PREPARATION AND EVALUATION OF Sn-117m ANNEXIN FOR VULNERABLE PLAQUE

Jaime Simón[a]*, Jason A. Rogers[a], George St. George[a], R.Keith Frank[a], Scot H. Ellebracht[a], Nigel R. Stevenson[b], David W. Mueller[b] and, Gilbert R. Gonzales[b]

[a]IsoTherapeutics Group LLC: 1004 S. Velasco, Angleton, Texas 77515;
[b]Clear Vascular, Inc.: 21 Waterway Avenue, Suite 225, The Woodlands, Texas 77380
**Corresponding author e-mail: jimsimon@isotherapeutics.com*

Introduction

Annexin was labeled with high specific activity Sn-117 by using a DOTA-based bifunctional chelating agent. The conjugate retained its biological activity in an *in vitro* binding test. In addition, the conjugate showed targeting in two different mouse models and in early clinical trials. Also, an early indication of efficacy in one mouse model was observed. Based on these results, further development of this agent for diagnosis and therapy of vulnerable plaque is warranted.

Description of the Work or Project

Sn-117m was prepared by the reaction of Cd-116 with 50 MeV alpha particles. The isotope was separated from the target by ion exchange columns to produce very pure, high specific activity Sn-117m. The metal was chelated to aminobenzyl-DOTA (ABD) at low pH in a microwave. The resulting chelate was further purified using reverse phase HPLC.

Purified Sn-117m-ABD was treated with thiophosgene to generate the isothiocyanate and reacted with annexin at a pH of 9. The resulting conjugate was purified using size exclusion chromatography.

The Sn-117m-Annexin produced by the above process was evaluated for biological activity by a cell binding assay, evaluated in two different mouse models and finally in humans.

Conclusions

- High purity Sn-117m with specific activities of 15,000 – 20,000 Ci/g were achievable
- Chelation of Sn-117m with ABD was achievable in close to quantitative yields
- Sn-117m-ABD was used to conjugate to annexin with yields of 30-60 %
- Sn-117m-annexin retained its biological activity in a cell binding test
- Sn-117m-annexin gave positive results in two different mice models
- Early stage clinical trials show targeting of the conjugate in vulnerable plaque
- Early toxicology data show low toxicity for Sn-117m-annexin at therapeutic doses

Keywords: nuclear medicine, accelerator produced isotopes, Sn-117m, high specific activity, annexin, vulnerable plaque