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Targeted alpha-emitter therapy of neuroendocrine tumors using 212Pb-octreotate (AlphaMedix TM)

Objectives:

The high potency of alpha-emitters combined with high affinity of the somatostatin analogs provides the fundamental strength and rationale for using Targeted Alpha-emitter Therapy (TAT) in neuroendocrine cancers (NETs). The 212Pb-octreotate analog, (AlphaMedix™) will be the next generation of peptide receptor radionuclide therapy for the metastatic NETs patients. RadioMedix and Orano Med initiated the Phase I, non-randomized, open-label, dose escalation study of AlphaMedix™ to determine the safety, bio-distribution, and preliminary effectiveness of this drug in adult subjects with somatostatin receptor expressing NETs. The Investigational New Drug application was approved by U.S. FDA (IND# 135150) and BRANY IRB of New York. The clinical trial site is the Excel Diagnostics and Nuclear Oncology Center in Houston.

Methods:

Subjects with histologically confirmed NETs and prior positive somatostatin analog scans, with no prior history 177Lu/90Y/111In peptide receptor radionuclide therapy (PRRT), were enrolled in this study. Each subject underwent a screening visit within 14 days prior to receiving the investigational agent. Vital signs, laboratory tests, and ECG were measured before and at multiple time points after the drug administration. These assessments were repeated through the follow-up phase of the study. For the efficacy assessment, the imaging studies including CT/MRI, 18F-FDG-PET/CT, and other known imaging modalities were used to monitor any change in the size and function of the tumor. The quality of life (QOL) were also monitored using ECOG performance status and the EORTC-QLQ-C30 QOL questionnaire. The treatment regimen started with single intravenous (IV) administration of ascending doses of AlphaMedix™. Each cohort consisted of 3 subjects meeting the inclusion and exclusion criteria of the protocol. There was an incremental 30% increase of the dose between each cohort. Dosing was continued until the tumor response or DLT is observed. The Single Ascending Dose (SAD) regimen has been converted to a Multiple Ascending Dose (MAD) regimen which consists of 3 IV injections of selected doses of drug administrated at 8 (+/-1) week intervals.

Results:

As of November 2018, we have enrolled nine patients (6 females and 3 males) with SSTR expressing metastatic NETs. All subjects well-tolerated treatments with single ascending or the first multi-ascending doses of AlphaMedix™. Few mild adverse events were reported during the follow-up visits (nausea and mild hair loss in 2/9 patients; the abdominal pain and diarrhea in 3/9 patients, the fatigue in 2/9 patients). There was no dose-limiting toxicity.

Conclusion:

The AlphaMedix™ treatment has shown a favorable safety profile at the currently tested doses. The efficacy and the safety study are still ongoing. The favorable properties of 212Pb causing irreversible damage to the double stranded DNA of tumor cells can potentially translate into longer progression-free survival of the patients with metastatic SSTR (+) NETs.

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Email Address

itworowska@radiomedix.com

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Primary authors: Dr DELPASSAND, Ebrahim S. (RadioMedix Inc; Excel Diagnostics and Nuclear Oncology Center); Dr TWOROWSKA, Izabela (RadioMedix Inc)

Co-authors: Dr MUZAMMIL, Ali (Excel Diagnostics and Nuclear Oncology Center); Dr SAIDI, Amal (Orano Med LLC); Dr HE, Bin (Rapid LLC); Dr FREY, Eric (Rapid LLC); Dr SHANOON, Farah (Excel Diagnostics and Nuclear Oncology Center); Dr SGOUROS, George (Rapid LLC); Dr TORGUE, Julien (Orano Med LLC); Dr BOLEK, Luke (Excel Diagnostics and Nuclear Oncology Center); Dr GHALY, Michael (Rapid LLC); Dr STALLONS, Tania (Orano Med LLC)

Presenter: Dr DELPASSAND, Ebrahim S. (RadioMedix Inc; Excel Diagnostics and Nuclear Oncology Center)