REAL-WORLD DATA ON THE EFFICACY AND SAFETY OF PAZOPANIB AS FIRST-LINE TREATMENT FOR ADVANCED RENAL CELL CARCINOMA AT VIETNAM NATIONAL CANCER HOSPITAL

Nguyen Thi Huong Giang[1*], Hoang Ngoc Giap[1]
Nguyen Thu Phuong[1,2], Can Thi Anh Hong[1]

ABSTRACT

Background: Pazopanib is an effective first-line treatment for advanced renal cell carcinoma (RCC), but its efficacy and safety in the Vietnamese population are not well-documented. This study evaluates the outcomes and adverse effects of pazopanib at Vietnam National Cancer Hospital, with a focus on the impact of initial dosing.

Methods: A retrospective and prospective study of 60 patients with advanced RCC treated with pazopanib between January 2018 and July 2024. The initial doses were 200 mg, 400 mg, 600 mg or 800 mg. Primary endpoints were overall response rate (ORR) and disease control rate (DCR), with secondary endpoints including progression-free survival (PFS), overall survival (OS), and adverse events.

Results: The ORR was 45%, with 3.3% achieving complete response and 41.7% partial response. Median PFS was 13.1 months, and median OS was 21.5 months. The initial dose of pazopanib did not significantly affect OS (25.5 months for 800 mg vs. 20.5 months for lower doses, p=0.945). Common adverse effects included elevated liver enzymes and fatigue.

Conclusions: Pazopanib is effective and well-tolerated in the Vietnamese population, with no significant impact of initial dosing on overall survival. Dose adjustments based on tolerability may be beneficial. Further research with larger samples and longer follow-up is needed to confirm these findings.

Keywords: Renal cell carcinoma; pazopanib; advanced stage.

1. INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignancy originating from the kidneys, accounting for approximately 85% of all kidney cancers. It is a significant global health burden, with incidence rising partly due to improvements in imaging technologies. In Vietnam, RCC accounts for an estimated 2,246 new cases and 1,112 deaths annually[1]. Early-stage RCC is typically treated with surgery; however, 20-30% of patients will experience recurrence or metastasis[2].

While international guidelines now recommend first-line combination therapies, such as immune-oncology (IO) agents with tyrosine kinase inhibitors (TKIs) or dual IO combinations for advanced RCC[3], the high cost of these regimens makes them inaccessible to many patients in Vietnam. As a result, pazopanib, a TKI, remains the most widely used and affordable option in routine clinical practice. Although its efficacy has been established in clinical trials, real-world data in Vietnamese

[1]Vietnam National Cancer Hospital;
[2]Hanoi Medical University.
*Corresponding Author: bsgiang9bvk@gmail.com

Date received: 04/9/2024
Date reviewed: 11/9/2024
Date accepted for publication: 10/4/2025

patients are limited. This study aims to evaluate the effectiveness and safety of pazopanib in advanced RCC in Vietnam, with particular attention to the impact of initial dosing.

2. SUBJECTS AND METHODS

2.1. Subjects

This retrospective and prospective observational study was conducted at Vietnam National Cancer Hospital from January 2018 to July 2024. Sixty patients with histologically confirmed advanced RCC receiving pazopanib as first-line systemic therapy were included.

2.2. Inclusion Criteria

- Patients aged 18 years or older with histologically confirmed RCC.

- Locally advanced disease that is not amenable to surgery OR recurrent or metastatic disease.

- ECOG performance status 0-2.

- Receipt of at least two cycles of pazopanib.

2.3. Exclusion Criteria

- Patients with prior systemic therapy for RCC.

- Uncontrolled comorbidities or significant medical conditions that could interfere with treatment.

2.4. Methods

This is retrospective and prospective observational study. Clinical data were collected from medical records and patient interviews, including demographic characteristics, pathological subtype, initial pazopanib dose, and treatment response. The initial pazopanib dose was determined by the treating physician based on patient performance status and comorbidities, with options including 200mg, 400mg, 600mg, or 800mg daily. Efficacy was assessed via overall response rate (ORR), disease control rate (DCR), progression-free survival (PFS) and overall survival (OS). Tumor response was evaluated using RECIST 1.1. Adverse events were recorded and graded using CTCAE v5.0.

2.5. Data Analysis

Survival data were analyzed using Kaplan-Meier methods and comparisons were made using the log-rank test.

3. RESULTS

The cohort had a median age of 57.2 ± 11.9 years, with 80% male patients. The most common comorbidities were hypertension (21.7%) and diabetes mellitus (16.7%). Of the 60 patients, 55% were diagnosed with advanced RCC, while 45% had recurrent disease. Clear cell RCC (ccRCC) was the predominant histological subtype, accounting for 85% of cases.

