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Trial record **1 of 1** for: CZOL446EIT14

Previous Study | Return to List | Next Study

Safety and Efficacy of Zoledronic Acid in Patients With Breast Cancer With Metastatic Bone Lesions

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT00375427

First received: September 12, 2006
Last updated: April 9, 2012
Last verified: July 2011
History of Changes

Full Text View | Tabular View | **Study Results** | Disclaimer | How to Read a Study Record

Results First Received: February 28, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Breast Cancer With Bone Metastasis
Intervention:	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
Total enrollment was 430; five participants were screened but not treated.

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 Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Participant Flow: Overall Study

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks
STARTED	**209** [1]	**216**
COMPLETED	**149**	**142**
NOT COMPLETED	**60**	**74**
Adverse Event	**21**	**27**
Abnormal test procedure result(s)	**0**	**1**
Abnormal laboratory value(s)	**1**	**2**

Unsatisfactory therapeutic effect	**4**	**4**
Patient no longer requires study drug	**3**	**7**
Protocol Violation	**10**	**8**
Withdrawal by Subject	**9**	**13**
Lost to Follow-up	**1**	**1**
Administrative reasons	**0**	**1**
Death	**11**	**10**

[1] Total enrollment was 430 but five patients were screened but not treated.

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 Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.
Total	Total of all reporting groups

Baseline Measures

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks	Total
Number of Participants [units: participants]	**209**	**216**	**425**
Age [units: years] Mean (Standard Deviation)	**60.4 (11.9)**	**59.8 (11.8)**	**60.1 (11.9)**
Gender [units: participants]			
Female	**209**	**216**	**425**
Male	**0**	**0**	**0**

Outcome Measures

Hide All Outcome Measures

1. Primary: Annual Overall Skeletal Morbidity Rate (SMR) [Time Frame: 12 months]

Measure Type	Primary
Measure Title	Annual Overall Skeletal Morbidity Rate (SMR)
Measure Description	The SMR was computed by summing all Skeletal Related Event(s) (SREs)which occurred during the observation period and dividing it by the ratio “days of observation period / 365.25”, for each participant. SRE was defined as: pathologic bone fracture, spinal cord compression, surgery to bone both curative and prophylactic, radiation therapy to bone, or hypercalcemia of malignancy. SMR (years) = 365.25 x SMR(days) where SMR (days) = total number of SREs / total SRE risk period (days). Risk period for SMR was computed as the days from randomization date to the date of last visit.
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.
Intent-to-treat (ITT) population will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**209**	**216**
Annual Overall Skeletal Morbidity Rate (SMR) [units: Number of Skeletal Events per Year] Mean (Standard Deviation)	**0.26 (0.81)**	**0.22 (0.57)**

No statistical analysis provided for Annual Overall Skeletal Morbidity Rate (SMR)

2. Secondary: Percentage of Participants Experiencing Skeletal Related Event(s) (SREs) [Time Frame: 12 month]

Measure Type	Secondary
Measure Title	Percentage of Participants Experiencing Skeletal Related Event(s) (SREs)
Measure Description	Skeletal Related Events (SREs) are defined as a: • pathologic bone fracture such as non-vertebral and vertebral compression fractures • spinal cord compression identified by positive diagnosis documented by X-ray evidence • surgery to bone both curative and prophylactic • radiation therapy to bone including palliative, therapeutic or prophylactic • hypercalcemia of malignancy, defined as a corrected serum calcium > 12 mg/dl (3.00 mmol/l) or a lower level of hypercalcemia which is symptomatic and which requires active treatment other than rehydration.
Time Frame	12 month
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 will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**

