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

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Introduction

- Immune checkpoint inhibitor–based combinations are the current standard first-line treatment for **metastatic renal cell carcinoma (mRCC).**

First Barrier : Immunotherapy Cost
Second Barrier: Intolerance to full dose TKI

1 LIMITED AFFORDABILITY AND ACCESS

- TKIs remain the predominant first-line therapy in many low- and middle-income countries.
- Limited affordability and access to immunotherapy.

2 POOR TOLERANCE TO FULL DOSE

- Standard dose: 800 mg daily
- Issues:
  - Toxicities
  - Dose reductions
  - Treatment discontinuation

INDIAN KIDNEY CANCER REGISTRY

- **One fourth** of mRCC patients treated with first-line TKI required dose reduction from standard dosing during the treatment course.

APOLON STUDY COHORT

- One third had pazopanib discontinuation related to adverse event.
- Nearly half (47%) required dose reduction during course of treatment.

RATIONALE FOR STUDY :Using maximum tolerable dose of TKI concept is being replaced by biologic effective dose . Dose reduction of TKI is frequently practised in real world to improve tolerance and adherance. But effectiveness of reduced dose pazopanib approach is not well documented

Methodology

Retrospective observational study

INCLUSION CRITERIA

- Patients diagnosed with renal cell carcinoma who received first line systemic therapy with reduced dose (400 mg) pazopanib between January 2016 to December 2023.

EXCLUSION CRITERIA

- Incomplete records regarding pazopanib dosing details.
- Patients who received prior tyrosine kinase inhibitors or immunotherapy in the adjuvant setting.

PRIMARY OBJECTIVE

- To assess response rates, toxicities, survival outcomes of reduced dose pazopanib as first line systemic therapy.

SECONDARY OBJECTIVES

- To document patterns of subsequent treatment lines received by this patient cohort.

Results : Clinical Profile

Characteristics (N=84)	Patient numbers(%)
Median age	57.5yrs (19–76 yrs)
Gender	
Male	66(78.5)
Female	18(21.4)
ECOG status	
0	2(2.4)
1	44(52.4)
2	27(32.1)
3	11(13.1)
Histological subtype	
Clear cell	67(79.7)
Unclassified	17(20.2)

Characteristics	Patient numbers(%)
Stage at time of diagnosis	
I	3(3.8)
II	9(10.7)
III	17(20.2)
IV	55 (65.5)
IMDC Risk status	
Favourable	21(25.0)
Intermediate	44(52.4)
Poor	11(13.1)
Not available	8(9.5)

Results : Outcomes

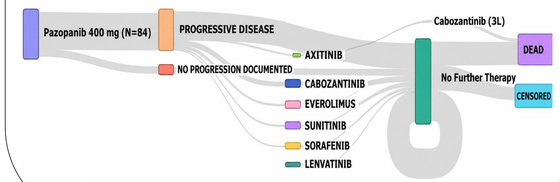
Response rates at first evaluation	Patient no. (%)
Complete Response (CR)	1(1.2)
Partial Response (PR)	23(27.4)
Stable disease (SD)	45(53.5)
Progressive disease(PD)	13(15.5)
Not evaluable	2(2.4)
Over all response rate(ORR)	24(28.6)
Clinical benefit rate(CBR)	69(82.1)
Clinical outcomes	
Median Progression free survival(PFS)	8.9 months
Median Overall survival(OS)	28.6 months

Results : Adverse events

Adverse events	Event number (%)
Diarrhea	
Grade 1 & 2	20(23.8)
Grade ≥3	1(1.2)
Hand-foot syndrome	
Grade 1 & 2	16(19)
Grade ≥3	2(2.4)
Transaminitis	
Grade 1 & 2	6(7.1)
Grade ≥3	1(1.2)
Hypertension (Including worsening)	
Grade 1 & 2	11(13.1)
Grade ≥3	1(1.2)
Fatigue	
Grade 1 & 2	10(11.9)
Grade ≥3	0(0)

Adverse events	Event number (%)
Hyponatremia	
Grade 1 & 2	9(10.7)
Grade ≥3	0(0)
Hypothyroidism	11(13.1)
Skin & hair depigmentation	30(35.7)
Altered taste (Grade not available)	8(9.5)
Grade ≥3 adverse events related to pazopanib	5(5.9)
Pazopanib related treatment discontinuation	2(2.4)
Dose de-escalation during treatment	11(13.09)

Post Progression Therapy



Comparison :Outcomes

Variable	Our study	Sternberg et al	Comparz study	TMH study	Apolon study	Parachute study	Principal study	SPAZO study	Pazoreal study
Number	84	290	554	28	217	190	657	278	376
Dose	RDP	SDP	SDP	SDP	SDP	SDP	SDP	SDP	SDP
ORR	28.6%	31 %	NA	22.4%	48.3%	24.4%	30.3%	30.3%	NA
CBR	82.1%	69%	NA	60.7%	83%	68.5%	NA	NA	NA
Median PFS (months)	8.9	11.1	10.5	7.9	10.6	10	10.3	11.1	NA
Median OS (months)	28.6	NA	NA	12.8	29.1	NA	29.9	22.2	35.9

RDP :Reduced dose Pazopanib,SDP: Standard dose Pazopanib, PFS: progression-free survival, OS: overall survival, ORR :Over all response rate,CBR :Clinical benefit rate,NA : Not available

References: 1. Sternberg *et al., J Clin Oncol.* 2010; 2. COMPARZ (Motzer *et al., N Engl J Med.* 2013); 3. TMH Study (Ramaswamy *et al., Clin Genitourin Cancer.* 2017); 4. APOLON (Barthelemy *et al., ESMO Real World Data Digit Oncol.* 2025); 5. PARACHUTE (Erman *et al., BMC Cancer.* 2021); 6. PRINCIPAL (Schmidinger *et al., Oncologist.* 2019); 7. SPAZO (Pérez-Valderrama *et al., Ann Oncol.* 2016); 8. PAZOREAL (Doehn *et al., Cancers (Basel).* 2022).

Variable	Our study	Comparz	Parachute study	Pazoreal
Number	84	554	190	376
Dose	RDP	SDP	SDP	SDP
Grade ≥3 adverse events	5.9%	NA	NA	7.9%
Treatment discontinuation due to toxicity	2.4%	NA	10.9%	17.6%
Dose interruption (>1 week)	20.2%	44%	40.5%	NA
Dose reduction during treatment	13.1%	44%	33.7%	NA

LIMITATIONS : Single centre Retrospective design
STRENGTHS : Captures a real world population often excluded or underrepresented in clinical trial because of poor performance status.

Conclusion

Reduced dose pazopanib (400mg) is a pragmatic tolerability focussed first line treatment option for anti-VEGF TKI naïve & immunotherapy inaccessible patients to reproduce comparable treatment outcomes with reduced adverse events