Table 1: Patient characteristic

Patient	N = 60 (100%)
Age	
Average	57.2 ± 11.9 (Years)
Gender	
Male	48 (80%)
Female	12 (20%)
Performance status	
PS 0	40 (66.7%)
PS 1	11 (18.3%)

PS 2	9 (15%)
Denovo/Recurrence	
De novo metastatic	33 (55%)
Recurrence	27 (45%)
Histopathology	
Clear cell carcinoma	51 (85%)
Non-clear cell carcinoma	9 (15%)
IMDC risk group	
Low risk	3 (5%)
Intermediate risk	27 (45%)
High risk	9 (15%)
Indeterminate	21 (35%)
Initial dose of Pazopanib	
200 mg	5 (8.3%)
400 mg	26 43.3%)
600 mg	17 (28.3%)
800 mg	12 (20%)

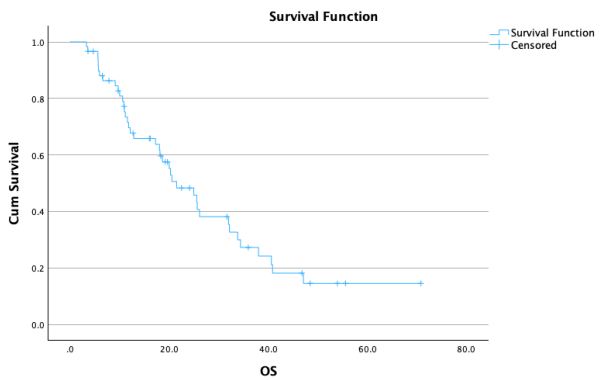

Figure 1: Overall survival

Pazopanib was administered as first-line treatment at an initial dose of 400 mg in 43.3% of patients, with the remainder receiving lower or higher doses based on tolerability. The median treatment duration was 46.8 months. The ORR was 45%, with 3.3% of patients achieving a complete response and 41.7% achieving a partial response. Disease stabilization was observed in 40% of patients, while 15% experienced disease progression during the initial assessment.

After a median follow-up time of 46.8 months, the median PFS was 13.1 months (95% CI: 10.6-15.5), and the median OS was 21.5 months (95% CI: 15.0-28.0). The estimated one-year and two-year OS rates were 67.8% and 48.3%, respectively.

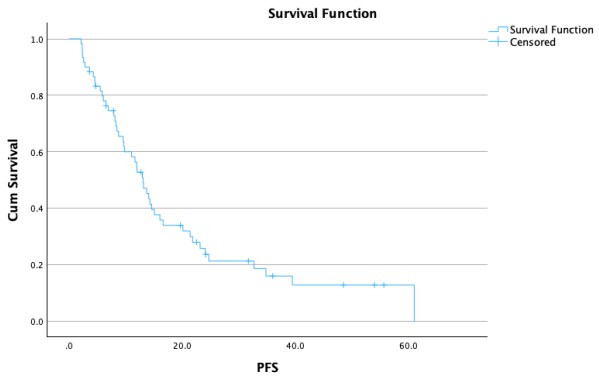

Figure 2: Progression free survival

The analysis of the initial dose of pazopanib indicated that the dose had no significant impact on overall survival. Patients on higher initial doses (800 mg) showed similar survival outcomes as those

on lower doses. The median OS for patients on the 800 mg dose was 25.5 months, while those on lower doses had a median OS of 20.5 months (p=0.945).

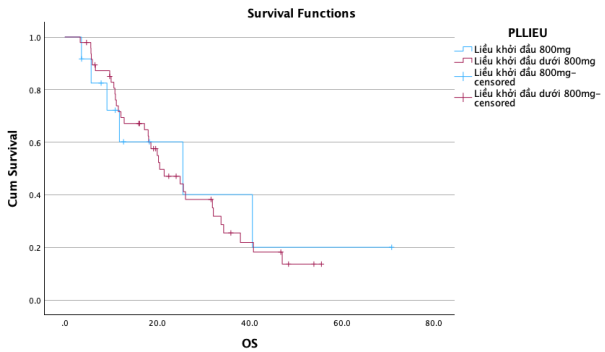

Figure 3: OS according to initial dose of Pazopanib

Regarding adverse effects, 71.7% of patients experienced some form of toxicity, with the most common being increased liver enzymes (43.3%) and fatigue (38.3%). Severe adverse events (CTCAE grade 3-4) occurred in 10% of patients, with the most notable being elevated liver enzymes and hypertension. No patient discontinued treatment due to adverse effects.

