01. Title: Integrating Immunotherapy and Targeted Therapy in Advanced Hepatocellular Carcinoma: Clinical Outcomes of Lenvatinib–Pembrolizumab Combination Therapy

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Background: Advanced unresectable hepatocellular carcinoma (uHCC) is associated with poor prognosis and limited treatment options. Combination therapy with lenvatinib, a multikinase inhibitor, and pembrolizumab, an immune checkpoint inhibitor, has demonstrated promising antitumor activity in recent studies. However, variability in liver function status and prior systemic therapy exposure continues to influence clinical outcomes. This review evaluates the efficacy and safety profile of lenvatinib–pembrolizumab therapy in advanced uHCC.

Objective: To assess the clinical efficacy, safety, and prognostic factors associated with lenvatinib plus pembrolizumab therapy in patients with advanced unresectable hepatocellular carcinoma.

Methodology: A literature review was conducted using published clinical trials and real-world studies evaluating lenvatinib combined with pembrolizumab in advanced uHCC. Key outcomes analyzed included disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and treatment-related adverse effects. Prognostic variables such as Child–Pugh classification, Albumin-Bilirubin (ALBI) score, and prior systemic therapy exposure were additionally reviewed.

Result: Reviewed studies demonstrated favourable efficacy and acceptable tolerability of lenvatinib–pembrolizumab therapy in advanced uHCC. In a prospective cohort involving 71 patients, 81.7% were categorized as Barcelona Clinic Liver Cancer (BCLC) stage C. Disease control rates exceeded 80% in first-line settings and approached 70% in previously treated patients. Median progression-free survival was approximately 9 months. Liver function, assessed using ALBI scores, remained relatively stable during treatment. Common adverse effects included hypertension, fatigue, and hepatic dysfunction, while severe toxicities were infrequent.

Conclusion: Current evidence supports lenvatinib combined with pembrolizumab as an effective and generally well-tolerated therapeutic strategy in advanced unresectable hepatocellular carcinoma. Treatment outcomes appear to be influenced by baseline liver function and prior immunotherapy exposure. Larger prospective randomized studies are required to further validate long-term efficacy and safety outcomes.

Key Words: Hepatocellular Carcinoma; Lenvatinib; Pembrolizumab; Immunotherapy; Targeted Therapy; Unresectable HCC; Disease Control Rate; Progression-Free Survival; ALBI Score; Systemic Therapy

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