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Congress Abstract

Immunotherapy and Targeted Therapy for Metastatic Renal Cell Carcinoma

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Background: The introduction of targeted therapy and immune checkpoint inhibitors has significantly improved treatment outcomes in patients with locally advanced and metastatic renal cell carcinoma (mRCC). However, tumor heterogeneity and the development of alternative signaling pathways may contribute to treatment resistance, emphasizing the need for effective combination strategies.

Objective: To evaluate the efficacy of contemporary immunotherapy-based combinations in the first-line treatment of metastatic renal cell carcinoma and identify clinical factors relevant to treatment selection.

Materials and Methods: Published data from randomized phase III studies of first-line systemic therapy for advanced and metastatic renal cell carcinoma were analyzed. Particular attention was given to nivolumab plus ipilimumab and lenvatinib plus pembrolizumab compared with sunitinib. Treatment efficacy was assessed using progression-free survival (PFS), overall survival (OS), objective response rate (ORR), and outcomes according to International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk groups.

Results: In the CLEAR trial, lenvatinib plus pembrolizumab significantly prolonged median PFS compared with sunitinib (23.9 vs 9.2 months) and improved overall survival. In patients with intermediate/poor IMDC risk, median PFS was 22.1 months with lenvatinib plus pembrolizumab versus 5.9 months with sunitinib, while ORR was 72.4% versus 28.8%, respectively. Long-term results of the CheckMate 214 trial demonstrated a sustained survival benefit with nivolumab plus ipilimumab compared with sunitinib. The final analysis after a median follow-up of 9.3 years showed an OS hazard ratio of 0.71 in the intention-to-treat population and 0.69 in patients with intermediate/poor IMDC risk. Durable responses were maintained across long-term follow-up.

Conclusions: Immunotherapy-based combinations have substantially improved the treatment of metastatic renal cell carcinoma. Lenvatinib plus pembrolizumab provides significant improvements in PFS and objective response compared with sunitinib, while nivolumab plus ipilimumab demonstrates durable long-term survival benefits. Selection of first-line therapy should consider IMDC risk group, tumor burden, metastatic sites, clinical condition, histological characteristics, and individual patient factors.

Keywords: Renal Cell Carcinoma; Immunotherapy; Targeted Therapy; Lenvatinib; Pembrolizumab; Nivolumab