SUMMARY

FDA CBER Patient-Focused Drug Development Listening Meeting

Patient and Care Partner Perspectives on Safety Considerations for Approved Gene Therapy Treatments for Rare Diseases

September 20, 2024

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Introduction

On September 20, 2024, the U.S. Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) hosted the first of two 2024 listening meetings for patients with rare diseases and their care partners.[1] This meeting aimed to 1) hear patient and care partner perspectives on short-term and long-term risks of approved gene therapy (GT) products; 2) learn what types of information patients would find helpful in their decision-making when considering GT; 3) learn about patient considerations and experience with participating in long-term postmarket studies; and 4) help inform patient-centered protocols for long-term studies of GTs.

Gene therapy aims to modify a gene or replace a faulty gene to treat a disease or medical condition. Gene therapies can work by several mechanisms, such as:[2]

1. Replacing a disease-causing gene with a healthy copy of the gene;
2. Inactivating a disease-causing gene that is not functioning properly; or
3. Introducing a new or modified gene into the body to help treat a disease.[3]

While the scientific underpinnings that made GT possible have been recognized since the mid-20th century, the first GT approvals in the United States occurred in 2017 with the chimeric antigen receptor CAR T-cell products tisagenlecleucel (Kymriah) and axicabtagene ciloleucel (Yescarta) and directly administered GT voretigene neparvovec-rzyl (Luxturna). Since the first approvals in 2017, gene therapy continues to grow at a rapid pace. By the end of 2024, FDA had approved 22 gene therapies, most for rare diseases.[4]

The Importance of Patient Engagement

Patients are uniquely positioned to inform the understanding of the therapeutic context for drug development and evaluation. Patient engagement involves patients, care partners, and patient advocates sharing their experiences, perspectives, needs, and priorities. This input can help identify patients' priorities related to treatment benefits, risks, and burden, and determine effective methods for communicating information to health care professionals.

The FDA has established several patient engagement initiatives[5] including the FDA Patient Representative Program,[6] the Patient-Focused Drug Development (PFDD) Initiative,[7] the Patient Engagement Collaborative,[8] and Patient Listening Sessions.[9] CBER staff actively participate in and collaborate with the offices that house these programs, including attending patient listening sessions to engage directly with patient advocacy organizations.

CBER's Office of Therapeutic Products' (OTP) RegenMedEd program regularly engages with patients, caregivers, and advocates to explore opportunities to help advance development of regenerative medicine therapies like GTs.[10]

[1] 2024 CBER Patient and Care Partner Listening Meetings | FDA

[2] What is Gene Therapy? | FDA

[3] What is Gene Therapy

[4] https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

[5] FDA Patient Listening Sessions | FDA

[6] FDA Patient Representative Program

[7] The Patient-Focused Drug Development Initiative

[8] Patient Engagement Collaborative

[9] Patient Listening Sessions

[10] OTP Events, Meetings, and Workshops | FDA

Figure 1. Top Referral Sources

Additionally, CBER staff have provided feedback to patient organizations and patient advocacy groups on natural history studies, patient preference studies, and other regulatory science activities that can promote efforts related to drug development. The FDA also collaborates with a variety of national patient advocacy organizations to connect with patient-led rare disease organizations, which allows the FDA to gain a better understanding of the complexities inherent to living with a rare disease. Further, these collaborations improve the FDA's grasp of how new therapies and data collection can best be integrated into patients' lives.

Meeting Overview

CBER announced two patient listening meetings on its website on July 11, 2024, and simultaneously opened registration for the September 2024 meeting. To promote and recruit participants for the meeting, CBER posted the announcement on the FDA website and shared the announcement in the "What's New at CBER" listserv and other FDA newsletters. Additionally, CBER posted on the FDA LinkedIn and CBER X accounts. As a result, 36% of referrals came from a friend or colleague and 28% came from FDA newsletters or emails, among other referral sources (**Figure 1**). CBER also conducted targeted outreach to sister agencies, patient advocacy groups, and organizations.[11]

The half-day meeting consisted of two sessions. The first, entitled "Patient and Caregiver Safety Considerations in Decision-making About Gene Therapy," focused on the types of information and considerations patients would find helpful when considering a gene therapy product. The second session, "Partnering with Patients and Caregivers on Long-term Studies After Receiving a Gene Therapy," reviewed factors that contribute to patient and care partner willingness to participate in long-term studies and data collection.

