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Clinical Outcomes and Toxicity Profile of Cabozantinib in Advanced Neuroendocrine Tumors: A Multi-Center Real World Analysis

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BACKGROUND

Cabozantinib is a multi-kinase inhibitor that has recently emerged as a standard treatment option for progressive neuroendocrine tumors (NETs) following the phase III CABINET trial. However, real-world outcomes across heterogeneous patient populations remain limited.

METHODS

We conducted a retrospective multi-institutional cohort study using IRB-approved institutional NET registries. Eligible patients had advanced NETs treated with cabozantinib in routine clinical practice between 2018 and 2026. Endpoints included objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and time-to-treatment discontinuation (TTD). Survival outcomes were estimated using the Kaplan-Meier method and compared using log-rank testing. ORR comparisons were performed using Fisher's exact test. Adverse events were graded according to CTCAE criteria.

RESULTS

Fifty-two patients were included; 27 (51.9%) were male and most had preserved performance status (ECOG 0–1; 43/49, 87.8%). Most had heavily pretreated disease, with ≥3 prior systemic therapy lines in 36/52 (69.2%). Among 48 patients with available histologic grade, most had grade 2 disease (58.3%), followed by grade 3 (22.9%) and grade 1 (18.8%). Starting doses were 40 mg in 70.0%, 60 mg in 24.0%, and 20 mg in 6.0%. Among 37 evaluable patients, ORR was 13.5% and DCR was 73.0%, including partial response in 13.5% and stable disease in 59.5%. Median PFS was 9.1 months (95% CI, 6.9–11.3), median OS was 14.5 months (95% CI, 10.4–23.3), and median TTD was 8.4 months (95% CI, 5.0–15.8). Exploratory subgroup analyses showed no statistically significant differences in ORR or

PFS by primary site, grade, age, or sex. ORR was numerically higher in pancreatic versus extra-pancreatic NETs (25.0% vs 5.9%, p=0.17) and in grade 3 versus grade 1/2 tumors (30.0% vs 8.0%, p=0.13). Treatment-related AEs were predominantly grade 1–2 (44/52, 84.6%). The most common AEs were fatigue (26.9%), palmar-plantar erythrodysesthesia (26.9%), diarrhea (11.5%), nausea/vomiting (11.5%), and thromboembolic events (11.5%). Grade ≥3 AEs occurred in 8/52 (15.4%), most commonly thromboembolic events (5.8%), hypertension (3.8%), and thrombocytopenia (3.8%).

CONCLUSIONS

In this multi-institutional real-world analysis, cabozantinib demonstrated clinically meaningful antitumor activity in a heavily pretreated NET population. Clinical benefit was observed across tumor grades, primary sites, age groups, and sexes, supporting the broad applicability of cabozantinib in routine practice. Toxicities were largely low grade, likely reflecting frequent use of reduced starting doses, and outcomes remained favorable despite this approach. These findings support cabozantinib as an effective later-line therapy and warrant prospective evaluation of dose-optimized strategies to improve tolerability without compromising efficacy.

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