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A CAR-T bottleneck: Centers that collect patient cells feel crunch from growing demand

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The arrival of CAR-T cancer treatments and the expected coming age of cell therapies are opening new frontiers for what medicines look like: Cells are taken from patients, then tweaked or supercharged in a lab, and finally given back to patients.

But the emergence of those treatments has put a pinch on the places that collect those cells from patients. The crunch is only expected to grow as more CAR-T candidates and other cell therapies enter clinical trials and win approval.

These facilities, called apheresis centers, have already seen a spike in the number of patients coming through their doors with the first two CAR-T products on the market, in some cases forcing cancer patients to have to wait several days for a slot. Adding to the burden, center directors say, is that each company with a product or experimental therapy insists on performing its own audit to ensure its collection protocols are followed.

At Memorial Sloan Kettering Cancer Center in New York, where there isn't much room for the apheresis center to grow, it has instead added staff — mostly nurses and technicians — and expanded the hours it is open, said Dr. Miguel-Angel Perales, the deputy chief of the adult bone marrow transplantation service.

"In Manhattan, you can't just say you're going to add 10 chairs for apheresis," Perales said. "You can't just have them line up on First Avenue."

The University of Pennsylvania is also planning on hiring more staff "to handle the increased volume in the research setting and in the clinical setting," said Dr. David Porter, the director of cell therapy and transplantation.

Other centers said they haven't had to add staff or hours yet, but are anticipating a further strain on their resources. Company audits alone can take up days of staff time for paperwork and visits to monitor processes that center staff say are in many ways the same across therapies.

Staff at apheresis centers and their attached labs have had to show several times, for example, that they know how to open the boxes used to ship cells.

"We're auditing the same process again and again," said Heather Steinmetz, the quality assurance manager for UCLA's program.

Center directors are trying to figure out whether and how they can streamline the industry auditing process, leaving them more time to serve patients. One idea: give a central body the authority to audit the centers on behalf of all the companies, checking that they understand the common steps among the products and helping them navigate the nuances that do exist between treatments.

"It's very frustrating to have to be trained and retrained on the same thing, but you have to be retrained because it's a different company," Porter said. While there are some differences among the different companies' products and procedures, Porter said, "having to get approved independently for each product has been very intensive."

Apheresis centers have for years been where hospitals collect bone marrow stem cells to transplant into patients with blood cancers. More recently, as CAR-T therapies entered trials and the first two became approved, the centers have used their collection machines to stockpile patients' T cells — the immune cells that are modified and reintroduced to the body in massive numbers as part of the treatment.

The machines draw the patient's blood out through one tube, separate the target cells, and then return the rest of the blood and its components back to the patient through another line — like a high-tech version of panning for gold.

Then those cells are shipped off to the biopharma companies' manufacturing facilities, where they are engineered to bolster their cancer-attacking powers, and then returned to hospitals to be re-infused back into patients.

The group aiming to become the central auditor is a nonprofit called Be the Match BioTherapies, a subsidiary of Be the Match, which runs the country's bone marrow donor registry and facilitates marrow transplants. The biotherapies group was started in 2016 as executives saw that the apheresis centers and cell laboratories they had been working with for decades were anticipating the advent of cell therapies. (Perales and Porter are both on the board of Be the Match.)

Be the Match BioTherapies envisions standardizing the gathering of cells for therapies as much as possible while preserving what it calls the biopharma companies' "secret sauce" — the steps that are and have to be unique to their treatments. It could also train apheresis centers' staffs how to manage those differences so they're not left to decipher each company's to-do list on their own.

Some of the distinctions are clear — whereas one company requires the cells to be shipped to the manufacturing site frozen, another one stipulates that the cells be sent fresh. But others are more subtle — a matter of just how many cells need to be included in a collection, or how many and what kind of anticoagulants should be added to the cells so they don't clump together.

“Centers that have relied on us for 30 years can continue to rely on us for these therapies as well,” said Amy Hines, the director of collection networks at Be the Match BioTherapies.

Hines said her group has been talking with cell therapy companies and that they are coming around to the idea that there has to be a more efficient way to conduct audits.

“What I’m hearing from centers and from some of the companies is that everyone has come at this from their own angle, but now transplant and apheresis centers are saying, ‘Wait, wait, wait,’” she said. “And that’s caused companies to look at it differently.”

The question remains whether companies will actually get on board. They might not trust an outside group to ensure that the procedures at apheresis centers are up to their standards and those required of them by regulators. In statements, Novartis and Gilead — the two companies with approved CAR-T treatments — didn’t indicate much enthusiasm for a general auditing process.

“We continue to look for ways of improving our quality and processes,” the Novartis statement said.

“We are learning from our early experience,” Gilead spokesman Nathan Kaiser said. “We will continue to look for ways to improve efficiency while also ensuring patient safety and product quality and meeting FDA requirements