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Trial record **1 of 1** for: CZOL446G2419

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A Study to Evaluate the Safety and Efficacy of Zoledronic Acid in the Prevention or Delaying of Bone Metastasis in Patients With Stage IIIA and IIIB Non-small Cell Lung Cancer (NSCLC)

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

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

ClinicalTrials.gov Identifier:
NCT00172042

First received: September 13, 2005
Last updated: April 13, 2015
Last verified: April 2015
History of Changes

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Results First Received: June 16, 2011

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Open Label; Primary Purpose: Prevention
Condition:	Non-Small-Cell Lung Cancer
Intervention:	Drug: Zoledronic acid 4 mg

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	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Participant Flow: Overall Study

	Zoledronic Acid	Control
STARTED	**226**	**211**
COMPLETED	**68**	**86**
NOT COMPLETED	**158**	**125**
Adverse Event	**27**	**13**
Abnormal laboratory value(s)	**5**	**1**
Abnormal test procedure(s)	**0**	**3**
Unsatisfactory therapeutic effect	**13**	**11**
Patient no longer requires study drug	**10**	**8**

Protocol Violation	**8**	**7**
Withdrawal by Subject	**37**	**25**
Lost to Follow-up	**3**	**5**
Administrative problems	**13**	**10**
Death	**42**	**42**

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	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.
Total	Total of all reporting groups

Baseline Measures

	Zoledronic Acid	**Control**	**Total**
Number of Participants			

[units: participants]	**226**	**211**	**437**
Age [units: years] Mean (Standard Deviation)	**59.2 (9.19)**	**60.0 (9.27)**	**59.6 (9.23)**
Gender [units: participants]			
Female	**65**	**65**	**130**
Male	**161**	**146**	**307**

Outcome Measures

Hide All Outcome Measures

1. Primary: Progression-Free Survival [Time Frame: Up to 24 months]

Measure Type	Primary
Measure Title	Progression-Free Survival
Measure Description	Progression-free survival is defined as the time from randomization to the date of the first documented progression or recurrence of disease or death from any cause. Time to disease progression (TTP) was assessed by the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines with evaluations every 3 months.
Time Frame	Up to 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.
Intent-to-Treat Population consisting of all randomized participants.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	Control
Number of Participants Analyzed [units: participants]	**226**	**211**
Progression-Free Survival [units: Months] Median (95% Confidence Interval)	**9.0 (6.8 to 12.4)**	**11.3 (7.7 to 15.8)**

No statistical analysis provided for Progression-Free Survival

2. Primary: Kaplan-Meier Estimates for Progression-free Survival [Time Frame: Months 6, 12, 18, and 24]

Measure Type	Primary
Measure Title	Kaplan-Meier Estimates for Progression-free Survival
Measure Description	Progression-free survival is defined as the time from randomization to the date of the first documented progression or recurrence of disease or death from any cause. Time to disease progression (TTP) was assessed by the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines with evaluations every 3 months.
Time Frame	Months 6, 12, 18, and 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 Population consisting of all randomized participants.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	**Control**
Number of Participants Analyzed [units: participants]	**226**	**211**
Kaplan-Meier Estimates for Progression-free Survival [units: Percentage of participants] Number (95% Confidence Interval)		
6 months	**63.0 (56.2 to 69.0)**	**67.9 (61.0 to 73.9)**
12 months	**44.4 (37.6 to 51.0)**	**48.8 (41.6 to 55.5)**
18 months	**30.7 (24.4 to 37.2)**	**40.6 (33.7 to 47.5)**
24 months	**25.7 (19.8 to 32.0)**	**36.0 (29.2 to 42.8)**

No statistical analysis provided for Kaplan-Meier Estimates for Progression-free Survival

