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Trial record **1 of 1** for: CZOL446H2301E2

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3 yr Efficacy & Safety Study of Zoledronic Acid in Post-menopausal Women With Osteoporosis Treated With Zol Acid for 6 Yrs

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT00718861

First received: July 18, 2008
Last updated: October 2, 2014
Last verified: September 2014
History of Changes

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Results First Received: November 8, 2013

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:	Post-menopausal Osteoporosis
Interventions:	Drug: Placebo Drug: Zoledronic acid

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
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Participant Flow: Overall Study

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
STARTED	95 [1]	95
Safety Set	92 [2]	95
Modified Intent to Treat	67 [3]	69 [3]
COMPLETED	74	77
NOT COMPLETED	21	18
Withdrawal by Subject	15	10
Adverse Event	2	1
Lost to Follow-up	2	1
Administrative Problems	1	1
Death	1	5

[1] "Started" indicates Randomized and Intent-to Treat (ITT) population
[2] 3 patients randomized but never received study drug
[3] ITT patients with DXA total hip measure at extension 2 baseline and year 9

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.
The intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).
Total	Total of all reporting groups

Baseline Measures

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)	Total
Number of Participants [units: participants]	**95**	**95**	**190**
Age [units: Years] Mean (Standard Deviation)	**78 (4.71)**	**78.1 (4.85)**	**78.1 (4.77)**
Gender [units: participants]			
Female	**95**	**95**	**190**
Male	**0**	**0**	**0**

Outcome Measures

Hide All Outcome Measures

1. Primary: Percentage Change in Total Hip Bone Mineral Density BMD at Year 6 (Baseline) and Year 9 [Time Frame: Year 6 (baseline) and Year 9]

Measure Type	Primary
Measure Title	Percentage Change in Total Hip Bone Mineral Density BMD at Year 6 (Baseline) and Year 9
Measure Description	Bone Mineral Density (BMD) measured by dual energy x-ray absorptiometry (DXA). DXA consists of two X-ray beams with different energy levels that are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Percentage change from Year 6 = 100*(Year 9 – Year 6)/Year 6.
Time Frame	Year 6 (baseline) and Year 9
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 modified intent-to-treat (MITT) population included all patients in the ITT population who had DXA measurements of the total hip at Visit 11 (Year 6) and Visit 15 (Year 9). This was the primary population for the primary efficacy parameter.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**67**	**69**
Percentage Change in Total Hip Bone Mineral Density BMD at Year 6 (Baseline) and Year 9 [units: Percentage Change of BMD] Least Squares Mean (Standard Error)	**-0.54 (0.433)**	**-1.31 (0.427)**

No statistical analysis provided for Percentage Change in Total Hip Bone Mineral Density BMD at Year 6 (Baseline) and Year 9

2. Secondary: Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7 and 8 Compared to Year 6 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8]

Measure Type	Secondary
Measure Title	Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7 and 8 Compared to Year 6
Measure Description	Bone Mineral Density (BMD) measured by dual energy x-ray absorptiometry (DXA). DXA consists of two X-ray beams with different energy levels that are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Percentage change from Year 6 = 100*(Year 9 – Year 6)/Year 6.
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8

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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at Year 6 and follow-up visits as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**95**	**95**
Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7 and 8 Compared to Year 6 [units: percentage change of BMD] Least Squares Mean (Standard Error)		
Year 7 (n=83,76)	**-0.28 (0.336)**	**-0.83 (0.347)**
Year 8 (n=73,72)	**-0.14 (0.311)**	**-1.06 (0.315)**

No statistical analysis provided for Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7 and 8 Compared to Year 6

3. Secondary: Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 6 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 6
Measure Description	Bone Mineral Density (BMD) measured by dual energy x-ray absorptiometry (DXA). DXA consists of two X-ray beams with different energy levels that are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Percentage change from Year 6 = 100*(Year 9 – Year 6)/Year 6.
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at Year 6 and follow-up visits as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Number of Participants Analyzed [units: participants]	**95**	**95**
Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 6 [units: percentage change of BMD] Least Squares Mean (Standard Error)		
Year 7 (n=83,76)	**-0.78 (0.433)**	**-1.24 (0.447)**
Year 8 (n=73,72)	**0.00 (0.521)**	**-0.88 (0.528)**
Year 9 (n=67,69)	**-1.11 (0.554)**	**-1.17 (0.547)**

No statistical analysis provided for Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 6

