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Editorial

CAR T Cell Therapy: A New Weapon to Fight Bladder Cancer

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HIGHLIGHTS

- CAR-T cell therapy as a super promising immunotherapy approach has opened new gates for the treatment of cancers.
- Despite the challenges of this method in the treatment of solid cancers such as bladder cancer, there is still an attempt to smooth the way.
- CAR-based therapies for bladder cancers have entered the clinical trials and could be the future for treating this type of cancer if the challenges are overcome.

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ABSTRACT

It has been a while since chimeric antigen receptor (CAR)-T cell therapy was introduced as an attractive immunotherapeutic approach to fighting cancer. Despite the remarkable success of this approach in treating blood malignancies such as acute lymphoblastic leukemia (ALL), treatment of solid cancers such as bladder cancer still has many challenges and problems. This work highlights CAR-based cell therapy's preclinical and clinical studies in bladder cancer, their successes, and the challenges involved in translating this procedure into the clinic.

Keywords: CAR-T Cell Therapy; Bladder Cancer; Immunotherapy; Clinical Trials

Editorial: It has been ten years since Emily Whitehead (the first child in the world who received engineered T cells) was cancer-free. The girl who lived thanks to CAR-T cell therapy.

CAR T-cell therapy is a brilliant immunotherapy approach in which a patient's T cells are harvested from the body and genetically engineered to express a chimeric antigen receptor against a tumor-associated or tumor-specific antigen. These cells are then returned to the patient's body to attack cancer cells and eradicate them. This method was first used to treat ALL and had promising results (1). To date, the FDA has approved five CAR T-cell products, all of which are for blood malignancies. This treatment generally has more favorable effects on liquid tumors than solid ones. Solid tumors are highly resistant to this treatment due to their complex organization (acidic and hypoxic core) and the establishment of an immunosuppressive niche. A tremendous amount of research has been done and continues to be done to overcome the challenges of CAR-T cell therapy in solid cancers. So far, no CAR-T cell-based therapy product has been approved by the

Table 1. Clinical trials of CAR-based immunotherapies for bladder cancer

Trial Number	Status	Phase	Cell type	Antigenes
NCT03185486	Unknown	I/II	T lymphocyte	PSMA, FRa
NCT03960060	Active, not recruiting	I	T lymphocyte	ROR2
NCT03740256	Recruiting	I	T lymphocyte	HER2
NCT04660939	Recruiting	I	Macrophage	HER2

FDA, but many clinical trials are underway, and the number is growing.

Bladder cancer, the second most common urological malignancy in terms of prevalence and mortality, does not fully respond to standard treatments such as surgery, chemotherapy, radiotherapy, and immunotherapy with bacillus calmette-guérin (BCG). Therefore, there is still a demand for new and more effective treatments for bladder cancer, and CAR-T cell therapy can be one of the best options for this purpose.

Preclinical studies of T cell therapy for bladder cancer have shown that this immunotherapy can effectively treat bladder cancer. In a study by Grunewald et al., The effect of combining CAR T cells against Human EGFR and CD44V6 with Decitabine (a DNA methyltransferase inhibitor) was investigated. Their results showed that T cells could kill bladder cancer cells, and this cytotoxic effect was enhanced by adding Decitabine (2).

CAR-T cells can be helpful in personal medicine to overcome the heterogeneity and genetic instability of bladder cancer. In a study by Yu et al., The effect of CAR-T cells against MUC1 antigen on patient-derived bladder cancer organoids was investigated. CAR-T cells could identify tumor cells and destroy them (3).

To date, 4 CAR-dependent immunotherapy clinical trials for bladder cancer have been reported in early stages (according to Clinicaltrials.gov). In these trials, T lymphocytes and macrophages were used as CAR carriers (Table 1).

Conclusions

CAR-T cell therapy could be an excellent candidate for fighting bladder cancer in the future by overcoming the challenges of this approach in solid tumors such as on-target off-tumor toxicity, cytokine release syndrome (CRS), graft versus host disease (GVHD) and antigen escaping.

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Ethics statement

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Data availability

None.

Abbreviations

ALL	Acute lymphoblastic leukemia
BCG	Bacillus calmette-guérin
CAR	Chimeric antigen receptor
CRS	Cytokine release syndrome
GVHD	Graft versus host disease

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Author (s) biosketches

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