

Allogeneic CAR-T Therapy Technologies: Has the Promise Been Met?

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Abstract

This last decade, chimeric antigen receptor (CAR) T-cell therapy has become a real treatment option for patients with B-cell malignancies, while multiple efforts are being made to extend this therapy to other malignancies and broader patient populations. However, several limitations remain, including those associated with the time-consuming and highly personalized manufacturing of autologous CAR-Ts. Technologies to establish “off-the-shelf” allogeneic CAR-Ts with low alloreactivity are currently being developed, with a strong focus on gene-editing technologies. Although these technologies have many advantages, they have also strong limitations, including double-strand breaks in the DNA with multiple associated safety risks as well as the lack of modulation. As an alternative, non-gene-editing technologies provide an interesting approach to support the development of allogeneic CAR-Ts in the future, with possibilities of fine-tuning gene expression and easy development. Here, we will review the different ways allogeneic CAR-Ts can be manufactured and discuss which technologies are currently used. The biggest hurdles for successful therapy of allogeneic CAR-Ts will be summarized, and finally, an overview of the current clinical evidence for allogeneic CAR-Ts in comparison to its autologous counterpart will be given.

Keywords: allogeneic; chimeric antigen receptor; off-the-shelf; gene editing