Number of Participants Analyzed [units: participants]	**209**	**216**
Percentage of Participants Experiencing Skeletal Related Event(s) (SREs) [units: Percentage of Participants]		
Patient with any SRE	**14.83**	**15.28**
Vertebral pathological fracture	**1.44**	**1.85**
Non vertebral pathological fracture	**3.35**	**2.31**
Spinal cord compression	**0.96**	**0.46**
Radiation to bone	**10.53**	**11.11**
Surgery to bone	**0.96**	**0.46**
Hypercalcemia of malignancy	**0.48**	**1.85**

No statistical analysis provided for Percentage of Participants Experiencing Skeletal Related Event(s) (SREs)

3. Secondary: Annual Incidence of Any Skeletal Related Events (SREs) [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Annual Incidence of Any Skeletal Related Events (SREs)
Measure Description	Skeletal Related Events (SREs) are defined as a: • pathologic bone fracture such as non-vertebral and vertebral • spinal cord compression identified by X-rays evidence • surgery to bone both curative and prophylactic • radiation therapy to bone including palliative, therapeutic or prophylactic

	• hypercalcemia of malignancy, defined as a corrected serum calcium > 12 mg/dl (3.00 mmol/l) or a lower level of hypercalcemia which is symptomatic and which requires active treatment other than rehydration. Annual incidence for each SRE was computed in the same way as annual overall SMR.
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.
Intent-to-treat (ITT) population will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**209**	**216**
Annual Incidence of Any Skeletal Related Events (SREs) [units: Number of SRE per Year] Mean (Standard Deviation)		
Vertebral pathological fracture rate	**0.02 (0.19)**	**0.02 (0.15)**

Non-vertebral pathological fracture rate	**0.08 (0.58)**	**0.03 (0.20)**
Spinal cord compression rate	**0.01 (0.10)**	**0.00 (0.07)**
Radiation to bone rate	**0.17 (0.67)**	**0.14 (0.43)**
Surgery to bone rate	**0.02 (0.21)**	**0.00 (0.07)**
Hypercalcemia of malignancy rate	**0.01 (0.08)**	**0.02 (0.16)**

No statistical analysis provided for Annual Incidence of Any Skeletal Related Events (SREs)

4. Secondary: Median Time to First Skeletal Related Event(s) (SRE) [Time Frame: 12 month]

Measure Type	Secondary
Measure Title	Median Time to First Skeletal Related Event(s) (SRE)
Measure Description	Median Time to first skeletal related event (SRE) is defined as the time from randomization to the date of first occurrence of any SRE which includes at least one of the following: radiation therapy to bone, pathologic bone fracture, spinal cord compression, surgery to bone, and hypercalcemia of malignancy (HCM). Due to the few numbers of SRE, Kaplan-Meier estimate never reaches a failure probability >=25%; so median time, 25th and 75th percentiles are not determined.For this reason only the estimated percentage of patient SRE free are reported at each time point.
Time Frame	12 month
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.
No text entered.

Reporting Groups

	Description

Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks
Number of Participants Analyzed [units: participants]	**209**	**216**
Median Time to First Skeletal Related Event(s) (SRE) [units: Day]	**NA** [1]	**NA** [1]

[1] NA=Not evaluable. Due to the low incidence of SRE, K-M estimates never reach a failure probability ≥25%; so median time, 25th and 75th percentiles aren't determined. Time can't be estimated because of insufficient SRE to reach the quartiles

No statistical analysis provided for Median Time to First Skeletal Related Event(s) (SRE)

5. Secondary: Percentage of Participants Skeletal Related Event (SRE) Free [Time Frame: 12 months]

Measure Type	Secondary
Measure Title	Percentage of Participants Skeletal Related Event (SRE) Free
Measure Description	Percentage of participants SRE free is defined as the Kaplan-Meier estimate of participants free of any Skeletal Related Events(SRE) at each time point. Skeletal Related Events (SREs) are: • pathologic bone fracture; non-vertebral and vertebral • spinal cord compression identified by X-rays • surgery to bone both curative and prophylactic

