

NEUROENDOCRINOLOGY

Improved progression-free survival with everolimus plus octreotide in carcinoid syndrome

Everolimus plus octreotide improves progression-free survival in patients with advanced neuroendocrine tumors (NETs) associated with carcinoid syndrome compared with placebo plus octreotide.

The diagnosed incidence of advanced NETs has risen more than fivefold over the past three decades. These tumors, which are not curable, can arise from neuroendocrine cells spread throughout the body. Median survival is approximately 4 years for patients with advanced disease. Though less aggressive than other cancers, NETs are also generally more resistant to treatment. For NETs arising from primary sites other than the pancreas, which are often called carcinoids, no FDA-approved drugs for oncologic control are currently available.

“Our initial reason for the investigation of mTOR inhibitors in NETs lies in the realization that genetic cancer syndromes in which the mTOR pathway is affected, for example, tuberous sclerosis, neurofibromatosis and von Hippel Lindau disease, are associated with development of NETs,” reflects senior investigator James C. Yao from the University of Texas MD Anderson Cancer Center. “Preclinical studies have shown mTOR inhibition may delay the growth of carcinoid tumors.”

The investigators tested the hypothesis that everolimus plus octreotide delays tumor growth compared with standard therapy (that is, octreotide alone) in a randomized controlled phase III study. Everolimus plus octreotide increased progression-free survival by 5.1 months

compared with octreotide alone. The study was affected by imbalances in randomization, as patients in worse clinical condition were assigned to the everolimus group, and by informative censoring, which caused the central review of radiological data to lose statistical power. Nevertheless, the findings by Pavel and colleagues, along with data from a previous study in pancreatic NETs, support the efficacy of everolimus in advanced NETs.

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Original article Pavel, M. E. *et al.* Everolimus plus octreotide long-acting repeatable for the treatment of advanced neuroendocrine tumours associated with carcinoid syndrome (RADIANT-2): a randomised, placebo-controlled, phase 3 study. *Lancet* doi:10.1016/S0140-6736(11)61742-X