NEUROENDOCRINE CANCER

CLARINET: NEW OPTION FOR NETS

Neuroendocrine tumours (NETs) are rare, and patients are typically diagnosed with inoperable disease or distant metastases. Moreover, few approved treatment options with antiproliferative efficacy exist for the treatment of advanced-stage NETs. Somatostatin analogues have a favourable safety profile and antiproliferative efficacy has been observed *in vitro*, in small uncontrolled retrospective studies and, in a small randomized study of 85 patients, the somatostatin analogue octreotide (PROMID study) showed antitumour effects in low-grade intestinal NETs.

Caplin and coauthors conducted a randomized, phase III double-blind, placebo-controlled trial (CLARINET) of the long-acting agent lanreotide. In this 96-week multinational trial, 204 patients from 14 different countries with grade 1 or grade 2 well-differentiated or moderately differentiated tumours were randomly assigned to lanreotide or placebo. Primary tumours were located in the pancreas, midgut, hindgut or were of unknown origin.

The primary end point of the study was progression-free survival (PFS)—centrally assessed using RECIST criteria—or death. PFS was significantly prolonged with lanreotide compared with placebo (median PFS not reached versus 18 months). Caplin summarizes the results, “after 2 years of treatment with lanreotide, the risk of disease progression or death was reduced by 53%.” At 24 months, 65.1% of patients treated with lanreotide had not progressed compared with only 33% in the placebo group. Moreover, the antiproliferative effect of lanreotide was independent of tumour hepatic volume ($\leq 25\%$ versus $>25\%$). The rates of adverse events were similar in both arms, although lanreotide was associated with more gastrointestinal adverse events.

Caplin explains the significance of these findings: “Although CLARINET included predominantly patients with stable disease, the practical outcome of this trial is that lanreotide may be considered a potential first-line antitumour agent in intestinal and pancreatic NETs.” He further concludes, “the CLARINET study demonstrated not only significant antitumour effect of lanreotide, but also showed impressive results in patients with grade 2 NETs and those who had $>25\%$ of their liver replaced by tumour metastases.”

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