*(endpoint - baseline)
Time Frame	Month 6, Month 12, Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat (ITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the efficacy variable.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**65**	**63**
Percentage Change From Baseline in Lumbar Spine Bone Mass Density (BMD) [units: Percent change in BMD] Least Squares Mean (Standard Error)		
Month 6 (n=61, n=61)	**4.87 (0.412)**	**0.10 (0.412)**
Month 12 (n=60, n=62)	**5.51 (0.437)**	**0.84 (0.430)**

Month 24 (n=58, n=61)	**7.73 (0.459)**	**1.61 (0.448)**

No statistical analysis provided for Percentage Change From Baseline in Lumbar Spine Bone Mass Density (BMD)

12. Secondary: Percentage Change From Baseline in Total Hip BMD (g/CM^2) [Time Frame: Month 6, Month 12, Month 24]

Measure Type	Secondary
Measure Title	Percentage Change From Baseline in Total Hip BMD (g/CM^2)
Measure Description	Dual energy x-ray absorptiometry (DXA) Least Square Means (LSM) were analyzed using an ANCOVA model with treatment and baseline value as explanatory variables. Percent change in total hip BMD at Months 6, 12, and 24 relative to baseline as measured by DXA in a subset of at least 100 evaluable subjects at selected sites. Percentage change from baseline = 100*(endpoint - baseline)
Time Frame	Month 6, Month 12, Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat (ITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the efficacy variable.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**64**	**65**
Percentage Change From Baseline in Total Hip BMD (g/CM^2) [units: Percent change in BMD] Least Squares Mean (Standard Error)		
Month 6 (n=60, n=63)	**1.38 (0.294)**	**-0.44 (0.287)**
Month 12 (n=58, n=64)	**1.66 (0.283)**	**0.26 (0.269)**
Month 24 (n=56, n=63)	**2.31 (0.346)**	**0.16 (0.326)**

No statistical analysis provided for Percentage Change From Baseline in Total Hip BMD (g/CM^2)

13. Secondary: Percentage Change From Baseline in Femoral Neck BMD (g/CM^2) [Time Frame: Month 6, Month 12, Month 24]

Measure Type	Secondary
Measure Title	Percentage Change From Baseline in Femoral Neck BMD (g/CM^2)
Measure Description	Dual energy x-ray absorptiometry (DXA) Least Square Means (LSM) were analyzed using an ANCOVA model with treatment and baseline value as explanatory variables. Percent change in total femoral neck BMD at Months 6, 12, and

	24 relative to baseline as measured by DXA in a subset of at least 100 evaluable subjects at selected sites. Percentage change from baseline = 100*(endpoint - baseline)
Time Frame	Month 6, Month 12, Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat (ITT) population included all randomized subjects who had a baseline and at least one post-baseline assessment of the efficacy variable.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	**Placebo**
Number of Participants Analyzed [units: participants]	**64**	**65**
Percentage Change From Baseline in Femoral Neck BMD (g/CM^2) [units: Percent change in BMD] Least Squares Mean (Standard Error)		
Month 6 (n=60, n=63)	**2.21 (0.448)**	**0.58 (0.437)**
Month 12 (n=58, n=64)	**2.06 (0.465)**	**0.59 (0.443)**
Month 24 (n=56, n=63)	**3.39 (0.544)**	**0.09 (0.513)**

No statistical analysis provided for Percentage Change From Baseline in Femoral Neck BMD (g/CM^2)

14. Secondary: Serum Beta C-terminal Telopeptides of Type I Collagen(b-CTx) by Visits [Time Frame: Baseline, Month 3, Month 6, Month 12, Month 15, month 18, Month 24]

Measure Type	Secondary
Measure Title	Serum Beta C-terminal Telopeptides of Type I Collagen(b-CTx) by Visits
Measure Description	No text entered.
Time Frame	Baseline, Month 3, Month 6, Month 12, Month 15, month 18, Month 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The ITT, Intent to Treat population, includes all participants who received a single a dose of treatment and had data available for analysis. n = the number of subjects with evaluable measurements at visit, as determined by the efficacy window.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The intravenous (i.v.) infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year.

