O5

^{177}Lutetium-DOTA-Octreotate Therapy in Somatostatin Receptor-Expressing Neuroendocrine Neoplasms; First Trial in U.S.A

Ebrahim S. Delpassand, M.D.

^{177}Lu-(DOTA0,Tyr3) Octreotate is a promising therapy for patients with somatostatin receptor positive neuroendocrine Tumors. European studies of this therapy have shown significant improvement in disease state with little toxicity. In a recent study conducted by Erasmus Medical Center, 125 patients were treated with cumulative doses of 177Lu-(DOTA0,Tyr3) of up to 600-800mCi. A complete radiological response was found in 3 (2%) patients, a partial response in 32 (26%), a minor response in 24 (19%), stable disease in 44 (35%), and progressive in 22 (18%) patients. A significant improvement in symptoms and quality of life were also observed in the majority of patients. Median time to progression was greater than 36 months.

Excel Diagnostics and Nuclear Oncology Center has recently obtained approval from the FDA to begin a phase III trial of 177Lu-(DOTA0,Tyr3) Octreotate. This trial is based on the Erasmus protocol and is the first in the US to offer this therapy to patients with NETs. This will be a nonrandomized study to provide treatment to patients with disseminated neuroendocrine malignancies and to observe the potential for efficacy and the side effects of this drug. This therapy protocol calls for IV infusion of 200 mCi of ^{177}Lu-DOTATATE every 6-11 weeks to a cumulative dose of 800 mCi. For kidney protection, patients will receive an infusion of Aminosyn II 7%, 200 ml/hr 30 minutes prior to therapy and up to 3.5 hrs after.

Inclusion criteria are (1) Patients with biopsy proven Gastroenteropancreatic (GEP tumors including bronchial Carcinoid (2) Presence of somatostatin-receptors on the know tumor lesions demonstrated by OctreoScan within 6 months of the first dose of radiolabeled Octreotate therapy. (3) Life Expectancy greater than 12 weeks. (4) Serum creatinine ≤ 150 µmol/liter or 1.7 mg/dL and a measured creatinine clearance (or measured GFR using plasma clearance methods, not gamma camera based) of ≥ 50ML/min (5) Hemoglobin (Hgb) concentration≥ 5.5 mmol/L (≥ 8.9 g/dL);

WBC ≥ $2*10^{9}$/L ($2000/mm^3$); platelets ≥ $100*10^{9}$/L ($100*10^3/mm^3$). (6) Total Bilirubin≤ 3X UNL. (7) Serum Albumin > 30g/L or serum albumin≤ 30g/L but normal prothrombin time. (8) All patients must have a Karnofski performance status of at least 60% and (9) Patients must be greater than 18 years of age. Patients younger than 18 years will be presented to FDA for compassionate use on a case by case basis.

Patients will be evaluated for adverse effects, acute and long term hematological, kidney and liver toxicity. The primary endpoint of this trial is to determine progression free survival (PFS). The distributions of duration of PFS will be estimated using the Kaplan-Meier method. Comparison of PFS to historical controls will be determined using the exact binomial test. Secondary endpoints include Additional secondary endpoints of this trial are to determine Radiological response by PRECIST criteria, clinical response and biochemical Response compared to historical controls. This clinical trial is actively recruiting patients. Detail information about the protocol will be presented in the poster.