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Treatment Outcomes of Well-Differentiated High-Grade Neuroendocrine Tumors

A. Liu[1], B. Ueberroth[1], P. McGarrah[2], S. Buckner Petty[3], A. Kendi[4], J. Starr[5], T. Hobday[2], T. Halfdanarson[2], M. Sonbol[6]; [1]Mayo Clinic, AZ/United States of America, [2]Division of Medical oncology, Department of Oncology, Mayo Clinic College of Medicine, MN/United States of America, [3]Division of Biomedical Statistics and Informatics, Mayo Clinic/United States of America, [4]Department of Radiology, Mayo Clinic, MN/United States of America, [5]Mayo Clinic, FL/United States of America, [6]Medical Oncology, Mayo Clinic, AZ/United States of America

BACKGROUND: Recent World Health Organization (WHO) classification of neuroendocrine neoplasms (NET) has defined high-grade well-differentiated NET (NET G3) as a distinct entity that is clinically different from the poorly differentiated neuroendocrine carcinoma (NEC). The optimal treatment for NET G3 has not been well-described. This study aims to evaluate NET G3 response to different treatment regimens.

METHODS: This is a retrospective study of NET G3 patients within the Mayo Clinic database (Arizona, Florida, and Minnesota). Patient demographics along with treatment characteristics and responses and survival were assessed. Primary end points were progression-free survival (PFS) and overall survival (OS). Secondary end points were objective response rate (ORR) and disease control rate (DCR).

RESULTS: Seventy-one patients with NET G3 were identified. Systemic treatment data was available in 30 patients with median age of 59.5 years at time of diagnosis. The primary tumor was most commonly pancreatic (73.3%). Ki-67 index was ≥55% in 26.7% of cases. 56.7% of cases had >1 metastatic site. Treatment regimens included: capecitabine + temozolomide (CAPTEM) (n=20), lutetium 177 DOTATATE (PRRT) (n=10), carboplatin/cisplatin + etoposide (EP) (n=7), everolimus (n=2), and FOLFOX (n=7).

CAPTEM was the most commonly used regimen (10 first-line, and 10 second-line) with ORR of 35%, disease control rate (DCR) of 65%, and median PFS of 9.4 months (95% CI 2.96-12.78). Both EP and FOLFOX showed comparable activity with ORR of 28.6% in both and PFS of 3.42 and 13.04 months, respectively. PRRT was used in 10 patients with ORR of 20%, DCR in 50%, and median PFS of 8.28 months.

CONCLUSION: Among NET G3 patients, CAPTEM was found to be the most commonly used treatment with clinically meaningful efficacy and disease control. Other potentially active treatment options include FOLFOX, EP, and PRRT. Prospective studies evaluating different treatments effects in NET G3 patients are needed to determine an optimal treatment strategy.

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