Get full control of your T cell isolation for your CAR T cell therapy manufacturing

Marine de Lageneste[1], Melissa Maggioni[1], Genna Luciani[2], Meerah Vijeyakumaran[3] and Debalina Basak[3]

1) Cytiva, Switzerland; 2) Cytiva, Canada; 3) Centre of Commercialization of Regenerative Medicine, Canada

Introduction

Cell therapies offer potential treatments for currently untreatable malignancies. Approaches such as chimeric antigen receptor (CAR) T cell therapies are being evaluated in numerous clinical trials with a number of them emerging as approved therapies, particularly in hematological tumors. Due to the growing numbers of these therapies and the complex workflow required to produce them, additional tools are needed to produce a consistent product in a closed, automated process. The Sefia Select™ cell processing system is a functionally closed instrument that was developed to enable automation of different processing steps within the CAR T cell workflow. MagnetSelect is an expanded offering for the Sefia Select system to enable magnetic T cell isolation to provide greater automation potential in the cell therapy process.

MagnetSelect application

In this study, we focus on the first part of the CAR T cell workflow: the automated magnetic isolation of CD4/CD8+ cells from fresh or frozen leukapheresis using MagnetSelect application and CT-400.1 single-use kit on the Sefia Select cell processing system (Fig 2).

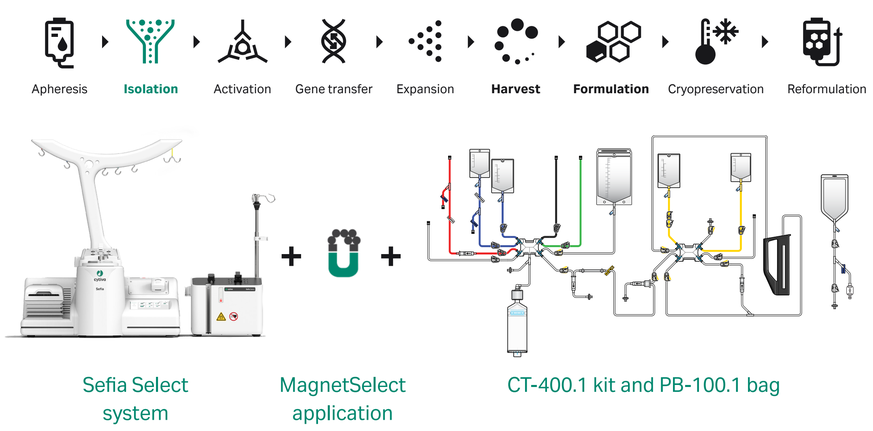

Fig 2. Sefia Select system, MagnetSelect application, CT-400.1 single-use kit and, PB-100.1 processing bag.

MagnetSelect is a modular application composed of different optional phases, schematically represented in Figure 3. During the magnetic isolation step, the user can select a single or serial isolation depending of input material composition.

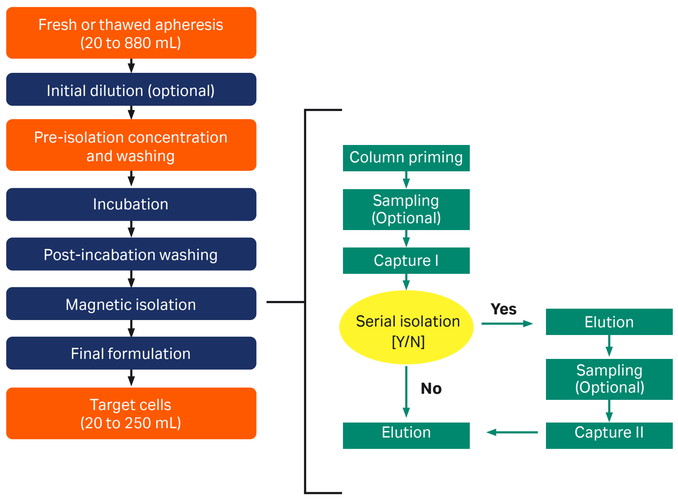

Fig 3. MagnetSelect application workflow.

The table below summarizes the initial products tested to generate results as well as application workflow used for each scenario.

Scenario	Description	Cell composition	Application recommendation
1	Fresh healthy leukapheresis		Single isolation
2	Frozen healthy leukapheresis	*See* Figure 5	Dilution + single isolation
3	Patient model		Serial isolation

Figure 4 below represents the average total viable cells (TVC) in initial products from each scenario that was used to generate results using the MagnetSelect application.