Measured Values

	Zoledronic Acid	Placebo
Number of Participants Analyzed [units: participants]	**64**	**66**
Serum Beta C-terminal Telopeptides of Type I Collagen(b-CTx) by Visits [units: ng/mL] Mean (Standard Error)		
Baseline (n-64) (n=66)	**0.3646 (0.02094)**	**0.3933 (0.02955)**
Month 3 (n=63) (n=65)	**0.0990 (0.00800)**	**0.3647 (0.02989)**
Month 6 (n=62) (n=64)	**0.1384 (0.00914)**	**0.3540 (0.02576)**
Month 12 (n=63) (n=64)	**0.1669 (0.00925)**	**0.4042 (0.03056)**
Month 15 (n=55) (n=58)	**0.0996 (0.00590)**	**0.3576 (0.02519)**
Month 18 (n=55) (n=60)	**0.1320 (0.00661)**	**0.3954 (0.03001)**
Month 24 (n=55) (n=62)	**0.1760 (0.01248)**	**0.4060 (0.02640)**

No statistical analysis provided for Serum Beta C-terminal Telopeptides of Type I Collagen(b-CTx) by Visits

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The i.v. infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The i.v. infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year

Serious Adverse Events

	Zoledronic Acid	Placebo
Total, serious adverse events		
# participants affected / at risk	**149/588 (25.34%)**	**154/611 (25.20%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**1/588 (0.17%)**	**1/611 (0.16%)**
Bone marrow failure † 1		

# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Lymphadenopathy [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Pernicious anaemia [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Cardiac disorders		
Acute myocardial infarction [†1]		
# participants affected / at risk	5/588 (0.85%)	1/611 (0.16%)
Angina pectoris [†1]		
# participants affected / at risk	6/588 (1.02%)	7/611 (1.15%)
Angina unstable [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Arrhythmia [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Arteriosclerosis coronary artery [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Atrial fibrillation [†1]		
# participants affected / at risk	7/588 (1.19%)	5/611 (0.82%)
Atrial flutter [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Cardiac arrest [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Cardiac failure [†1]		
# participants affected / at risk	1/588 (0.17%)	4/611 (0.65%)
Cardiac failure chronic [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cardiac failure congestive [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Cardio-respiratory arrest [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cardiopulmonary failure [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cardiovascular insufficiency [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Coronary artery disease [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Coronary artery stenosis [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Mitral valve incompetence [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Myocardial infarction [†1]		
# participants affected / at risk	4/588 (0.68%)	1/611 (0.16%)
Myocardial ischaemia [†1]		
# participants affected / at risk	3/588 (0.51%)	1/611 (0.16%)
Myocarditis [†1]		

# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Tachycardia [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Ventricular tachycardia [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Congenital, familial and genetic disorders		
Exomphalos [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Phimosis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Ear and labyrinth disorders		
Sudden hearing loss [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Vertigo [†1]		
# participants affected / at risk	3/588 (0.51%)	1/611 (0.16%)
Endocrine disorders		
Hyperthyroidism [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Eye disorders		
Cataract [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Heterophoria [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Retinal degeneration [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Retinal detachment [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Gastrointestinal disorders		
Abdominal pain [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Anal haemorrhage [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Ascites [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Colitis ischaemic [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Constipation [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Diarrhoea [†1]		
# participants affected / at risk	0/588 (0.00%)	3/611 (0.49%)
Diverticular perforation [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Diverticulum intestinal [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Duodenal ulcer [†1]		

# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Enterovesical fistula [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Faecaloma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Femoral hernia [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Gastric ulcer [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Gastritis [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Gastritis erosive [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Haematemesis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Hiatus hernia [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Ileus [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Inguinal hernia [†1]		
# participants affected / at risk	3/588 (0.51%)	2/611 (0.33%)
Inguinal hernia, obstructive [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Intestinal congestion [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Melaena [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Nausea [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Oesophagitis [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Pancreatitis acute [†1]		
# participants affected / at risk	2/588 (0.34%)	1/611 (0.16%)
Pancreatitis chronic [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Peritonitis [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Poor dental condition [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Rectal haemorrhage [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Rectal polyp [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Reflux oesophagitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)

