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

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Objective: Landmark clinical trials such as the Checkmate 214 trial[1] have demonstrated that patients with previously untreated advanced renal cell carcinoma who received first line dual immunotherapy regimes (IO/IO), or combination therapy consisting of an immune checkpoint inhibitor with a targeted agent- tyrosine kinase inhibitor (IO/TKI) had improved outcomes compared to those receiving single-agent TKI. In light of these findings this study aimed to compare the real-world outcomes of patients with metastatic renal cell carcinoma treated at the Royal United Hospital, Bath, UK, receiving first line SACT with IO/IO, IO-TKI and TKI only regimes.

Methods: This is a single centre, retrospective cohort study looking at data from 2018- 2026. There were 115 patients included (IO/IO n=24, IO/TKI n=21, TKI n=70). The primary outcome was progression free survival (PFS). Secondary outcomes included treatment response rates and how frequently toxicities contributed to treatment discontinuation.

Results: Per NHS guidelines, there were no IMDC favourable risk patients in the IO/IO cohort. Thus analysis separated the outcomes of intermediate- and poor-risk groups. There were 81 patients with intermediate/poor risk scores. The overall median PFS for these patients was 10m (95% CI [7, 12m]), for IO/IO (n=24)- 8m (95% CI [4, 13m]), IO/TKI (n=13)- 10m (95% CI [9, 14]) and TKI (n=44)- 10m (95% CI [7, 13m]). In the intermediate/poor risk groups the ORR for IO/IO was 41.7%, IO+TKI was 85% and TKI was 59% (p=0.02). In the favourable risk patient cohort the ORR for IO/TKI was 87.5% and for TKI alone was 80%. Toxicities lead to treatment discontinuation in 3 (12.5%) patients receiving IO/IO, 1 (4.7%) IO/TKI and 18 (25.7%) TKI patients.

Conclusions: There was no statistically significant variation in PFS for intermediate- and poor-risk patients with mRCC across first-line SACT regimens. IO/TKI demonstrated the highest ORR and lowest toxicity-related discontinuation rate. Study limitations include the small sample size. Due to evolving additional treatment options early-year treatments may not fully reflect today's prescribing practice. Subsequent analysis could examine grade 3 toxicity rates and incorporate patient-reported quality-of life outcomes to enhance shared clinical decision-making.