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Phase I Trial of ⁹⁰Y-DOTA-tyr³-Octreotide in Children and Young Adults

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Purpose: A Phase I trial of ⁹⁰Y-DOTA-tyr³-Octreotide was conducted in children and young adults with somatostatin receptor positive tumors as indicated by SPECT imaging with ¹¹¹In-DTPA-Octreotide.

Methods: A 3X3 design was utilized to determine highest tolerable dose of ⁹⁰Y-DOTA-tyr³-Octreotide while limiting renal radiation dose to ≤ 21 Gy. Activity levels of administered ⁹⁰Y-DOTA-tyr³-Octreotide were 1.11, 1.48 and 1.85 GBq/m²/cycle in 3 cycles at 6 week intervals, co-administered with Aminosyn II for renal protection. Eligibility criteria included age 2-25 years, progressive disease, positive ¹¹¹In-DTPA-Octreotide scan, glomerular filtration rate ≥ 80 ml/min/m², bone marrow cellularity $\geq 40\%$ or stored autologous hematopoietic stem cells, Lansky Play Scale $\geq 60\%$, and informed consent.

Results: Seventeen subjects, ages 2 to 24 years, received at least one dose of ⁹⁰Y-DOTA-tyr³-Octreotide; diagnoses included neuroblastoma, embryonal and astrocytic brain tumors, paraganglioma, MEN IIB, and neuroendocrine tumors. There were no dose limiting toxicities and no individual dose reductions due to renal or hematologic toxicity. There were no complete responses; 3/15 subjects experienced partial response, 5/15 had minor responses, 5/15 experienced stable disease, 2/15 patients had progressive disease. Two subjects withdrew.

Conclusions: Molecularly targeted peptide radiotherapy with ⁹⁰Y-DOTA-tyr³-Octreotide demonstrated a 20% PR plus 33% MR rate in a Phase I trial in children and young adults with somatostatin receptor positive tumors. No dose limiting toxicities were observed. The recommended Phase II dosing is three cycles of 1.85GBq/m²/dose ⁹⁰Y-DOTA-tyr³-Octreotide co-administered with amino acids. In the future, higher doses may be attainable through the use of dosimetry guided therapy.