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EDITORIAL

# New treatments of pancreatic neuroendocrine tumors: why using them? How to use them?

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Neuroendocrine tumor has long been considered as a rare tumor, although its prevalence makes it one of the most frequent gastrointestinal malignancies [1]. In the eighties, streptozotocin-based chemotherapy allowed substantial improvements in the management of advanced pancreatic neuroendocrine tumors (PNETs) [2, 3]. Subsequently, somatostatin analogues were shown to be useful for the control of symptomatic PNETs and also able to delay tumor progression in slow-growing midgut carcinoids [4].

Based on large double-blind randomized trials, sunitinib [5] and everolimus [6] have been approved last year for the treatment of patients with advanced well-differentiated PNETs. Both drugs significantly improve progression-free survival and provide substantial clinical benefit for patients with advanced PNETs [7, 8]. The availability of those novel drugs is now raising several questions such as the optimal patient management and best possible placement in the current armamentarium of patients with PNETs. While currently limited to the treatment of well-differentiated PNETs, questions will also be raised on the potential of those drugs for the treatment of midgut carcinoids. New agents have led to redefine algorithms used for the treatment of patients with PNETs and to establish the role of progression-free survival as a valid endpoint for clinical trials in PNETs [8].

In this special issue of *Targeted Oncology* authors will attempt to address some of those questions. Angiogenesis has been shown to play a major role in PNET carcinogenesis and as such has offered multiple targets for therapeutic interventions. Inhibition of angiogenesis at the level of VEGFR and PDGFR tyrosine kinases with sunitinib and mTOR with everolimus has been shown to translate into clinical benefit using sunitinib and everolimus, respectively [9]. Mechanisms by which tumors may respond to those drugs as well as mechanisms of resistance are important for new generations of compounds that will now be develop in PNETs. Sunitinib being a paradigm antiangiogenic agent, understanding its indication and management will be crucial for routine practice and will be detailed in this special issue [10]. New agents that are currently in development are also comprehensively described [11]. The disease being often limited to the liver, hepatic-directed therapies will certainly remain important options and are extensively described [12]. Finally, the challenge of using sunitinib in clinical practice stands on the radiological evaluation of patients to define those benefiting the most of novel targeted treatments [13]. In most cases, tumor evaluations made on RECIST criteria are often poorly predictive of progression-free benefit of targeted agents in PNETs, requiring redefining response evaluation based on novel criteria such as the CHOI criteria previously used to predict activity of imatinib in gastrointestinal stromal tumors.

In this issue we have aim-providing physicians in charge of patients with a review that could help them to better understand the mechanisms of action of novel drugs in PNETs and to provide them with practical tools that they will use to treat patients and to design novel clinical trials. The multidisciplinary approach that the treatment of PNET

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patients deserves will be further addressed in another special issue of *Targeted Oncology* that will shortly follow the current issue of the journal. In the future issue, we will also discuss more in deep the role of surgery, cytotoxic chemotherapy, novel somatostatin analogues, and targeted agents in PNETs and midgut carcinoids.

**Conflict of interest** Eric Raymond and Philippe Ruszniewski are consultant for Pfizer, Novartis and Ipsen.

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