

First-Line Tivozanib in Favorable and Very Favorable Risk Metastatic Renal Cell Carcinoma: Real-World Evidence from the TIVOREAL-SOGUG Study

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BACKGROUND

The **optimal first-line (1L) treatment** for favorable-risk metastatic renal cell carcinoma (mRCC) remains debated in the immune checkpoint inhibitor (ICI) era. Real-world data on **VEGFR-TKI monotherapy** in IMDC favorable-risk subgroups are limited. This **TIVOREAL-SOGUG** subanalysis assessed outcomes with 1L tivozanib in **favorable-risk (FR)** mRCC, with a specific focus on a **very favorable-risk (VFR)** subgroup.

METHODS

TIVOREAL-SOGUG is a multicenter, 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.

Favorable-risk: IMDC criteria (0 risk factors)

Very favorable-risk: subgroup defined according to Zarba et al. by all of the following:

- Time from diagnosis to systemic therapy >3 years
- Karnofsky performance status 90-100%
- Absence of brain, liver, or bone metastases

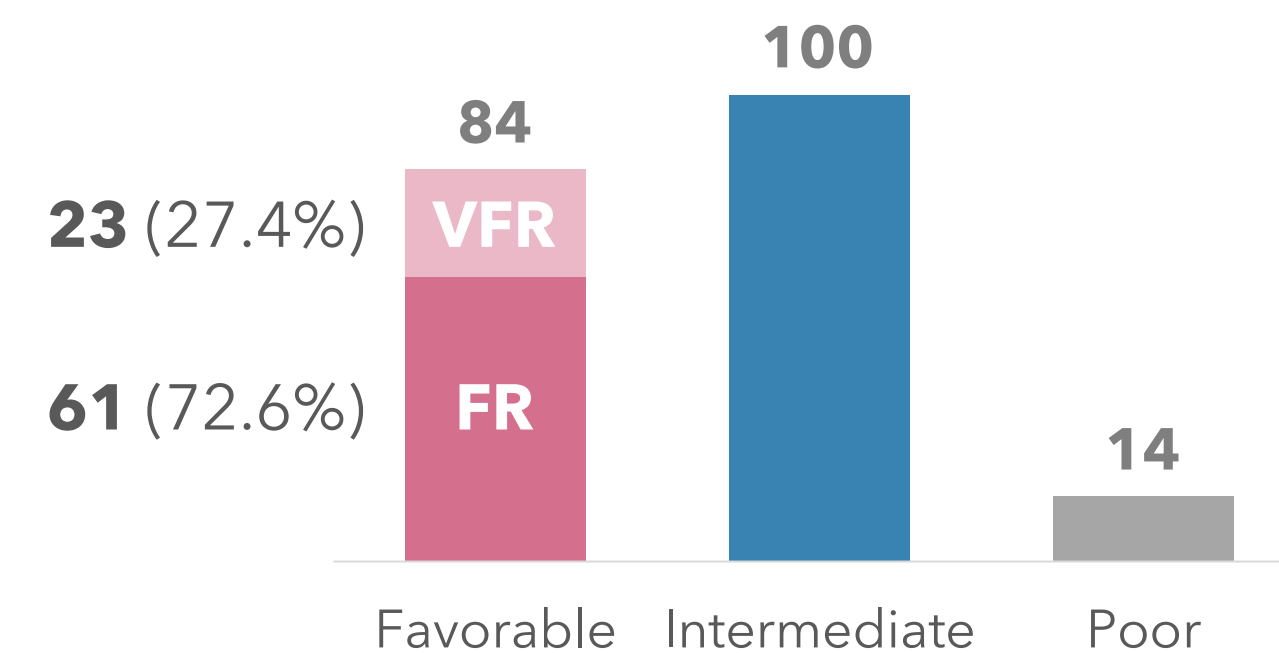
Endpoints:

- Primary: TTF
- Secondary: ORR, PFS, OS, safety, subsequent therapies

RESULTS

PATIENT CHARACTERISTICS

Patients by IMDC risk group (n = 198)

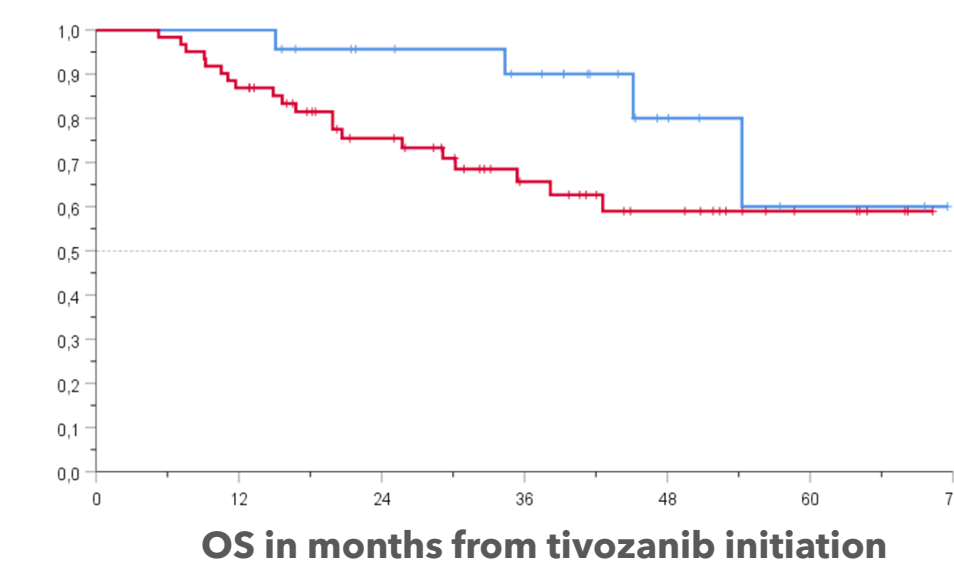
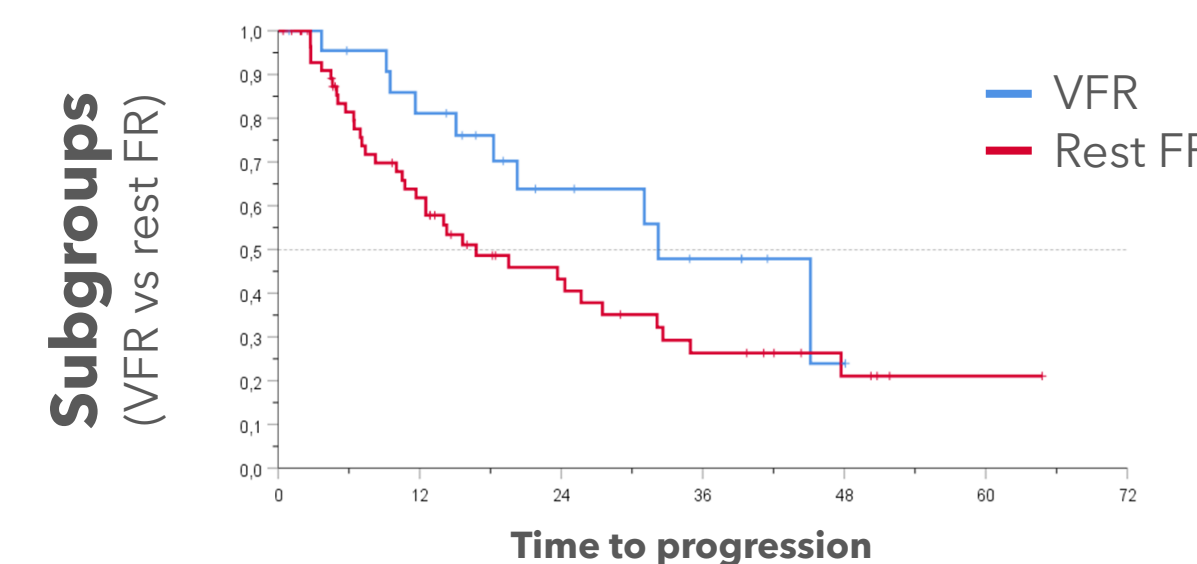
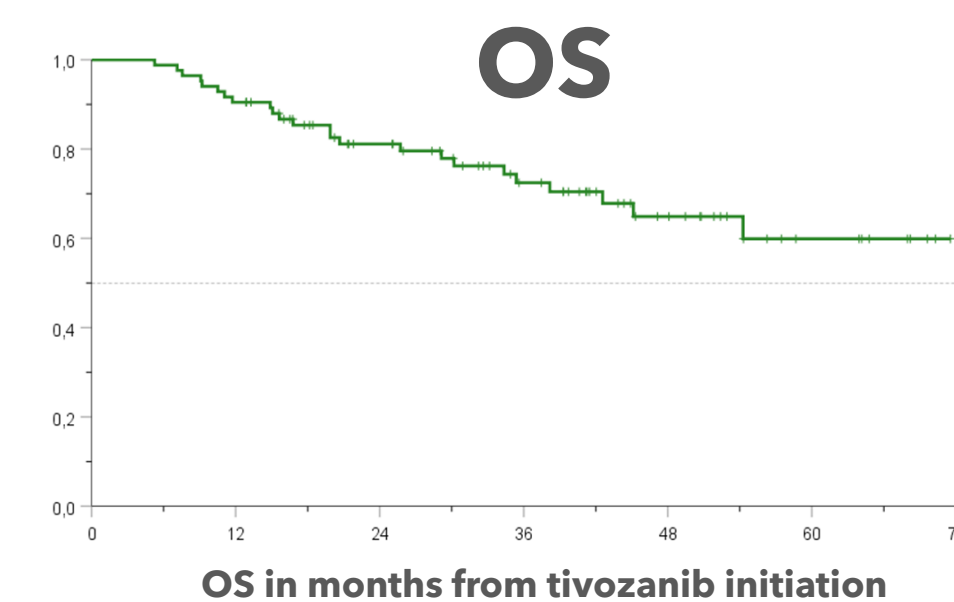
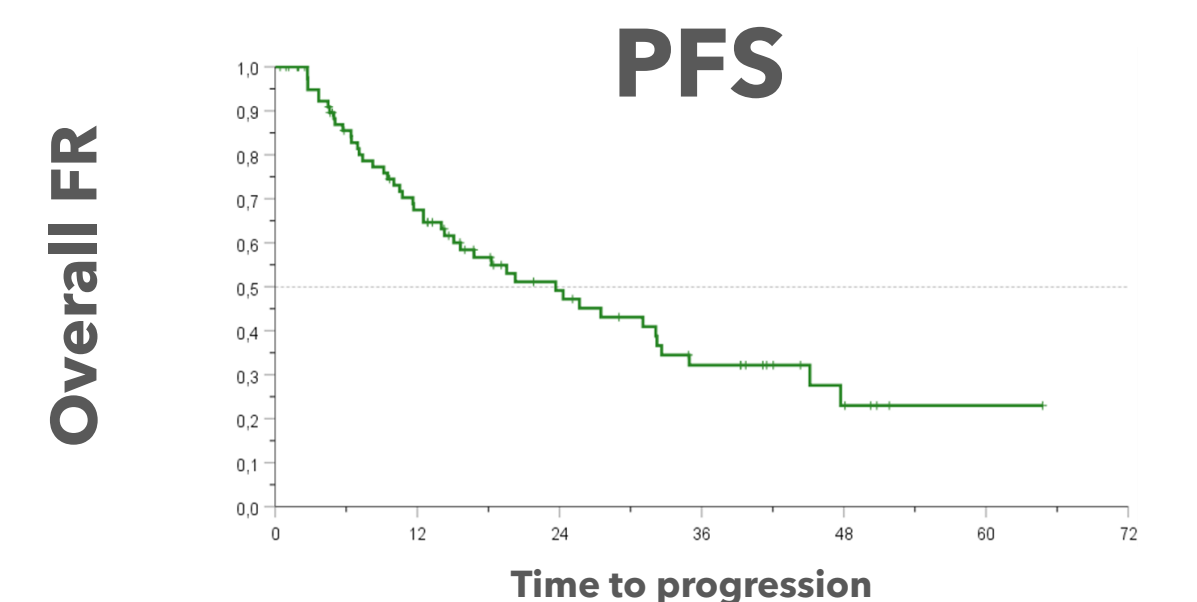