3. Primary: Percentage of Participants With Progression-Free Survival Events [Time Frame: Up to 24 months]

Measure Type	Primary
Measure Title	Percentage of Participants With Progression-Free Survival Events
Measure Description	Percentage of Participants with the Progression-free survival events: disease progression and death. Time to disease progression (TTP) was assessed by the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines with evaluations every 3 months.
Time Frame	Up to 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.
Intent-to-Treat Population consisting of all randomized participants.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	**Control**
Number of Participants Analyzed		

[units: participants]	**226**	**211**
Percentage of Participants With Progression-Free Survival Events [units: Percentage of participants]		
Disease Progression	**60.2**	**55.5**
Death	**8.4**	**5.7**

No statistical analysis provided for Percentage of Participants With Progression-Free Survival Events

4. Secondary: Percentage of Participants With Bone Metastases at 6, 12, 18, and 24 Months [Time Frame: Months 6, 12, 18 and 24]

Measure Type	Secondary
Measure Title	Percentage of Participants With Bone Metastases at 6, 12, 18, and 24 Months
Measure Description	Percentage of participants developing at least 1 bone metastasis, whether or not symptomatic. Bone scans were scheduled at screening and at 6-monthly intervals after study entry, or when symptoms suggested the presence of bone metastases. Positive bone scans required confirmation by x-ray, magnetic resonance imaging (MRI), or computed tomography (CT).
Time Frame	Months 6, 12, 18 and 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 Population consisting of all randomized participants.

Reporting Groups

	Description

Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	Control
Number of Participants Analyzed [units: participants]	**226**	**211**
Percentage of Participants With Bone Metastases at 6, 12, 18, and 24 Months [units: Percentage of participants]		
6 months	**2.2**	**4.3**
12 months	**4.0**	**7.1**
18 months	**6.2**	**8.1**
24 months	**6.6**	**9.0**

No statistical analysis provided for Percentage of Participants With Bone Metastases at 6, 12, 18, and 24 Months

5. Secondary: Kaplan-Meier Estimate of the Time to Occurrence of Bone Metastases [Time Frame: Months 6, 12, 18, and 24]

Measure Type	Secondary
Measure Title	Kaplan-Meier Estimate of the Time to Occurrence of Bone Metastases
Measure Description	Time to occurrence of bone metastases was defined as the time from randomization to the date of the first documented bone metastases which could be asymptomatic or symptomatic at the time of detection. Bone scans were scheduled at screening and at 6-monthly intervals after study entry, or when symptoms suggested the presence of bone metastases. Positive bone scans required confirmation by x-ray, magnetic resonance imaging (MRI), or computed tomography (CT).

Time Frame	Months 6, 12, 18, and 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 Population consisting of all randomized participants. Any participant without documented bone metastases at the date of analysis was to be censored at the date of the last bone scan.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	**Control**
Number of Participants Analyzed [units: participants]	**226**	**211**
Kaplan-Meier Estimate of the Time to Occurrence of Bone Metastases [units: Percentage of participants] Number (95% Confidence Interval)		
6 months	**2.7 (0.4 to 5.1)**	**1.9 (0.0 to 4.0)**
12 months	**4.2 (1.1 to 7.3)**	**9.0 (4.3 to 13.7)**
18 months	**11.1 (5.4 to 16.8)**	**12.6 (6.9 to 18.3)**

24 months	**12.4 (6.2 to 18.5)**	**13.7 (7.7 to 19.7)**

No statistical analysis provided for Kaplan-Meier Estimate of the Time to Occurrence of Bone Metastases

6. Secondary: Percentage of Participants With Skeletal Related Events (SREs) at 12 and 24 Months From Study Entry [Time Frame: Months 12 and 24]

Measure Type	Secondary
Measure Title	Percentage of Participants With Skeletal Related Events (SREs) at 12 and 24 Months From Study Entry
Measure Description	Skeletal Related Events were defined as radiation therapy or surgery to bone, spinal cord compression event or a pathologic bone fracture event.
Time Frame	Months 12 and 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 Population consisting of all randomized participants.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	Control
Number of Participants Analyzed [units: participants]	**226**	**211**
Percentage of Participants With Skeletal Related Events (SREs) at 12 and 24 Months From Study Entry [units: Percentage of participants]		
12 months	**2.2**	**1.4**
24 months	**2.2**	**1.4**

