NOVEL TREATMENTS FOR ARTHRITIS IN HUMANS AND ANIMALS USING SN-117M COLLOIDS AND LABELED MOLECULES

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Introduction

Joint disorders, such as osteoarthritis (OA) and rheumatoid arthritis (RA), are common in every society and represent one of the largest medical burdens to healthcare today. Canine osteoarthritis is the leading cause of pain and discomfort that can be so extreme as to even lead to the need for euthanasia. It is now possible to address these serious issues with novel tin-117m based colloids that can be used in joint radiosynoviorthesis (RSO, radiosynovectomy) procedures. Additionally, to address systemic problems a labeled molecule that targets CD-206 macrophages specifically found in the inflammatory RA joints is being developed.

Discussion

Sn-117m has been used in the manufacturing of a novel and unique homogeneous colloid. A production technique has been developed that employs the decomposition of urea to release ammonia uniformly throughout the colloid solution. This raises the pH in a very reproducible and controlled manner that 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 both OA and RA in animal models. The ideal size of the colloid (2-20 μm) results in no leakage from the joint and complete phagocytosis of the particles which allows for deeper irradiation of the inflamed synovium tissue as the engulfing macrophages traverse the tissue. 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 2018. Multi-national human trials for this product will also begin next year.

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 demonstrated that the existing DTPA in this construction does not retain Sn-117m in 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.

Conclusions

Joint disorders such as OA and RA represent one of the world's largest medical problems. A Sn-117m homogeneous colloid has been developed that shows very promising results in animal trials and has the potential to replace existing commercial RSO isotopes in human RA and OA. A [Sn-117m]-DOTA-mannosyl-dextran composition also shows favorable bio-distribution and promise to treat RA systemically.

Keywords: Sn-117m, nuclear medicine, arthritis, radiosynoviorthesis, radiosynovectomy