Sex		Overall FR (n=84)	
		n	%
Male		64	76.2
		20	23.8
Female		61	72.6
		23	27.4
Age, years	Median	68.7 (46 - 89)	
	< 75	61	72.6
	≥ 75	23	27.4

Lung was the most frequent metastatic site across subgroups (**65.4%**). VFR patients showed higher rates of **soft-tissue (26.1%)** and **pancreatic (30.4%)** metastases, with no bone or liver involvement.

EFFICACY

Median follow-up: **41.3 months (95% CI 36.0 - 46.7)**



ENDPOINTS	Overall FR (N=84)	VFR (n=23)	Rest FR (n=61)
ORR, % (CR %)	48.8 (7.1)	65.2 (13)	42.6 (4.9)
Median TTF, Months (95% CI)	14.7 (9.2 - 20.1)	31.1 (8.0 - 54.1)	12.5 (8.0 - 17.0)
Median PFS, Months (95% CI)	23.7 (11.8 - 28.8)	32.2 (21.1 - 43.4)	16.8 (5.8 - 27.7)
Median OS, Months (95% CI)	NR	NR	NR
2-year survival probability, %	85.4 (77.2 - 92.8)	95.7 (88.1 - 100.0)	75.5 (63.9 - 87.1)
5-year survival probability, %	67.8 (55.8 - 79.8)	60 (21.6 - 98.4)	59.0 (43.8 - 74.2)

Log-rank Mantel Cox (p NS)

SAFETY

Global tolerability	Overall FR (N=84) n (%)	VFR (n=23) n (%)	Rest FR (n=61) n (%)
Full-dose treatment	40 (47.6)	11 (47.8)	29 (47.5)
Dose reduction	13 (15.5)	3 (13.0)	10 (16.4)
Discontinuation due to toxicity	8 (9.5)	2 (8.7)	6 (9.8)

Most **adverse events** were **grade 1-2** fatigue, diarrhea, mucositis, hypertension and dysphonia, while **grade ≥3** events were infrequent and mainly limited to hypertension.

SUBSEQUENT TREATMENT

Among patients discontinuing 1L tivozanib (n=61), **47 (77.0%) received subsequent treatment:** second line consisted predominantly of ICIs (89.4%; mostly nivolumab), with VEGFR-TKIs in 10.6%, and 42.6% of second-line recipients went on to third or later lines, mainly VEGFR-TKIs.

CONCLUSIONS

- 1 First-line tivozanib showed durable disease control and long-term survival in IMDC favorable-risk mRCC in routine clinical practice.
- 2 VFR patients showed numerically higher ORR and longer TTF and PFS than other FR patients.
- 3 Tivozanib showed a favorable safety profile, with mainly low-grade toxicity and infrequent discontinuations.
- 4 ICIs and cabozantinib remain effective salvage options after progression in this setting.

ABBREVIATIONS: CI, confidence interval; FR, favorable risk; IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; mRCC, metastatic renal cell carcinoma; NS, not significant; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SOGUG, Spanish Genitourinary Oncology Group; TTF, time to treatment failure; VEGFR-TKI, vascular endothelial growth factor receptor tyrosine kinase inhibitor; VFR, very favorable risk.

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