No statistical analysis provided for Percentage of Participants With Skeletal Related Events (SREs) at 12 and 24 Months From Study Entry

7. Secondary: Kaplan-Meier Estimates of the Time to the First Skeletal Related Event (SRE) [Time Frame: Months 6,12, 18, and 24]

Measure Type	Secondary
Measure Title	Kaplan-Meier Estimates of the Time to the First Skeletal Related Event (SRE)
Measure Description	Time to the first skeletal related event defined as the time from randomization to the date of occurrence of the first SRE. Skeletal Related Events were defined as radiation therapy or surgery to bone, spinal cord compression event or a pathologic bone fracture event
Time Frame	Months 6,12, 18, and 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 Population consisting of all randomized participants. Any participant in whom no SRE had been observed during the study was to be censored at the date of the last visit or the date of death whichever was the earlier.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	Control
Number of Participants Analyzed [units: participants]	**226**	**211**
Kaplan-Meier Estimates of the Time to the First Skeletal Related Event (SRE) [units: Percentage of participants] Number (95% Confidence Interval)		
6 month	**1.0 (0.0 to 2.3)**	**0.0 (0.0 to 0.0)**
12 month	**2.7 (0.4 to 5.0)**	**1.8 (0.0 to 3.9)**
18 month	**2.7 (0.4 to 5.0)**	**1.8 (0.0 to 3.9)**
24 month	**2.7 (0.4 to 5.0)**	**1.8 (0.0 to 3.9)**

No statistical analysis provided for Kaplan-Meier Estimates of the Time to the First Skeletal Related Event (SRE)

8. Secondary: Kaplan-Meier Estimates for Overall Survival [Time Frame: Months 6, 12, 18, and 24]

Measure Type	Secondary

Measure Title	Kaplan-Meier Estimates for Overall Survival
Measure Description	No text entered.
Time Frame	Months 6, 12, 18, and 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 Population consisting of all randomized participants.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Measured Values

	Zoledronic Acid	**Control**
Number of Participants Analyzed [units: participants]	**226**	**211**
Kaplan-Meier Estimates for Overall Survival [units: Percentage of participants] Number (95% Confidence Interval)		
6 months	**92.8 (88.4 to 95.5)**	**93.6 (89.3 to 96.3)**
12 months	**81.8 (76.0 to 86.4)**	**81.8 (75.7 to 86.5)**

18 months	**72.4 (65.7 to 78.0)**	**71.0 (64.0 to 76.9)**
24 months	**59.5 (51.9 to 66.2)**	**63.6 (56.1 to 70.1)**

No statistical analysis provided for Kaplan-Meier Estimates for Overall Survival

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	Safety results are subsequently presented according to treatment actually received at the start of the study (224 in zoledronic acid arm, 213 in control arm); two patients were randomized to the zoledronic acid arm but did not receive study drug at the start of the study hence included into control arm for safety analysis.

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Serious Adverse Events

	Zoledronic Acid	**Control**
Total, serious adverse events		
# participants affected / at risk	**71/224 (31.70%)**	**84/213 (39.44%)**
Blood and lymphatic system disorders		

Anaemia † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**2/213 (0.94%)**
Febrile neutropenia † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**2/213 (0.94%)**
Neutropenia † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**2/213 (0.94%)**
Pancytopenia † [1]		
# participants affected / at risk	**2/224 (0.89%)**	**0/213 (0.00%)**
Thrombocytopenia † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Cardiac disorders		
Acute myocardial infarction † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Angina pectoris † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Angina unstable † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Atrial fibrillation † [1]		
# participants affected / at risk	**2/224 (0.89%)**	**2/213 (0.94%)**
Atrial flutter † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Bradycardia † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Cardiac failure † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**3/213 (1.41%)**

