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Locoregional and Immunotherapy Integration for Hepatocellular Carcinoma: Mechanistic Rationale and Trial Landscape

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PURPOSE

This educational review analyzes the rationale and current trial landscape of combined treatment approaches including either transarterial chemoembolization (TACE) or transarterial radioembolization (TARE) and Immunotherapy for Hepatocellular Carcinoma (HCC).

BACKGROUND

- HCC is a leading cause of cancer-related mortality and its incidence is increasing
- Both TACE and TARE have long been the standard of care treatments for intermediate-stage HCC.
- TACE and TARE may modulate the tumor microenvironment and upregulate pro-inflammatory cytokines, thereby increasing immune checkpoint molecules.[7]
- This upregulation in turn increases the efficacy of PD-L1 inhibitors.

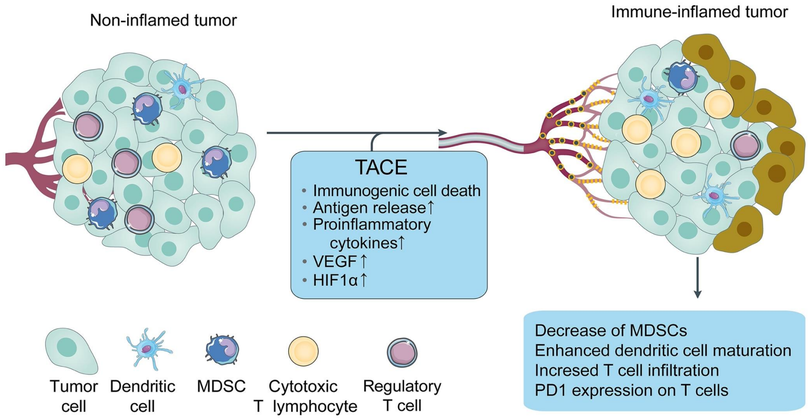

Figure 1, TACE Altering the Tumor Microenvironment, adapted from Zhong et. al

METHODS

A systematic literature review was conducted evaluating PubMed-indexed clinical trials and randomized control trials containing the search parameters “TACE and immunotherapy” or “TARE and immunotherapy” as a treatment for HCC.

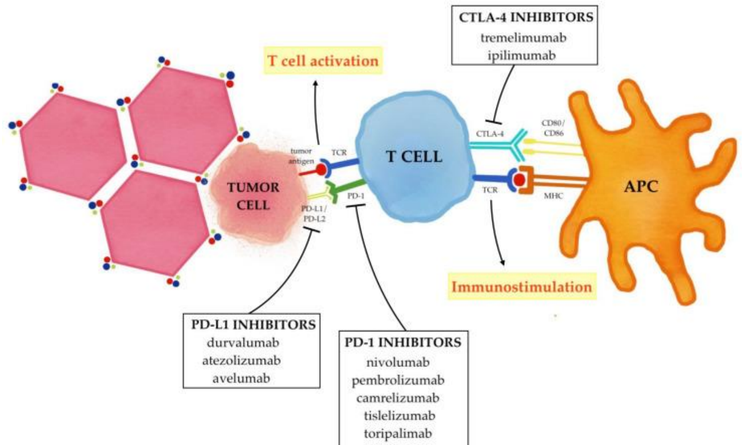

Figure 2, Immunotherapy Overview and Mechanisms, adapted from Brandi et. al

Combination Therapy	Progression-Free Survival (PFS)*	Overall Survival (OS)*	Disease Control Rate (DCR)*	Objective Response Rate (ORR)*	Phase	Study Name
TACE + Pemrolizumab	8.95 months	33.5 months	Not reported	53%	Ib	PETAL[2]
TACE + Sintilimab	8.4 months	Not yet reached	95.0% (76.4 to 99.1)	60% (38.7% to 78.1%)	II	Li et al.[3]
TACE + radiotherapy + Avelumumab	14.9 months (8.2–21.6)	23.7 months (15.2–32.2)	85% (69–95%)	73% (55–87%)	II	START-FIT[1]
TARE + Pemrolizumab	9.95 months (4.14-15.24)	27.30 months (10.15-39.52)	84.6% (65.1-95.6)	30.8% (14.3-51.8)	II	HCRN GI15-225[5]

Table 1, Summary of Preliminary Trials
***outcomes according to mRESIST criteria**

RESULTS

The studies reviewed were either phase I or II trials on patients with unresectable HCC, all of which yielded improved outcomes after combination therapy. The studies reported similar safety profiles as the monotherapies, reporting mostly manageable gastrointestinal side effects[1-5]

CONCLUSIONS

Thus far, early prospective studies in patients with intermediate to advanced-stage HCC have demonstrated improved survival using a combination approach as opposed to TACE or TARE monotherapy. However, this treatment combination needs to be investigated in later phase studies before informing clinical practice.

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