SN-117M – A NEW ISOTOPE FOR TREATING ARTHRITIS

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Introduction

Joint disorders, including rheumatoid arthritis (RA) and osteoarthritis (OA), are common in every society and represent some of the largest medical burdens to human healthcare today. Osteoarthritis in dogs is the leading cause of pain and discomfort that can be so extreme as to even lead to the need for euthanasia. These serious issues are now starting to be addressed with a novel Sn-117m based colloid that can be used in joint radiosynoviorthesis (RSO, aka radiosynovectomy) procedures. Additionally, systemic problems can also be addressed with a Sn-117m labeled molecule that targets CD-206 macrophages abundantly found in the inflammatory RA joints.

Discussion

Sn-117m has been incorporated into a novel and unique homogeneous colloid. We employ a technique where the slow decomposition of urea releases ammonia uniformly throughout the colloid solution and raises the pH in a very reproducible and controlled manner. This results in a colloid with a tight particle size distribution (around 5 μm). This colloid has very high retention (>99.8% after 5 half-lives) in the injected joint and has demonstrated efficacious treatment of arthritis in animal models. An ideal size range of the colloid (2-20 μm) results in no leakage from the joint (or the need for joint splinting to prevent leakage) and complete phagocytosis of the particles by migrating macrophages which allows for the engulfed colloid to irradiate the deeper inflamed synovium. The colloid has demonstrated suitability for treating both small and medium sized joints and may even be useful in larger joints. This cGMP product has completed several successful canine OA trials and will be commercially available in the US as a veterinary product later this year. Multi-national human trials for this product are also set to begin.

High specific activity Sn-117m has been used to label a mannosyl-dextran macromolecule. A similar imaging molecule ([Tc-99m]-tilmanocept) has demonstrated great specificity for RA. Initial attempts found that the DTPA in this construct did not retain Sn-117m in a physiological pH environment. To overcome this, the molecule was modified to accommodate Sn-117m using a DOTA chelate which is known to be stable *in-vivo*. This novel theranostic molecule mimics the biodistribution of [Tc-99m]-tilmanocept and allows for a therapeutic effect similar to the Sn-117m colloid product, but on a systemic basis that is particularly suitable for treating RA.

Conclusions

Joint disorders such as RA and OA represent some of the world's largest medical problems. A Sn-117m homogeneous colloid has been developed for the RSO treatment of canine OA. This commercial product is also ideal for treating human arthritis and multi-national clinical trials are underway. A [Sn-117m]-DOTA-mannosyl-dextran composition under development also shows promise to image and treat RA systemically.