Expert perspective: NAVNEET MAJHAIL, MD

Clinical trial recruitment faces new challenges as CGT market matures

Less than a decade after the first cell and gene therapies (CGTs) were approved by the FDA, the treatment landscape has fundamentally shifted. Patients who have had few or no medicines to treat serious and life-threatening conditions can now choose between commercially available drugs or a range of clinical trials with new treatments.

This evolution presents new challenges for biopharma companies trying to recruit patients and sites for clinical trials. At Sarah Cannon Cancer Network, which operates one of the largest cell and gene therapy programs in the country, the shift is dramatic, said Navneet Majhail, MD, Physician-in-Chief of Blood Cancers at the organization. Through 2022, nearly three-quarters of patients receiving CAR T therapies were enrolled in clinical trials, which are supported by Sarah Cannon Research Institute, while one quarter were on commercial therapy. Today, that ratio has flipped.

The change reflects the success of the CAR T field in moving from experimental to standard care. But it also means companies developing new therapies must work harder to demonstrate why patients should choose an investigational treatment over proven alternatives.

For major cancer centers like Sarah Cannon, which performed more than 1,500 transplants and cell therapies last year, the challenge extends beyond patient recruitment to managing an increasingly broad portfolio of both clinical trials and commercial therapies, while ensuring that each patient gets the treatment that is best for them.

Barriers Standing in the Way

Majhail said there are four main categories of obstacles that compound the difficulty of running effective cell and gene therapy trials.

Patient-level barriers remain one of the most fundamental hurdles. Geographic distance to specialized centers, insurance coverage gaps, and socioeconomic factors create the same access problems that have long plagued clinical trials. But CGTs add layers of complexity.

"These CGTs are available at specialized centers with the right expertise, the infrastructure, the people, the capacity and everything else," Majhail said. "Sometimes people travel a couple of hours to get there for treatment, and if a trial requires you to come back every so often or live close by for a certain amount of time, there can be those geographic barriers."

The second challenge involves investigators themselves. Unlike traditional cancer trials where virtually any oncologist might enroll patients, CGTs require specialized expertise that is still relatively scarce, given the recent rapid growth of the CGT space.

"The way these therapies are and where they're heading, it'll be hard for just one person to know it all and do it well," Majhail said. "You need to have collaborative multidisciplinary teams that come together to offer these therapies collectively."

Health center capacity is the third bottleneck. Even experienced programs face constraints as they juggle increasing numbers of commercial treatments and competing clinical trials.

The fourth barrier involves the products themselves—manufacturing timelines, supply chain requirements, and slot availability that can add complexity, even when patients and treatment centers are prepared and willing.

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>
> **— Navneet Majhail, MD**
> *Physician-in-Chief of Blood Cancers at Sarah Cannon Cancer Network*

When Protocols Meet Reality

Majhail says there are often disconnects between how clinical trials are designed and how they work in practice that can make it more difficult to operate successfully. He points to examples where well-intentioned protocols create operational challenges for the centers trying to implement them.

"Sometimes these trials come through and we are like, you wrote this whole protocol, got it through FDA, but I'm not sure you had a cell therapy expert actually take a look at this and ask, 'is this even workable?'" Majhail said.

The problems range from basic logistics to patient experience. Some protocols specify product shipping or storage requirements that don't align with how hospitals actually handle cell therapies. Others demand that patients spend

many hours in clinic for outpatient procedures, which can deter some patients from signing up for a trial and present scheduling conflicts for hospital staff.

"You want to push something in the outpatient setting, but you're asking the patient to be there for 10 hours of the day. How do you make that work in a clinic?" Majhail said.

The disconnect becomes more costly as competition intensifies. Sites have limited capacity and multiple trial options, making operational feasibility a key factor in which studies they choose to support.

Building Trials That Work

Despite the challenges, Majhail said there are three key strategic approaches that can help CGT clinical trials succeed.

The foundation starts with assembling the right team at clinical sites. This goes beyond finding qualified investigators to building entire support structures that can handle the complexity of CGT trials.

"It's about the team—setting up the right team to both facilitate opening a trial, enrolling patients on them, and then supporting patients as they go through the process," Majhail said.

The second element involves fostering a research culture that views clinical trials as potentially the best treatment option for patients, not just an alternative when commercial therapies fail.

"You can open as many trials as you want, but if there's not a culture that facilitates or encourages looking at research clinical trials, which I think most of us agree is the best therapy for patients, then it's not going to happen," he said.

The third recommendation addresses the protocol design problems directly. Majhail urges companies to partner with experienced centers early in clinical development to ensure trials integrate smoothly into real-world workflows.

For companies entering the field, this means engaging with treatment centers not just as trial sites, but as partners in designing studies that can be implemented successfully.

The Autoimmune Challenge Ahead

As CGTs expand beyond cancer into broader areas, such as autoimmune disease, Majhail expects fundamentally different approaches to patient management and trial design will be required.

While cancer patients typically remain within oncology teams throughout their treatment journey, autoimmune patients will need coordination with rheumatologists, neurologists, and other specialists who haven't traditionally worked with cell therapy centers. It also means understanding that patients have different risk-value calculations to make. For example, side effects that cancer patients might accept as necessary trade-offs could carry different weight for autoimmune patients with well-controlled conditions.

"For many of our cancer patients, if you lose your hair, it's kind of almost expected as you go," Majhail said. "But to say to a young woman with lupus, you're going to lose your hair with this, but you've got these other therapies. I think these are some risk-benefit conversations that'll be very interesting in that setting."

Working Through Real-World Pain Points

As competition for clinical trial participants intensifies, Majhail's advice for the industry focuses on bridging the gap between laboratory innovation and clinical reality. Companies that understand operational challenges early will have advantages in recruiting both sites and patients.

This collaboration needs to start during protocol development, not after FDA approval.

"Working with experienced centers and people who've done this is important as you're trying to think about commercializing your therapy," he said. By working together to eliminate real world pain points for patients, physicians and treatment centers, "that gets everyone to a happy place." he said.

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