Enhancing Hepatocellular Carcinoma Outcomes: Integrating Immune Checkpoint Inhibitors with Interventional Oncology

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Introduction

- **Hepatocellular carcinoma (HCC):**
  - 6th most common cancer worldwide
  - Major cause of cancer-related mortality
  - Often diagnosed at advanced stages with limited curative options [1,2]
- **Locoregional therapies:**
  - Transarterial chemoembolization (TACE) and Yttrium-90 (Y-90) radioembolization (TARE)
  - Standard treatments for intermediate-stage disease
  - Provide tumor control, but limited long-term survival [2-4]
- **IO-ICI combinations:**
  - Show promise in enhancing tumor control and immune activation
  - Supported by updated guideline and ongoing clinical trials
  - Emerging as a promising strategy across disease stages

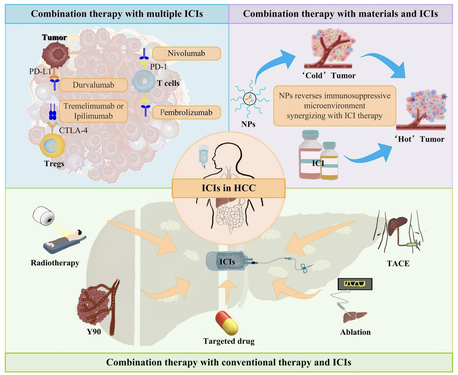

Figure 1. Combination Strategies with ICIs (*Tong et al., 2025*).

Purpose

- To review the rationale, clinical evidence, and role of IO-ICI combinations across different stages of HCC

Methods

- Targeted literature review (2020-2025)
- Included clinical studies, meta-analyses, and guidelines
- Focused on efficacy, safety, and immunologic mechanisms of IO-ICI mechanisms

Results

Overall Findings
- IO-ICI combinations enhance tumor control and immune activation
- Guidelines and trials are expanding their role across all HCC stages

TACE & ICIs: TACE promotes PD-L1 upregulation in the tumor microenvironment, potentially enhancing ICI efficacy
- Show improved survival and response rates across multiple studies

Y-90 & ICIs: Y-90 trigger antigen release and promote immune cell recruitment, contributing to ICI's enhanced activity through immune priming
- Y-90 offers longer time to progression than TACE
- Offer durable control with high response rates but variable toxicity by study

Ablation & ICIs: Complement ICIs by inducing immunogenic cell death and promoting antigen release, demonstrating synergistic immune activation and reduced recurrence

Advanced Disease: Early-phase studies integrating hepatic arterial infusion chemotherapy (HAIC), TACE, and ICIs in advanced HCC show:
- Favorable safety with manageable AEs
- Encouraging efficacy, though results remain preliminary

IO-ICI Combination	Median PFS (mos)	Median OS (mos)	ORR (%)	DCR (%)	Grade ≥3 AEs (%)	Author (Year)
TACE + Camrelizumab	6.1	13.3	35.3	-	5.9	Zhang et al. (2022)
TACE + ICIs	↑ vs. ICIs alone	↑ vs. ICIs alone	↑	↑	-	Li et al. (2025); Yu et al. (2025)
Y-90 + ICIs	5.6–13.3	16.2–27	31–89	0	50–80	Hosseini et al. (2025)
RFA + ICIs	-	↑ survival	↑ response	↓ recurrence	Controllable	Xie et al. (2025)
HAIC-FOLFOX + TKI + ICIs	11	↑ vs. TKI/ICIs	61.6	87.9	ALT/AST ↑, thrombocytopenia	Tan et al. (2023); Liu et al. (2024)

Table 1. Combination Therapy Outcomes in HCC.

Discussion

- IO procedures + ICIs + anti-angiogenic agents activate complementary mechanisms, offering a multifaceted approach to HCC treatment.
- TACE and Y-90 provide localized tumor control and enhance immunogenicity [5-8] via:
  - Antigen release
  - PD-L1 upregulation
  - Immune cell recruitment
- Anti-angiogenic agents improve immune infiltration, amplifying ICI efficacy

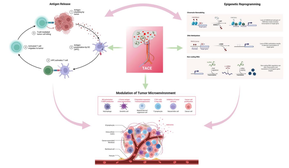

Figure 2. Rationale for Combining Locoregional Techniques with ICIs (*Chen et al., 2024*).

Conclusion & Future Directions

- IO-ICI combinations activate complementary mechanisms that improve tumor control and immune response.
- Not yet standard of care, accumulating evidence suggests these multimodal strategies may outperform monotherapies.
- Multimodal strategies are most promising in patients with limited IO or ICI response
- Biomarker-driven patient selection
- **Ongoing trials:** EMERALD-1, CheckMate 74W, and CA 209-678,
- Prospective trials to validate combinations and optimize sequencing

References

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