Transarterial Chemoembolization Alone and with Immunotherapy for Treating Hepatocellular Carcinoma: Current Evidence

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Purpose

- Transarterial chemoembolization (TACE) has long been a standard treatment for intermediate-stage hepatocellular carcinoma (HCC). Several recent studies suggest that concurrent treatment with TACE and immunotherapy can improve survival metrics for several subtypes of HCC patients.
- This exhibit will review the current evidence surrounding the efficacy of TACE alone, in combination with targeted therapies, and in conjunction with immunotherapy for the treatment of hepatocellular carcinoma.

Materials and Methods

- A systematic literature review was conducted using the PubMed and Google Scholar databases to identify relevant clinical studies between 2020 and 2025. Randomized studies and those with relatively large sample sizes were preferred.
- The literature review focused on the current role of TACE in the treatment of HCC. Studies that compared TACE alone and in combination with targeted therapy and immunotherapy were also selected.
- The selected studies were reviewed for endpoints and clinical outcomes, as well as reported adverse effects (AE).

Studies

Recent Literature

Study	Study design	TACE & Immunotherapy	Findings	Limitations and AE
LEAP-012 2025	• Multicenter, randomized, double-blind • Unresectable, non-metastatic HCC • N = 480	Group 1 • **Lenvatinib** (multi-kinase inhibitor with anti-VEGF activity) & **Pembrolizumab** (PD-1 inhibitor) with **TACE** Group 2 • Dual **placebo** with **TACE**	• Increased Median progression-free survival (PFS) with combination treatment: 14.6 vs 10.0 months • Increased 24-month survival rate combination treatment: 75% vs 69% placebo • More Grade 3 or worse treatment-related adverse events in combination treatment: 71% vs 32%	• Overall survival (OS) data • Patient-reported outcomes • Concerning side effects and AE from combination therapy included hypertension, thrombocytopenia, and death (n=4).
EMERALD-01 2025	• Multiregional, randomized, double-blind, placebo-controlled • Unresectable HCC that is amenable to embolization • N = 618	Group 1 • **TACE** alone Group 2 • **Durvalumab** (PD-L1 inhibitor) with **TACE** Group 3 • **Durvalumab** (PD-L1 inhibitor) & **Bevacizumab** (VEGF Inhibitor) with **TACE**	• Increased Median PFS for Cobo treatment - Group 3: 15M, Group 2: 10M, Group 1: 8M • Group 3 had Higher incidence of serious AE, maximum grade 3–4 adverse events, and adverse events leading to discontinuation than other groups. N=16 deaths following an AE. • Higher hemorrhagic events occurred in Group 3 in those with varices at baseline.	• OS data • Patient-reported outcomes • Full analysis of liver function • Avoiding Bevacizumab use at the same time as TACE (side effects) • High rate of concerning side effects and AE from combination therapy, such as hypertension, anemia, and death.
Guo et al. 2025	• Meta-analysis of 20 studies • Patients with unresectable HCC who received TACE with molecular targeted therapy (MTT) and those who received TACE and MTT with immunotherapy (most commonly camrelizumab, pembrolizumab, nivolumab, sintilimab, and tislelizumab) • N = 2587	Group 1 • **TACE** with MTT Group 2 • **TACE** with MTT and immunotherapy	• The addition of immune checkpoint inhibitors (ICI) to TACE and MTT significantly improved overall survival. • PFS was significantly prolonged with the addition of ICI. • Objective response rate (ORR) and disease control rate (DCR) increased with the addition of ICI. • The addition of ICI to TACE and tyrosine kinase inhibitors (TKI) improved OS, PFS, ORR, and DCR without a significant increase in adverse events. • The safety profile of combination therapy was comparable to TACE plus TKI without a significant increase in adverse events.	• The study utilized both retrospective and prospective studies with varying baseline characteristics, with only a few randomized studies. • Variability in immunotherapy and targeted agents • Inconsistent reporting of adverse events across studies • Among the most reported adverse events are hypertension, fever, abdominal pain, nausea, vomiting, hand-foot syndrome, proteinuria, diarrhea, and hypothyroidism.

Why combination treatment:

TACE can lead to a hypoxic tumor microenvironment and induce immunogenic cell death in cancer cells. This combination induces vascular endothelial growth factor, creating an immunosuppressive environment supporting anti-tumor immunity.

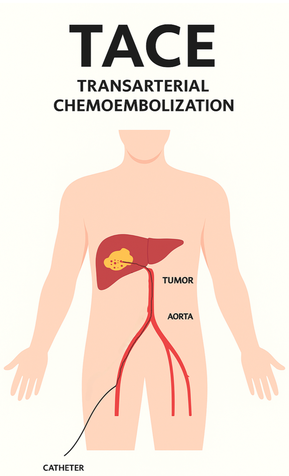

Figure 1 is a simplified schematic illustrating access to a hepatocellular carcinoma tumor and targeted delivery of chemoembolic agents.

Results

- TACE in combination with various immunotherapy regimens significantly improves several survival metrics, including one-year survival, progression-free survival at follow-up, and disease-free survival.
- The examined studies were not congruous in all regards, such as overall survival and adverse events.

Conclusions

- TACE with immunotherapy could set a new standard of care, but a personalized approach will be needed for combination therapy until new clinical guidelines can be established.
- Advancements in immunotherapy have sparked investigations into combination therapy with existing techniques such as TACE for the treatment of HCC. These combination therapies appear to reduce disease burden and improve patient outcomes.
- Differences between the studies regarding outcomes such as OS may be due to differences in study design, such as the focus on tumor microvascular involvement. Results were further limited by factors such as inadequate long-term follow-up periods. Further research into the topic can focus on standardizing patient populations and increasing the duration of follow-up.
- Ongoing studies are yielding encouraging results regarding combination therapy, and will continue to improve treatment strategies for HCC.

References

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