	• radiation therapy to bone (palliative, therapeutic or prophylactic) • hypercalcemia of malignancy, defined as a corrected serum calcium > 12 mg/dl (3.00 mmol/l) or a lower level which is symptomatic and requires treatment other than rehydration.
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.
Intent-to-treat (ITT) population will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**209**	**216**
Percentage of Participants Skeletal Related Event (SRE) Free [units: Percentage of participants] Number (95% Confidence Interval)		
At Month 1	**99 (96 to 100)**	**98 (95 to 99)**

At Month 2	**98 (94 to 99)**	**98 (94 to 99)**
At Month 3	**96 (92 to 98)**	**97 (93 to 98)**
At Month 4	**94 (90 to 97)**	**95 (91 to 97)**
At Month 5	**94 (89 to 96)**	**93 (89 to 96)**
At Month 6	**93 (89 to 96)**	**92 (87 to 95)**
At Month 7	**88 (83 to 92)**	**90 (85 to 93)**
At Month 8	**86 (80 to 90)**	**88 (83 to 92)**
At Month 9	**85 (79 to 90)**	**85 (79 to 89)**
At Month 10	**84 (78 to 89)**	**83 (77 to 88)**
At Month 11	**83 (77 to 88)**	**83 (77 to 88)**
At Month 12	**78 (63 to 87)**	**82 (75 to 87)**

No statistical analysis provided for Percentage of Participants Skeletal Related Event (SRE) Free

6. Secondary: Composite Bone Pain Score According to the Brief Pain Inventory (BPI) Questionnaire [Time Frame: At Baseline, Month 3, Month 6, Month 9 and Month 12]

Measure Type	Secondary

Measure Title	Composite Bone Pain Score According to the Brief Pain Inventory (BPI) Questionnaire
Measure Description	Bone pain was assessed by means of a pain score obtained using the Brief Pain Inventory (BPI) questionnaire. The BPI can produce three pain scores: worst pain, a composite pain score, and a pain interference score. The composite pain score, which is the average of questions 3, 4, 5 and 6 of the questionnaire was used in this study. Pain was rated on a scale of 0 (no pain) to 10 (pain as bad as you can imagine). The outcome is given as the median score for participants at baseline, and 3, 6, 9 and 12 months of treatment
Time Frame	At Baseline, Month 3, Month 6, Month 9 and Month 12
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 will include all randomized patients. All ITT patients with BPI questionnaire filled up at baseline were included.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**186**	**185**
Composite Bone Pain Score According to the Brief Pain Inventory (BPI)		

Questionnaire [units: score on a scale] Mean (Standard Deviation)		
Baseline (N= 186, 185)	**2.0 (1.8)**	**2.1 (1.9)**
Month 3 (N= 156, 163)	**2.3 (2.0)**	**2.2 (1.9)**
Month 6 (N= 143, 160)	**2.3 (2.2)**	**1.9 (1.8)**
Month 9 (N= 131, 130)	**2.3 (2.2)**	**2.1 (2.0)**
Month 12 (N= 135, 124)	**2.4 (2.3)**	**2.1 (2.0)**

No statistical analysis provided for Composite Bone Pain Score According to the Brief Pain Inventory (BPI) Questionnaire

7. Secondary: Evaluation of Pain According to Verbal Rating Scale (VRS) Based on Median Score Value [Time Frame: At Baseline, Month 3, Month 6, Month 9 and Month 12]

