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Phase II Trial of Cabozantinib in Patients with Carcinoid and Pancreatic Neuroendocrine Tumors

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BACKGROUND: Activation of VEGFR2 and MET is implicated in driving growth of neuroendocrine tumors (NET). Cabozantinib inhibits VEGFR2, MET, AXL, and RET. We performed a two-cohort phase II study to evaluate the efficacy of cabozantinib in patients with advanced carcinoid or pancreatic NET (pNET) (NCT01466036).

METHODS: Patients (pts) with progressive, well-differentiated carcinoid or pNET were treated with cabozantinib 60 mg daily. Pts were restaged after every 2 cycles for the first 6 cycles, then every 3 cycles. The primary endpoint was response rate (RECIST 1.1).

RESULTS: 41 pts with carcinoid (median age 63 yrs, 44% male, %ECOG PS 0/1=51/49) and 20 pts with pNET (median age 55 yrs, 60% male, %ECOG PS 0/1=40/60) were accrued. Carcinoid pts completed a median of 8 (range 0-44) 28-day treatment cycles; pNET pts completed a median of 10 (0-35) cycles. 3/20 (15%) pts with pNET achieved PR (95% CI, 5-36%); 15/20 had SD. 6/41 (15%) pts with carcinoid achieved PR (95% CI, 7-28%); 26/41 had SD. Median PFS was 21.8 mo (95% CI, 8.5-32.0 mo) in pts with pNET and 31.4 mo (95% CI, 8.5 mo-NR) in pts with carcinoid. 14 pts remained on treatment at time of data analysis. Reasons

for discontinuation among those who stopped therapy were progression/death (51%), withdrawal of consent/investigator decision (28%), adverse events (21%). Gr 3/4 toxicity included hypertension (13%), hypophosphatemia (11%), diarrhea (10%), lymphopenia (7%), thrombocytopenia (5%), fatigue (5%), increased lipase/amylase (7%). 81% (43/53) of pts completing ≥ 1 cycle required dose reduction from the initial 60 mg dose.

CONCLUSION: Treatment with cabozantinib was associated with objective tumor responses and encouraging PFS durations in patients with advanced carcinoid and pNET. While dose reduction was common, treatment was tolerable. A randomized phase III trial to confirm activity of cabozantinib in carcinoid and pNET is being developed through the Alliance for Clinical Trials in Oncology.