4. Secondary: Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0 [Time Frame: Year 0 (core baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0
Measure Description	Bone Mineral Density (BMD) measured by dual energy x-ray absorptiometry (DXA). DXA consists of two X-ray beams with different energy levels that are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Percentage change from Year 0 = 100*(Year 9 – Year 0)/Year 0.
Time Frame	Year 0 (core baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at Year 0 and follow-up visits as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Number of Participants Analyzed [units: participants]	**95**	**95**
Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0 [units: percentage change of BMD] Least Squares Mean (Standard Error)		
Year 7 (n=83,75)	**4.81 (0.619)**	**3.73 (0.640)**
Year 8 (n=72,71)	**5.35 (0.677)**	**3.65 (0.684)**
Year 9 (n=67,68)	**4.64 (0.760)**	**3.68 (0.752)**

No statistical analysis provided for Percentage Change of Total Hip Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0

5. Secondary: Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0 [Time Frame: Year 0 (core baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0
Measure Description	Bone Mineral Density (BMD) measured by dual energy x-ray absorptiometry (DXA). DXA consists of two X-ray beams with different energy levels that are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Percentage change from Year 0 = 100*(Year 9 – Year 0)/Year 0.
Time Frame	Year 0 (core baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at Year 0 and follow-up visits as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Number of Participants Analyzed [units: participants]	**95**	**95**
Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0 [units: percentage change of BMD] Least Squares Mean (Standard Error)		

Year 7 (n=83,75)	**5.11 (0.921)**	**3.86 (0.952)**
Year 8 (n=72,71)	**6.12 (1.041)**	**4.43 (1.052)**
Year 9 (n=67,68)	**4.16 (0.963)**	**3.88 (0.954)**

No statistical analysis provided for Percentage Change of Femoral Neck Bone Mineral Density (BMD) at Year 7, 8 and 9 Compared to Year 0

6. Secondary: Biomarkers (Bone Markers) Serum C-terminal Telopeptide of Type I Collagen (CTx) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Biomarkers (Bone Markers) Serum C-terminal Telopeptide of Type I Collagen (CTx) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9
Measure Description	Bone marker analysis: All patients had blood samples collected for analysis of serum c-terminal telopeptide of type I collagen (CTx). Serum CTX assays measure a fragment of the C-terminal telopeptide of type 1 collagen released during resorption of mature bone
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at each visit as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**95**	**95**
Biomarkers (Bone Markers) Serum C-terminal Telopeptide of Type I Collagen (CTx) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [units: ng/ml] Median (Full Range)		
Year 6 (n=59, 58)	**0.19 (0.1 to 0.6)**	**0.18 (0.1 to 0.5)**
Year 7 (n=56, 51)	**0.2 (0.1 to 0.4)**	**0.22 (0.1 to 0.5)**
Year 8 (n=51, 52)	**0.22 (0.1 to 0.4)**	**0.2 (0.1 to 0.4)**
Year 9 (n=51,54)	**0.22 (0.1 to 0.6)**	**0.22 (0.1 to 0.7)**

No statistical analysis provided for Biomarkers (Bone Markers) Serum C-terminal Telopeptide of Type I Collagen (CTx) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9

7. Secondary: Biomarkers (Bone Markers)Serum N-terminal Propeptide of Type I Collagen (P1NP) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Biomarkers (Bone Markers)Serum N-terminal Propeptide of Type I Collagen (P1NP) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9
Measure Description	Bone marker analysis: All patients had blood samples collected for analysis of serum n-terminal propeptide of type I collagen (P1NP) The P1NP concentration is directly proportional to the amount of new collagen laid down during bone formation.
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at each visit as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**95**	**95**
Biomarkers (Bone Markers)Serum N-terminal Propeptide of Type I Collagen (P1NP) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [units: ng/ml] Median (Full Range)		
Year 6 (n=88, 86)	**25.89 (10.8 to 69.1)**	**24.98 (9.9 to 65.6)**
Year 7 (n=58, 65)	**25.69 (12.3 to 52.9)**	**27.79 (11.7 to 140.2)**
Year 8 (n=54, 57)	**26.07 (10.9 to 59.9)**	**25.19 (13.1 to 68.1)**
Year 9 (n=52,56)	**26.74 (12.4 to 133.4)**	**27.41 (11.3 to 119.4)**

No statistical analysis provided for Biomarkers (Bone Markers)Serum N-terminal Propeptide of Type I Collagen (P1NP) at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9

