Real world analysis of first line systemic anti-cancer treatment for metastatic Renal cell carcinoma

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OBJECTIVE

The introduction of immunotherapy treatment options has transformed management for patients with metastatic renal carcinomas (mRCC). Landmark trials have demonstrated that patients with previously untreated advanced renal cell carcinoma who received first line dual immunotherapy (IO-IO) [1] or combination IO-tyrosine kinase inhibitor (IO-TKI) [2,3] had improved outcomes compared to those who received single-agent TKI. Median progression free survival (PFS) for IO-IO vs. TKI was 11.6 vs. 8.4 months [1] and IO-TKI vs. TKI were 16.6 vs. 8.3 months [2] and 13.8 vs. 7.2 months [3].

Aim- To compare real-world outcomes of patients with mRCC treated with first line IO-IO, IO-TKI and TKI at the Royal United Hospital, Bath, UK

METHODOLOGY

Single center, retrospective cohort study

Inclusion criteria:

1. No prior SACT for mRCC
2. Availability of complete clinical data
3. Treatment initiation between October 2015 and September 2025

Primary outcome- Progression free survival

Secondary outcomes-

- How frequently **toxicities** contributed to treatment discontinuation
- **Treatment response rates** evaluated using computed tomography (CT) scans performed at 3 monthly intervals

RESULTS

	Dual IO *(N = 24)*	Combination IO + TKI (n= 21)	TKI monotherapy *(n=70)*
Median age (range)- yr	69.5 (32-80)	66 (44-81)	74 (53-87)
Sex- no. (%)			
Male	17 (71%)	16 (76%)	48 (69%)
Female	5 (29%)	5 (24%)	22 (31%)
IMDC prognostic risk			
Favourable	0	8 (38%)	26 (37%)
Intermediate	17 (71%)	8 (38%)	34 (49%)
Poor	7 (29%)	5 (24%)	10 (14%)
Most common sites of metastasis - no. (%)			
Bone	6 (25%)	9 (43%)	24 (34%)
Liver	6 (25%)	5 (24%)	11(16%)
Lung	17 (71%)	15 (71%)	34 (49%)
Lymph nodes	8 (33%)	12 (57%)	30 (43%)
Nephrectomy - no. (%)	9 (38%)	9 (43%)	57 (81%)
Sarcomatoid changes - no. (%)	1 (4%)	3 (14%)	5 (7%)
Clear cell component - no. (%)	22 (92%)	18 (86%)	66 (94%)

Table 1. Baseline data. IMDC= International Metastatic RCC Database Consortium Risk Model for Metastatic Renal Cell Carcinoma

RESULTS CONTINUED

Progression free survival (PFS)

Of the 115 patients, 20.9%, 18.3% and 60.9% were treated with IO-IO, IO-TKI and TKI, respectively. Median PFS for all patients receiving first-line SACT was 12 months (m), for IO-IO it was 8m (95% CI 4-13m), IO-TKI was 13m (CI 95% 7-18 m) and TKI was 12m (CI 95% 9-17m) .

In adherence with NHS guidelines, there were no IMDC favourable risk patients in the IO-IO cohort. Consequently, our comparative analysis separated the clinical outcomes of intermediate- and poor-risk patients of which there were 81 patients (70.4%). Median PFS for the intermediate/poor risk cohort was 10m (95% CI [7, 12m]), for IO-IO it was 8m (95% CI 4-13m), IO-TKI was 10m (95% CI 9-14m) and TKI was 10m (95% CI 7-13m) . There was no statistically significant difference between groups (IO-IO vs TKI p=0.34, IO-IO vs IO/TKI p=0.9), TKI vs IO-TKI p=0.4).

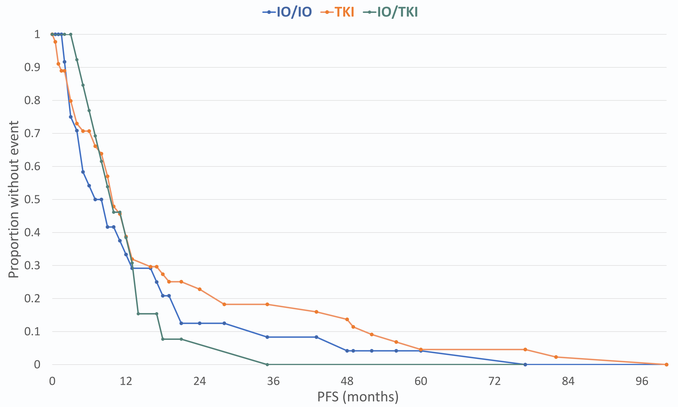

Figure 1. Kaplan–Meier curve showing progression free survival in patients with IMDC intermediate and poor risk mRCC's by first line SACT

Toxicity

Treatment related toxicities and adverse events were cited as the reason or part of the reason for treatment discontinuation in 3 (12.5%) patients receiving IO-IO. Only 1 (4.7%) patient stopped IO-TKI therapy due to toxicities, and TKI monotherapy was discontinued in 18 (25.7%) of patients due to toxicities.

Best confirmed treatment response

(A)

	Dual IO n=0 n (%)	IO+TKI n=8 n (%)	TKI n=26 n (%)
CR	0	0 (0)	0 (0)
PR	0	7 (87.5)	21 (80)
SD	0	1 (12.5)	2 (8)
PD	0	0 (0)	3 (12)
ORR	**n/a**	**87.5%**	**80%**

(B)

	Dual IO n=24 n (%)	IO+TKI n=13 n (%)	TKI n=44* n (%)
CR	1 (4.2)	0 (0)	4 (9)
PR	9 (37.5)	11 (85)	22 (50)
SD	5 (20.8)	1 (7.5)	3 (7)
PD	9 (37.5)	1 (7.5)	9 (20.5)
ORR	**41.70%**	**85%**	**59%**

Figure 2. CR- complete response, PR- Partial response, S- stable disease, PD- progressive disease, ORR- objective response rate
*(A) Comparing treatment response rates for first line SACT for patients with an **IMDC favourable risk** score.*
*(B) Comparing treatment response rates for patients with an **IMDC intermediate or poor risk** score.*
**6 patients in TKI group not Evaluable due to early death.*

The differences between SACT groups ORR's was statistically significant (favourable risk p=0.002, intermediate/poor risk p=0.02) using a Chi-square test for association.

CONCLUSION

- There was no statistically significant variation in PFS for intermediate- and poor-risk mRCC patients across first-line SACT regimens.
- IO-TKI demonstrated the highest ORR and lowest toxicity-related discontinuation rate.
- Study limitations include small sample size, and the earliest part of our cohort may not reflect today's prescribing practice due to newer therapies emerging.
- Subsequent analysis could examine grade 3 toxicity rates and incorporate patient-reported quality-of life outcomes to enhance shared clinical decision-making.

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