Cardiopulmonary failure † 1		
# participants affected / at risk	**0/224 (0.00%)**	**2/213 (0.94%)**
Myocardial infarction † 1		
# participants affected / at risk	**2/224 (0.89%)**	**2/213 (0.94%)**
Palpitations † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Pericardial effusion † 1		
# participants affected / at risk	**2/224 (0.89%)**	**1/213 (0.47%)**
Sinus tachycardia † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Ear and labyrinth disorders		
Hypoacusis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**2/213 (0.94%)**
Vertigo † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Gastrointestinal disorders		
Abdominal pain † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Abdominal pain upper † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Constipation † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Diarrhoea † 1		
# participants affected / at risk	**1/224 (0.45%)**	**3/213 (1.41%)**
Dysphagia † 1		

# participants affected / at risk	1/224 (0.45%)	1/213 (0.47%)
Gastric haemorrhage † 1		
# participants affected / at risk	0/224 (0.00%)	1/213 (0.47%)
Gastritis † 1		
# participants affected / at risk	1/224 (0.45%)	0/213 (0.00%)
Gastropleural fistula † 1		
# participants affected / at risk	0/224 (0.00%)	1/213 (0.47%)
Haematemesis † 1		
# participants affected / at risk	1/224 (0.45%)	0/213 (0.00%)
Melaena † 1		
# participants affected / at risk	1/224 (0.45%)	1/213 (0.47%)
Mesenteric artery thrombosis † 1		
# participants affected / at risk	0/224 (0.00%)	1/213 (0.47%)
Nausea † 1		
# participants affected / at risk	1/224 (0.45%)	0/213 (0.00%)
Oesophageal stenosis † 1		
# participants affected / at risk	2/224 (0.89%)	1/213 (0.47%)
Oesophagitis † 1		
# participants affected / at risk	0/224 (0.00%)	1/213 (0.47%)
Subileus † 1		
# participants affected / at risk	1/224 (0.45%)	0/213 (0.00%)
Vomiting † 1		
# participants affected / at risk	1/224 (0.45%)	1/213 (0.47%)
General disorders		
Chest discomfort † 1		
# participants affected / at risk	0/224 (0.00%)	2/213 (0.94%)

Chest pain † 1		
# participants affected / at risk	**1/224 (0.45%)**	**4/213 (1.88%)**
Disease progression † 1		
# participants affected / at risk	**2/224 (0.89%)**	**4/213 (1.88%)**
Fatigue † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
General physical health deterioration † 1		
# participants affected / at risk	**4/224 (1.79%)**	**2/213 (0.94%)**
Influenza like illness † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Pain † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Pyrexia † 1		
# participants affected / at risk	**8/224 (3.57%)**	**4/213 (1.88%)**
Sudden death † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Infections and infestations		
Appendicitis † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Bronchitis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Bronchopneumonia † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Dental fistula † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**

Empyema † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Enterocolitis infectious † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Herpes zoster † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Lower respiratory tract infection † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Lung abscess † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Lung infection † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Neutropenic sepsis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Pneumonia † 1		
# participants affected / at risk	**7/224 (3.13%)**	**10/213 (4.69%)**
Post procedural infection † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Pyelonephritis acute † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Respiratory tract infection † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Septic shock † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**

Injury, poisoning and procedural complications		
Ankle fracture † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Fall † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Foot fracture † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Hip fracture † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Jaw fracture † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Pneumothorax traumatic † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Procedural pain † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Radiation pneumonitis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**3/213 (1.41%)**
Road traffic accident † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Tendon rupture † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Investigations		
Blood creatinine increased † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Electrocardiogram repolarisation abnormality † 1		

# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Metabolism and nutrition disorders		
Dehydration † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Diabetes mellitus † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Hypocalcaemia † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Musculoskeletal and connective tissue disorders		
Back pain † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Bone pain † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Osteoarthritis † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Osteonecrosis of jaw † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Pain in extremity † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Colon cancer † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Lung carcinoma cell type unspecified recurrent † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**