8. Secondary: Biomarkers (Bone Markers) Serum Bone-specific Alkaline Phosphatase (BSAP). at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Biomarkers (Bone Markers) Serum Bone-specific Alkaline Phosphatase (BSAP). at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9
Measure Description	Bone marker analysis: All patients had blood samples collected for analysis of serum bone-specific alkaline phosphatase (BSAP).Bone-specific alkaline phosphatase (BSAP) is a useful marker of active bone formation.
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with measurements at each visit as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**95**	**95**
Biomarkers (Bone Markers) Serum Bone-specific Alkaline Phosphatase (BSAP). at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9 [units: ng/ml] Median (Full Range)		
Year 6 (n=59, 62)	**8.16 (4.9 to 15.9)**	**8.95 (3.9 to 16.2)**
Year 7 (n=58, 65)	**8.4 (4.7 to 15.7)**	**10.00 (5.1 to 19.6)**
Year 8 (n=54, 57)	**7.84 (5.4 to 16.4)**	**9.57 (5.6 to 15.8)**
Year 9 (n=52, 56)	**8.46 (5.1 to 18.3)**	**9.94 (6.2 to 20.7)**

No statistical analysis provided for Biomarkers (Bone Markers) Serum Bone-specific Alkaline Phosphatase (BSAP). at Year 6 (Extension 2 Baseline), Year 7, Year 8, Year 9

9. Secondary: Number of Participants With New/Worsening Morphometric Vertebral Fractures at Year 9 Compared to Year 6 [Time Frame: Year 6 (extension 2 baseline), Year 9 (3 years of study duration)]

Measure Type	Secondary
Measure Title	Number of Participants With New/Worsening Morphometric Vertebral Fractures at Year 9 Compared to Year 6

Measure Description	Morphometric 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 fracture was defined as an SQ reading that was greater than the baseline SQ reading.
Time Frame	Year 6 (extension 2 baseline), Year 9 (3 years of study duration)
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n= the number of patients with the event

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Number of Participants Analyzed [units: participants]	**95**	**95**
Number of Participants With New/Worsening Morphometric Vertebral Fractures at Year 9 Compared to Year 6 [units: participants]		
New Morphometric vertebral fracture	**3**	**5**
New/worsening Morphometric vertebra	**3**	**5**

No statistical analysis provided for Number of Participants With New/Worsening Morphometric Vertebral Fractures at Year 9 Compared to Year 6

10. Secondary: Mean of Time to First Clinical Fracture [Time Frame: over 3 years of study duration]

Measure Type	Secondary
Measure Title	Mean of Time to First Clinical Fracture
Measure Description	The mean of time to the first clinical fracture is estimated from the area under the Kaplan-Meier curve.
Time Frame	over 3 years of study duration
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Number of Participants Analyzed [units: participants]	**95**	**95**
Mean of Time to First Clinical Fracture [units: Days] Mean (Standard Error)	**1212.05 (22.96)**	**1204.65 (26.35)**

No statistical analysis provided for Mean of Time to First Clinical Fracture

11. Secondary: Change in Height at Years 7, 8 and 9 Relative to Year 6 [Time Frame: Year 6 (extension 2 baseline), Year 7, Year 8, Year 9]

Measure Type	Secondary
Measure Title	Change in Height at Years 7, 8 and 9 Relative to Year 6
Measure Description	Height was measured using a stadiometer in millimeters (mm). A stadiometer is a piece of medical equipment used for measuring height. It is usually constructed out of a ruler and a sliding horizontal headpiece which is adjusted to rest on the top of the head.
Time Frame	Year 6 (extension 2 baseline), Year 7, Year 8, Year 9
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 intent-to-treat (ITT) population included all patients who were enrolled in the extension study at Visit 12. This included patients who were randomized to Z9 and Z6P3 groups. n = the number of patients with evaluable measurements at both Year 6 and the post-Year 6 visit, as determined by the analysis window.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Measured Values

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Number of Participants Analyzed [units: participants]	**95**	**95**
Change in Height at Years 7, 8 and 9 Relative to Year 6 [units: millimeters (mm)] Least Squares Mean (Standard Error)		

Year 7 (n=58, 51)	**-5.29 (1.171)**	**-4.84 (1.199)**
Year 8 (n=55, 49)	**-10.16 (1.875)**	**-9.90 (2.006)**
Year 9 (n=52, 48)	**-13.31 (1.975)**	**-11.65 (2.085)**

No statistical analysis provided for Change in Height at Years 7, 8 and 9 Relative to Year 6

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	The safety population included all patients in the Intent to Treat (ITT) population who received at least 1 dose of study drug during this second extension study. Adverse Events data used the safety population.

