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-D1-Dataset.csv (consort)

Description: Dataset NCT00869206-D1-Dataset.csv (consort) is one of 10 datasets associated with PubMed ID 28030702. This dataset contains information in the Consort Diagram.

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).

There is a typo in the consort diagram that indicates 903 patients received randomized treatment and 8 never started from each arm. The data provided in dataset NCT00869206-D1-Dataset.csv contains 18 patients from Arm A and 25 patients from Arm B that did not receive treatment. These patients can be identified by looking at OF001 (Reason off Treatment) and setting to either "Treatment never started" or "Patient withdrawal/refusal prior to beginning protocol therapy."

The data for number of deaths (OF001 = "Death on Study") provided in this submission are the correct data and will not match the publication exactly.

NCT00869206-D1-Dataset.csv (consort) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient ID	PATID		
Treatment Assigned	TREAT_ASSIGNED	Arm B: Zoledronic Acid Q 12 Wks, Arm A: Zoledronic Acid Q 4 Wks	
>= 2 Yrs of SRE	srege1_9	No, Yes	
Reason off treatment	OF001	Other, Death On Study, Adverse Event/Side Effect/Complication, Patient withdrawal/refusal and withdrew consent to be followed, Alternative therapy, Progressive disease, Treatment completed per protocol, Patient withdrawal/refusal and consented to be followed, Patient developed other disease, Treatment never started, Patient withdrawal/refusal prior to	Missing means the patient was still on treatment at time of publication.

		beginning protocol therapy, Patient did not respond to therapy, LTFU	
Skeletal-related event forms submitted	numsrepts	Yes, No	
Included in the primary analysis	primaryanaly	Yes	
Included in the secondary analysis	secondaryanaly	Yes	