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## Efficacy and Safety of Cabozantinib in Advanced Neuroendocrine Tumors By Hormone Functional Status: Subgroup Analysis of Phase 3 CABINET Trial

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### BACKGROUND

In the CABINET trial (Alliance A021602), cabozantinib (CABO) significantly prolonged progression-free survival (PFS) compared to placebo (PB) in patients (pts) with advanced, previously treated extrapancreatic NET (epNET) or pancreatic NET (pNET) (Chan et al., NEJM, 2025). Here we report outcomes according to functional status based on hormone secretion.

### METHODS

Pts with progressive, locally advanced or metastatic epNET or pNET were randomized 2:1 in separate cohorts to receive CABO 60 mg daily vs PB. Pts with functional NET due to hormone secretion and non-functional NET were included. In this post hoc analysis, we analyzed PFS by blinded independent central review and adverse events (AEs) for pts receiving CABO vs PB according to functional status. Cox regression models were used with stratification on primary tumor site (epNET vs pNET). Subset analyses were conducted in pts with functional and non-functional tumors. Due to small numbers, results for those with unknown functional status are not included.

## RESULTS

Among 298 pts enrolled in both cohorts, 74 had functional NET (CABO, n=47; PB, n=27); 179 had non-functional NET (CABO, n=123; PB, n= 56); 45 had unknown functional status (CABO, n=28; PB, n=17). For functional NET, primary tumor sites were GI tract (n=50; 68%), pancreas (n=15; 20%), unknown (n=4; 5%), lung (n=3; 4%), thymus (n=2; 3%). Secreted hormones that were reported included serotonin (55%), somatostatin (18%), gastrin (16%), glucagon (4%), insulin (4%), ACTH (1%), VIP (1%). For non-functional NET, primary tumor sites were pancreas (n=75; 42%), GI tract (n=42; 23%), lung (n=30; 17%), unknown (n=17; 9%), thymus (n=8; 4%), other (n=7; 4%). Concurrent SSA was received by 91% and 53% of pts with functional and non-functional NET, respectively. In both subgroups, CABO was associated with improved PFS compared to PB (functional NET: stratified hazard ratio [sHR], 0.40; 95% confidence interval [CI]: 0.20-0.82, P= 0.012; non-functional NET: sHR, 0.26; 95% CI: 0.17-0.41, P<0.001). The most frequent grade 3/4 AEs attributed to CABO vs PB in pts with functional NET included hypertension (21% vs 11%), diarrhea (9% vs 11%), and fatigue (2% vs 15%); in pts with non-functional NET, grade 3/4 AEs included hypertension (21% vs 4%) and fatigue (18% vs 4%).

## CONCLUSIONS

Subset analyses of the CABINET trial suggest that CABO is effective in pts with functional or non-functional epNET or pNET. Efficacy and safety results for pts with functional or non-functional NET treated with CABO are consistent with results for the entire trial.

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