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Serious Adverse Events

	Z9 (Zoledronic Acid 9)	**Z6P3 (Zoledronic Acid 6 Placebo 3)**
Total, serious adverse events		
# participants affected / at risk	**24/92 (26.09%)**	**28/95 (29.47%)**
Blood and lymphatic system disorders		
Agranulocytosis † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Anaemia † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Cardiac disorders		
Acute myocardial infarction † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Arrhythmia † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Atrial fibrillation † 1		
# participants affected / at risk	**1/92 (1.09%)**	**1/95 (1.05%)**
Cardiac failure † 1		
# participants affected / at risk	**1/92 (1.09%)**	**1/95 (1.05%)**
Cardiomyopathy † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Coronary artery disease † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Myocardial ischaemia † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**

Palpitations † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Eye disorders		
Cataract † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Gastrointestinal disorders		
Colitis ischaemic † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Gastritis † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Oesophageal discomfort † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
General disorders		
Chest pain † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Death † 1		
# participants affected / at risk	**0/92 (0.00%)**	**2/95 (2.11%)**
Pyrexia † 1		
# participants affected / at risk	**1/92 (1.09%)**	**1/95 (1.05%)**
Sudden death † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Infections and infestations		
Bronchitis † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Diverticulitis † 1		
# participants affected / at risk	**1/92 (1.09%)**	**1/95 (1.05%)**
Lower respiratory tract infection † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Pneumonia † 1		
# participants affected / at risk	**1/92 (1.09%)**	**2/95 (2.11%)**
Urinary tract infection † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Vestibular neuronitis † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Injury, poisoning and procedural complications		
Concussion † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Contusion † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Facial bones fracture † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Fall † 1		
# participants affected / at risk	**0/92 (0.00%)**	**2/95 (2.11%)**
Femur fracture † 1		

# participants affected / at risk	0/92 (0.00%)	2/95 (2.11%)
Fractured sacrum † 1		
# participants affected / at risk	0/92 (0.00%)	2/95 (2.11%)
Hip fracture † 1		
# participants affected / at risk	1/92 (1.09%)	1/95 (1.05%)
Lumbar vertebral fracture † 1		
# participants affected / at risk	1/92 (1.09%)	1/95 (1.05%)
Pelvic fracture † 1		
# participants affected / at risk	1/92 (1.09%)	2/95 (2.11%)
Pubis fracture † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Radius fracture † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Thoracic vertebral fracture † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Wrist fracture † 1		
# participants affected / at risk	0/92 (0.00%)	1/95 (1.05%)
Metabolism and nutrition disorders		
Dehydration † 1		
# participants affected / at risk	0/92 (0.00%)	1/95 (1.05%)
Hyponatraemia † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Iron deficiency † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	2/92 (2.17%)	0/95 (0.00%)
Back pain † 1		
# participants affected / at risk	2/92 (2.17%)	0/95 (0.00%)
Intervertebral disc protrusion † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Osteoarthritis † 1		
# participants affected / at risk	0/92 (0.00%)	3/95 (3.16%)
Pain in extremity † 1		
# participants affected / at risk	2/92 (2.17%)	0/95 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Basal cell carcinoma † 1		
# participants affected / at risk	1/92 (1.09%)	1/95 (1.05%)
Brain neoplasm † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Breast cancer † 1		
# participants affected / at risk	1/92 (1.09%)	0/95 (0.00%)
Colon cancer † 1		
# participants affected / at risk	0/92 (0.00%)	1/95 (1.05%)

Gastrointestinal tract adenoma † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Invasive lobular breast carcinoma † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Lung neoplasm malignant † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Lymphoma † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Nervous system disorders		
Cerebral haemorrhage † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Cerebral infarction † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Cerebrovascular accident † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Ischaemic stroke † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Psychiatric disorders		
Depression † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Renal and urinary disorders		
Acute prerenal failure † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Renal failure acute † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Reproductive system and breast disorders		
Uterine prolapse † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Respiratory, thoracic and mediastinal disorders		
Pleural effusion † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**
Skin and subcutaneous tissue disorders		
Pemphigoid † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Skin lesion † 1		
# participants affected / at risk	**1/92 (1.09%)**	**1/95 (1.05%)**
Surgical and medical procedures		
Spinal fusion surgery † 1		
# participants affected / at risk	**0/92 (0.00%)**	**1/95 (1.05%)**
Vascular disorders		
Peripheral arterial occlusive disease † 1		
# participants affected / at risk	**1/92 (1.09%)**	**0/95 (0.00%)**

