IPSEN
Innovation for patient care

CLARINET® Backgrounder

The FDA priority review and approval of Somatuline® Depot® (lanreotide) injection was based on the Controlled Study of Lanreotide Antiproliferative Response in Neuroendocrine Tumors (CLARINET) – a 96-week landmark registrational study of 204 patients enrolled in 48 centers across 14 countries. The trial showed Somatuline® reduced the risk of disease progression or death by 53% as compared to placebo in patients with advanced gastrointestinal and pancreatic neuroendocrine tumors.

Participants

Trial participants had well or moderately differentiated non-functioning enteropancreatic neuroendocrine tumors and a proliferation index (Ki67) of less than 10%.

- Primary tumor locations: pancreas (45%), midgut (35%), hindgut (7%) and unknown (13%). Most patients (96%) had stable disease and were treatment-naïve (86%).

Trial Design

In this investigational, Phase III, double-blind, placebo-controlled study, participants were randomized to treatment with either Somatuline® 120 mg (n=101) or placebo (n=103). The primary efficacy endpoint was time to either disease progression (assessed by central independent radiological review using the Response Evaluation Criteria in Solid Tumors, RECIST 1.0) or death. Two baseline CT (computed tomography) or MRI (magnetic resonance imaging) scans (12 to 24 weeks) were performed, followed by additional scans at 12-week intervals during the first year and 24-week intervals during the second year up to 96 weeks.

Results

Median progression-free survival (PFS -- length of time during and after treatment for a disease that a patient lives with the disease but does not get worse) for those taking placebo was 18.0 months and 33.0% of that treatment group had not progressed or died at 96 weeks. In contrast, the median PFS for Somatuline® treated patients was not reached and 65.1% had not progressed or died at 96 weeks (stratified logrank test, $p<0.001$). This represented a 53% reduction in risk of disease progression or death based on a hazard ratio of 0.47 (95% CI: 0.30–0.73).

- The improvement in PFS with Somatuline® was seen regardless of patient or disease characteristic.

Safety data from the CLARINET® study were consistent with the known safety profile of Somatuline®. Similar proportions of each treatment group experienced adverse events (Somatuline® 88%; placebo 90%). One half of the Somatuline® group experienced treatment-related adverse events (vs. 28% with placebo), most commonly diarrhea (26% vs. 9%, respectively), followed by abdominal pain and cholelithiasis (gallstones). Six patients experienced adverse events leading to withdrawal, three in each group, with only one considered by the investigator to be treatment-related in the Somatuline® group. Fifty-seven patients experienced 122 serious adverse events; eight were considered treatment-related (Somatuline®, seven events; placebo, one event).

CLARINET® was published in the July 17, 2014 edition of the New England Journal of Medicine and is available online at NEJM.org (N. Engl. J. Med. 2014; 371: 224-233.