Targeted Immuno Infiltration: Catheter Directed Delivery Awakens the Tumor Microenvironment

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Purpose

- Catheter-directed immunotherapy (CDIT) is an evolving approach in interventional oncology that enables locoregional delivery of immunomodulatory agents directly into the tumor microenvironment.
- CDIT leverages minimally invasive catheter techniques while limiting systemic exposure.
- Explored current advances in CDIT, emphasizing technological innovations, biologic rationale, and integration with multimodal oncologic strategies.

Materials & Methods

- A systematic review of PubMed-indexed studies was conducted, focusing on preclinical models, early-phase clinical trials, and translational reports evaluating catheter-directed delivery of immune checkpoint inhibitors, cytokines, and adoptive cellular therapies.
- Therapeutic platforms, including nanoparticles, as well as procedural techniques involving arterial infusion were examined.
- Outcomes assessed included immune response modulation, safety, and feasibility.

Results

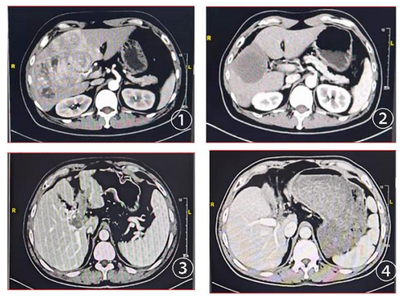

Figure 1: CT scans at baseline and after treatment assessment for two advanced patients with HCC treated with HAIC combined lenvatinib and PD-1. (1) Baseline CT scans of the first patient; (2) CT scans of the first patient after two cycles of the combined treatment; (3) baseline CT scans of the second patient with portal vein tumor thrombus; (4) the portal vein tumor thrombus disappeared after the combined treatment.

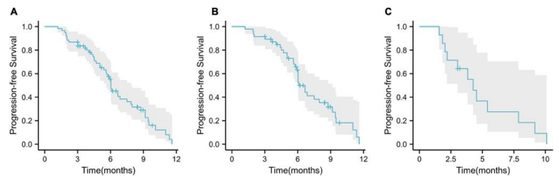

Figure 2: Kaplan–Meier curves for progression-free survival. (A) Overall population progression-free survival; (B) progression-free survival in first-line patients; (C) progression-free survival in second-line patients.

- In advanced hepatocellular carcinoma (HCC), hepatic arterial infusion of PD-1 inhibitors combined with lenvatinib and chemotherapy achieved an objective response rate (ORR) of 36.1% by RECIST and 57.4% by mRECIST.[1]
- Adverse events were predominantly grade 1–2; grade greater than or equal to three events occurred in 8.5% of patients, most commonly hypertension and transaminase elevation.[1]
- In a phase I trial, intratumoral delivery of the TLR9 agonist cavrotolimod in combination with systemic checkpoint inhibitors induced robust dendritic cell activation and enhanced CD8+ T-cell infiltration, with minimal systemic toxicity.[2]
- Additionally, a tumor microenvironment-based gene expression classifier (TMEscore) outperformed PD-L1 combined positive score in predicting checkpoint inhibitor response in advanced gastric cancer (AUC = 0.891 vs. 0.817, $p < 0.001$).[3]

Conclusions

- Catheter-directed immunotherapy represents a promising frontier to potentiate localized immune responses while mitigating systemic adverse effects.
- Advances in immunobiology, delivery technologies, and image guidance are rapidly expanding the potential of this approach.
- Further well-designed clinical trials are required to establish optimal protocols, dosing strategies, and tumor-specific indications.

References

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