For each session, patients, caregivers, patient advocates, and other stakeholders (**Appendix 2**) presented their perspectives on approved GT products. Discussions identified factors that impact decision-making for receiving GT and participating in long-term post-treatment studies. Following each session, subject matter experts from OTP and CBER's Office of Biostatistics and Pharmacovigilance (OBPV) (**Appendix 2**) asked the speakers clarifying questions. Periodically, patients and care partners in attendance were asked to respond to polling questions (**Appendix 3**), which provided demographic information as well as participants' views on the topics.

This report summarizes the main topics and perspectives discussed during the September 20, 2024, patient listening meeting. To supplement the insights gathered at the meeting, stakeholders were encouraged to submit comments to the public docket (FDA-2024-N-3208-0001),[12] open from September 18, 2024, to November 19, 2024; one comment was submitted (**Appendix 1**).

[11] National Center for Advancing Translational Science (NCATS), National Heart Lung and Blood Institute (NHLBI), National Organization for Rare Diseases (NORD), Global Genes, and National Health Council

[12] Regulations.gov

SESSION 1

Patient and Caregiver Safety Considerations in Decision-Making about Gene Therapy

Prior to patient presentations, opening remarks for session one acknowledged OTP was overseeing over 2,600 investigational products, approximately half of which are GTs. However, the newness of the gene therapies, and their use primarily in small, rare-disease populations so far may contribute to uncertainty in the balance of benefits and risks for some GT products. Common safety- and risk-related questions include the following: Have enough patients been treated to know all the risks? When might adverse events happen (e.g., shortly after therapy, or many years later), how severe will they be, and can they be treated? Do certain factors place some people at increased risk of particular adverse events as compared with others?

In support of the FDA's goal to understand patient and caregiver considerations, speakers addressed three primary questions for Session 1 of the listening meeting:

1. What risks or uncertainties did you or would you consider when determining whether to receive an approved gene therapy?
2. What do you believe patients and care partners making decisions on behalf of patients should know about gene therapy?
3. In a scenario where more than one treatment option is available to treat a disease or condition, what information would you want to know?

Stakeholder Perspectives on Patient and Caregiver Decision-Making About Gene Therapy

Seventeen speakers (**Appendix 2**) shared their perspectives during this session, and their comments are summarized below:

- A man with hereditary amyloid amyloidosis described his experience receiving GT and the uncertainties involved, such as understanding how the therapy worked and if enough trial data were available to validate the risk. The speaker stressed that patients should be fully informed of whether they can switch to another treatment if there is a poor response to the current option.
- The Executive Director and Cofounder of Decoding Developmental Epilepsies and mother of a child with SCN8A developmental epilepsy highlighted recent projects and surveys indicating community support for GT options in developmental and epileptic encephalopathy. Caregivers in this therapeutic area call for transparent and intensive education on various aspects of GT, such as how the therapy is administered and how long the benefit lasts.
- A parent of a child with mucopolysaccharidosis (MPS) and advocate for the National MPS Society discussed considerations for comparing standard-of-care treatment with GTs, mentioning that peer-reviewed comparisons are essential. In addition to considerations such as the likelihood of treatment failure or long-term effects after treatment, MPS families must factor in logistical concerns, like how many school or work days they will have to miss or if they will have to travel extensively to the treatment facility.
- On behalf of the National MS Society, a speaker highlighted risk-benefit concerns patients and caregivers have regarding GT for multiple sclerosis, including the duration of efficacy, burdens of long-term follow-up, and the potential for complications such as organ damage or immune system reactions.
- A father of two young adults with Friedrich Ataxia (FA) spoke about his family's experience weighing different treatment options, noting his concern about how receiving one GT may preclude the ability to receive another GT or non-GT treatment in the future, since multiple treatments may be needed to treat all symptoms of FA. These concerns led him to believe that more research is needed to evaluate the risks and benefits of GTs administered in combination with other therapies.
- The Scientific Director for the Dravet Syndrome Foundation highlighted that per an externally led patient-focused drug development meeting,[13] 98% of caregivers expressed interest in GT and are seeking clear data on its potential risks and benefits, particularly the risk for adverse events or worsening symptoms.

[13] FDA User Fee Programs. Externally led Patient-Focused Drug Development Meetings. Accessed October 7, 2024. https://dravetfoundation.org/dsf-funded-research/externally-led-pfdd-meeting/.

