CALGB-70604

A Randomized, Phase III Study of Standard Dosing Versus Longer Dosing Interval of Zoledronic Acid in Metastatic Cancer

ClinicalTrial.gov Identifier: NCT00869206

Study Background

Trial Description

This randomized phase III trial studies two different schedules of zoledronic acid to compare how well they work in reducing bone-related complications in patients with breast cancer, prostate cancer, or multiple myeloma that has spread to other places in the body and have bone involvement. Bone-related complications are a major cause of morbidity in patients with metastatic prostate cancer, breast cancer, and multiple myeloma. Zoledronic acid may stop the growth of cancer cells in the bone and may help relieve some of the symptoms caused by bone metastases. It is not yet known whether giving zoledronic acid more or less frequently is more effective in treating patients with metastatic cancer that has spread to the bone.

Arms:

Arm I (zoledronic acid every 4 weeks): (Experimental): Patients receive zoledronic acid IV over at least 15 minutes every 4 weeks for up to 2 years in the absence of disease progression or unacceptable toxicity.

Arm II (zoledronic acid every 12 weeks): (Experimental): Patients receive zoledronic acid IV over at least 15 minutes every 12 weeks for up to 2 years in the absence of disease progression or unacceptable toxicity.

Objectives:

PRIMARY OBJECTIVES:

I. To determine whether every-12-week therapy with zoledronic acid is not inferior to every-4-week therapy for patients with metastatic breast cancer, metastatic prostate cancer, or multiple myeloma involving bone, as measured by the proportion who experience at least one skeletal related event within 24 months after randomization.

SECONDARY OBJECTIVES:

I. To compare pain scores (Brief Pain Inventory) of patients with metastatic breast cancer, metastatic prostate cancer, or myeloma

involving bone receiving every 12 week dosing of zoledronic acid to those receiving every 4 week dosing.

II. To compare the functional status (Eastern Cooperative Oncology Group [ECOG] performance status) of patients with metastatic breast cancer, metastatic prostate cancer, or myeloma involving bone receiving every 12 week dosing of zoledronic acid to those receiving every 4 week dosing.

III. To compare the incidence of osteonecrosis of the jaw in patients with metastatic breast cancer, metastatic prostate cancer, or myeloma involving bone receiving every 12 week dosing of zoledronic acid to those receiving every 4 week dosing.

IV. To compare the incidence of renal dysfunction in patients with metastatic breast cancer, metastatic prostate cancer, or myeloma involving bone receiving every 12 week dosing of zoledronic acid to those receiving every 4 week dosing.

V. To compare the skeletal morbidity rate of these patients, defined as the number of skeletal-related events per year, of patients receiving every 12 week dosing to those receiving every 4 week dosing.

VI. To compare the suppression of serum markers of bone resorption of patients with metastatic breast cancer, metastatic prostate cancer, or myeloma involving bone receiving every 12 week dosing of zoledronic acid to those receiving every 4 week dosing.

VII. To determine whether every 12 week therapy with zoledronic acid is not inferior to every-4-week therapy for each subgroup of patients with either breast cancer, prostate cancer, or multiple myeloma, as measured by the proportion who experience at least one skeletal related event within 24 months after randomization.

OUTLINE: Patients are randomized to 1 of 2 treatment arms.

ARM I: Patients receive zoledronic acid intravenously (IV) over at least 15 minutes every 4 weeks for up to 2 years in the absence of disease progression or unacceptable toxicity.

ARM II: Patients receive zoledronic acid IV over at least 15 minutes every 12 weeks for up to 2 years in the absence of disease progression or unacceptable toxicity.

After completion of study treatment, patients are followed up every 4 weeks for 2 years from registration.

Study Milestones:

Start date: March 2009

Primary Completion Date: June 2014

Publication Information:

Analysis Type: Primary

PubMed ID: 28030702

Citation: AL. Himelstein. Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in Patients With Bone Metastases: A Randomized Clinical Trial. JAMA 2017. 48-58.

Associated Datasets:

NCT00869206-D1-Dataset.csv (consort),

NCT00869206-D2-Dataset.csv (patchar),

NCT00869206-D3-Dataset.csv (ske_events),

NCT00869206-D4-Dataset.csv (master_bone),

NCT00869206-D5-Dataset.csv (bpigrowth),

NCT00869206-D6-Dataset.csv (pscmh),

NCT00869206-D7-Dataset.csv (renal),

NCT00869206-D8-Dataset.csv (bonedems1),

NCT00869206-D9-Dataset.csv (incsre),

NCT00869206-D10-Dataset.csv (delay)

Dataset Information:

Dataset Name: NCT00869206-D7-Dataset.csv (renal)

Description: Dataset NCT00869206-D7-Dataset.csv (renal) is one of 10 datasets associated with PubMed ID 28030702. This dataset contains information for the osteonecrosis of the jaw, kidney dysfunction, and skeletal morbidity rate secondary endpoints. There is a difference in our SRE follow-up time to what was in the manuscript due to updated data.

Unless indicated, missing values indicate the data was not collected.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

NCT00869206-D7-Dataset.csv (renal) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Prior SRE	priorsre	No, Yes	
Prior Bisphosphonate use	prior_bis	No, Yes	
Patient ID	patid		
Treatment Assigned	TREAT_ASSIGNED	Arm B: Zoledronic Acid Q 12 Wks, Arm A: Zoledronic Acid Q 4 Wks	
Creatinine	serum_creat	<= 1.4mg/dL, > 1.4mg/dL	
SRE Follow-up Time (Years)	srefutime		
Current diagnosis	DIAGNOSIS	Breast Adenocarcinoma, Prostate Adenocarcinoma, Multiple Myeloma	
Renal Dysfunction from the treatment form	renaldys	No, Yes, Missing	
Occurrences of Renal Dysfunction	num_renal	0, 1, 2, 4, 3, 13, 5, 6, 16, 14, 10, 7, 12	
Increased creatinine	serum_renal	0=No, 1=Yes	

level vs baseline			
Osteonecrosis any grade	osteo	No, Yes	
Hypocalcemia any grade	hypo	No, Yes	
Hypocalcemia grade 4	hypo_g4	No, Yes	
Adverse Events Evaluable	AE_eval	Yes, No	
Increased Creatinine Level, grade 3+, from the adverse event form	Creatg3	Yes	Missing values indicate there was no grade 3 increase creatinine reported.
Number of Skeletal Related Events	numsres	2, 1, 0, 3, 6, 4, 5, 7	
Average yearly SRE rate	sresperyr		