Measure Type	Secondary
Measure Title	Evaluation of Pain According to Verbal Rating Scale (VRS) Based on Median Score Value
Measure Description	Pain intensity at rest and on movement is rated by the patient by means of a validated 6-point Verbal Rating Scale (VRS) and refers to the pain which occurred during the last week before the assessment. Median score value is the median of all the observed scores (none=0, very mild=1, mild=2, moderate=3, severe=5 and very severe=6) at each time point.
Time Frame	At Baseline, Month 3, Month 6, Month 9 and Month 12
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 will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks
Number of Participants Analyzed [units: participants]	**209**	**216**
Evaluation of Pain According to Verbal Rating Scale (VRS) Based on Median Score Value [units: score on a scale] Median (Full Range)		
At Rest: Baseline	**1 (1.00 to 5.00)**	**1 (1.00 to 6.00)**
At Rest: Month 3	**2 (1.00 to 6.00)**	**2 (1.00 to 5.00)**
At Rest: Month 6	**2 (1.00 to 5.00)**	**1 (1.00 to 6.00)**
At Rest: Month 9	**1 (1.00 to 5.00)**	**1 (1.00 to 5.00)**
At Rest: Month 12	**2 (1.00 to 6.00)**	**1 (1.00 to 6.00)**
At Movement : Baseline	**2**	**2**

	(1.00 to 5.00)	**(1.00 to 6.00)**
At Movement : Month 3	**2 (1.00 to 6.00)**	**2 (1.00 to 6.00)**
At Movement : Month 6	**2 (1.00 to 6.00)**	**2 (1.00 to 6.00)**
At Movement : Month 9	**2 (1.00 to 6.00)**	**2 (1.00 to 6.00)**
At Movement : Month 12	**2.5 (1.00 to 6.00)**	**2 (1.00 to 6.00)**

No statistical analysis provided for Evaluation of Pain According to Verbal Rating Scale (VRS) Based on Median Score Value

8. Secondary: Use Of Analgesic Medications According to the Analgesic Score Scale [Time Frame: At Baseline, Month 3, Month 6, Month 9 and Month 12]

Measure Type	Secondary
Measure Title	Use Of Analgesic Medications According to the Analgesic Score Scale
Measure Description	The analgesic score used for this study is modified from the Radiation Therapy Oncology Group (RTOG) analgesic score scale. The scale represents type of medication administered from 0 to 4 where: 0 = None 1. = Minor analgesics (aspirin, NSAID, acetaminophen, propoxyphene, etc.) 2. = Tranquilisers, antidepressants, muscle relaxants, and steroids 3. = Mild narcotics (oxycodone, meperidine, codeine, etc.) 4. = Strong narcotics (morphine, hydromorphone, etc.) The outcome is given a the median score for the participants at Baseline and 3, 6, 9 and 12 months of treatment
Time Frame	At Baseline, Month 3, Month 6, Month 9 and Month 12
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 will include all randomized patients.

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**209**	**216**
Use Of Analgesic Medications According to the Analgesic Score Scale [units: score on a scale] Median (Full Range)		
Baseline	**0 (0 to 4)**	**0 (0 to 4)**
Month 3	**0 (0 to 4)**	**0 (0 to 4)**
Month 6	**0 (0 to 4)**	**0 (0 to 4)**

Month 9	**0 (0 to 4)**	**0 (0 to 4)**
Month 12	**0 (0 to 4)**	**0 (0 to 4)**

No statistical analysis provided for Use Of Analgesic Medications According to the Analgesic Score Scale

9. Secondary: Assessment of the Eastern Cooperative Oncology Group (ECOG) Performance Score [Time Frame: At Baseline, Month 3, Month 6, Month 9 and Month 12]

Measure Type	Secondary
Measure Title	Assessment of the Eastern Cooperative Oncology Group (ECOG) Performance Score
Measure Description	ECOG Performance Score has 4 grades. 0 = Fully active, able to carry out all pre-disease activities; 1 = Restricted in strenuous activity but ambulatory and able to carry out work of light or sedentary nature; 2 = Ambulatory and capable of all self-care but unable to carry out work activities. Active about 50% of waking hours; 3 = Capable of limited self-care, confined to bed/chair more than 50% of waking hours; 4 = Completely disabled; cannot carry on self-care. Totally confined to bed/chair. Outcome is given as median score for participants at Baseline and 3, 6 , 9 and 12 months of treatment
Time Frame	At Baseline, Month 3, Month 6, Month 9 and Month 12
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 will include all randomized patients.