- The CEO of Help 4 HD International, whose family member passed away from Huntington's disease (HD), discussed community feedback on GT and a forthcoming white paper on risk-benefit evaluation. While concerns about off-target effects or post-therapy improvement exist in the HD community, Huntington's disease is a terminal illness with a diminishing quality of life, so families are typically willing to try an available therapy even if all long-term risks are not yet identified.

- A patient advocate for Voices for ALS highlighted the unique safety and efficacy concerns expressed by individuals with terminal, heterogenous, and rare diseases. Having had a family member pass away from amyloidosis, the speaker discussed issues affecting both the amyotrophic lateral sclerosis and amyloidosis communities, indicating that studies should address whether the therapy was tested in a presymptomatic population, and if there will be long-term data available about this population. It was suggested that the following be available: a postmarket patient registry for data collection, more information on drug labels about approval for presymptomatic populations, and brief educational materials provided in accessible language for families considering a particular GT.

- A presenter on behalf of Response Evaluation in Neurofibromatosis and Schwannomatosis and parent of a young adult with neurofibromatosis type 1 discussed efforts of a working group established in 2022 to develop standardized response criteria or endpoints for GT trials. Their patient preference study, which will be published next year, will investigate perceived risk-benefit for patients and caregivers, such as the potential for new malignancies or the ability to receive standard treatment after GT.

- The Executive Vice President of Public Policy and Advocacy at the Muscular Dystrophy Association highlighted that due to the severe and rapid progression of untreated spinal muscular atrophy (SMA) and Duchenne muscular dystrophy (DMD), patients and caregivers must often make quick decisions regarding whether to receive GT because of the rapid progression and limited treatment eligibility window associated with untreated SMA and DMD. Families are particularly concerned about durability, whether the current therapy's risks and benefits outweigh those of a future option, and the need for more long-term efficacy data. Additional concerns exist within the community around educating patients and caregivers on the signs of a successful therapy.

- The Founder and Executive Director of TESS Research Foundation and a parent of children with SLC13A5 epilepsy was joined by the foundation's Scientific Director to discuss the need for more gene therapies for this disease. Patients and care partners want improved education about the outcome of GT treatment, such as whether all disease symptoms will be addressed, if the number of daily medications will be reduced, and what the long-term impact will be.

- A woman with myelodysplastic syndrome spoke about her experience weighing the risks and benefits of GT for her disease, particularly concerning long-term effects or outcomes for patients with compromised immune systems. She spoke about the need for improved financial equity in accessing GT treatment, as well as registries where candidates can access additional information on patient experience with and outcomes of a particular treatment.

- A pediatrician and mother of a teenager with Wiskott-Aldrich syndrome shared her family's experience in selecting GT versus standard-of-care for the disease, highlighting how the benefits and improved quality of life provided to her son outweighed potential risks. She stated that all patients and their families should be able to access available GTs and make an informed decision regarding treatment.

- A patient with limb-girdle muscular dystrophy (LGMD) type R2 and General Counsel for the Jain Foundation shared that there are currently no approved therapies, particularly adeno-associated viral (AAV)-based GT, for any subtype of LGMD. Common concerns with GT treatment in the LGMD community include toxicity, short duration of lasting benefit, and difficult access due to financial constraints.

- A speaker from Juju and Friends CLN2 Warrior Foundation and mother of a child with CLN2 Batten disease spoke about the need for complete, transparent, and comprehensible information for patients and caregivers regarding available therapies, potential adverse events, long-term outcomes, and robust follow-up protocols to monitor efficacy. She added that more mental health resources should be made available for families navigating treatment options for rare disease conditions.

- An independent advocate, pharmacist, and adult patient with phenylketonuria discussed the tension between having a treatment option that is available but not accessible to patients due to sociocultural, economic, and other barriers. She stressed that in order for patients to be proactive partners in supporting research and approval for GTs, they must be able to understand the science behind the therapy by receiving written materials in plain language and have equitable access to treatment.

- A patient ambassador for Friedreich's Ataxia Research Alliance and PhD candidate stated that due to the risks of disease progression, patients with FA would rather have earlier access to a GT approved based on surrogate endpoints than waiting for additional evidence of clinical efficacy via primary endpoints. She stated that because FA is a multisystemic disease and there is an upper limit to the safe expression of the deficient protein frataxin, the FDA should incentivize GT studies early to address the safety and efficacy of multiple or combination therapies, such as GT and protein replacement therapy. She added that pharmaceutical companies should provide comprehensive training on GT to clinicians and facilities administering their product.

