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EDITORIAL

Targeting neuroendocrine tumor: mixing standard options with novel therapies

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While chemotherapy remains frequently used in neuroendocrine tumors [1, 2], sunitinib [3] and everolimus [4] have been more recently approved expanding treatment options for patients with advanced/metastatic pancreatic neuroendocrine tumors. Mixing standard options including surgery and chemotherapy with novel therapies has become a common challenge for physicians in charge of treatment for patients with neuroendocrine tumors. Clinical guidelines, standards, options, and recommendations are progressively incorporating novel drugs in treatment algorithms. However, several prevalent questions remain to be answered: do we know the mechanisms of action and resistance to targeted therapies, is there a place for targeted therapies before or after surgery, are targeted therapies combinable with liver targeted options, shall we use targeted agents prior or after chemotherapy, and is there a place for combining chemotherapy with targeted agents?

In the June 2012 issue of *Targeted Oncology*, we extensively discussed the efficacy of sunitinib in pancreatic neuroendocrine tumors [5–8]. However, tumor progressions occurring during treatment suggest that acquired resistance to sunitinib may become an important issue in the next few years. In this issue of *Targeted Oncology*, Tijeras-Raballand et al. have deciphered mechanisms of resistance to sunitinib and defined resistance pathways that may help identifying drugs that could counteract resistance to sunitinib.

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At a cellular level, neuroendocrine tumor cell survival involves multiple signaling pathways among which the PI3k/AKT/mTOR pathway was shown to play a major role described by Cingarlini et al. Based on preclinical data, everolimus has been tested in clinical trials and demonstrated striking activity prolonging progression-free survival in patients with advanced pancreatic neuroendocrine tumors [4]. Although not reaching the level of evidence required for approval, everolimus also showed activity in patients with non-pancreatic neuroendocrine tumors [9]. In this issue, Grozinsky-Glasberg and Pavel comprehensively summarize trials with mTOR inhibitors in neuroendocrine tumors and comments on ongoing trials that may broader the indications of rapalogues in these diseases.

While targeted agents are becoming more prevalent, standard options will also move progressively and indications will certainly be redefined as we accumulate more clinical trial data [10]. In this issue, we also wanted to update data on the so-called classical chemotherapy and novel cytotoxic agents available for the treatment of neuroendocrine tumors. Therefore, we asked Meyer et al. to discuss the place of streptozotocin-based chemotherapy and Hammel et al. offered to briefly summarize novel cytotoxic drugs such as temozolomide in the treatment of metastatic neuroendocrine tumors. Surgical resection remains one of the commonly used strategies for the treatment of neuroendocrine tumors. In this issue of *Targeted Oncology*, Gaujoux et al. have summarized the indications of surgical resection for patients with neuroendocrine tumors. While surgery may be used to remove the primary tumor offering hopes for cure, surgical resection of metastases may also now be discussed with specialized surgeons to extend overall survival and delay symptomatic progressions in a limited subset of patients. As such, surgery keeps a central place as a targeted option in the armamentarium for neuroendocrine tumors.

We hope that this second issue of *Targeted Oncology* focusing on endocrine tumors will bring sufficient information to fulfill expectations of new comers in this filed as well as experts interested to get a comprehensive view of the complex treatment landscape of advanced neuroendocrine tumors [11].

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Conflict of interest Eric Raymond and Sandrine Faivre are consultants for Novartis, Pfizer, and IPSEN.

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