Reporting Groups

	Description

Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions.

Measured Values

	Zoledronic Acid Every 3 Months	**Zoledronic Acid Every 4 Weeks**
Number of Participants Analyzed [units: participants]	**209**	**216**
Assessment of the Eastern Cooperative Oncology Group (ECOG) Performance Score [units: score on a scale] Median (Full Range)		
Baseline	**0 (0 to 2)**	**0 (0 to 2)**
Month 3	**0 (0 to 3)**	**0 (0 to 3)**
Month 6	**0 (0 to 2)**	**0 (0 to 2)**
Month 9	**0 (0 to 2)**	**0 (0 to 2)**
Month 12	**0 (0 to 4)**	**0 (0 to 4)**

No statistical analysis provided for Assessment of the Eastern Cooperative Oncology Group (ECOG) Performance Score

Serious Adverse Events

Hide Serious Adverse Events

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

Reporting Groups

	Description
Zoledronic Acid Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions

Serious Adverse Events

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks
Total, serious adverse events		
# participants affected / at risk	**21/209 (10.05%)**	**29/216 (13.43%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**2/216 (0.93%)**
Febrile neutropenia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**2/216 (0.93%)**
Thrombocytopenia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**2/216 (0.93%)**

Cardiac disorders		
Acute myocardial infarction † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Cardiac failure † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Eye disorders		
Diplopia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Gastrointestinal disorders		
Gastric haemorrhage † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Nausea † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Oral pain † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**2/216 (0.93%)**
Vomiting † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**2/216 (0.93%)**
General disorders		
Mucosal inflammation † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Pain † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Hepatobiliary disorders		
Jaundice † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**

Infections and infestations		
Acute sinusitis † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Pneumonia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Sepsis † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Skin infection † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Injury, poisoning and procedural complications		
Femur fracture † [1]		
# participants affected / at risk	**2/209 (0.96%)**	**1/216 (0.46%)**
Humerus fracture † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Metabolism and nutrition disorders		
Cachexia † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**1/216 (0.46%)**
Hypercalcaemia † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Musculoskeletal and connective tissue disorders		
Bone pain † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**2/216 (0.93%)**
Jaw disorder † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Musculoskeletal chest pain † [1]		

# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Osteitis † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Osteonecrosis † [1]		
# participants affected / at risk	**4/209 (1.91%)**	**3/216 (1.39%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Malignant neoplasm progression † [1]		
# participants affected / at risk	**2/209 (0.96%)**	**1/216 (0.46%)**
Metastases to central nervous system † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Nervous system disorders		
Cranial nerve paralysis † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Epilepsy † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Ischaemic cerebral infarction † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Paraparesis † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Psychiatric disorders		
Depression † [1]		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Sopor † [1]		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**

Respiratory, thoracic and mediastinal disorders		
Dyspnoea † 1		
# participants affected / at risk	**2/209 (0.96%)**	**2/216 (0.93%)**
Dyspnoea exertional † 1		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Haemoptysis † 1		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Pleural effusion † 1		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Pulmonary embolism † 1		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Surgical and medical procedures		
Breast operation † 1		
# participants affected / at risk	**1/209 (0.48%)**	**0/216 (0.00%)**
Laparoscopic surgery † 1		
# participants affected / at risk	**0/209 (0.00%)**	**1/216 (0.46%)**
Vascular disorders		
Deep vein thrombosis † 1		
# participants affected / at risk	**1/209 (0.48%)**	**1/216 (0.46%)**

† 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 Every 3 Months	Zoledronic acid given as a 15-minute (at least) i.v. infusion every three months. The dose of study drug was the same as administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Randomized participants received a maximum of 4 infusions in this group.
Zoledronic Acid Every 4 Weeks	Zoledronic acid given as a 15-minute (at least) i.v. infusion every 4 weeks. The dose of study drug was the as same administered before study entry; that is, 4 mg or a reduced dose, i.e. 3.5 mg, or 3.3 mg or 3.0 mg. Participants randomized to this group received up to 12 infusions

