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EDITORIAL

Treatment with somatostatin analogues may delay progression of neuroendocrine tumours

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Neuroendocrine tumours (NETs) are typically slow growing, hormone producing malignancies diagnosed at advanced stages. Somatostatin analogues have been successfully used to reduce hormone-induced symptoms, but their impact on tumour growth has been debated. One randomised trial addressing this question has been published, the PROMID study [1], in which 85 patients with small intestinal NETs were randomised to treatment with long acting octreotide LAR or placebo. In the study octreotide showed an antiproliferative effect with time to tumour progression of 14 months in the treatment arm compared to 6 months for placebo-treated patients (HR = 0.34; 95% CI 0.20–0.59; p = 0.000072). This effect was demonstrated in patients regardless of the presence of a carcinoid syndrome.

Recently, a large, international, multicentre trial was published, the CLARINET study [2], which included 204 patients with advanced, non-functioning gastrointestinal NETs, randomised to either lanreotide autogel 120 mg every fourth week or placebo and treated for 96 weeks. The majority of patients had their primary tumour in the pancreas or small intestine. Progression-free survival (PFS) was significantly longer (median not reached) in the treatment arm at the end of follow-up compared to 18 months in the placebo arm (HR = 0.47; 95% CI 0.30–0.73; $p < 0.001$). The surprisingly long PFS in both arms in this study may be related to the fact that 96% of the patients had stable disease at inclusion. Hepatic tumour load did not have an impact on the outcome as it did in the PROMID study. Despite this, both the PROMID and the CLARINET studies point in the same direction, somatostatin analogues not only ameliorate hormone-induced symptoms, they also have an antiproliferative effect in small intestinal NETs of grade 1 and 2 (Ki67 < 10%). However, the data for pancreatic NETs has to be interpreted with some caution as this is based on a limited number of patients and events (HR = 0.58; CI 0.32–1.04; p-value not shown). These results are suggestive but not fully conclusive and further studies are needed to establish the anti-tumour effect of somatostatin analogues on pancreatic NET growth.

Both studies demonstrate that somatostatin analogues are safe and well-tolerated. The results have changed the indication for somatostatin analogue treatment in NET patients from being only symptomatic treatment to having an anti-tumour effect. In the updated Nordic Guidelines for gastroenteropancreatic neuroendocrine neoplasms published in this issue of Acta Oncologica [3] somatostatin analogue treatment is recommended for small intestinal NETs with residual disease with or without endocrine symptoms. Furthermore, treatment in endocrine pancreatic NETs with Ki67 < 10% may be considered, but for this group other treatments with well-established effects are also available.

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