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TACE with Locally Injected Immunotherapy for Hepatocellular Carcinoma: An Area of Untapped Potential

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BACKGROUND

- Systemic administration has typically been the preferred route for immunotherapies.
- Numerous early-stage trials have examined the synergistic effect of transarterial chemo-embolization (TACE) and systemic immunotherapy as a treatment regimen for Hepatocellular Carcinoma (HCC).
- Local Immunotherapy may offer potential advantages.
  - Minimizing systemic toxicity
  - Increasing local bioavailability

PURPOSE

Trials augmenting TACE with locally administered immunotherapy are limited. This review will examine these preliminary trials, investigating their potential for clinical use.

LITERATURE

Combining TACE and local delivery of TLR9 – termed (TACIE)[2]

- Rat models showed robust tumor regression in the transcatheter arterial chemo-immuno-embolization (TACIE) group compared to TACE alone.
- Relative tumor volume compared to baseline was **341.8 ± 115.4%** in the TACE group and **79.4 ± 49.5%** in TACIE group ($p < 0.01$)
- TACIE group had **favorable safety profile with minimal adverse effects**

TACE combined with Dendritic Cell (DC) Vaccine[1]

- 48 participants were randomized to receive either TACE plus preconditioning cyclophosphamide or TACE plus preconditioning cyclophosphamide and DC infusions.
- Local action was ensured by pulsating a dendritic cell (DC) vaccine with tumor lysate of the HepG2 cell line, allowing the DCs to hone only to the liver and function primarily against tumor antigens.

Outcome	TACE + Cyclophosphamide + DC Vaccination	TACE + Cyclophosphamide (Control)
Median Progression-Free Survival (PFS)	18.6 months	10.4 months
Median Overall Survival (OS)	25.7 months	21.5 months
Overall Response Rate (mRECIST)	75%	54%
Disease Control Rate (mRECIST)	88%	67%

Table 1, Treatment Outcomes[1]

TACE followed by intraarterial sintilimab and bevacizumab[4]

- Phase II study using local administration of a PD-L1 inhibitor and VEGF inhibitor in advanced HCC.
- Showed promising efficacy/safety with 29 patients.

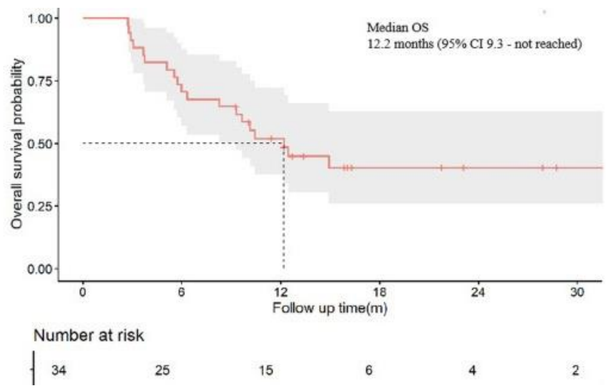

Figure 1, Kaplan-Meier Curve of Overall Survival, adapted from Mu et al.

CONCLUSIONS

Locally administered immunotherapy has proven to be an effective adjuvant to TACE in preclinical and early clinical trials. The next step would be comparing this method with systemic administration as a combination therapy with TACE.

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