Upper gastrointestinal haemorrhage [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Vomiting [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
General disorders		
Adverse drug reaction [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Asthenia [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Chest pain [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Death [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Device failure [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Device occlusion [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Impaired healing [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Malaise [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Non-cardiac chest pain [†1]		
# participants affected / at risk	3/588 (0.51%)	0/611 (0.00%)
Pyrexia [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Sudden death [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Hepatobiliary disorders		
Cholecystitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cholecystitis acute [†1]		
# participants affected / at risk	3/588 (0.51%)	1/611 (0.16%)
Cholelithiasis [†1]		
# participants affected / at risk	2/588 (0.34%)	4/611 (0.65%)
Hepatitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Jaundice [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Immune system disorders		
Hypersensitivity [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Infections and infestations		
Abdominal abscess [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Anal abscess [†1]		

# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Appendicitis [†1]		
# participants affected / at risk	2/588 (0.34%)	1/611 (0.16%)
Bronchopneumonia [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Chronic sinusitis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Device related infection [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Diverticulitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Gastroenteritis [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Gastroenteritis viral [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Herpes zoster [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Incision site abscess [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Infective exacerbation of chronic obstructive airways disease [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Lung infection [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Osteomyelitis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pneumonia [†1]		
# participants affected / at risk	6/588 (1.02%)	9/611 (1.47%)
Pyelonephritis [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Respiratory tract infection [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Sepsis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Tracheobronchitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Urinary tract infection [†1]		
# participants affected / at risk	0/588 (0.00%)	4/611 (0.65%)
Vestibular neuronitis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Viral infection [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Injury, poisoning and procedural complications		
Alcohol poisoning [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Arterial injury [†1]		

# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Contusion [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Fall [†1]		
# participants affected / at risk	3/588 (0.51%)	1/611 (0.16%)
Incisional hernia [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Injury [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Joint dislocation [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Joint sprain [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Meniscus lesion [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pneumothorax traumatic [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Post procedural haemorrhage [†1]		
# participants affected / at risk	0/588 (0.00%)	3/611 (0.49%)
Road traffic accident [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Tendon rupture [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Traumatic fracture [†1]		
# participants affected / at risk	16/588 (2.72%)	10/611 (1.64%)
Traumatic lung injury [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Vascular graft complication [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Wound [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Metabolism and nutrition disorders		
Decreased appetite [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Metabolic acidosis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Musculoskeletal and connective tissue disorders		
Arthralgia [†1]		
# participants affected / at risk	0/588 (0.00%)	3/611 (0.49%)
Arthritis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Arthropathy [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Back pain [†1]		
# participants affected / at risk	2/588 (0.34%)	1/611 (0.16%)

Bone pain [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Bunion [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Foot deformity [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Intervertebral disc protrusion [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Muscular weakness [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Neck pain [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Osteoarthritis [†1]		
# participants affected / at risk	7/588 (1.19%)	3/611 (0.49%)
Osteonecrosis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pain in extremity [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pathological fracture [†1]		
# participants affected / at risk	4/588 (0.68%)	5/611 (0.82%)
Pseudarthrosis [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Rheumatoid arthritis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Rotator cuff syndrome [†1]		
# participants affected / at risk	2/588 (0.34%)	1/611 (0.16%)
Sensation of heaviness [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Spinal osteoarthritis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Spondyloarthropathy [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Tendonitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Bladder cancer [†1]		
# participants affected / at risk	4/588 (0.68%)	2/611 (0.33%)
Bladder cancer stage 0, with cancer in situ [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Bladder transitional cell carcinoma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Brain neoplasm benign [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)

Colon adenoma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Colon cancer [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Gastric cancer [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Gastrointestinal carcinoma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Haemangioma [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Hepatic neoplasm malignant [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Hypopharyngeal cancer [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Lung neoplasm malignant [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Lymph node cancer metastatic [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Meningioma [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Metastases to liver [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Metastases to lymph nodes [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Metastases to the mediastinum [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Metastasis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Multiple myeloma [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Oesophageal carcinoma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Oesophageal neoplasm [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Prostate cancer [†1]		
# participants affected / at risk	6/588 (1.02%)	4/611 (0.65%)
Prostate cancer metastatic [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Prostatic adenoma [†1]		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Rectal cancer [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Renal cancer [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Renal cell carcinoma [†1]		

# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Small cell lung cancer extensive stage † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Squamous cell carcinoma † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Thyroid adenoma † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Nervous system disorders		
Alcohol induced persisting dementia † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Balance disorder † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Brain compression † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Carotid artery stenosis † 1		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Carpal tunnel syndrome † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Cerebellar infarction † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Cerebral atrophy † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cerebral infarction † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Cerebral ischaemia † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Cerebrovascular accident † 1		
# participants affected / at risk	6/588 (1.02%)	5/611 (0.82%)
Cerebrovascular insufficiency † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Cervical root pain † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Coma † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Convulsion † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Dementia † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Dizziness † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Encephalitis † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Haemorrhage intracranial † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Headache † 1		

# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Hemiparesis [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Hypoglycaemic coma [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Hypoxic-ischaemic encephalopathy [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Intracranial aneurysm [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Ischaemic stroke [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Loss of consciousness [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Monoparesis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Paraesthesia [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Parkinson's disease [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Radicular pain [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Syncope [†1]		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Transient ischaemic attack [†1]		
# participants affected / at risk	4/588 (0.68%)	3/611 (0.49%)
Psychiatric disorders		
Depression [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Encopresis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Panic attack [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Renal and urinary disorders		
Bladder neck obstruction [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Calculus ureteric [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Dysuria [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Haematuria [†1]		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Microalbuminuria [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Nephrolithiasis [†1]		
# participants affected / at risk	3/588 (0.51%)	2/611 (0.33%)

Renal artery stenosis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Renal colic [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Renal failure [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Renal failure acute [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Urethral polyp [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Urethral stenosis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Urinary retention [†1]		
# participants affected / at risk	3/588 (0.51%)	3/611 (0.49%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia [†1]		
# participants affected / at risk	2/588 (0.34%)	3/611 (0.49%)
Epididymal cyst [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Epididymitis [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Prostatomegaly [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Testicular swelling [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Atelectasis [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Bronchitis chronic [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Chronic obstructive pulmonary disease [†1]		
# participants affected / at risk	4/588 (0.68%)	7/611 (1.15%)
Cough [†1]		
# participants affected / at risk	2/588 (0.34%)	0/611 (0.00%)
Dyspnoea [†1]		
# participants affected / at risk	4/588 (0.68%)	4/611 (0.65%)
Dyspnoea exertional [†1]		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Emphysema [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Foreign body aspiration [†1]		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Haemothorax [†1]		

# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Lung consolidation † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pleural effusion † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Pleurisy † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pneumonia aspiration † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Pneumothorax † 1		
# participants affected / at risk	0/588 (0.00%)	2/611 (0.33%)
Pulmonary embolism † 1		
# participants affected / at risk	1/588 (0.17%)	2/611 (0.33%)
Respiratory failure † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Skin and subcutaneous tissue disorders		
Actinic keratosis † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Skin irritation † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Social circumstances		
Walking disability † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Vascular disorders		
Aortic aneurysm † 1		
# participants affected / at risk	2/588 (0.34%)	1/611 (0.16%)
Arterial haemorrhage † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Arteriosclerosis † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Arteritis † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Deep vein thrombosis † 1		
# participants affected / at risk	1/588 (0.17%)	0/611 (0.00%)
Femoral arterial stenosis † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Hypertension † 1		
# participants affected / at risk	3/588 (0.51%)	3/611 (0.49%)
Hypertensive crisis † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Hypovolaemic shock † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Intermittent claudication † 1		
# participants affected / at risk	1/588 (0.17%)	1/611 (0.16%)
Intra-abdominal haemorrhage † 1		

# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Peripheral artery aneurysm † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Peripheral ischaemia † 1		
# participants affected / at risk	2/588 (0.34%)	2/611 (0.33%)
Varicose vein † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Vascular calcification † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)
Venous insufficiency † 1		
# participants affected / at risk	0/588 (0.00%)	1/611 (0.16%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Zoledronic Acid	5 mg/100 ml administered via a peripheral intravenous site as a slow infusion over 15 minutes. The i.v. infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year
Placebo	100 ml Placebo administered via a peripheral intravenous site as a slow infusion over 15 minutes. The i.v. infusion was delivered via vented infusion line (to allow constant flow) and 20-22 gauge angiocatheter, and preceded and followed by a 10 ml normal saline flush of the intravenous line for a total volume infused of 120 ml once a year

