Cell Collection & Cellular Starting Materials Considerations
June 14, 2023

Q: How can CAR-T developers and collection centers collaborate to ensure good product quality for the patients?

A: The most important thing developers and collections centers can do to effectively collaborate is to communicate transparently. It is important for the manufacturer to effectively share what cellular products they want in the bag and what products should be minimized. This includes not only the absolute count of target cells but tolerance for off-target cells like red blood cells and granulocytes.

Additionally, one of the most impactful ways we can ensure the best starting material for drug manufacture is obtained is through sharing of collected product outcome data. If the Apheresis center is not permitted to draw a sample of the final collected product prior to shipment, they have no idea if they met the product criteria for manufacture. If Apheresis providers understand "what is in the bag", they can adjust upcoming collections to optimize target cell collection. This is a relatively new therapy for the medical field with new connections between these stakeholders; transparent and standard communication is key to making lasting improvements.

Q: The industry believes there will be a trend toward 'standardized' source material. Could you comment on what standardization looks like for apheresis: what is already standardized, what can / cannot be standardized?

A: There needs to be a working definition in the industry for "standardized" source material. Providing concrete, collaborative definitions is a place to start. For example, when we talk about standardizing source material, are we referring to defining the percent allowable red cell content, percent platelet content in the collected product, or both? Or are we referring to standardizing the collection procedure using patient/donor pre-procedure cell counts (optimally flow cytometry) to guide processing volumes for that specific collection scenario? The standard use of prediction algorithms via pre-counts is present at many collection sites but has not yet reached industry-wide adoption. This is potentially because there has not been enough support at apheresis centers to adapt to all the requirements such therapies bring to the apheresis landscape.

Similar obstacles exist on the manufacturing side as well. It is difficult to standardize apheresis starting materials (even loosely) when some manufacturers detail very specific cell populations and absolute counts and others require collection of "as many MNCs as you can". Yet there is inherent difficulty in tight standardization as the Spectra Optia is meant to be configurable to the inherent variability of heterogenous patient and donor populations requiring apheresis. Everything from disease status, effects of previous therapies, vascular access needs, and emotional acceptance of the procedure can have a huge impact on the overall collection outcome. Each collection procedure requires different instrument adjustments based on how the patient's individual blood reacts when in the circuit. It is critical that we define and operationalize "standardization" so that the efforts eventually bring optimal outcomes for patients.

Q: As autologous cell therapies become earlier (1st and 2nd line) treatments, how does this change the technical considerations and /or patient preparation during the apheresis process?

A: This is a great question and at this time we do not have sufficient objective data to support our answer, BUT it stands to reason that we should see a collection process that is able to be completed not only in a shorter time frame but also with easier collection of the target cells. Patients in later stages of treatment have often been through many different treatments with drugs/complications (i.e., sepsis) that can affect the availability of the target cell in the peripheral blood. And while we have good information about how certain drugs impair that availability in the hematologic cancer space, we do not have sufficient information for other disease indications. Patient populations that can benefit from autologous cell therapies are changing and the effects of their disease status, prior therapies, as well as prior complications require that we capture this data to become informed.

In addition, when we discuss technical considerations, we need to consider how first line autologous cell therapies may impact current apheresis resources. Apheresis is a unique sub-specialty requiring specific training and expertise. If autologous therapies move to first line, how will this impact the hospital apheresis program? Would adoption of community collection sites be the way to support access to front-line hospital apheresis programs? We feel there is still a lot of practical and technical considerations that need to be explored collaboratively.

Q: When you describe the patient population for the buffy coat, are you referring to autologous CAR T?

A: The differences in the buffy coat slide were meant to refer to a patient or donor who has been mobilized versus a patient or donor who was not mobilized. Information we have about the differences in buffy coat separation is based on autologous CAR-T collections. However, the same principle applies to allogeneic CAR-T collections from un-mobilized donors. They will have a thinner buffy coat after separation because they have not received mobilization as a stem cell donor/patient have and there are not as many immune cells available for the device to collect.

Q: Are there challenges widely shared by cell therapy developers that apheresis centers and Terumo might collaborate with interested developers to address & minimize?

A: Yes, we have been involved with many cell therapy developers and apheresis centers to address or minimize issues with starting materials. We have a few case studies that we can share to show how this collaboration has improved starting material, helped developers get the cells they need, and helped apheresis operators optimize the instrument and decreased collection days.