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Reduced-Dose Pazopanib as First-Line Therapy in Metastatic Renal Cell Carcinoma: Real-World Evidence from an Immunotherapy-Inaccessible Cohort

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Background: Immune checkpoint inhibitor (ICI)-based combinations are the current standard first-line treatment for metastatic renal cell carcinoma (mRCC). However, tyrosine kinase inhibitors (TKIs) continue to be widely used in many low- and middle-income countries (LMICs) due to financial barriers limiting access immunotherapy. Dose optimization of TKIs is frequently practiced in real-world settings to mitigate toxicity and improve treatment adherence. Data on outcomes with reduced-dose pazopanib and subsequent treatment patterns remain limited.

Objectives: To evaluate the effectiveness and safety of reduced-dose pazopanib (400 mg daily) as first-line systemic therapy in anti-VEGF TKI-naïve patients with mRCC who were unable to access immunotherapy because of financial constraints.

Methods: This retrospective study included patients aged ≥18 years with histologically confirmed RCC who received pazopanib 400 mg daily as first-line systemic therapy between January 2016 and December 2023. Clinical characteristics, response rates, toxicities were extracted from hospital records. Survival outcomes were estimated using the Kaplan–Meier method.

Results: Eighty-four patients received reduced-dose pazopanib during the study period. Median age was 57.5 years (range, 19–76). Most patients were male (79%) and had clear-cell histology (79.7%). De novo metastatic disease was present in 66%.Nearly half (45.1%) had an Eastern Cooperative Oncology Group (ECOG) performance status ≥2. Nephrectomy was performed in 52 patients (61.9%), including radical nephrectomy in 29 (58%) and cytoreductive nephrectomy in 23 (42%). Clinical benefit at first response assessment was observed in 69 patients (82.1%). At a median follow-up of 41.3 months, median progression-free survival was 8.9 months (95% CI, 6.7–11.0) and median overall survival was 28.6 months (95% CI, 19.0–38.1). The most common adverse events were skin/hair

depigmentation (35.7%), diarrhea (25%), hand–foot syndrome (21.4%), and hypertension (14.3%). Grade 3–4 adverse events occurred in five patients (5.9%), and treatment discontinuation due to toxicity occurred in two patients (2.4%). No treatment-related deaths were reported.

Conclusions: In an LMIC setting where access to immunotherapy remains limited, reduced-dose pazopanib represents a feasible and pragmatic first-line treatment option for mRCC, including those with borderline performance status. It demonstrated clinically meaningful response rates and survival outcomes with a favourable toxicity profile.