

 TARGETED THERAPIES

## Widening the treatment NET

The incidence of neuroendocrine tumours (NETs) is increasing, and treatment options are limited. Mouse model of NETs are responsive to the antiangiogenic agent sunitinib. In 2006, results from the first phase I trial investigating this agent in patients with various types of NETs were published. Among four patients with advanced-stage NETs, one had a major tumour response and two patients had long-term partial responses. Phase II data provided new hope, which led to the launch of a phase III, randomized, placebo-controlled trial in patients with pancreatic NETs. This phase III trial reported on the safety of a continuous daily dose of sunitinib in patients with advanced-stage pancreatic NETs, which provided benefits in terms of progression-free survival (PFS) and overall survival, while maintaining an acceptable quality of life. Data from

this pivotal phase III trial was the basis for the FDA and EMA approval of sunitinib in pancreatic NETs. Sandrine Faivre, lead author of the latest report, elaborates: “this was one of the first large international phase III trials to demonstrate the feasibility of this randomized approach in patients with rare tumours, such as NETs.”

The recent phase III report included long-term follow-up monitoring of patients receiving sunitinib; an impressive doubling of PFS from 5.8 months with placebo to 12.6 months was demonstrated (HR 0.32,  $P = 0.00001$ ), which translated into a median overall survival improvement of nearly 10 months, 5 years after study closure. Faivre opines, “we show a sustained benefit favouring sunitinib in terms of overall survival, despite a limited number of patients and the fact that 69% of patients crossed over from placebo to sunitinib.”

The results of this phase III trial confirm previous findings and pave the way for future trials using antiangiogenic treatments, either as single agents or in combination, for patients with pancreatic or other gastrointestinal NETs. “Considering recent data showing a PFS benefit of sunitinib in the adjuvant setting in renal-cell carcinoma, results of our study might provide new avenues for developing trials investigating antiangiogenic agents following surgical resection of pancreatic NETs,” concludes Faivre.

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**ORIGINAL ARTICLE** Faivre, S. *et al.* Sunitinib in pancreatic neuroendocrine tumours: updated progression-free survival and final overall survival from a phase III randomized study. *Ann. Oncol.* <http://dx.doi.org/10.1093/annonc/mdv561> (2016)



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