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212Pb-AlphaMedix™ Targeted Alpha Therapy (TAT): A Potential Breakthrough in Treatment of Metastatic SSTR Expressing NET



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BACKGROUND: Peptide Receptor Radioligand Therapy (PRRT) with beta emitter such as Lu-177 DOTATATE has been shown to be an effective treatment for patients with metastatic somatostatin receptor (SSTR) positive NETs. Alpha emitters such as Pb-212 have significantly higher Linear Energy Transfer (LET), causing double strand DNA damage, but less collateral damage to the normal tissues. We present the safety and preliminary effectiveness of 212Pb AlphaMedix™ (212Pb-DOTAMTATE), a novel SSTR analogue for Targeted Alpha-emitter Therapy (TAT), in SSTR(+) NET patients.(IND 135150).

METHODS: Sixteen subjects, 7 men and 9 women, median age 68 (range 27-75), PRRT naïve patients with unresectable or metastatic SSTR (+) NETs from different primary sites were enrolled in a classic 3+3 dose escalation design. Response to treatment was measured per RECIST 1.1 and the effect on quality of life was measured with the EORTC-QLQ-C30 QOL questionnaire.

RESULTS: Effective and safe dose was determined to be 67.6 $\mu\text{Ci}/\text{kg}$. Cumulative dose ranging from 18.4 to 23.6, across 4 cycles. By RECIST criteria 5 out of 6 subjects showed Objective Radiological Response (ORR=83%). Ga-68 DOTATATE PET/CT revealed complete response in 4 and partial response in 2 patients.

No clinically significant drug related toxicity was noted up to 18 months after treatment. Quality of life was significantly improved.

CONCLUSION: 212Pb -AlphaMedix™ was well tolerated. Dramatic decreases in tumor burden and a positive impact on quality of life were seen in 6 out of 6 patients who received four cycles of 212Pb -AlphaMedix™ at the highest dose tested. ORR of 83% with 212Pb -AlphaMedix™ compares with 13% ORR for Lutathera (Lu-177 DOTATATE). is extremely promising. This FIH study illustrates that PRRT with 212Pb -AlphaMedix™ is highly effective, and well tolerated. If proven in larger cohorts, this treatment modality will be a major breakthrough in treatment of patients with unresectable, metastatic SSTR expressing NETs.

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