B-16

[212Pb]PSC-PEG2-TOC Therapy for NET Leads to Complete Responses in Mice Bearing SSTR2 Positive Tumors – Comparison to [177Lu]DOTATATE in a Preclinical Model

Michael K. Schultz[1,2], Dijie Liu[2], Mengshi Li[2], Brianna S. Cagle[2], Zhiming Dai[2], Dongyoul Lee[2], Kelly Orcutt[2], Edwin Sagastume[2], Nicholas J. Baumhover[2], Ivy Vance[2], Amos Hedt[2], Yusuf Menda[1], Frances L. Johnson[2].

[1]Department of Radiology, University of Iowa; [2]Viewpoint Molecular Targeting, Inc.

BACKGROUND

Peptide-based targeted alpha-particle radiotherapy has emerged as a promising approach to cancer treatment. $^{203}Pb/^{212}Pb$ is the only elementally identical isotope pair for this application. Tyr^3-Octreotide (TOC) peptide ligands targeting SSTR2 have been widely investigated preclinically and clinically. [^{177}Lu]DOTATATE was approved by the US FDA to treat patients with gastroenteropancreatic neuroendocrine tumors. However, the objective response rate (18%) reported in the Phase III trial leaves significant room for improvement. In this study, we modified TOC with a Pb specific chelator (PSC) and PEG2 linker and evaluated the in vivo biodistribution profiles and efficacy of [$^{203/212}$Pb]PSC-PEG2-TOC in preclinical mouse model in comparison with [^{177}Lu]DOTATATE.

METHODS

PSC-PEG2-TOC was radiolabeled with ^{203}Pb and ^{212}Pb by published methods1, 2. [^{177}Lu]DOTATATE was synthesized and radiolabeled using published methods3. Biodistributions were conducted in female athymic nu/nu mice bearing AR42J tumor xenografts following intravenous injection of 74 kBq of ^{203}Pb-labeled PSC-PEG2-TOC at 1, 3, 6 and 24 h post-injection (pi). Single or fractionated doses of [^{212}Pb]PSC-PEG2-TOC (total activity at 4.44 MBq) were administered to mice bearing AR42J tumors for efficacy evaluation. Administered fractionated doses of [^{177}Lu]DOTATATE were based on previous literature. Tumor volume, body weight, complete blood count, and serum chemistry were monitored.

RESULTS

PSC-PEG2-TOC labeled efficiently with ^{203}Pb at high specific activity (50-100 MBq/nmol). 24-h radiochemical purity and maintained near quantitative levels in excipients. *In vivo* biodistribution studies demonstrated high tumor uptake and rapid renal clearance for [^{203}Pb]PSC-PEG2-TOC. The administration of 4 fractionated doses of [^{212}Pb]PSC-PEG2-TOC produced 100% complete tumor responses at 100 days post therapy initiation and was well-tolerated compared to [^{177}Lu]DOTATATE, which produced improved PFS (28.5 days), but no complete responses.

CONCLUSIONS

These data demonstrate that [$^{203/212}$Pb]PSC-PEG2-TOC has the potential to produce a higher rate of objective tumor responses than beta-particle emitting therapeutics for NETs.

ABSTRACT ID 21938