Ongoing, Double-Blind, Randomized, Placebo-Controlled Clinical Trial Investigating the Efficacy and Safety of Somatuline® Depot (Lanreotide) Injection in the Treatment of Carcinoid Syndrome – Update on the Current Status

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INTRODUCTION

Carcinoid syndrome occurs when a carcinoid tumor secretes certain amines and peptides that bypass the liver and are secreted into the bloodstream. It is usually the result of liver metastases. The most common symptoms are flushing and/or diarrhea

- Somatostatin receptors are found on 80%-90% of all carcinoid tumors[1]
- Somatostatin analogs (SSAs) are widely used to treat carcinoid syndrome
- Lanreotide is an SSA approved in >50 countries for the treatment of acromegaly and/or for the treatment of symptoms associated with carcinoid syndrome
  - For now it is currently approved in the US only for the treatment of acromegaly
  - Somatuline® Depot Injection is a prolonged-release formulation of lanreotide that is presented as a ready-to-use, pre-filled syringe administered via deep subcutaneous injection every four weeks
- This ongoing clinical trial will evaluate the safety and efficacy of lanreotide versus placebo for the control of symptoms associated with carcinoid syndrome

STUDY OBJECTIVES

- To evaluate the efficacy of lanreotide for the control of symptoms (diarrhea and/or flushing) associated with carcinoid syndrome
- To characterize the effect of lanreotide versus placebo on biomarkers of tumor activity
- To characterize the pharmacokinetic profile (C_{min}) of lanreotide in patients with carcinoid syndrome
- To evaluate the safety of lanreotide

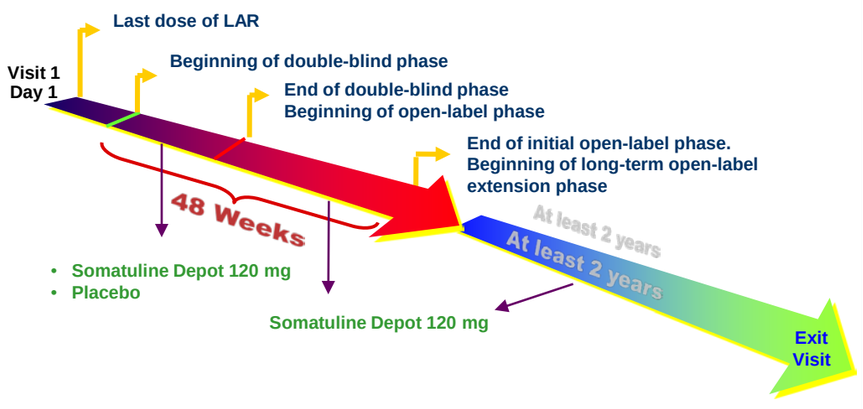
METHODS

Study design

- Ongoing, multi-center, Phase 3/4 study of patients with carcinoid syndrome with three phases (**Figure 1**)
  - 16-week, double-blind, randomized, placebo-controlled phase
  - Followed by a 32-week open-label phase
  - Long-term open-label phase available for patients in countries where lanreotide is not yet approved for the treatment of carcinoid syndrome

METHODS

Figure 1. Study Design



Study treatments

- **Double-blind phase:** Patients are randomized in a 1:1 ratio to one of the following treatments administered as a deep subcutaneous injection every four weeks:
  - 120 mg lanreotide
  - Placebo: saline solution
- **Initial open-label and long-term open-label phases:** All patients receive 120 mg lanreotide
- **Throughout the study:** Patients are allowed to use subcutaneous octreotide, as needed, to control the symptoms associated with carcinoid syndrome (diarrhea and/or flushing)

Primary endpoint

- The usage (% of days) of subcutaneous octreotide required to control the symptoms (diarrhea and/or flushing) associated with carcinoid syndrome during the double-blind phase of the study

Participating Countries

- **12 Countries:** Brazil, Croatia, Czech Republic, India, Latvia, Poland, Russia, Serbia, South Africa, Turkey, Ukraine, and United States

Patients

- **Target enrollment:** 100 patients

- **Key inclusion criteria:**
  - Age ≥18 years at first dosing
  - Histopathologically confirmed carcinoid tumor, or a carcinoid tumor of unknown location with liver metastases (documented by biopsy), and a history of carcinoid syndrome (diarrhea and/or flushing)
  - SSA treatment-naïve or responsive to conventional doses of octreotide
  - Willing to receive subcutaneous octreotide injections as rescue medication, as needed, to control symptoms associated with carcinoid syndrome
  - Confirmation of positive somatostatin receptor status
  - Documented absence of tumor progression
- **Key exclusion criteria:**
  - History of carcinoid syndrome refractory to treatment with conventional doses of SSAs
  - Treatment with interferon, chemotherapy and/or radiotherapy, a radiolabelled SSA and/or tumor debulking <3 months prior to study entry
  - Short bowel syndrome
  - Uncontrolled diabetes and/or hypertension
  - Severe renal and/or severe liver impairment

Key study assessments

- **Efficacy:** Symptoms and rescue medication use, biomarkers for tumor activity (plasma CgA, 5-H1AA) and a QoL questionnaire
- **Safety:** Physical exams, adverse events, biochemistry/hematology, gallbladder echography, electrocardiogram and anti-lanreotide antibodies

Pharmacokinetics

- Lanreotide serum concentrations are measured during the open-label phase at the following time points:
  - **Week 16:** Before and 4 hrs after lanreotide administration
  - **Week 20:** Before lanreotide administration
  - **Week 48 (Exit Visit):** At exit visit or before lanreotide administration if continuing into long-term open-label extension

Patient recruitment for this study is ongoing

REFERENCES

1. Kulke MH and Mayer RJ. *N Engl J Med* 1999; 340:858-68.
2. Oberg et al. *Ann Oncol* 2004;15:966-73.

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