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Real-world Outcomes of First-line Immune Checkpoint Inhibitor–Tyrosine Kinase Inhibitor Combination Therapy in Metastatic Renal Cell Carcinoma: A Regional Cancer Centre Experience

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Background:

Immune checkpoint inhibitor (ICI) in combination with a Tyrosine Kinase Inhibitor (TKI) provides fast and durable response which is valuable in International Metastatic RCC Database Consortium (IMDC) intermediate and poor risk groups, especially those with increased disease burden. However, initial studies like the CheckMate 9ER and JAVELIN Renal 101 reported grade ≥3 toxicities in over 70 %raising concerns of tolerability in routine clinical practice.

Objective:

To evaluate the safety and efficacy of first line (1L) ICI-TKI combination therapies in IMDC intermediate and poor risk groups

Methods:

Retrospective service evaluation study of mRCC patients managed at JCUH with 1L ICI-TKI from November 2020 to October 2025 with a median follow-up duration of 27 months.

Results:

45 patients were eligible for analyses, with a median age of 65 years (range:28-87) of which 68.9% were males, and 31.1% females. 80% were clear cell histology remaining were non-clear cell variants. Sites of metastasis at diagnosis were lung, bone, liver and brain in 48.9%, 40%, 35.6% and 8.9% respectively. 64.4% were IMDC intermediate risk and 35.6% were IMDC poor risk. First-line regimens included pembrolizumab-lenvatinib (60%), avelumab-axitinib (31.1%), and nivolumab-cabozantinib (8.9%).

Median progression free survival (PFS) across all groups was 16.7 months (95%CI: 3.6-29.8); Median PFS was better in IMDC intermediate risk group 23.7 months (95%CI: 8.7-39.4), in contrast to 14.2 months (95%CI: 10.2-18.3) in the IMDC i poor risk groups . Median overall survival (OS) across all IMDC groups was 18.8 months (95%CI: 4.7-32.9). The intermediate IMDC group had a longer OS of 28.0 months (95%CI: 8.8-47.3), compared to the poor risk group of 10.4 months (95%CI: 0.0-22.4), with log-rank p=0.03. 24.4% had TKI dose reduction and 37.8% reported grade ≥3 toxicities.

Conclusion:

This study showed that 1L ICI-TKI therapy demonstrates clinical benefit with better tolerability with low ,Grade ≥3 toxicities . The survival outcomes were not as impressive compared to initial trials. A retrospective design, less stringent reporting, frailer patients, increased disease burden and treatment interruptions routinely encountered in practice may be reflective of the differences noted. Nevertheless, this raises the question of improved patient selection strategies for this therapy.