† 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	The safety population included all patients in the Intent to Treat (ITT) population who received at least 1 dose of study drug during this second extension study. Adverse Events data used the safety population.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Z9 (Zoledronic Acid 9)	Group Z9 patients were those who had been treated with zoledronic acid for up to 9 years in the core (CZOL446H2301) and extension studies (CZOL446H2301E1 and CZOL446H2301E2).
Z6P3 (Zoledronic Acid 6 Placebo 3)	Group Z6P3 patients were those who had been treated with zoledronic acid for 6 years in the core (CZOL446H2301) and the first extension study (CZOL446H2301E1) followed by up to 3 years of placebo in the second extension study (CZOL446H2301E2).

Other Adverse Events

	Z9 (Zoledronic Acid 9)	Z6P3 (Zoledronic Acid 6 Placebo 3)
Total, other (not including serious) adverse events		
# participants affected / at risk	**62/92 (67.39%)**	**58/95 (61.05%)**
Cardiac disorders		
Atrial fibrillation † 1		
# participants affected / at risk	**5/92 (5.43%)**	**1/95 (1.05%)**
Eye disorders		
Cataract † 1		
# participants affected / at risk	**8/92 (8.70%)**	**5/95 (5.26%)**
Gastrointestinal disorders		
Diarrhoea † 1		
# participants affected / at risk	**1/92 (1.09%)**	**6/95 (6.32%)**
General disorders		
Fatigue † 1		
# participants affected / at risk	**5/92 (5.43%)**	**2/95 (2.11%)**
Infections and infestations		
Bronchitis † 1		
# participants affected / at risk	**5/92 (5.43%)**	**9/95 (9.47%)**
Cystitis † 1		
# participants affected / at risk	**5/92 (5.43%)**	**5/95 (5.26%)**
Nasopharyngitis † 1		
# participants affected / at risk	**9/92 (9.78%)**	**5/95 (5.26%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**3/92 (3.26%)**	**5/95 (5.26%)**

Urinary tract infection † 1		
# participants affected / at risk	**10/92 (10.87%)**	**8/95 (8.42%)**
Injury, poisoning and procedural complications		
Contusion † 1		
# participants affected / at risk	**2/92 (2.17%)**	**7/95 (7.37%)**
Fall † 1		
# participants affected / at risk	**8/92 (8.70%)**	**11/95 (11.58%)**
Investigations		
Creatinine renal clearance decreased † 1		
# participants affected / at risk	**6/92 (6.52%)**	**0/95 (0.00%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**17/92 (18.48%)**	**12/95 (12.63%)**
Back pain † 1		
# participants affected / at risk	**3/92 (3.26%)**	**13/95 (13.68%)**
Musculoskeletal pain † 1		
# participants affected / at risk	**5/92 (5.43%)**	**8/95 (8.42%)**
Osteoarthritis † 1		
# participants affected / at risk	**6/92 (6.52%)**	**13/95 (13.68%)**
Pain in extremity † 1		
# participants affected / at risk	**9/92 (9.78%)**	**1/95 (1.05%)**
Nervous system disorders		
Sciatica † 1		
# participants affected / at risk	**1/92 (1.09%)**	**5/95 (5.26%)**
Psychiatric disorders		
Insomnia † 1		
# participants affected / at risk	**5/92 (5.43%)**	**1/95 (1.05%)**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**10/92 (10.87%)**	**8/95 (8.42%)**

† 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:** Principal Investigators are NOT employed by the organization sponsoring the study. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. 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 pooled data (i.e.,data from all sites) in clinical trial.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis Pharmaceuticals
phone: 8627788300

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00718861 History of Changes
Other Study ID Numbers:	**CZOL446H2301E2** 2007-005383-27 (EudraCT Number)
Study First Received:	July 18, 2008
Results First Received:	November 8, 2013
Last Updated:	October 2, 2014
Health Authority:	United States: Food and Drug Administration European Union: European Medicines Agency Australia: Department of Health and Ageing Therapeutic Goods Administration Argentina: Ministry of Health Canada: Canadian Institutes of Health Research Colombia: INVIMA Instituto Nacional de Vigilancia de Medicamentos y Alimentos New Zealand: Medsafe Norway: Norwegian Medicines Agency Russia: Ministry of Health of the Russian Federation Switzerland: Swissmedic Thailand: Ministry of Public Health