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Association of Progression-Free Survival with Overall Survival in Patients with Neuroendocrine Tumor Treated with Somatostatin Analogs

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Background: Progression-free survival (PFS) is commonly used as a primary endpoint in NET clinical trials. Whether PFS is associated with OS is uncertain. We assessed the association between PFS and OS in a large observational cohort of patients with NETs treated with somatostatin analogs (SSA).

Methods: We identified 440 patients at our institution who had received single-agent SSA for metastatic NETs and were evaluable for tumor progression and overall survival. We used a landmark analysis to assess OS in patients with progressive disease (PD) or without PD at 6 month intervals, from 6 to 24 months after treatment initiation. Adjusted hazard ratios were assessed with Cox proportional hazards models. Kaplan-Meier estimates were used to calculate median OS for patients with PD vs. those without PD at each landmark time. PFS was defined as time of treatment initiation to time of first progression, death or censoring. OS was measured from landmark time to time of death, or censoring.

Results: Of the 440 pts, 224 had small bowel NETs, 93 had pancreatic NETs and 123 other NETs. 311 patients progressed and 215 died. Median follow-up was 7.1 yrs. PFS was associated with OS at the 6, 12, 18 month landmarks (see table): those who progressed by each landmark time had shorter median OS times than those who did not progress.

Conclusions: In this observational cohort of patients with metastatic NETs treated with SSA, PFS was associated with OS. Our findings support the use of PFS as an endpoint in NET clinical trials.

PFS and OS in NET Pts Treated with SSA (N=440)

Landmark time	No PD (N)	No PD (Median OS)	PD (N)	PD (Median OS)	Adjusted HR[a] (95%CI)
6 mo	338	7.6 yrs	96	3.5 yrs	1.77 (1.28, 2.45), p=0.0006
12 mo	272	7.2 yrs	146	3.8 yrs	1.60 (1.16, 2.20), p=0.0036
18 mo	222	7.1 yrs	179	3.7 yrs	1.82 (1.28, 2.58), p=0.0009
24 mo	186	6.8 yrs	180	4.1 yrs	1.46 (0.99, 2.14), p=0.06

a. Adjusted for age, gender, elevated CgA, tumor grade and tumor origin and post-progression treatment