Metastases to central nervous system † 1		
# participants affected / at risk	**6/224 (2.68%)**	**10/213 (4.69%)**
Metastases to liver † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Metastases to lung † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Metastases to lymph nodes † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Metastases to meninges † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Metastases to spleen † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Neoplasm progression † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Non-small cell lung cancer † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Nervous system disorders		
Ataxia † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Cerebral haemorrhage † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Cerebrovascular accident † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Dizziness † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**

Encephalopathy † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Epilepsy † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**3/213 (1.41%)**
Headache † [1]		
# participants affected / at risk	**3/224 (1.34%)**	**1/213 (0.47%)**
Intracranial pressure increased † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Loss of consciousness † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Neuropathy peripheral † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Speech disorder † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Spinal cord compression † [1]		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Syncope † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Psychiatric disorders		
Anxiety † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Confusional state † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**2/213 (0.94%)**
Disorientation † [1]		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Renal and urinary disorders		

Haematuria † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Nephrolithiasis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Renal failure † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**4/224 (1.79%)**	**0/213 (0.00%)**
Dyspnoea † 1		
# participants affected / at risk	**12/224 (5.36%)**	**10/213 (4.69%)**
Haemoptysis † 1		
# participants affected / at risk	**3/224 (1.34%)**	**5/213 (2.35%)**
Lung disorder † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Pleural effusion † 1		
# participants affected / at risk	**3/224 (1.34%)**	**1/213 (0.47%)**
Pneumothorax † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Productive cough † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Pulmonary embolism † 1		
# participants affected / at risk	**5/224 (2.23%)**	**5/213 (2.35%)**
Pulmonary fibrosis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**

Pulmonary haemorrhage † 1		
# participants affected / at risk	**3/224 (1.34%)**	**1/213 (0.47%)**
Pulmonary oedema † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Respiratory failure † 1		
# participants affected / at risk	**1/224 (0.45%)**	**3/213 (1.41%)**
Stridor † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Tachypnoea † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Vascular disorders		
Deep vein thrombosis † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Labile blood pressure † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**
Phlebitis † 1		
# participants affected / at risk	**1/224 (0.45%)**	**0/213 (0.00%)**
Superior vena caval occlusion † 1		
# participants affected / at risk	**1/224 (0.45%)**	**1/213 (0.47%)**
Thrombosis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**2/213 (0.94%)**
Venous thrombosis † 1		
# participants affected / at risk	**0/224 (0.00%)**	**1/213 (0.47%)**

† 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	Safety results are subsequently presented according to treatment actually received at the start of the study (224 in zoledronic acid arm, 213 in control arm); two patients were randomized to the zoledronic acid arm but did not receive study drug at the start of the study hence included into control arm for safety analysis.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Zoledronic Acid	Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks for 24 months. Dosage was adjusted for participants with mild or moderate renal impairment.
Control	No investigational treatment. If a participant developed bone metastases, treatment was started with Zoledronic acid 4 mg intravenous infusion over at least 15 minutes every 3 to 4 weeks until 24 months from the date of study entry had elapsed.

Other Adverse Events

	Zoledronic Acid	Control
Total, other (not including serious) adverse events		
# participants affected / at risk	**166/224 (74.11%)**	**139/213 (65.26%)**
Blood and lymphatic system disorders		
Anaemia † [1]		
# participants affected / at risk	**23/224 (10.27%)**	**23/213 (10.80%)**