Other Adverse Events

	Zoledronic Acid	Placebo
Total, other (not including serious) adverse events		
# participants affected / at risk	399/588 (67.86%)	256/611 (41.90%)
General disorders		
Chills † 1		
# participants affected / at risk	40/588 (6.80%)	5/611 (0.82%)
Fatigue † 1		
# participants affected / at risk	40/588 (6.80%)	13/611 (2.13%)
Influenza like illness † 1		
# participants affected / at risk	30/588 (5.10%)	14/611 (2.29%)
Pyrexia † 1		
# participants affected / at risk	143/588 (24.32%)	21/611 (3.44%)
Infections and infestations		

Influenza † 1		
# participants affected / at risk	**30/588 (5.10%)**	**28/611 (4.58%)**
Nasopharyngitis † 1		
# participants affected / at risk	**50/588 (8.50%)**	**49/611 (8.02%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**123/588 (20.92%)**	**65/611 (10.64%)**
Back pain † 1		
# participants affected / at risk	**82/588 (13.95%)**	**73/611 (11.95%)**
Musculoskeletal pain † 1		
# participants affected / at risk	**30/588 (5.10%)**	**19/611 (3.11%)**
Myalgia † 1		
# participants affected / at risk	**129/588 (21.94%)**	**25/611 (4.09%)**
Pain in extremity † 1		
# participants affected / at risk	**43/588 (7.31%)**	**23/611 (3.76%)**
Nervous system disorders		
Headache † 1		
# participants affected / at risk	**80/588 (13.61%)**	**27/611 (4.42%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**47/588 (7.99%)**	**43/611 (7.04%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☑ Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. **Restriction Description:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not

prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial; or the publication of the trial results in their entirety.

Results Point of Contact:

Name/Title: Novartis Study Director
Organization: Novartis Pharmaceuticals
phone: 862-778-8300

No publications provided by Novartis

Publications automatically indexed to this study:

Boonen S, Reginster JY, Kaufman JM, Lippuner K, Zanchetta J, Langdahl B, Rizzoli R, Lipschitz S, Dimai HP, Witvrouw R, Eriksen E, Brixen K, Russo L, Claessens F, Papanastasiou P, Antunez O, Su G, Bucci-Rechtweg C, Hruska J, Incera E, Vanderschueren D, Orwoll E. Fracture risk and zoledronic acid therapy in men with osteoporosis. N Engl J Med. 2012 Nov;367(18):1714-23. doi: 10.1056/NEJMoa1204061.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00439647 History of Changes
Other Study ID Numbers:	**CZOL446M2309**
Study First Received:	February 22, 2007
Results First Received:	October 10, 2011
Last Updated:	October 10, 2011
Health Authority:	Argentina: National Administration of Drugs, Foods and Medical Technology Belgium: Federal Agency for Medicines and Health Products, FAMHP Brazil: National Health Surveillance Agency Czech Republic: State Institute for Drug Control Denmark: Danish Medicines Agency Finland: Finnish Medicines Agency Germany: Federal Institute for Drugs and Medical Devices Hungary: National Institute of Pharmacy Norway: Norwegian Medicines Agency Portugal: National Pharmacy and Medicines Institute Romania: Ministry of Health and the Family Spain: Spanish Agency of Medicines Slovakia: State Institute for Drug Control Sweden: Medical Products Agency Switzerland: Swiss Agency for Therapeudic Products United Kingdom: Medicines and Healthcare Products Regulatory Agency South Africa: Medicines Control Council (MCC) Iceland:"Lyfjastofnun" Icelandic Medicines Control Agency Poland: Central Register of Clinical Trials. The office for Registration of Medicinal Products, Medical Devices and Biocidal Products Italy: Ministero della Salute Austria: Bundesamt für Sicherheit im Gesundheitswesen. AGES PharmMed, WIN/NATA Australia:Therapeutic Goods Administration (TGA) Russia:Federal Service on Surveillance in Healthcare and Social Development of Russian Federation