TVC in input product

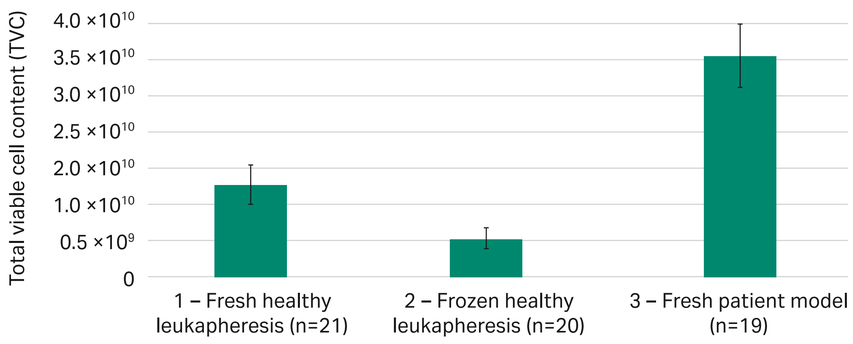

Fig 4. Average TVC in input products tested.

The autologous CAR T cell workflow

The autologous CAR T cell manufacturing process is composed of different steps starting with a leukapheresis unit collected from patients (Fig 1). Frozen leukapheresis units are thawed, diluted, and washed before moving to the next step. The cell isolation step can correspond to peripheral blood mononuclear cells (PBMC) enrichment or to T cell selection via magnetic beads. After cell isolation, selective activation, viral-based transduction, and large-scale bioreactor expansion are performed to reach the appropriate cell amount. The cells are harvested by concentrating, washing, and diluting the cells with different solutions including cryoprotectant and finally split into several doses. CAR T cell doses are cryopreserved to be shipped and injected into the patient.

The Sefia Select system allows you to automate multiple steps of the CAR T cell workflow, thanks to the use of different applications.

Here we show the results obtained using the new MagnetSelect application as an automated solution for initial product dilution and for subsequent magnetic T cell isolation from different types of initial cellular products.

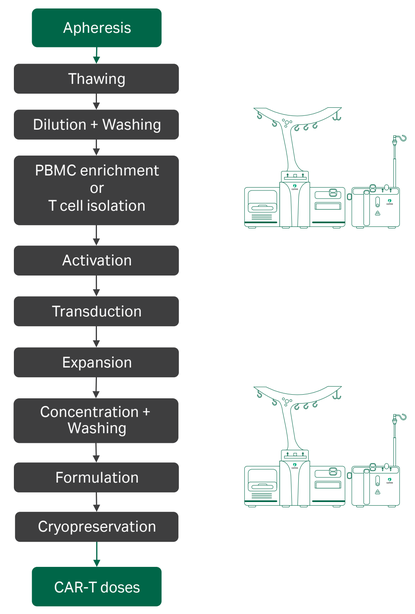

Fig 1. Autologous CAR T cell workflow.

Results

Initial product phenotypes

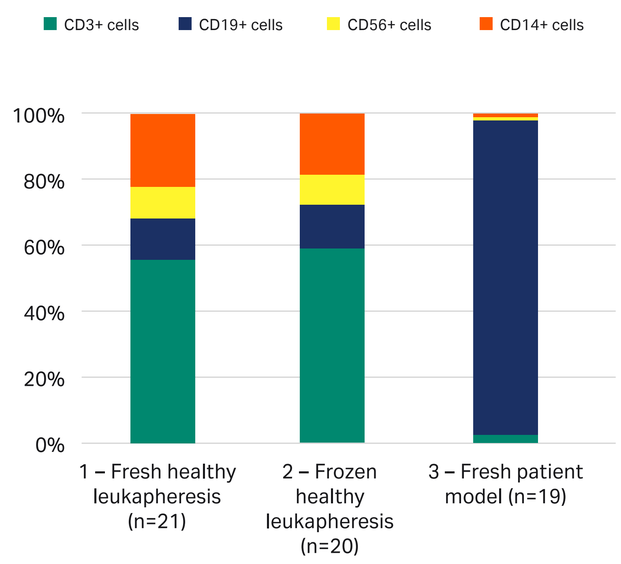

Fig 5. Cell composition of initial products tested pre MagnetSelect application.

