Tumor Infiltration and Cytokine Biomarkers of Prostate Stem Cell Antigen (PSCA)-Directed GoCAR-T® Cells in Patients with Advanced Pancreatic Tumors

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Background

GoCAR-T is a novel off-the-shelf CAR-T cell therapy specifically designed to address unmet needs in solid tumors. By harnessing the natural immune system and engaging T cells within tumors, GoCAR-T enables effective intra-tumoral infiltration, persistence, and cytokine production to boost CAR-T performance.

Methods

We conducted a phase 1 trial in patients with advanced, metastatic, or inoperable pancreatic cancer who were treated with GoCAR-T cells. The primary endpoints were safety and response to treatment. We assessed infiltration, T cell persistence, and cytokine biomarkers.

Results

GoCAR-T cells exhibited enhanced survival and persistence up to 9 months. A subset of patients achieved partial or complete tumor responses. Intratumoral infiltration was observed in all patients, with the highest intensity of CAR staining in patient 5B-5, who also had the highest number of infiltrating CAR+ T cells.

Conclusion

GoCAR-T cells offer a promising strategy for the treatment of advanced pancreatic cancer by effectively infiltrating and persisting within tumors, leading to improved efficacy. Further research is needed to optimize CAR design and enhance clinical outcomes.

References


GoCAR-T Cells Infiltrated Tumor Metastases

- **Patient 5A**: Tumor-intrinsic factors include high expression of HLA-DRB5, HLA-DQA1, and P4HA2. Upregulated genes include CCL5, CCL8, GBP4, and LAMC2.

- **Patient 5B**: Tumor-intrinsic factors include high expression of LILRA3, LAMC2, and ARG1. Upregulated genes include CCL3/L1, SPP1, and LAMC2.

Differential Gene Expression in Tumor Microenvironment

- **NLRP3**: Inflamed and activated macrophages were observed in all patients, with increased expression of inflammasome components.

- **IL17A**: Expression was associated with the presence of Th17 proinflammatory cells, contributing to tumor progression.

Conclusions

- GoCAR-T cells infiltrated and persisted within tumors, consistent with the phase 1 trial data.

- The expression of tumor-intrinsic factors and upregulated genes suggests a complex interplay of immune cell infiltration and cytokine production, potentially influencing tumor response.

- Future studies should focus on optimizing CAR design and enhancing immune responses to maximize clinical efficacy.