Validation of the IMDC Prognostic Model in Patients With Metastatic Renal Cell Carcinoma Treated With First-Line Tivozanib: TIVOREAL-SOGUG, A Spanish Real-World Experience

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INTRODUCTION

The **IMDC prognostic classification** was originally developed and validated in patients with metastatic renal cell carcinoma (mRCC) treated with VEGFR-TKIs. However, it was established before the availability of tivozanib and modern agents that improve overall survival (OS), such as nivolumab and cabozantinib.

Objective: TIVOREAL-SOGUG aimed to validate the IMDC classification in patients with clear-cell mRCC treated with first-line tivozanib in contemporary real-world practice.

METHODS

TIVOREAL-SOGUG is a multicentre, retrospective, real-world study of **198** adult patients with **clear-cell mRCC** receiving **first-line tivozanib** (Aug 2017 – Aug 2024) at 14 Spanish oncology centers of SOGUG.

Patients were categorized into **IMDC risk groups**: favourable (FR), intermediate (IR), and poor-risk (PR).

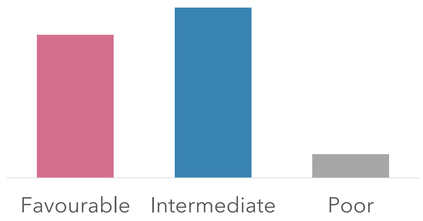
Endpoints:
- Validation of the IMDC model in terms of ORR, TTF, PFS, and OS.
- Safety, subsequent therapies were assessed descriptively.

Statistics:
- Kaplan–Meier, log-rank, Cox models
- Response per RECIST 1.1.

RESULTS

PATIENT CHARACTERISTICS

Patients by IMDC risk group



	n=198	%
FR	84	42.4
IR	100	50.5
PR	14	7.1

Median follow-up 42 months (95% CI 37.9 – 46.2)

Baseline characteristics in overall population (n= 198)

Characteristics		Overall (n= 198)	%
Sex	Male	146	73.7
	Female	52	26.3
Age	Median (range)	69.2 (40 – 89)	
	< 75 years	130	65.7
	≥ 75 years	68	34.3
ECOG	0	116	58.6
	1	52	26.3
	2	22	11.1
	3 – 4	3	1.5
	Unknown	5	2.5

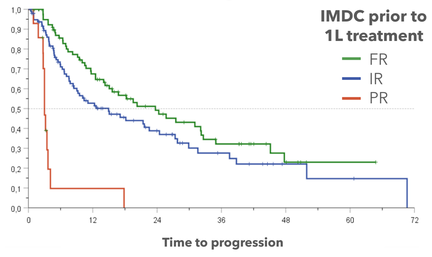
Lung was the most common metastatic site (63.1%), followed by lymph nodes (34.3%) and bone (25.3%). Most patients had multiple metastatic sites.

EFFICACY

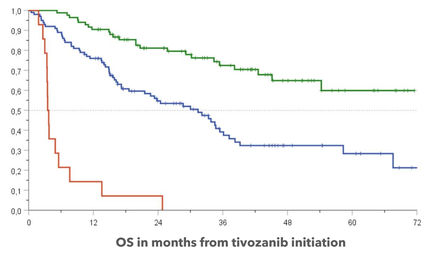
Key efficacy endpoints in the Overall population and by IMDC subgroup

Efficacy endpoints	Overall cohort (N=198)	FR (n=84)	IR (n=100)	PR (n=14)
ORR, % (CR %)	36.4 (5.1)	48.8 (7.1)	29.0 (4.0)	-
Median TFF Months (95% CI)	10.0 (7.2 – 12.8)	14.7 (9.2 – 20.1)	8.3 (5.4 – 11.3)	3.0 (2.7 – 3.3)
Median PFS Months (95% CI)	15.6 (10.5 – 20.8)	23.7 (11.8 - 28.8)	14.9 (7.3 – 22.6)	3.0 (2.6 – 3.4)
Median OS Months (95% CI)	36.1 (28.0 – 44.3)	NR	31.4 (22.0 – 40.8)	3.5 (3.1 – 3.9)
		*Log-rank Mantel Cox (**p < 0.001**)*		

PFS



OS



The IMDC model showed clear prognostic separation for TTF, PFS and OS (global p<0.001 across FR, IR and PR)

SAFETY

Tolerability of tivozanib	Overall population (N=198) (%)
Full-dose	89 (44.9)
Dose reduction	26 (13.1)
Discontinuation due to toxicity	18 (9.1)

- Adverse events were mainly grade 1–2 (fatigue, diarrhea, hypertension, mucositis, dysphonia).
- Grade ≥3 events were uncommon and primarily limited to hypertension.
- The safety profile was consistent with known tivozanib data.

SUBSEQUENT TREATMENTS

Subsequent Treatment After 1L Tivozanib		N (%)
Discontinuation of first-line tivozanib		154 (100)
Received ≥1 subsequent active therapies		100 (64.9)
Main agents used	Nivolumab	84
	Cabozantinib	44

CONCLUSIONS

1. The IMDC model retained strong prognostic discrimination across risk groups in first-line tivozanib–treated mRCC.
2. Significant differences in TTF, PFS and OS across IMDC risk groups validate the model's use in the current multi-agent treatment era.
3. Tivozanib showed meaningful activity with a favourable safety profile, with low discontinuation rates and preserved dosing in most patients.
4. Sequential use of tivozanib followed by nivolumab and/or cabozantinib provided prolonged OS, especially in IMDC favorable-risk patients.

ABBREVIATIONS: **CI**, confidence interval; **ECOG**, Eastern Cooperative Oncology Group; **FR**, favourable risk; **IMDC**, International Metastatic Renal Cell Carcinoma Database Consortium; **IR**, intermediate risk; **mRCC**, metastatic renal cell carcinoma; **NR**, not reached; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **PR**, poor risk; **SOGUG**, Spanish Genitourinary Oncology Group; **TTF**, time to treatment failure; **VEGFR-TKI**, vascular endothelial growth factor receptor tyrosine kinase inhibitor.

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