Final product phenotypes

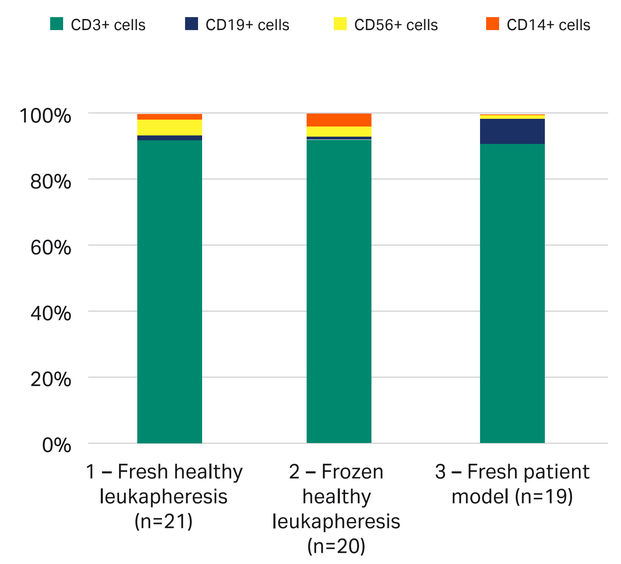

Fig 6. Cell composition of final products post MagnetSelect.

Performances post MagnetSelect

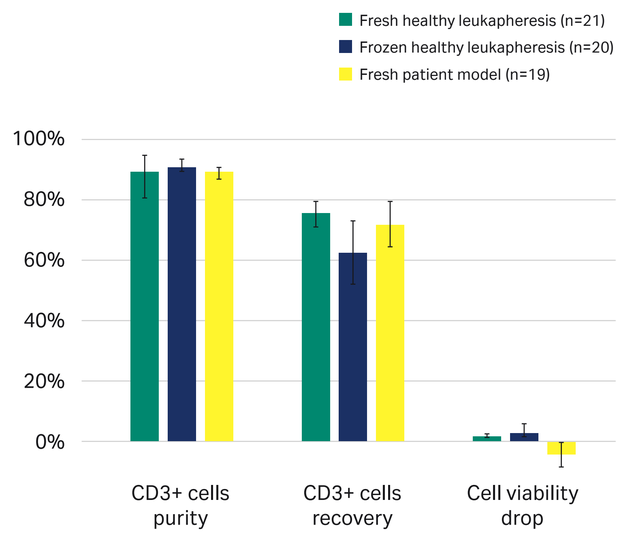

Fig 7. Performances obtained for each scenario post MagnetSelect.

Total duration MagnetSelect

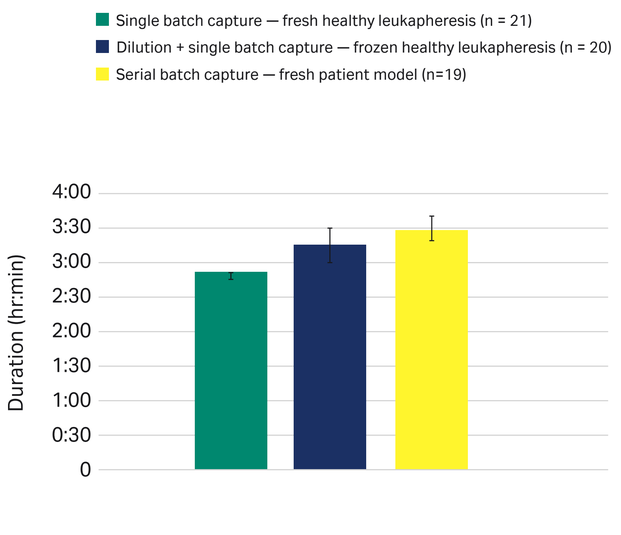

Fig 8. Total duration of MagnetSelect application depending of workflow selected.

Conclusions

We have shown that the MagnetSelect application:

- Is a fully automated magnetic T cell isolation solution for both fresh and frozen initial products.
- Allows reproducible T cell isolation with high purity and recovery, independent of the composition of the initial product.
- Can accommodate a variety of initial products thanks to the flexibility in the parameter setting that can be adapted in relation to the type and composition of the initial product to process

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CY40982-15Jan24-PO