

From the Editor

Well-differentiated neuroendocrine tumors (NETs) represent both a diverse set of tumors that can occur in many organs and sites, as well as a meaningful number of patients in most oncologic practices. Prior to the advent of drugs that now target the biological aspects of NETs, systemic treatments had little impact on outcome despite the often indolent nature of the disease.



Debu Tripathy

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Editor-in-Chief

In this issue of the *American Journal of Hematology/Oncology*[®], an overview of therapies titled “Are We Making Progress in Treatment of the Neuroendocrine Tumors?” highlights the importance of basic biology progress in developing effective treatments for NETs. First among these is the known presence of somatostatin (SS) receptors on many NETs. Octreotide and lanreotide, SS analogs, had been used to mitigate symptoms of carcinoid syndrome; ultimately, however, the former was shown to actually improve the time to tumor progression in 2009.¹ Subsequently, radioactive SS analogs yielded similar benefits to nonradioactive analogs. An influential report

that highlighted genomic lesions in NETs pointed to the PTEN/PI3K/mTOR pathway.² This eventually led to a landmark trial that resulted in the first approval of this agent for NET.

The activation of angiogenesis is complex. It is mediated through hypoxia pathways and multiple receptor-initiated proliferation pathways. Many tumors co-opt these pathways, but only some are successfully treated with antiangiogenic agents. The results of biological studies suggested this phenotype as a potential target. There is an effect on response rate from adding bevacizumab to everolimus, both with antiangiogenic activity, when treating pancreatic NETs, but without a difference in PFS.^{3,4} However, the antiangiogenic drug sunitinib is active and approved as a single agent, perhaps due to its multikinase-inhibiting activity that may also have antiproliferative effects.⁵

Further clues are being followed for NETs, including immune checkpoint and cyclin-dependent kinase inhibition, again highlighting the importance of studying biology to lead the direction of oncology treatment, especially for tumors that are rarer and more diverse. Collaborations among centers that tend to see larger cohorts of these patients has complemented scientific advances, and the coming years will likely result in even more progress.

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