Dose escalation of octreotide LAR is safe and effective in patients with advanced gastrointestinal neuroendocrine tumours for control of symptoms and tumor progression

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To the Editor,

Octreotide is a powerful drug for patients with gastroentero-pancreatic neuroendocrine tumors (GEP-NET). We recently reviewed in this Journal the role of somatostatin analogs as antiproliferative agents, but so far no results from randomized controlled trials were available (1). Meanwhile, the PROMID-study has established that a monthly dose of 30 mg octreotide-Long Acting Release (LAR) controls tumor growth in patients with advanced midgut neuroendocrine tumors, resulting in an important benefit in progression free survival compared to placebo (14.3 versus 6 months, hazard ratio = 0.34 ; 95% CI, 0.20 to 0.59 ; p = 0.000072) (2). It is important to recall that this somatostatin analogue mainly exerts its actions through the somatostatin-2 and 3-receptors, but saturation is incomplete at the classical doses of octreotide-LAR of up to 30 mg monthly (3).

Symptoms of carcinoid syndrome have been reported to respond in only 50% of cases to the standard dose of octreotide-LAR (4). However, a prospective study reported an improved effect of a high-dose treatment with octreotide pamoate in patients with advanced malignant midgut carcinoid tumours (5). In this study, 12 patients received doses of octreotide of 160 mg every 2-4 weeks resulting in 75% of patients with tumour growth stabilisation for a median of 12 months and the majority of patients experiencing an amelioration of symptoms.

A recent retrospective study also reported on 54 patients with GEP-NET that received octreotide-LAR, of which 30 required dose escalation above the conventional dose for tumor control (range : 40-90 mg, median of 8.5 doses received) with no treatment-related toxicities (6). In a survey (7), and updated by Woltering (3), in 392 patients with carcinoid tumors, just over 65% (n = 256) of the total population changed octreotide dosing. In particular, up to 40% of patients received doses of octreotide-LAR above the 30 mg monthly schedule, in order to control symptoms.

These, and other, findings have resulted in the recent adaptation of the National Comprehensive Cancer Network's guidelines and the Nordic guidelines, which state that dose and frequency of octreotide-LAR may be further increased (8,9). In our personal experience, even doses up to 60 mg every 2 weeks are well tolerated.

In conclusion, dose escalation of octreotide LAR represents an important and safe addition to our therapeutic arsenal for disease control in patients with advanced midgut neuroendocrine tumors, an approach which could postpone or abrogate the need to change to other, more costly therapies with a lower risk-benefit ratio.

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