Following the public presentations, FDA panelists (**Appendix 2**) had the opportunity to ask speakers clarifying questions. One panelist asked what sources of information patients and caregivers find most useful for decision-making related to treatment options. The speakers stated that for information about a GT trial, patients and caregivers may start with patient advocacy organizations. Peer-reviewed literature published through the FDA or scientific community is the main source of information for patient advocacy organizations. For evolving risks or safety data after approval, patients and caregivers often turn to their clinicians, multidisciplinary care center teams, and patient advocacy organizations. Since most advocacy organizations have an established rapport with patient communities, improved communication between the FDA and patient advocacy organizations was recommended to make data more accessible.

In addition to calling for earlier patient involvement in therapy development, speakers stressed the importance of patient-centric trial design concerning toxicity, especially at the preclinical stage. When evaluating a potential therapy, patients and caregivers want to see more transparent data about quality of life and actual morbidity, especially since they often look at toxicity data from patients who had already received the therapy.

The speakers also highlighted the challenge of presenting available risk-benefit data and resources on rare diseases in an online format that is comprehensible and accessible for patients and caregivers. The speakers encouraged the FDA to create a centralized, "one-stop" webpage where individuals are provided an overview of the disease, next steps after diagnosis, and links to clinical trial data, advisory committee meetings (if applicable), patient series webinars, guidance documents for industry, and other resources. Such a resource would be particularly helpful for families who can't easily access information through a large academic center or don't know a field expert who could inform them of the best treatment options.

SESSION 2

Partnering With Patients and Caregivers on Long-Term Studies After Receiving a Gene Therapy

Opening remarks for Session 2 discussed the importance of collecting long-term data and patient and care partner perspectives on barriers and incentives for participating in long-term data collection efforts.

Currently approved GTs are either ex-vivo genetically modified cells (cells modified outside of the body, e.g., CAR T-cell products) and viral vector-based products. Since the first GT was approved and made available to patients less than 10 years ago, there is still a lot to learn about different types of gene therapies. While these products are expected to produce long-lasting benefits, some serious adverse events may appear years after the treatment is administered.

Investigational programs are carried out in small numbers of patients and are short in duration; collection of reliable long-term data is critical to understanding GT safety and effectiveness. Collection of real-world data is one way to achieve this, including sources such as 1) electronic health records, medical claims, and billing databases; and 2) registries for a specific or related diseases or patients treated with a specific GT product/class.

For sponsors planning to develop a new registry, they may refer to FDA's 2024 guidance for industry entitled "Real-World Data: Assessing Registries To Support Regulatory Decision-Making for Drug and Biological Products,"[14] which provides considerations for designing a new registry or using an existing registry to support regulatory decision-making about a drug's effectiveness or safety.

Speakers addressed the following questions in this session:

1. What knowledge or factors might positively or negatively impact a patient's decision to participate in a gene therapy registry or other long-term study that captures gene therapy outcomes over a long period?
2. What is important to patients and their care partners about how a potential registry or other long-term study that includes gene therapy outcomes would be designed, operated, and managed?
3. What information about gene therapy outcomes in the long term is important to be communicated to patients?

Stakeholder Perspectives on Patient and Caregiver Decision-Making About Gene Therapy

Sixteen speakers (**Appendix 2**) shared their perspectives during this session and their comments are summarized below:

- A survivor of stage IV follicular lymphoma and patient advocate noted the ease of long-term follow-up for patients treated in large academic cancer centers. She noted that patients treated locally should be followed by their oncologists so they do not have to travel but buy-in from oncology practices may be difficult due to limited resources. Though data are collected and shared with pharmaceutical companies, it is not standard practice for that information to be shared in a central repository or be made public.

- A representative of the Speak Foundation, a patient-led advocacy organization for LGMD, emphasized that a long-term follow-up plan for medical monitoring is optimal and local data collection for long-term follow-up and information dissemination should be standard. This could potentially be achieved with private/public partnerships, one-stop websites, and other methods to explain potential risks.

- A mother of a son who passed away at age 25 from severe combined immunodeficiency (SCID) noted that while GT has led to success in treating the disease, long-term studies are necessary, especially in monitoring adverse events and life after treatment. She stressed that this information is essential to patient understanding and the ability to consent to GT; plain language summaries are crucial. Additionally, information regarding logistics of long-term follow-up should be shared with patients.

