

Treatment Response and Outcomes of Metastatic Grade 3 (G3) Pancreatic Neuroendocrine Carcinomas (HGNEC) Based on Pathologic Differentiation (Well Differentiated (WDNEC) versus Poorly Differentiated (PDNEC))

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Background: WHO criteria define HGNEC as tumors with Ki-67 index >20%. However, it is unknown if treatment response/outcomes vary based on cellular differentiation (WDNEC versus PDNEC). We conducted a retrospective review of pancreatic HGNEC treated at MSKCC to evaluate response to therapy, progression free survival (PFS), and overall survival (OS).

Methods: G3 pancreatic WDNEC or PDNEC patients treated from 2000-2014 were identified. Demographics, response to 3 lines of systemic therapy (by RECIST criteria based on radiology reports), PFS, and OS were determined.

Results: 45 patients were identified, 16 WDNEC (mean age 46.8, 43.8% male) and 29 PDNEC (mean age 58.2, 65.5% male). Median OS was 52.0 months in WDNEC versus 10.1 months in PDNEC ($p = 0.0009$). 10/16 (62.5%) WDNEC received platinum agents, 1/10 (10.0%) with partial response (PR), 5/10 (50.0%) with stable disease (SD), and 4/10 (40.0%) with progressive disease (PD). 27/29 (93.1%) PDNEC received platinum agents, 1/27 (3.7%) with complete response, 9/27 (33.3%) with PR, 10/27 (37.0%) with SD, and 7/27 (25.9%) with PD. Median PFS was 4.4 months for WDNEC versus 3.3 months for PDNEC ($p = 0.16$). 12/16 (75.0%) WDNEC received alkylating agents, 6/12 (50.0%) with PR, 3/12

(25.0%) with SD, 3/12 (25.0%) with PD. 6/29 (20.7%) PDNEC received alkylating agents, 3/6 (50.0%) with PR, 1/6 (16.7%) with SD, 2/6 (33.3%) with PD. Median PFS was 5.6 months for WDNEC versus 4.2 months for PDNEC ($p = 0.27$). 6/16 (37.5%) WDNEC received targeted agents, 1/6 (16.7%) with SD and 5/6 (83.3%) with PD. 1/29 (3.4%) PDNEC received a targeted agent; this patient had a PR.

Conclusion: In this series, WDNEC had significantly improved OS compared to PDNEC. Both WDNEC and PDNEC responded to alkylating agents; PDNEC had a higher response to platinum agents. Targeted agents were rarely used with signal of activity noted in few patients.