Gastrointestinal disorders		
Abdominal pain upper † 1		
# participants affected / at risk	**12/224 (5.36%)**	**7/213 (3.29%)**
Constipation † 1		
# participants affected / at risk	**32/224 (14.29%)**	**13/213 (6.10%)**
Diarrhoea † 1		
# participants affected / at risk	**12/224 (5.36%)**	**13/213 (6.10%)**
Nausea † 1		
# participants affected / at risk	**24/224 (10.71%)**	**23/213 (10.80%)**
Vomiting † 1		
# participants affected / at risk	**20/224 (8.93%)**	**9/213 (4.23%)**
General disorders		
Asthenia † 1		
# participants affected / at risk	**11/224 (4.91%)**	**15/213 (7.04%)**
Chest pain † 1		
# participants affected / at risk	**28/224 (12.50%)**	**19/213 (8.92%)**
Fatigue † 1		
# participants affected / at risk	**38/224 (16.96%)**	**26/213 (12.21%)**
Influenza like illness † 1		
# participants affected / at risk	**12/224 (5.36%)**	**3/213 (1.41%)**
Pyrexia † 1		
# participants affected / at risk	**46/224 (20.54%)**	**22/213 (10.33%)**
Infections and infestations		
Bronchitis † 1		
# participants affected / at risk	**6/224 (2.68%)**	**11/213 (5.16%)**

Nasopharyngitis † 1		
# participants affected / at risk	**17/224 (7.59%)**	**19/213 (8.92%)**
Respiratory tract infection † 1		
# participants affected / at risk	**15/224 (6.70%)**	**12/213 (5.63%)**
Upper respiratory tract infection † 1		
# participants affected / at risk	**7/224 (3.13%)**	**16/213 (7.51%)**
Investigations		
Weight decreased † 1		
# participants affected / at risk	**11/224 (4.91%)**	**12/213 (5.63%)**
Metabolism and nutrition disorders		
Decreased appetite † 1		
# participants affected / at risk	**31/224 (13.84%)**	**29/213 (13.62%)**
Hyperglycaemia † 1		
# participants affected / at risk	**4/224 (1.79%)**	**12/213 (5.63%)**
Musculoskeletal and connective tissue disorders		
Arthralgia † 1		
# participants affected / at risk	**17/224 (7.59%)**	**12/213 (5.63%)**
Back pain † 1		
# participants affected / at risk	**17/224 (7.59%)**	**14/213 (6.57%)**
Musculoskeletal pain † 1		
# participants affected / at risk	**10/224 (4.46%)**	**13/213 (6.10%)**
Myalgia † 1		
# participants affected / at risk	**16/224 (7.14%)**	**12/213 (5.63%)**
Pain in extremity † 1		
# participants affected / at risk	**11/224 (4.91%)**	**11/213 (5.16%)**

Nervous system disorders		
Dizziness † 1		
# participants affected / at risk	**15/224 (6.70%)**	**13/213 (6.10%)**
Headache † 1		
# participants affected / at risk	**19/224 (8.48%)**	**23/213 (10.80%)**
Psychiatric disorders		
Insomnia † 1		
# participants affected / at risk	**21/224 (9.38%)**	**16/213 (7.51%)**
Respiratory, thoracic and mediastinal disorders		
Cough † 1		
# participants affected / at risk	**60/224 (26.79%)**	**54/213 (25.35%)**
Dyspnoea † 1		
# participants affected / at risk	**46/224 (20.54%)**	**49/213 (23.00%)**
Haemoptysis † 1		
# participants affected / at risk	**20/224 (8.93%)**	**11/213 (5.16%)**
Productive cough † 1		
# participants affected / at risk	**11/224 (4.91%)**	**11/213 (5.16%)**
Skin and subcutaneous tissue disorders		
Rash † 1		
# participants affected / at risk	**17/224 (7.59%)**	**6/213 (2.82%)**

† 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 by Novartis

Publications automatically indexed to this study:

Scagliotti GV, Kosmidis P, de Marinis F, Schreurs AJ, Albert I, Engel-Riedel W, Schallier D, Barbera S, Kuo HP, Sallo V, Perez JR, Manegold C. Zoledronic acid in patients with stage IIIA/B NSCLC: results of a randomized, phase III study. Ann Oncol. 2012 Aug;23(8):2082-7. doi: 10.1093/annonc/mds128. Epub 2012 Jun 22.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
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