Table 2: Adverse events

Adverse event	All grade N (%)	Grade 3-4 N (%)
Fatigue	23 (38.3%)	0
Nausea/vomiting	7 (11.7%)	0
Diarrhea	6 (10%)	0
Hypertension	11 (18.3%)	2 (3.3%)
Rash	3 (5%)	0
Hair color change	12 (20%)	0
Anemia	10 (16.7%)	1 (1.7%)
Neutropenia	6 (10%)	2 (3.3%)
Thrombocytopenia	7 (11.7%)	0
Elevated liver enzyme	26 (43.3%)	3 (5%)
Elevated bilirubin	3 (5%)	0
Elevated creatinine	15 (25%)	0
All	**43 (71.7%)**	**6 (10%)**

4. DISCUSSION

The findings of this study confirm that pazopanib is an effective and tolerable first-line treatment option for advanced RCC in Vietnamese patients, aligning well with global clinical trial data. Notably, the overall response rate of 45% observed in this cohort exceeds that reported in the pivotal COMPARZ (31%) and PISCES (32%) trials, suggesting encouraging tumor control even in a real-world setting[4,5]particularly between approved targeted therapies with similar efficacy. This double-blind cross-over study evaluated patient preference

for pazopanib or sunitinib and the influence of health-related quality of life (HRQoL. The median progression-free survival of 13.1 months also compares favorably with the 8.4–9.2 months reported in those studies, indicating sustained disease control. Although the median overall survival of 21.5 months is slightly lower than the COMPARZ trial's 28.4 months, it remains clinically meaningful, particularly in the context of limited access to subsequent lines of therapy in Vietnam[4]. By contrast, modern IO+TKI regimens, such as pembrolizumab plus axitinib, have demonstrated ORR around 60% and median OS exceeding 45 months[6], while IO+IO combinations like nivolumab plus ipilimumab report ORR around 42% and median OS of 47 months[7], highlighting the efficacy gap where access to these regimens is limited.

Pazopanib was well-tolerated overall, though adverse effects were prevalent, particularly liver enzyme elevation and hypertension, which are commonly associated with VEGF inhibitors. The overall AE rate (71.7%) and grade 3-4 event rate (10%) were comparable to the COMPARZ trial, where any-grade AEs were reported in over 80% of patients and grade 3-4 events in approximately 33%[4]. Notably, no patients discontinued treatment due to toxicity in this study, suggesting manageable side effects with appropriate dose modification and monitoring.

Importantly, the initial dose of pazopanib did not have a significant impact on overall survival. This suggests that dose adjustments based on tolerability may be appropriate without compromising efficacy. Patients receiving 800mg as the initial dose had a comparable median OS to those on lower doses, which supports the flexibility in dosing to reduce side effects while maintaining treatment effectiveness.

5. CONCLUSION

Pazopanib is an effective and generally well-tolerated option for the first-line treatment of advanced RCC in the Vietnamese population. This study contributes valuable data to the body of evidence regarding pazopanib's role in RCC treatment within a resource-limited setting. The initial dose of pazopanib did not significantly affect overall survival, suggesting that dose adjustments based on tolerability may be appropriate without compromising efficacy. Further studies, particularly with larger sample sizes and longer follow-up, are needed to confirm these findings and explore potential improvements in patient management strategies. Given the promising results, pazopanib remains a cornerstone in the treatment of advanced RCC, though individual treatment plans should consider patient-specific factors, including comorbidities and treatment tolerability.

REFERENCES

[1]. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today, accessed.

[2]. Gupta K, Miller JD, Li JZ, Russell MW, Charbonneau C. Epidemiologic and socioeconomic burden of metastatic renal cell carcinoma (mRCC): A literature review. *Cancer Treat Rev*. 2008;34(3):193-205. doi:10.1016/j.ctrv.2007.12.001

[3]. NCCN guidelines, Kidney cancer, version 2.2024. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.

[4]. Motzer RJ, Hutson TE, Cella D, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med*. 2013;369(8):722-731. doi:10.1056/NEJMoa1303989

[5]. Escudier B, Porta C, Bono P, et al. Randomized, controlled, double-blind, cross-over trial assessing treatment preference for pazopanib versus sunitinib in patients with metastatic renal cell carcinoma: PISCES Study. *J Clin Oncol Off J Am Soc Clin Oncol*. 2014;32(14):1412-1418. doi:10.1200/JCO.2013.50.8267

[6]. Rini BI, Plimack ER, Stus V, et al. Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2019;380(12):1116-1127.doi:10.1056/NEJMoa1816714

[7]. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus Ipilimumab versus Sunitinib in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2018;378(14):1277-1290. doi:10.1056/NEJMoa1712126