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Outcomes with 5-Fluorouracil, Doxorubicin and Streptozocin (FAS) and Subsequent Therapies in Patients with Well Differentiated Pancreatic Neuroendocrine Tumors (PanNETs)

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BACKGROUND: Targeted agents for PanNETs improve progression free survival (PFS) with little tumor regression. Recent data suggest response rates (RR) of 33% to temozolomide (tem) regimens. We aimed to evaluate outcomes of PanNET patients (pts) on FAS and its impact on subsequent everolimus or tem-based therapies.

METHODS: Pts with advanced PanNET with measurable disease diagnosed from 1992 to 2013 were included in this single center, retrospective study. Bolus 5-FU 400 mg/m2, streptozocin 400 mg/m2 (both IV days 1-5), and doxorubicin 40 mg/m2 IV (day 1) were repeated every 28 days. RR was assessed using Response Evaluation Criteria in Solid Tumors version 1.1.

RESULTS: Of 243 eligible pts, 220 were evaluable for RR and PFS with median (m) age 56. The majority (92%) had metastatic, non-functional PanNETs and 26% received prior systemic therapy (somatostatin analogues in 65%). RR to FAS was 41% [95% confidence interval (CI), 36-48%]. After a median follow up of 61 months, mPFS was 20 [95% CI, 15-23] months, median time on therapy was 5.5 months and median overall survival was 63 [95% CI, 60-71] months. The main grade ≥ 3 toxicities were hematologic (10%) and gastrointestinal (5.5%). Dose reductions were required in 32% of pts, 3.4% due to cardiac toxicity. The mPFS on everolimus (n = 108; 68% second line) was 10 [8.0-14] months. Tem-based

regimens used as salvage (n = 54, 51% 4th line or beyond) resulted in a PR of 13% with mPFS of 5.2 [4.0-12] months.

CONCLUSION: In the largest cohort of PanNETs treated with chemotherapy reported, FAS demonstrated activity without significant safety concerns. FAS therapy did not appear to affect subsequent PFS with everolimus and this sequence is being evaluated prospectively in the SEQTOR study. Responses were noted with subsequent tem-based regimens although PFS was possibly limited by the line of therapy.