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Treatment Response and Clinical Outcomes of Well-differentiated (WD) High-grade (HG) Neuroendocrine Tumors (NETs) to ^{177}Lu-DOTATATE

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BACKGROUND: ^{177}Lu-DOTATATE is an approved therapy for SSTR-positive gastroenteropancreatic NETs. Little data are available on response and outcomes for WD HG NETs treated with ^{177}Lu-DOTATATE.

METHODS: Patients with progressive WD HG NETs treated with ^{177}Lu-DOTATATE at MSK from 2018-2020 were identified. Demographics, treatment response, PFS (estimated using Kaplan-Meier methods) were determined. Next-generation sequencing (NGS) was performed in tumor samples through an institutional platform (MSK-IMPACT).

RESULTS: 19 patients were identified (mean age 54, 63% female, 14/19 (74%) pancreatic NET). Median Ki-67 32% (range 22-56). All tumors were SSTR-avid on pre-treatment Ga68-DOTATATE. Median number of prior systemic/liver-directed treatments 4 (range 2-7). Thirteen patients (68%) completed all four treatment cycles; treatment incomplete in 6 patients (treatment-related toxicities (N=3), clinical progression (N=3)). Best response by radiographic report (17 evaluable pts): 12/17 (71%) partial response, 5/17 (29%) disease progression. Three patients with response received additional cycles of ^{177}Lu-DOTATATE at progression. Median PFS (from date of first ^{177}Lu-DOTATATE treatment until progression/death) was 11.8 months (95% CI 10.6 to 18.6). Five patients (26%) experienced dose modifying toxicity. Most common treatment-related toxicities were thrombocytopenia (9 patients, 47%; G3/4 in 1 patient, 5%), anemia (7 patients, 37%; G3/4 in 2 patients, 11%), leukopenia (6 patients, 32%; G3/4 in 0 patients), AST/ALT elevation (4 patients, 21%; G3/4 in 0 patients). NGS results were available

in the tumor of 13 patients (68%). Most observed alterations were in MEN1 (6/13, 46%), DAXX (4/13, 31%). No RB1 alterations identified.

CONCLUSION: We observed a meaningful disease response of 71% during WD HG NET treatment with ^{177}Lu-DOTATATE. In this heavily pre-treated population, more than half of patients received all four treatment cycles. Treatment-related toxicities were largely bone-marrow related. As would be expected in SSTR-avid tumors, most had alterations in chromatin remodeling genes (MEN1, DAXX) consistent with WDNETs, with no RB1 alterations identified.

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