- A caregiver of a person with DMD pointed out the difficulties in participating in long-term follow-up, including scheduling conflicts and time and effort needed to visit study sites. Increasing the frequency of remote visits and

[14] https://www.fda.gov/media/152503/download

using primary doctors' offices/local labs for follow-up visits would ease the burden on patients and caregivers. Long-term safety and benefits of GT recorded in a registry managed by a public/private company could be valuable to potential recipients. Use of modern technology, such as a dedicated web-based or phone app, could be used by patients to report unexpected adverse events. In the cases that severe safety concerns are noted, other patients can be informed of risks quickly.

- Another caregiver of a son with LGMD type 2DR3 stated that a major factor patients and caregivers consider before participating in a GT registry or long-term study includes their ability to keep up with the demands of follow-up and reporting. Open communication with doctors at the treatment site about follow-up and outcomes and periodic reports for a specific GT, including long-term safety and effectiveness, is critical.

- The Vice President of Research and Clinical Innovation at Parent Project Muscular Dystrophy, which focuses on DMD and Becker muscular dystrophy, highlighted the importance of making long-term study results more accessible and actionable for both patients and clinicians, as well as the need to leverage technology to achieve this goal. Long-term data collection, analysis, and sharing is vital in understanding how treatments work in the long run and how patients' needs evolve. Data sharing is imperative to patients as they consider receiving GT. Safety and efficacy data should be maintained by individual companies and institutions and made available in a manner that is understandable to the average patient in considering risks and benefits of GT.

- The Executive Director and Board Chair of the Emily Whitehead Foundation stated that a survey of 96 patients receiving CAR T-cell therapy showed travel, cost, and distance are major impediments to attending follow-up appointments. He said that a lack of education when treatments are administered also proves to be a barrier for patients in long-term follow-up for appropriate time periods. The survey also indicated that patients are open to using tools like electronic health records, mobile apps, and telehealth to make data collection more patient-friendly. Long-term data collection in this population is especially important in terms of tracking secondary malignancies, a known but poorly documented risk of treatment.

- A person with SMA type 3 discussed the approved GT onasemnogene abeparvovec-xioi (Zolgensma) for treatment of patients less than 2 years of age, a population in which safety data are still being collected and analyzed as children grow and develop. She noted that frequent updates regarding the long-term benefits and safety profiles of GT (or GT combined with other approved treatments), including delayed adverse events and opportunities to connect with other patients and families may incentivize patients to participate in observational studies.

- A patient with hemophilia A noted that there are currently three approved AAV-based GTs, two for hemophilia B and one for hemophilia A. Both forms of the disease are monogenic with well-defined biomarkers. He noted that long-term follow-up, ideally using a global registry, may reveal GT factors contributing to issues such as liver toxicities and the need for immunosuppression. Additionally, rare adverse events can only be captured using a robust, prospective, longitudinal global registry, which the World Federation of Hemophilia has established in collaboration with key stakeholders.

- A family member of two people living with DMD spoke about the importance of long-term studies or registries to assist families in making decisions about treatment. Important issues that arise when participating in these efforts include time commitment, financial burden, and data accessibility and security.

- A professor of microbiology, immunology, and molecular genetics, Co-director of the Center for Duchenne Muscular Dystrophy at the University of California, Los Angeles, and mother of a son with DMD noted that patient follow-up is most efficient when a local site is available or travel expenses are covered. She said that whenever possible, patients receiving GT should be followed for the rest of their lives. Patients appreciate when data are shared with them, which engenders an ongoing discussion that establishes partnerships with their families.

- CEO and Founder of Cure Duchenne and the mother of a 27-year-old patient with DMD recognized that long-term studies and registries provide critical risk-benefit data to all stakeholders beyond those captured in clinical trials. To be part of any successful registry or long-term study, there should be clear communication about how the data will be used and the burden of participation. Costs must be low and data should be disseminated to all key stakeholders in real time instead of by annual corporate updates. She also noted that unexpected safety signals following long-term treatment need to be followed and captured. Finally, a registry that is owned and managed by a third party may be a viable solution to achieving this goal.

- A patient with facioscapulohumeral muscular dystrophy (FSHD), a rare genetic form of muscular dystrophy, discussed the issues associated with long-term studies,

including time, travel, and costs associated with that travel. He said that the FSHD Society has created a registry amassing information that includes data uploaded from patients, which can be used to educate the medical community and communicate medical risks.

