Are Targeted Therapies a Consideration in Poorly Differentiated Neuroendocrine Tumors?

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Disclosures of potential conflicts of interest may be found at the end of this article.

I appreciated the very thorough and insightful article, “Targeted therapies in neuroendocrine tumors (NET): Clinical trial challenges and lessons learned” by Yao et al. [1]. Among the challenges not discussed was the treatment of poorly differentiated NETs (PDNETs). The National Comprehensive Cancer Network (NCCN) guidelines for NETs recommend following the NCCN guidelines for small cell lung cancer, based largely on reports of the responsiveness to platinum-based therapy when this entity was first described by Hainsworth et al. in 1988 [2, 3]. The close relationship between PDNETs and well or intermediately differentiated NETs is evidenced by the World Health Organization criteria for distinguishing these groups [4] and by recognition by the NCCN that octreotide therapy should be considered in some PDNETs [1]. Catena et al. also demonstrated that these tumors express mammalian target of rapamycin at “similar levels” regardless of “tumor site or proliferation rate” [5]. In fact, the RADIANT-2 study, which included only well and intermediately differentiated NETs,

led to the approval of everolimus for pancreatic NETs, perhaps again recognition of this close relationship [6]. A single small phase II study of everolimus use in patients previously treated for small cell lung cancer appears to show no obvious benefit, and the responsiveness to platinum-based chemotherapy for PDNETs might be similar to that of small cell lung cancer, but perhaps these extrapulmonary PDNETs are more closely related to their well and intermediately differentiated relatives. Based on the possible derivation from similar normal cells and the somewhat arbitrary World Health Organization distinction, particularly between intermediate and poorly differentiated NETs, it seems reasonable that future studies of targeted agents in the treatment of NETs should evaluate patients with PDNETs as well.

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