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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 a 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 such as CheckMate 9ER and JAVELIN Renal 101 reported grade ≥3 toxicities in over 70% of patients, raising concerns about tolerability in routine clinical practice.

Objective

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

Methods

Retrospective service evaluation of patients with mRCC managed at James Cook University Hospital who received 1L ICI–TKI therapy between November 2020 and October 2025. Median follow-up was 27 months.

Results: patient characteristics

- 45 patients eligible; median age 65 years (range 28–87)
- Sex: 68.9% % male, 31.1% female
- Metastatic sites at diagnosis: lung 48.9%, bone 40.0%, liver 35.6%, brain 8.9%
- IMDC risk: intermediate 64.4%, poor 35.6%
- TKI dose reduction required in 24.4% of patients

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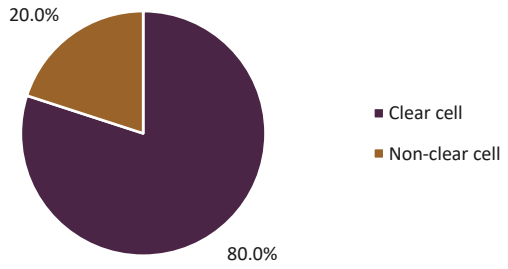
Survival outcomes

Outcome	Median, months	95% CI
PFS, all patients	**16.7**	3.6–29.8
PFS, IMDC intermediate	23.7	8.7–39.4
PFS, IMDC poor	14.2	10.2–18.3
OS, all patients	**18.8**	4.7–32.9
OS, IMDC intermediate	28.0	8.8–47.3
OS, IMDC poor	10.4	0.0–22.4

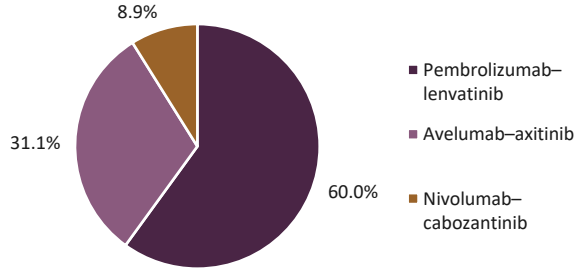
Log-rank p = 0.03 for the OS difference between IMDC intermediate and poor risk groups.

Figure 1. Histology



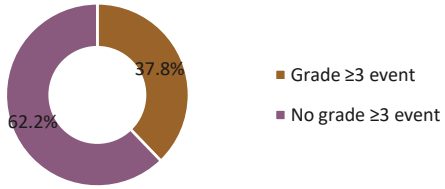
Clear cell vs non-clear cell variants (n = 45).

Figure 2. First-line regimen



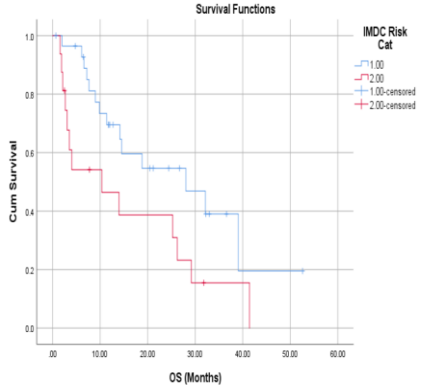
Distribution of 1L ICI–TKI regimens (n = 45).

Figure 3. Grade ≥3 toxicity



Grade ≥3 toxicity on 1L ICI–TKI therapy (n = 45).

Figure 4. Overall survival for IMDC intermediate and poor risk group



Conclusion 1L ICI–TKI therapy demonstrates clinical benefit with better tolerability and a lower rate of grade ≥3 toxicity than reported in registration trials. Survival outcomes were less impressive than in those trials; a retrospective design, less stringent reporting, frailer patients, greater disease burden and treatment interruptions routinely encountered in practice may account for the difference. This raises the question of improved patient selection strategies for this therapy.