MOLECULAR TARGETED THERAPY OF GI NEUROENDOCRINE TUMORS (pNETs, CARCINOIDS) AND OVERVIEW

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GI-NETs (pNETs, Carcinoids) are increasing in frequency both in Asia and throughout the world. In the past many patients died of tumor-mediated hormone/amine excess states resulting in functional syndromes. With the increased ability to control the hormone excess states medically the natural history of the tumor is becoming the major determinant of long-term survival. While most are indolent, a proportion is associated with aggressive growth and advanced metastatic disease. Until recently, little was known of their molecular pathogenesis except that it differed from common adenocarcinomas. Recently there has been not only an increased understanding of the molecular pathogenesis of these tumors and the fact that it differs for pNETs and carcinoids, as well as for carcinoids originating from different sites. Concomitant with this increased understand has come increased novel therapies. These include the development of cytotoxic receptor directed therapies using primarily the unique overexpression of somatostatin receptors by NETs (pNETs, Carcinoids) as well as various targeted molecular therapies. The latter therapies resulted primarily from an increased understanding of the importance of tyrosine kinase receptor activation as well as activation of the mTOR signaling cascade in the growth of NETs. Recent large double blind prospective studies (Phase 3) have provided evidence that both the tyrosine kinase inhibitor, sunitinib, as well as the mTOR inhibitor, everolimus are effective in pNETs resulting a more than a doubling of progressive free survival in patients with advanced disease. Each of these advances will be briefly discussed.