

SN-117M FOR METASTATIC BONE CANCER TREATMENT - MODERNIZING SN-117M-DTPA FOR REGULATORY APPROVAL

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Introduction

Sn-117m is a theranostic isotope used in for the treatment of metastatic bone cancer and bone pain with conversion electrons (CE) energy emission of ~0.14 MeV. The CE are mono-energetic with a maximum tissue range of 300µm. Early pre-clinical, and Phase 1/Phase 2 human trials utilized low specific activity (LSA) Sn-117m.¹ The specific activity (s.a.) of Sn-117m was 3 to 11 mCi/mg for use in the Sn-117m-DTPA therapeutic. The development of $\geq 1,000$ mCi/mg, high specific activity (HSA) cyclotron produced Sn-117m has been used in animal trials in preparation for FDA regulatory qualification for human trials.² The Sn-117m-DTPA product can use LSA and HSA Sn-117m with FDA regulatory ‘modernization’ requiring additional animal species for biodistribution (BD) and dosimetry before qualifying HSA Sn-117m for human use.

Description of the Work

Additional background work for FDA regulatory qualification of new radioisotopes is required. Previously mouse studies using only LSA Sn-117m-DTPA were acceptable. Presently regulatory qualification of cyclotron produced HSA Sn-117m using both LSA and HSA Sn-117m-DTPA for BD and dosimetry and end-product validation in rat studies are required.

Results

	<i>Srivastava mice</i>	<i>ITG mice 9/10/2020</i>	<i>ITG rat 9/24/2020</i>	<i>ITG rat 10/14/2020</i>
	% Injected Dose			
Bone	36%	38%	60%	61%
Blood	0.02%	0.06%	0.03%	0.02%
Liver	0.47%	0.69%	0.52%	0.37%
Muscle	0.31%	0.60%	0.60%	0.58%
	Bone to soft tissue ratio			
Blood	1955	816	1945	2446
Liver	72	45	85	110
Muscle	860	472	614	652

Conclusions

Clinical trials utilizing reactor and cyclotron produced Sn-117m has been ‘modernized’ for FDA regulatory submission to include higher specific activity Sn-117m to match prior studies that are decades old. Additionally, regulatory agency requirements of pre-clinical studies have evolved to include changes in animal species and newer isotope validation studies.

References

1. Srivastava SC, et al. (1998). Treatment of Metastatic Bone Pain with Tin-117m Stannic Diethylenetriaminepentaacetic Acid: A Phase I/II Clinical Study. Clin Cancer Research (vol. 4), pages 61-69.
2. Stevenson, NR, et al. (2015). Methods of Producing High Specific Activity Sn-117m with Commercial Cyclotrons. J. Radioanalytic Nuclear Chemistry (vol. 305), pages 99-108.