

RTOG 0517 – A Randomized Phase III Trial to Evaluate Radiopharmaceuticals and Zoledronic Acid in the Palliation of Osteoblastic Metastases from Lung, Breast and Prostate Cancer

Primary Objective: To determine if the addition of a radionucleotide (Strontium-89 [SR-89] or Samarium-153 [Sm-153]) to bisphosphonates for patients with asymptomatic or stable symptomatic bone metastasis will delay the time to development of malignant skeletal related events (SREs), defined as a pathological bone fracture, spinal cord compression, surgery to bone, or radiation to bone.

Eligibility Criteria:

- Histologically or cytologically proven diagnosis of solid tumor malignancy of lung, breast or prostate prior to registration.
- Appropriate diagnosis for protocol entry, based upon the following minimum diagnostic workup:
 - History/physical examination within 8 weeks prior to registration;
 - Bone scan within 4 weeks prior to registration; bone metastases must be visible on the scan. Other scanning modalities, such as MRI, PET scan, or plain radiography, may be used to confirm the bone scan, e.g., in the event of an equivocal bone scan.
 - Dental evaluation according to the dental exam checklist (carried out by the investigator, the investigator's designee, or by a qualified dental professional [dental hygienist or dentist]), including history of dental surgery (e.g. extraction or implant) within 8 weeks prior to registration and recorded on the dental exam checklist; **Note:** If the patient has received prior oral bisphosphonate therapy and has had a prior dental evaluation within 8 weeks of registration, the evaluation should not be repeated.
 - CBC/differential within 2 weeks prior to registration, with adequate bone marrow function defined as follows:
 - $WBC \geq 2,400$ cells/mm³;
 - $ANC \geq 1,800$ cells/mm³;
 - Platelets $\geq 60,000$ cells/mm³;
 - Hemoglobin ≥ 8.0 g/dl (**Note:** the use of transfusion or other intervention to achieve the required hemoglobin is permitted).
 - Serum creatinine < 3 mg/dl (265 μ mol/L) within 2 weeks prior to registration;
 - Total bilirubin < 2.5 mg/dl (43 μ mol/L) within 2 weeks prior to registration;
 - Pregnancy test (urine dipstick or serum) for women of childbearing potential within 2 weeks prior to registration;
- ≥ 18 years of age;
- Zubrod performance status 0-2 for patients with breast or prostate primaries; Zubrod performance status 0-1 for patients with lung primaries;
- Patients receiving systemic chemotherapy or hormonal therapy are eligible for this study. **See Section 6.0 and 7.0 for further details. Note: All patients must complete external beam radiation therapy ≥ 14 days prior to registration.** If patients have undergone CyberKnife treatment, treatment must be completed ≥ 14 days prior to registration.
- Patients may have received prior oral bisphosphonate therapy, such as Fosamax® or similar medications. Duration of bisphosphonate treatment prior to study entry must be documented, and all bisphosphonates other than the study drug must be discontinued prior to registration.
- Women of childbearing potential and male participants must agree to practice an adequate means of birth control throughout their participation in the study.
- Patient must sign study specific informed consent prior to study entry.

SCHEMA*:

S		R	
T	Site of Primary	A	Arm 1
R	1. Lung	N	* zolendronic acid, 4 mg IV, monthly, plus
A	2. Breast	D	Vitamin D and calcium supplement
T	3. Prostate	O	
I		M	Arm 2
F	Number of Bone Mets	I	* zolendronic acid, 4 mg IV, monthly, plus
Y	1. ≤ 2	Z	Vitamin D and calcium supplement, plus
	2. > 2	E	** single dose of SR-89 or Sm-153
			Within 6 weeks of randomization

- Zolendronic acid is given monthly for an indefinite period of time and discontinued at the discretion of the treating physician.
- Dose: SR-89 = 4mCi; Sm-153 = 1mCi/kg body weight

Patient Population

Histologically proven diagnosis of solid tumor malignancy of lung, breast, or prostate; bone metastases must be visible on bone scan performed within 4 weeks prior to study entry.

Required Sample Size: 352 patients