

TACE + Camrelizumab/Rivoceranib Improves OS in Unresectable HCC

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Patients with unresectable hepatocellular carcinoma (HCC) face limited survival benefits from transarterial chemoembolization (TACE) alone. New data from the CHANCE2005/CARES-005 trial indicate that combining TACE with camrelizumab and rivoceranib significantly improves overall survival in this population.¹

KEY TAKEAWAYS

- The Pivot: TACE alone has limited efficacy in unresectable HCC.
- The Data: TACE combined with camrelizumab and rivoceranib improved overall survival compared to TACE alone.¹
- The Action: Consider combination therapy for unresectable HCC, pending further phase III data.

Unresectable hepatocellular carcinoma (HCC) presents a significant clinical challenge, with transarterial chemoembolization (TACE) serving as a standard treatment. However, the efficacy of TACE alone in improving long-term survival for these patients has been limited.¹ The need for more effective systemic approaches, particularly those integrating immunotherapy and targeted therapy, has been a focus of ongoing research.¹

HCC is the most common primary liver cancer and a leading cause of cancer-related death worldwide. Its incidence is rising in many regions, often linked to underlying chronic liver diseases such as hepatitis B and C viral infections, non-alcoholic fatty liver disease (NAFLD), and alcohol-related liver disease. Patients with unresectable HCC, meaning the tumor cannot be completely removed by surgery or treated with local ablation, face a poor prognosis. TACE, a locoregional therapy, delivers chemotherapy agents directly to the tumor via its arterial blood supply, followed by embolization to block blood flow, thereby inducing tumor necrosis. While effective in controlling local disease and extending survival compared to no treatment, TACE monotherapy rarely achieves durable complete responses, and disease progression remains common. This necessitates the exploration of combination strategies that can address both local and systemic disease components.

The CHANCE2005/CARES-005 Trial

The CHANCE2005/CARES-005 study was a randomized phase II trial designed to evaluate the addition of camrelizumab (an anti-PD-1 antibody) and rivoceranib (a vascular endothelial growth factor receptor 2 inhibitor) to TACE for patients with unresectable HCC.¹ The trial compared two arms: TACE combined with camrelizumab and rivoceranib versus TACE alone.¹

The study aimed to determine if this combination therapy could offer a survival advantage over TACE monotherapy.¹ While the abstract does not specify the exact number of patients enrolled or the primary endpoint, it highlights the comparative nature of the trial in assessing the efficacy of the combination regimen.¹ The rationale for combining these agents stems from their distinct but complementary mechanisms of action. Camrelizumab, an immune checkpoint inhibitor, blocks the programmed cell death protein 1 (PD-1) pathway, thereby reactivating anti-tumor T-cell responses. Rivoceranib, an anti-angiogenic agent, inhibits VEGF receptor 2, disrupting the tumor's blood supply and potentially normalizing the tumor microenvironment, which can enhance the efficacy of immunotherapy. Preclinical and early clinical data suggest that anti-angiogenic therapies can synergize with immune checkpoint inhibitors by reducing immunosuppression within the tumor microenvironment and improving T-cell infiltration. The trial likely enrolled patients with confirmed unresectable HCC, possibly including those with Barcelona Clinic Liver Cancer (BCLC) stage B or C disease, who had adequate liver function and performance status to tolerate the treatments.

Key Findings

The trial demonstrated that TACE combined with camrelizumab and rivoceranib improved overall survival (OS) compared to TACE alone in patients with unresectable HCC.¹ Specific hazard ratios or p-values for OS were not provided in the abstract, but the statement indicates a positive outcome for the combination arm.¹ This suggests that the synergistic effects of immune checkpoint inhibition and anti-angiogenic therapy, when combined with locoregional TACE, may overcome some of the limitations of TACE monotherapy.¹

Another study, PMID 41107646, focused on the underutilization of staging laparoscopy prior to neoadjuvant systemic therapy in gastric cancer.² While this paper addresses a critical aspect of gastric cancer management, its findings are not directly related to the treatment approaches for unresectable HCC or the specific combination therapy evaluated in the CHANCE2005/CARES-005 trial.² The abstract for PMID 41107646 incorrectly describes the content of PMID 41734362, indicating a potential error in the provided research abstract.² Therefore, the information regarding gastric cancer staging laparoscopy is noted but not integrated into the discussion of HCC treatment efficacy.²

Limitations and Next Steps

As a phase II trial, CHANCE2005/CARES-005 provides preliminary evidence of efficacy.¹ The abstract does not detail safety profiles, specific adverse events, or quality of life outcomes, which are crucial for a comprehensive understanding of the treatment's clinical utility.¹ Further phase III trials with larger patient cohorts are necessary to confirm these survival benefits, establish the long-term safety profile, and define the optimal patient population for this combination therapy.¹ The absence of detailed statistical measures (e.g., HR, p-value) in the abstract limits a precise quantitative assessment of the observed improvement.¹

A more detailed reporting of adverse events, including their frequency, severity, and management, is essential for evaluating the risk-benefit profile of this complex regimen. Immunotherapy and anti-angiogenic agents each carry distinct toxicity profiles, and their combination may lead to additive or synergistic adverse effects. Furthermore, the abstract does not specify patient characteristics such as etiology of HCC (e.g., viral hepatitis, NAFLD), tumor burden, liver function (e.g., Child-Pugh score), or prior treatments, which could influence treatment response and generalizability.

of the findings. Future research should also explore biomarkers that can predict response to this combination therapy, allowing for more personalized treatment approaches and avoiding unnecessary toxicity in non-responders. The cost-effectiveness of this combination therapy compared to existing standards of care also warrants investigation in subsequent studies.

CLINICAL IMPLICATIONS

The CHANCE2005/CARES-005 trial offers a glimpse into a potentially more effective treatment strategy for unresectable hepatocellular carcinoma. For clinicians managing these complex cases, the prospect of combining TACE with an anti-PD-1 antibody like camrelizumab and an anti-VEGFR2 inhibitor such as rivoceranib suggests a new avenue beyond current standards. While the phase II nature and limited data in the abstract necessitate caution, the reported improvement in overall survival is a signal that warrants attention. It underscores the ongoing shift towards multi-modal approaches, integrating systemic therapies with locoregional treatments.

From an industry perspective, this trial highlights the continued investment in combination therapies, particularly those involving immune checkpoint inhibitors and targeted agents. Companies like Hengrui Pharma, which develops camrelizumab, and Elevar Therapeutics, associated with rivoceranib, will likely pursue further development and larger trials to solidify these findings. The market for HCC treatments remains competitive, and demonstrating a clear survival advantage, even in a phase II setting, can influence future research directions and potentially impact guideline recommendations if confirmed in subsequent studies. For patients, these results offer a degree of optimism. Unresectable HCC carries a poor prognosis, and any therapy that can extend overall survival is significant. While it is premature to alter clinical practice based solely on a phase II abstract, the data suggest that patients may eventually have access to more effective treatment options, potentially improving their quality of life and longevity. The integration of these agents into standard care would represent a meaningful step forward, moving beyond the current limitations of TACE monotherapy.

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