Overcoming ex vivo cell therapy manufacturing challenges through an in vivo lentiviral platform

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Introduction

Ex vivo CAR T-cell therapies have shown significant clinical success in treating hematological cancers. However, access to these life saving therapeutics has been severely limited due to the critical challenges in supply chain and manufacturing. Significant capital investments and costly overhead are required to produce these products, driving the cost to unattainable levels. With almost 200,000 new blood cancer diagnoses per year in the US,1 demand for life saving CAR T-cell therapies will undoubtedly continue to grow to levels unachievable with the current ex vivo manufacturing platforms and strategies, and skilled administration requirements. Umoja is pioneering a transformative in vivo CAR T-cell platform that would mitigate these challenges associated with ex vivo therapies, by using a universal, off-the-shelf, direct injection lentiviral vector to harness the patient’s own immune system to create cancer targeting CAR T-cells in vivo, thereby removing the complex ex vivo CAR T-cell generation.

Discussion

Eliminating the ex vivo CAR T-cell generation through use of Umoja’s in vivo lentiviral vector has significant advantages to the patient, including immediate, on-demand treatment and no harsh, lymphodepleting chemotherapy is required. The lentiviral vector can be made and stocked in hospitals well in advance to ensure rapid treatment.

Further, the in vivo lentivector manufacturing process uses a more consistent start cell line as compared to variable patient cells in ex vivo autologous and allogeneic donor cell therapies, meaning fewer and less complex manufacturing processes more similar to that of an efficient therapeutic. In addition to a more reliable supply chain, each batch of off-the-shelf CAR T-cell platform not only disrupts the ex vivo CAR T-cell therapy from lentiviral production to treatment, which allows for immediate treatment.

To highlight the advantages of Umoja’s in vivo CAR T-cell therapies over ex vivo autologous or allogeneic CAR T-cell therapies in the below areas:

1. Expediting treatment for critically ill patients
2. Decouples batch failure from patient outcomes
3. Reducing supply chain, process, storage, and distribution complexity
4. Reducing cost through batch scale up to thousands of doses

Figure 1: The difference in time to treatment between autologous and allogeneic ex vivo vs. in vivo CAR T-cell therapies. 2,3

Figure 2: The number of patients that can be treated per batch using current platforms for ex vivo autologous and allogeneic therapies vs. Umoja’s in vivo CAR T-cell therapy.4,5

Conclusions

1. In vivo CAR T-cell, direct injection lentivirus therapies can be manufactured prior to diagnosis and do not require harsh, lymphodepleting chemo prior to administration, which allows for immediate treatment.
2. The lentivirus production process is much faster and less complex than ex vivo CAR T-cell therapies and are more scalable; potentially creating enough doses to treat thousands of patients per batch instead of just one or hundreds.
3. The lentiviral drug product can be more easily and widely distributed on dry ice instead of the liquid nitrogen required for cell therapies, reaching a larger percentage of the population.

References: