Understanding the Patient Experience and Potential Barriers to Enrollment and Participation in Cell and Gene Therapy (CGT) Trials in Acute Myeloid Leukemia (AML)

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Background

CGT represents a rapidly advancing field in the treatment of cancer. Unlike traditional therapeutic approaches, CGT involves intricate processes that manipulate cells or genes to treat or even cure diseases. These therapies can include modifying a patient's own cells, inserting new genetic material, or using viral vectors to deliver genetic material to target specific cancer cells.

CGT trials have been in development for decades, but their popularity has surged since 2010, driven by breakthroughs in CAR-T cell therapies and gene-editing technologies like CRISPR.[1,2] These advancements have revolutionized the treatment of hematologic malignancies. However, their logistical and biological complexities, coupled with rigorous follow-up requirements and regulatory mandates for long-term monitoring, make the patient experience different from traditional therapies or non-CGT investigational studies. As CGT trials demonstrate clinical activity, it is critical to understand and address the barriers faced by patients and the broader CGT community to optimize trial enrollment, improve retention, and ultimately facilitate the successful translation of these therapies into clinical practice.

Despite the growing number of CGT trials, barriers limiting patient access and participation remain underexplored, particularly given the relative novelty of these therapies. Early research in clinical trial access has primarily focused on traditional treatments, leaving a gap in understanding the unique challenges of CGT trials. These barriers may include staffing shortages, institutional constraints, patient-related concerns, and resource limitations—all of which may impact trial enrollment, retention, and overall accessibility.

Study Aim & Objectives

This study survey is designed to investigate the key barriers limiting patient access to CGT trials by evaluating challenges across four major domains:

- **Staffing Barriers**: Assessing workforce limitations and the capacity of clinical teams to educate and support patients.
- **Institutional Barriers**: Examining administrative burdens, eligibility criteria, infrastructure requirements, and site readiness.
- **Patient Barriers**: Understanding factors such as lack of awareness, emotional distress, safety concerns, financial burdens, ethical considerations and logistical challenges.
- **Resource Barriers**: Identifying funding constraints, insurance coverage limitations, and disparities in access to CGT trial sites.

Methods

Survey Design and Administration

A two-step multiple choice survey and interview was conducted to assess staffing, institutional, patient-related, and resource barriers to enrollment into CGT trials for hematologic malignancies.

An initial survey, consisting of 6 questions, was administered between July 2024 and September 2024 to 7 study coordinators at 7 academic centers. Additionally, interviews were conducted with 2 social workers who have experience working with leukemia patients, providing an early qualitative understanding of patient perspective on CGT trials and their related barriers.

Based on initial responses, the survey was expanded in January 2025 to a more comprehensive 32-question multiple choice and open response format. This revised survey was distributed to a broader cohort, including study coordinators, research nurses, advanced practice providers, and transplant providers at academic centers, as well as patient advocacy partners. The survey responders were selected from academic centers who have had experience working with CGT trials.

The expanded questionnaire aimed to capture a more detailed and multi-perspective understanding of enrollment barriers, including provider workload and staffing limitations, institutional resources, financial and logistical challenges, and patient-specific concerns. Demographic data was collected to analyze potential associations between professional roles, institutional characteristics, and perceived barriers.

Qualitative Interviews

To complement the survey findings, interviews were conducted with key stakeholders to explore nuanced perspectives on trial enrollment challenges. Between January 2025 and February 2025, interviews were conducted with 8 transplant providers, 2 study coordinators, 1 BMT research nurse practitioner, and 2 patient advocacy representatives.

Data Analysis

Survey data was analyzed using descriptive statistics to identify trends in staffing, institutional, patient, and resource barriers that were perceived to limit enrollment in CGT trials among the different professional roles. Comparative analyses were performed to examine differences in responses based on job role, institutional setting, and prior experience with cell and gene therapy trials.

Respondent Demographics

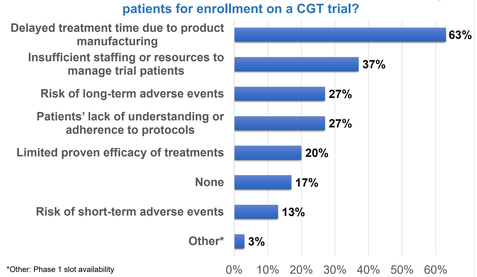
Table 1: Demographics Data of Survey Responders, Institution Type, and Cell & Gene Therapy Volume

Total Responders (n=30)							
Role	n	Years in Role	n	Expressed Role in CGT Trials			
Consenting provider	21	1-5 6-10 >10	5 4 12	Provide educational material, verify eligibility, lead informed consent discussion			
Study Coordinator	4	<1 1-5 6-10	1 2 1	Provide educational material, verify eligibility; lead informed consent discussions; coordinate/schedule trial activities			
Research Nurse	1	1-5	1	Provide educational material, coordinate/schedule trial activities			
Other (NP, trial navigator, medical director, no response)	4	1-5 >10	3 1	Provide educational material, verify eligibility; lead informed consent discussions; coordinate/schedule trial activities			
Geographic Region*		Allogeneic SCT Volume/yr		CAR-T Volume/yr**		Current Open Heme Malignancy CGT Trials	
Urban	25	<50 50-100 101-200 200+ Unsure	2 7 9 5 2	26-50 51-75 76-100 >100 Unsure	5 8 3 8 1	1-5 6-10 >10 Unsure	8 3 12 2
Suburban	4	101-200 200+	3 1	51-75 76-100 >100	1 1 2	6-10 >10	1 3

CAR-T: chimeric antigen receptor T-cell; NP: nurse practitioner; SCT: stem cell transplant
*geographic region not answered in one survey response; **CART volume includes commercial and investigations

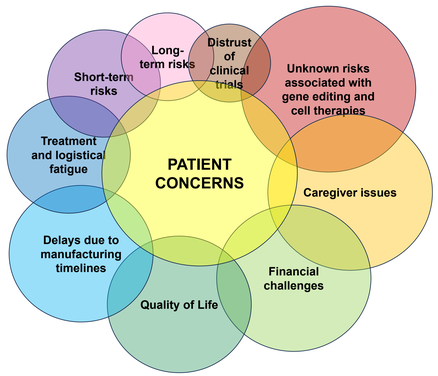
Results

What are the most common concerns you have when considering patients for enrollment on a CGT trial?

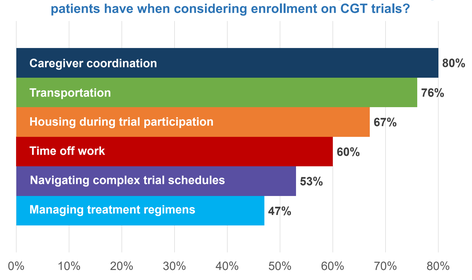


*Other: Phase 1 slot availability

What are the most common perceived or reported concerns patients have when considering enrollment on a CGT trial?



What are the most common perceived or reported logistical challenges patients have when considering enrollment on CGT trials?



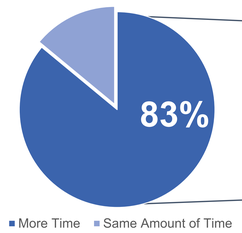
Does consenting a patient to a CGT trial take more, less, or the same amount of time when compared to a non-CGT trial?

83% of respondents reported CGT trials take more time to explain or consent than non-CGT trials

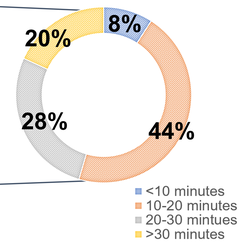
- Non-provider compared to provider respondents typically felt that it took more than 20+ minutes to explain CGT trials

93% of respondents reported that patients rely on discussions with the PI or site staff to help guide them through decisions regarding enrollment onto CGT trials

Despite the additional time commitment required to explain or consent patients to CGT trials, all respondents reported this did not influence their decision to offer CGT trial to patients.

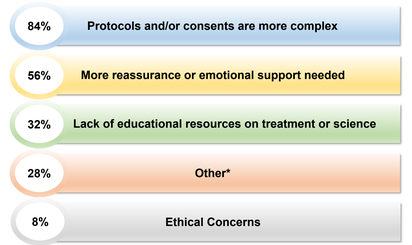


Time spent explaining or consenting patients to CGT trials vs non-CGT trials



Additional time required explaining or consenting patients to CGT trials vs non-CGT trials

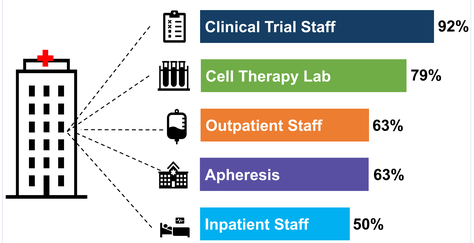
What factors lead to a longer consenting process in CGT trials?



*Risks of therapy; socioeconomic constraints of being on trial; clinical status of patients; complexity of science behind the protocols; privacy; use of cell products

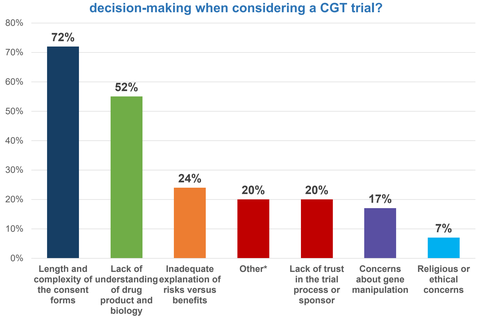
Do CGT trials add increased burden to workflow, staffing, and/or available resources?

80% of respondents noted CGT trials add an increased burden with some functions affected at a greater rate than others.



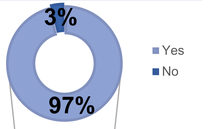
93% of respondents indicated that a dedicated CGT research team is needed to manage CGT trials.

What factors most often affect patient comprehension and informed decision-making when considering a CGT trial?

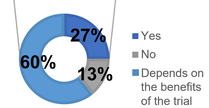


*Other: amount of time the provider can spend explaining the consent form; overwhelming treatment complexity with heavy logistical burden; changes in schedule; perceived patient's difficulty to adhere to the trial protocol; concerns about general research

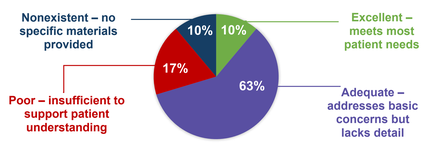
Do CGT trials have more labs and monitoring requirements than non-CGT trial?



Are patients less likely to participate in a CGT trial when there are excess labs and monitoring beyond what is required in SOC?



What is the quality of educational material provided by sponsors to support the CGT consent process?



What information/resources are most beneficial to patients considering enrollment on a CGT trial?

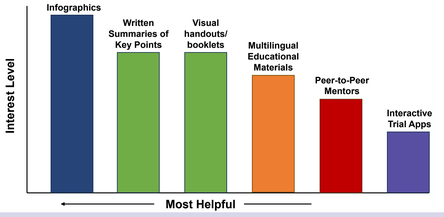


Table 2: Commonly Expressed Opinions From Interviewed Respondents

Theme	Representative Thoughts
Patient & Provider Perception	▪ Patients are generally aware of CGT trial benefits but often do not see them as significantly better than standard care or worth the treatment burden and time away from family. ▪ Patients who are suspicious of clinical trials in general would not enroll in CGT trial. And while some patients fear the unknowns of gene-editing, those with relapsed/refractory disease often have limited treatment options and are more likely to consent to CGT trials. ▪ Enrolling patients in CGT trials for aggressive malignancies is challenging due to the urgency of treatment and the complexity involved in coordinating many factors such as eligibility requirements, slot availability, donor matching, manufacturing, and treatment logistics. ▪ Some patients are aware of CAR-T therapy and have inquired about its use for treating AML, despite the absence of FDA-approved options. However, the limited data on CAR-T in AML presents challenges in effectively explaining these trials to patients. ▪ Consenting providers serve as the most trusted and effective resource for explaining and reassuring patients about CGT trials, as patients typically rely on their expertise and judgment in making the best treatment decisions. ▪ A peer-to-peer network or sharing trial success stories can significantly enhance patient confidence and increase enrollment in CGT trials.
Logistical and Financial Considerations	▪ With increased treatment complexities and monitoring requirements, CGT trials require commitment from caregivers not frequently seen in non-CGT trials. High rates of caregiver burnout pose a significant barrier to many patients considering CGT trials. ▪ Many centers have resources to assist with logistical and financial barriers, but support from sponsors and external funding is still heavily relied upon.

Conclusions

- The CTG trial informed consent process takes longer due to complex protocols and the need for increased patient reassurance and explanation
- 93% of respondents believe patients primarily rely on interactions with investigators and study staff as the primary resource for consenting to CGT trials
- Although consenting requires more time and resources, all respondents shared that this does not deter them from offering CGT trials to patients
- Delays in treatment due to drug product manufacturing is the primary concern of consenting staff when enrolling patients in CGT trials
- Most respondents agree that CGT trials require a dedicated research team familiar with complex therapies
- Centers with established CGT research teams reported increased capacity to offer trials and better management of patients enrolled in CGT trials
- 97% noted CGT trials require more lab work and monitoring than non-CGT trials, which may influence enrollment decisions based on perceived benefits
- Perceived patient concerns enrolling on a CGT trial are broad and varied
- Patient comprehension and decision making is hindered by the complexity of protocols and poor understanding of the drug products
- 90% found sponsor-provided educational materials insufficient, highlighting a gap in effectively explaining trial complexities and patient requirements
- Peer-to-peer support systems in addition to more traditional educational resources could improve trial enrollment and enhance the patient experience

References

1. Tao et al. Revolutionizing cancer treatment: enhancing CAR-T cell therapy with CRISPR/Cas9 gene editing technology. Front Immunol. 2024:15:1354825.
2. McKesson. Expanding Access to Cell and Gene Therapy. Retrieved from McKesson.com.

Limitations and Future Direction

Table 3: Limitations of Survey Study & Proposed Future Directions for Study, Sponsors, and Trial Sites

Limitation	Impact	Future Direction
Academic Center	▪ CGT trials are more prevalent and readily accessible at academic centers. ▪ Academic centers are more likely to have specialized infrastructure, experienced staff, and dedicated resources to support CGT trials, including logistical and financial assistance for patients ▪ Patients seeking care at academic centers may have already been introduced to CGT as a treatment option, increasing their likelihood of consenting to trial participation.	Survey community providers and healthcare team to capture the barriers faced by patients at community hospitals or non-specialized centers, where CGT availability and support systems may be more limited.
Geographical Location	▪ The surveyed centers were primarily located in urban and suburban areas, where higher socioeconomic status and access to healthcare may influence patient participation in CGT trials. ▪ Patients in rural or remote regions—who often experience greater financial, transportation, and logistical barriers—may be underrepresented in this survey.	Explore strategies to routinely provide logistical or caregiver support and alternative monitoring strategies to increase access to CGT trials.
CGT Current Treatment Landscape	▪ CGT is primarily utilized in the relapsed/refractory (R/R) setting for hematologic malignancies. ▪ R/R patients have likely undergone multiple lines of therapy and may experience higher rates of treatment fatigue, logistical exhaustion and caregiver/family burden thus making them less inclined to participate in a complex and intensive CGT trial.	Develop patient surveys to assess prior therapy burden in relation to willingness to participate in CGT trials. Solicit patient feedback on how institutions and sponsors can lessen such biases.
Survey Respondents	▪ The survey respondents were predominantly transplant providers with a research-focused background or individuals regularly involved in clinical trials, which may contribute to greater awareness and understanding of CGT trials which results in more confidence and commitment to enrolling patients. ▪ No patients were surveyed in this research, instead perceived patient concerns and challenges are reported which may not accurately provide the entirety of the patient experience.	Expand survey to more diverse respondents by incorporating perspectives from clinicians and other staff with varying levels of research engagement. Consider partnering with patient advocacy organizations to survey patients to better understand their experience.