Impact of Upfront Cytoreductive Nephrectomy on Overall Survival in Metastatic Renal Cell Carcinoma Patients Treated with First-line Immunotherapy: A Real-World Data Analysis

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Introduction

The role of cytoreductive nephrectomy (CN) in metastatic renal cell carcinoma (mRCC) has evolved with the advent of targeted therapies and immune checkpoint inhibitors (ICIs). While earlier studies supported CN in the cytokine era, its value in the context of modern systemic therapies remains debated. This study aimed to evaluate the impact of upfront CN on overall survival (OS) in mRCC patients receiving first-line immunotherapy using real-world data.

Methods

We conducted a retrospective study using the TriNetX US Collaborative Network database. Patients with mRCC who received first-line systemic therapy (ipilimumab-nivolumab, cabozantinib-nivolumab, axitinib-pembrolizumab, or lenvatinib-pembrolizumab) between 2008 and 2022 were included. Upfront CN was defined as nephrectomy performed before the initiation of systemic therapy. The primary outcome was OS, analyzed using Kaplan-Meier methodology and logistic regression.

Results

A total of 1,862 patients were included. Upfront CN was associated with significantly improved OS in patients receiving Ipi-Niv (HR 0.478, $p<0.0001$), Cab-Niv (HR 0.655, $p=0.0465$), and Axi-Pem (HR 0.416, $p<0.0001$). The benefit was particularly pronounced in those with intermediate IMDC risk scores. A trend towards lower mortality with CN was also observed in the Len-Pem group, although the sample size was limited.

Discussion

This real-world data analysis supports the use of upfront CN in mRCC patients receiving first-line ICI-based therapies. The observed OS benefit, particularly in intermediate-risk patients, suggests a synergistic effect between CN and immunotherapy. However, limitations include the retrospective design and potential confounding factors. Future research should focus on prospective trials to optimize patient selection and timing of CN, and investigate the mechanisms underlying the observed synergy. Further stratification of data to differentiate between radical and partial nephrectomy and direct comparison of mass recurrence in CN and ablative approaches like RFA when used with immunotherapy may yield additional insights.

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