T-3

Phase 2 Study to Evaluate the Safety, Pharmacokinetics, and Dose Response of Paltusotine Carcinoid Syndrome

Aman Chauhan, MD[1], Shagufta Shaheen, MD[2], Keith Usiskin, MD[3], Ade Odueyungbo, PhD[3], Cosina Mui, BSc[3], Joseph Dillon, MD[4].

[1]University of Kentucky Healthcare, [2]Stanford Medicine, [3]Crinetics Pharmaceuticals, [4]University of Iowa Carver College of Medicine.

BACKGROUND

Neuroendocrine tumors (NETs) are classified as functional or non-functional based on the presence of characteristic symptoms, related to tumoral secretion of biologically active peptides or amines. Carcinoid Syndrome (CS) is the commonest functional NET syndrome, seen at diagnosis in 19% of patients. It is characterized in over 80% of cases by watery diarrhea (mainly due to serotonin hypersecretion) or cutaneous flushing.

Somatostatin is a neuropeptide that inhibits the secretion of many hormones, including pituitary growth hormone and serotonin from functional NETs. While long-acting somatostatin receptor ligands (SRLs) are mainstay treatments for CS, relief of the symptoms at labeled doses is inadequate for many patients.

Paltusotine is a novel oral, nonpeptide, selective somatostatin receptor type 2 (SST2) agonist. It appears to be equally effective as long acting injectable SRLs in maintaining plasma IGF-1 levels in patients with acromegaly. Paltusotine was well tolerated in Phase 2 studies, with the most common adverse events (AEs) being headache, arthralgia, diarrhea, and abdominal pain.

METHODS

This randomized, open-label, parallel-group, multi-center study will examine the safety, tolerability, pharmacokinetics, and exploratory efficacy of paltusotine in patients with CS. Patients with documented well-differentiated, grade I or II, NETs with CS, who are either naïve to therapy with SRLs or have symptomatic control (bowel movement and flushing frequency) on SRLs, will be eligible to participate. The study includes a Screening Period of 2 weeks in patients naïve to SRLs and up to 12 weeks in patients washing out of SRLs. An electronic diary will be used to capture symptom frequency. Patients washing out of SRLs will be eligible for randomization when symptomatic worsening occurs over any 7-day period. After completion of screening, subjects will be randomly assigned to the 40 mg versus 80 mg daily open-label dose groups for 8 weeks. In addition to collection of safety data and serum paltusotine levels (to generate pharmacokinetic profiles in this patient population), a full suite of biomarkers and efficacy assessments will be explored for paltusotine in NETs. Following completion of the Randomized Treatment Phase, subjects may be eligible to enter the Open-Label Extension (OLE) Phase of the study in which they will receive paltusotine for an additional 50 weeks.

RESULTS

Currently enrolling. NCT05361668

CONCLUSIONS

Phase 2 clinical study with paltusotine, a somatostatin agonist, in progress

ABSTRACT ID 21388