Cleveland Clinic Innovations

PRODUCT
Biodegradable nanoparticles for treating bone metastasis

INDICATION
Therapeutic, delivery vehicle, nanoparticles, oncology

VALUE PROPOSITION
- Neutral NPs localize to tumor tissue in bone marrow.
- Regress tumor growth.
- Prevent bone loss.

DEVELOPMENT STAGE
Preclinical model studies have been completed.

INTELLECTUAL PROPERTY
US11013817B2
EP3439640A4
CA 3020329

RELATED PUBLICATIONS

Rahman MT, Kaung Y, Shannon L, Androjna C, Sharifi N, Labhasetwar V. Nanoparticle-mediated synergistic drug combination for treating bone metastasis. J Control Release. 357, 498-510, 2023.

Vijayaraghavalua S, Gao Y, Rahman MT, Rozica R, Sharifi N, Midura R, Labhasetwar V. Synergistic combination treatment to break cross-talk between cancer cells and bone cells to inhibit progression of bone metastasis, Biomaterials, 227,119558, 2020

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Nanoparticles for Drug Delivery to Treat Bone Metastasis

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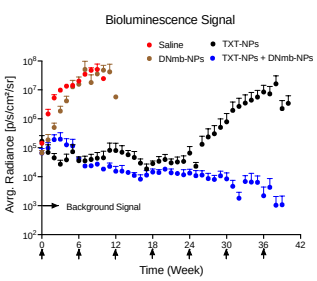
UNMET NEED
Bone is a common site for metastasis in a number of human cancers, in large part because of relatively slow blood flow together with bone marrow is an environment rich in growth factors and cytokines. Given that the cardiac output to the bone marrow is very low, intravenously administered anticancer chemotherapeutics do not achieve a therapeutic dose at bone metastatic sites to suppress tumor growth. A major fraction of the administered drug is either excreted and/or metabolized; or may accumulate in highly perfused body compartments. Studies reveal that existing bone-modifying therapies, particularly bisphosphonates, fail to substantially enhance clinical outcomes or survival and inflict osteonecrosis of jaws. Moreover, the success of existing nanoparticle therapeutics in targeting bone metastasis is limited. In addition, overexpression of cytokine RANKL in bone marrow promotes interactions between bone cells and cancer cells to drive tumor progression. There is an urgent need to develop nanoparticles that can target metastases in the bone and deliver therapeutics effectively that can target cancer cells as well as inhibit RANKL formation.

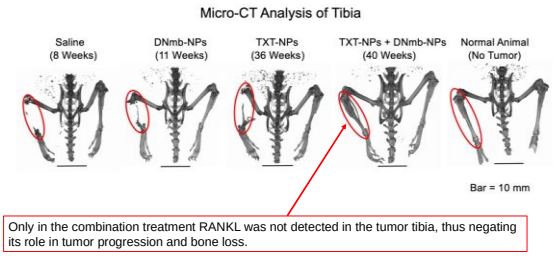
SOLUTION
Dr. Labhasetwar's lab has neutral-charge biodegradable nanoparticles (NPs) that encapsulate therapeutics and size to increase their access to the tumor tissue in bone marrow following intravenous injection while limiting side effects. The animal data demonstrate the potential of these NPs using Docetaxel, an anti-cancer drug (TXT-NPs) which, when delivered in combination with Denosumab (DNmb), a monoclonal antibody that binds to RANKL (TXT-NPs + DNmb-NPs) effectively regress tumor completely and preserving bone integrity in a prostate cancer model. Key features include:

- A neutral surface charge and the presence of polyvinyl alcohol result in reduced interactions with proteins and prevent rapid clearance.
- Significant prolongation of their circulation time in the bloodstream.
- NP size allows them to pass through the sinusoidal capillaries of bones while preventing clearance by the liver, thus mitigating the risk of toxicity.

The current innovation addresses a crucial unmet need by revolutionizing the delivery of a synergistic drug combination in NPs to treat bone metastasis, offering enhanced efficacy and reduced adverse effects.



Regression of Tumor



Inhibition of Bone Loss