Other Adverse Events

	Zoledronic Acid Every 3 Months	Zoledronic Acid Every 4 Weeks
Total, other (not including serious) adverse events		
# participants affected / at risk	**133/209 (63.64%)**	**161/216 (74.54%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**13/209 (6.22%)**	**21/216 (9.72%)**
Neutropenia † [1]		
# participants affected / at risk	**11/209 (5.26%)**	**18/216 (8.33%)**
Ear and labyrinth disorders		
Vertigo † [1]		

# participants affected / at risk	**2/209 (0.96%)**	**11/216 (5.09%)**
Gastrointestinal disorders		
Abdominal pain † [1]		
# participants affected / at risk	**12/209 (5.74%)**	**15/216 (6.94%)**
Abdominal pain upper † [1]		
# participants affected / at risk	**16/209 (7.66%)**	**20/216 (9.26%)**
Constipation † [1]		
# participants affected / at risk	**12/209 (5.74%)**	**15/216 (6.94%)**
Diarrhoea † [1]		
# participants affected / at risk	**12/209 (5.74%)**	**17/216 (7.87%)**
Nausea † [1]		
# participants affected / at risk	**24/209 (11.48%)**	**32/216 (14.81%)**
Vomiting † [1]		
# participants affected / at risk	**13/209 (6.22%)**	**21/216 (9.72%)**
General disorders		
Asthenia † [1]		
# participants affected / at risk	**18/209 (8.61%)**	**33/216 (15.28%)**
Fatigue † [1]		
# participants affected / at risk	**10/209 (4.78%)**	**12/216 (5.56%)**
Pain † [1]		
# participants affected / at risk	**10/209 (4.78%)**	**15/216 (6.94%)**
Pyrexia † [1]		
# participants affected / at risk	**22/209 (10.53%)**	**28/216 (12.96%)**
Investigations		
Gamma-glutamyltransferase increased † [1]		

# participants affected / at risk	8/209 (3.83%)	12/216 (5.56%)
Metabolism and nutrition disorders		
Anorexia † [1]		
# participants affected / at risk	5/209 (2.39%)	12/216 (5.56%)
Musculoskeletal and connective tissue disorders		
Arthralgia † [1]		
# participants affected / at risk	9/209 (4.31%)	13/216 (6.02%)
Back pain † [1]		
# participants affected / at risk	7/209 (3.35%)	13/216 (6.02%)
Bone pain † [1]		
# participants affected / at risk	56/209 (26.79%)	64/216 (29.63%)
Pain in extremity † [1]		
# participants affected / at risk	8/209 (3.83%)	12/216 (5.56%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Malignant neoplasm progression † [1]		
# participants affected / at risk	67/209 (32.06%)	68/216 (31.48%)
Nervous system disorders		
Headache † [1]		
# participants affected / at risk	14/209 (6.70%)	15/216 (6.94%)
Paraesthesia † [1]		
# participants affected / at risk	11/209 (5.26%)	8/216 (3.70%)
Respiratory, thoracic and mediastinal disorders		
Cough † [1]		
# participants affected / at risk	14/209 (6.70%)	12/216 (5.56%)

Dyspnoea † 1		
# participants affected / at risk	**9/209 (4.31%)**	**13/216 (6.02%)**
Skin and subcutaneous tissue disorders		
Rash † 1		
# participants affected / at risk	**3/209 (1.44%)**	**12/216 (5.56%)**

† 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.

Results Point of Contact:

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

No publications provided

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00375427 History of Changes
Other Study ID Numbers:	**CZOL446EIT14**
Study First Received:	September 12, 2006
Results First Received:	February 28, 2011
Last Updated:	April 9, 2012
Health Authority:	Italy: Ethics Committee