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Real-World Outcomes of Delayed Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma Following Systemic Therapy: A Tertiary Centre Experience

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Introduction

The role of cytoreductive nephrectomy in metastatic renal cell carcinoma patients has been an area of interest since the era of Interferon, cytokine therapy and the tyrosine kinase inhibitor therapy. Now that immune checkpoint inhibitors producing long term durable responses are established in the treatment of mRCC patients, it is important to evaluate real world data to understand which patients are proceeding to cytoreductive nephrectomy and if they are benefiting from this procedure. Here we report real-world pathological and clinical outcomes of delayed CN following first-line systemic therapy at a tertiary referral center.

Methods

We conducted a retrospective analysis of all mRCC patients who underwent delayed CN after first-line systemic therapy (tyrosine kinase inhibitors [TKI] or ipilimumab/nivolumab [IPI/NIVO]) between 2019-2023 . Baseline characteristics, treatment details, and surgical outcomes were collected.

Results

Eleven patients were included (median age 64 years; 8 males, 3 female). All had ECOG performance status 0–1. Ten tumors demonstrated clear cell histology; one was classified as metastatic renal tumor not otherwise specified. Mean primary tumor size was 105.9 mm. Metastatic sites included lung only (n=8), lymph nodes only (n=1), lung and adrenal (n=1), and lung and pancreas (n=1)). Nine patients received first-line IPI/NIVO, one received pazopanib, and one received cabozantinib. Median time from systemic therapy initiation to surgery was 22 months. Four patients underwent open nephrectomy; seven underwent robotic-assisted surgery. Complete pathological response (pCR) was observed in 5 of 11 patients (45%), all of whom had received IPI/NIVO. Of these, four received four cycles and one received two cycles (discontinued due to grade 3 transaminitis). At last follow-up, four of five pCR patients remained progression-free; one progressed and was switched to second-line cabozantinib. Both TKI-treated patients had viable tumors at surgery and subsequently progressed to second-line therapy.

Ten patients remain alive; one died from a non-cancer-related cause without evidence of disease recurrence.

Conclusion

Delayed cytoreductive nephrectomy following first-line ipilimumab/nivolumab was associated with a 45% complete pathological response rate in this real-world cohort. These findings support the potential benefit of immunotherapy-induced tumor regression prior to surgery and highlight the importance of careful patient selection. Given the limitations of this small retrospective study, prospective randomized trials are needed to define optimal timing and patient selection criteria for delayed CN in mRCC.