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Abstract Title : IMV101, a novel CD19-targeted In Vivo CAR T therapy exhibits potent efficacy and tolerable safety profiles in preclinical models

Category: 700s - Transplantation and Adoptive Cell Therapies

Review Category: 702. CAR-T Cell Therapies: Basic and Translational

Authors

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Abstract Body

Background: Autologous CD19 CAR-T cell therapy has shown remarkable efficacy in B-cell hematologic malignancies, yet its widespread application is constrained by prolonged manufacturing time, complex processes, and high costs. To address these challenges, we developed IMV101, a novel lentiviral vector pseudotyped with a mutated MxV glycoprotein and integrated with a T cell targeting module TCM3, enabling selective transduction of T cells and generating CD19-targeted CAR-T cells in vivo. In this study, we systematically evaluated the in vitro and in vivo properties of IMV101 to support its future development.

Methods: The T cell specificity of IMV101 was tested using in vitro transduction assays with various cell lines. In vitro cytotoxicity was assessed by co-culturing IMV101 or control virus transduced T cells with CD19+ cancer cells at various effector-to-target ratios, cytokine secretion were also analyzed following target cell stimulation. In vivo efficacy was investigated in immunocompromise mice engrafted with Nalm6-Luc tumor cells, following immune reconstitution with either human PBMCs or CD34+ hematopoietic stem cells. Biodistribution, pharmacokinetics of IMV101 virus or IMV101 transduced cells were detected at various timepoint post virus injections.

Results: In our study, IMV101 showed efficient T cell transduction at series titers with minimal infection of B cell derived cancer cell line. Moreover, IMV101 showed negligible infection in various primary epithelial cells and tumor cell lines, indicating high target specificity. In vitro, IMV101 transduced T cells can effectively eliminated CD19+ tumor cells in a dose-dependent manner and secreted effector cytokines (IL-2, IFN-γ, TNF-α) upon target cell recognition without IL-6 or IL-10 production. In Nalm6-Luc xenografted M-NSG mouse models, IMV101 significantly inhibited tumor growth across all doses ($1\sim25\times10^6$ TU/mice). Following IMV101 administration, robust CAR-T cell expansion was observed in peripheral blood, reaching a Cmax of about 2×10^5 CAR-T cells/mL between days 13 and 21, and then declined in parallel with tumor regression. In immunocompetent, non–tumor-bearing mice, biodistribution studies revealed that virus particles were confined to the spleen 24 hours post-dosing and were undetectable in any tissues been tested at day 7, including bone marrow, spleen, heart, lung, kidney, ovary, stomach, pancreas, intestine, lymph node and tumors. Tissue distribution using IMV101-CD19-GFP confirmed predominant expression of GFP in spleen/lymph nodes, with low levels of GFP in the liver which was not accompanied with increased liver enzymes. Further multi-color immunohistochemistry assay revealed that the GFP expression was predominantly colocalized with human T cells and, to a lesser extent, with murine splenic macrophages, indicating T-cell–specific transduction of IMV101 in vivo and phagocytosis of the viral particles.

Conclusions: IMV101 demonstrates high specificity of T cells transduction, potent *in vitro* and *in vivo* anti-tumor activity, effective expansion in peripheral blood of the in vivo generated CAR-T and a favorable safety profile in murine models. This comprehensive data supports its further clinical development for both B cell malignancies and autoimmune disease.

Keywords: Translational Research, Research

Disclosure : None declared