- The VP of Science Communications for the Foundation Fighting Blindness, an organization that funds research for treatments and cures for rare inherited retinal diseases, stated that the foundation hosts a large registry of patients, both those who have been in clinical trials and those who have not. Luxturna was approved in 2017 for people with a specific form of Leber congenital amaurosis mutations in the RPE65 gene. A post-authorization safety study demonstrated that most adverse events during therapy administration were mild, transient, and treatable and most patients had significantly improved vision, providing data that are invaluable to other patients who consider receiving GT versus prior standard of care. In terms of participation in follow-up studies or clinical trials, patients are most concerned about cost, time, travel, and eligibility for treatments and surgery.

- A caregiver from the sickle cell disease community spoke about the importance of the design of, approaches to, and collaboration necessary for disease registries for sickle cell patients. Patients and families want transparent platforms that allow for their input and open communication. Knowledge surrounding where data are going and feedback on what has been found is desired. Good design, access, collaboration, communication, and data security are also critical components to gathering long-term data.

- The Cofounder of Angle Therapeutics, which develops non-AAV gene therapy, and a patient with muscular dystrophy, said that one of the most important things patients and caregivers need to be aware of before enrolling in a GT trial is that treatment doesn't necessarily mean improvement in the disease. He noted that the burdens of travel are some of the biggest issues in deciding to be in a trial, including time away from work, expense, and other physical difficulties for a patient. Additionally, being in a GT trial run by a company or university means that entity has exclusivity over the data. To mitigate this barrier, registries should be standardized across diseases and patients.

Following the Session 2 speaker presentations, the FDA panel had the opportunity to ask speakers clarifying questions.

Discussion on obtaining information about potential risks centered around patient communication regarding uncertainty in treatment. However, if patients understand this uncertainty, they should be encouraged to consult with their doctors to help make risk-benefit assessments. Additionally, speakers agreed that trusted sources, like listening meetings and patient advocacy organizations disseminating information, must be used to communicate with and educate patients.

An FDA panelist asked a speaker to elaborate on ways to improve product labels to better communicate risks to patients, citing the example of Boxed Warnings for secondary malignancies attributable to CAR T-cell therapies based on lab testing for product presence. The speaker shared how major media outlets and social media have broadly communicated information about secondary malignancies caused by CAR T-cell therapies because of this labeling without context or knowledge of the disease being treated, which has been detrimental to patient decision-making. However, she stated that public misunderstanding of the science behind these effects misses the nuance behind both the disease being treated and the treatment itself. The speaker stressed that there should be a more balanced approach to disseminating information about these therapies, including success stories.[15]

Another issue discussed was the frequency and format for disseminating updates to patients and their caregivers. Both the patient and caregiver who responded agreed that patients want information updates as frequently as possible. And while physicians are the preferred conduit for reporting information to their patients, the method of communication isn't as important as the message.

Finally, the importance of plain-language summaries for those who are involved in long-term studies was elaborated upon. For example, plain-language summaries in medical journal articles have become a more common option. However, these kinds of communications should be more frequent and not only during the publication phase since patients and caregivers prefer to receive information in a way they can easily grasp.

[15] Note: the FDA panelist's question was about suggestions for optimizing product labeling to better communicate risks to patients. The FDA strives to ensure there is a balanced approach to disseminating information about CAR T-cell therapies. For more information, please visit **FDA Requires Boxed Warning for T cell Malignancies Following Treatment with BCMA-Directed or CD19-Directed Autologous Chimeric Antigen Receptor (CAR) T cell Immunotherapies | FDA**

Conclusion

This virtual listening meeting hosted by CBER provided patients, caregivers, and other stakeholders the opportunity to share valuable insights on the safety of GT products and the decision-making processes leading to treatment and participation in long-term studies. Contributors engaged in a discussion on short- and long-term risks of approved GT products, what types of information are helpful when considering treatment with a GT, experiences with long-term postmarketing studies, and how patient-centered protocols for long-term studies of GT can be improved.

Appendix 1: Docket Comments

As a supplement to the insights provided at the listening meeting, stakeholders were encouraged to submit comments to Docket FDA-2024-N-3208-0001, which was open from September 18, 2024, to November 19, 2024. One comment was submitted to the docket. Rachel DeConti, the mother and caregiver of a patient living with LGMD type 2D/R3 and a speaker in Session 2 of the listening meeting, posted her statement and slide deck presented at the meeting. This docket comment can be found at Regulations.gov.

