



Samarium-153-DOTMP treatment of spontaneously-occurring bone cancer in dogs as a proof-of-concept model

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Abstract

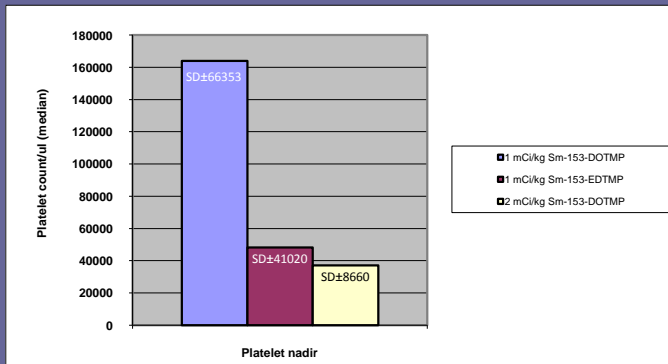
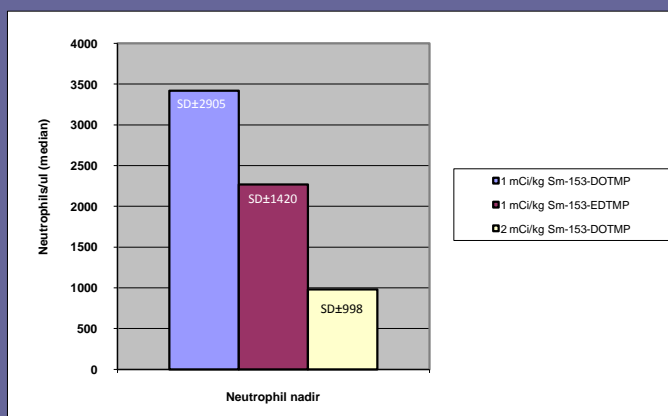
Objectives : Primary and metastatic bone cancer are significant sources of morbidity and mortality in cancer patients. Available treatments include bisphosphonates, anti-inflammatory and opioid pain medication, and radiation therapy. Targeted radioisotopes deliver radiation directly to affected tissue while sparing surrounding normal tissue. Samarium-153-DOTMP consists of samarium-153 which is an excellent radioisotope for imaging and treatment, and DOTMP which is a superior chelator relative to other available constructs. Our objective was to confirm localization of the chelate to known sites of bone tumors in dogs, and to identify myelosuppression or other toxicity.

Methods : Dogs with spontaneously-occurring bone cancer (7 primary appendicular osteosarcoma and 2 metastatic carcinoma and 1 metastatic multilobular tumor of bone) were recruited from the hospital population at the University of Missouri Veterinary Medical Teaching Hospital. Each dog was evaluated with blood count, biochemical profile, urinalysis, and technetium-99m-MDP skeletal scintigraphy. Dogs were treated with 1-2 mCi/kg samarium-153-DOTMP intravenously and monitored using weekly blood counts and quality-of-life assessments (including lameness). Gamma scintigraphy was acquired at 20-24 hours post injection for most cases.

Results : Treatment was well tolerated. There was excellent correlation between pretreatment technetium and post-treatment samarium-153-DOTMP scintigraphy. Region of interest ratios of uptake between tumor and contralateral normal bone ranged from 12.6-45.7 and ratio of tumor to adjacent bone ranged from 8.6-24.8. Two dogs experienced transient peritumoral swelling after injection. At 1 mCi/kg (n=7) and in 1 dog treated at 2 mCi/kg, no dog experienced a dose-limiting hematologic toxicity. In 1 dog treated at 2 and another treated at 2.3 mCi/kg, grade 4 asymptomatic thrombocytopenia and neutropenia were seen.

Conclusions : Given the favorable toxicity profile, higher doses should be explored to maximize the therapeutic ratio for samarium-153-DOTMP, a novel skeletal targeted radiotherapeutic agent.

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Cases- OSA

Post ^{99m}Tc-MDP

Distal radius osteosarcoma, St. Bernard, 1 mCi/kg

Post ¹⁵³Sm-DOTMP

Post ^{99m}Tc-MDP

Distal femur osteosarcoma, Mixed breed, 1 mCi/kg

Post ¹⁵³Sm-DOTMP

Post ^{99m}Tc-MDP

Distal radius osteosarcoma, Akita, 1 mCi/kg

Post ¹⁵³Sm-DOTMP

Post ^{99m}Tc-MDP

Distal radius osteosarcoma, St. Bernard, 1 mCi/kg

Post ¹⁵³Sm-DOTMP

Post ^{99m}Tc-MDP

Distal radius osteosarcoma, Doberman, 1 mCi/kg

Post ¹⁵³Sm-DOTMP

Tibial osteosarcoma, Labrador retriever, 2 mCi/kg, pre-treatment scans →

A: AP view after ^{99m}Tc-MDP
 B: AP view on PET/CT Oct 2010 (bottom) and Mar 2011 (top)
 C: Lateral view on PET/CT
 D: Lateral view after ^{99m}Tc-MDP

Cases- Other

Metastatic multilobular tumor of bone, Lab mix, 2 mCi/kg

Metastatic squamous cell carcinoma, standard Schnauzer, 1 mCi/kg, pre-tx scan only

Metastatic salivary carcinoma, Pit bull mix, 1 mCi/kg

Ulnar osteosarcoma, Golden retriever, 2 mCi/kg, pre-tx scan only