Appendix 2: Speakers and FDA Panelists

Speakers

Session 1:

1. Steve Bedsole
2. Gabi Conecker, *Decoding Developmental Epilepsies/ DEE-P Connections*
3. Stephanie Cozine, *National MPS Society*
4. Alicia DeVinney, *MS Society*
5. D. Rolf Hill
6. Dr. Veronica Hood, *Dravet Syndrome Foundation*
7. Katie Jackson, *Help 4 HD International*
8. Michelle Lorenz, *Voices for ALS*
9. Miranda McManus, *Response Evaluation in Neurofibromatosis and Schwannomatosis (ReiNS)*
10. Paul Melmeyer, *Muscular Dystrophy Association*
11. Kimberly Nye and Dr. Tanya Brown, *TESS Research Foundation*
12. Joan Powell, *MDS Patient and Advocate*
13. Dr. Priya Stephen, *Wiskott Aldrich Foundation*
14. Joshua Thayer, *Jain Foundation*
15. Cristina Vargas, *Juju and Friends CLN2 Warrior Foundation*
16. Jennifer Weiland Payne
17. Shandra Trantham, *Friedreich Ataxia Research Alliance (FARA)*

Note: Two speakers, Rama Boddanapalli and Michelle Stevens, were slated to speak but did not participate.

Session 1:

1. Laurie Adami, *LA Patient Advocacy*
2. Kathryn Bryant Knudsen, *Speak Foundation*
3. Barbara Ballard, *SCID Angels for Life Foundation*
4. Rupjani Bhattacharya
5. Rachel DeConti, *LGMD2D Foundation*
6. Dr. Eric Camino, *Parent Project Muscular Dystrophy*
7. George Eastwood, *Emily Whitehead Foundation*
8. Lauren Gibbs, *Cure SMA*
9. Radek Kaczmarek, *World Federation of Hemophilia*
10. Sheryl Marrazzo, *4 Jake's Sake Charitable Foundation*
11. Dr. M. Carrie Miceli, *University of California, Los Angeles*
12. Debra Miller, *Cure Duchenne*
13. David Rubin
14. Ben Shaberman, *Foundation for Blindness*
15. Adrienne Shapiro, *Axis Advocacy*
16. Donavon Decker, *Angle Therapeutics*

FDA Panelists

1. Dr. Shelby Elenburg, Physician, Clinical Team Lead, General Medicine Branch 1, Division of Clinical Evaluation General Medicine, Office of Clinical Evaluation, Office of Therapeutic Products
2. Dr. Avanti Golikeri, Medical Officer, General Medicine Branch 1, Division of Clinical Evaluation General Medicine, Office of Clinical Evaluation, Office of Therapeutic Products
3. Dr. Megha Kaushal, Branch Chief, Benign Hematology Branch, Division of Clinical Evaluation Hematology, Office of Clinical Evaluation, Office of Therapeutic Products
4. Dr. Richard Forshee, Deputy Director, Office of Biostatistics and Pharmacovigilance
5. Dr. Larissa Lapteva, Associate Director, Office of Biostatistics and Pharmacovigilance
6. Dr. Adamma Mba-Jonas, Branch Chief, Division of Pharmacovigilance, Pharmacovigilance Branch 1, Office of Biostatistics and Pharmacovigilance
7. Dr. Xinyi Ng, Visiting Scientist, Benefit-Risk Assessment Branch, Division of Analytics and Benefit-Risk Assessment, Office of Biostatistics and Pharmacovigilance

Appendix 3: Polling Question Data

During the meeting, FDA used the meeting platform's polling to pose the following questions to attendees. Patients and caregivers were self-identified and answered on a voluntary basis. The results, presented below, were used to provide context for the speaker comments.

Demographic Questions

Question 1: Geographically, where do you live?

Question 2: How would you describe your level of knowledge of gene therapies?

Question 3: What does gene therapy mean to you as a patient or care partner? Please select the one you can relate to the most.

Question 4: How do you prefer to receive information about the risks of gene therapy? Please select as many as apply.

Question 5: We would like to know about the patients and care partners joining today's event. Please select the response that best describes you.

Question 6: How would you describe you or your loved one's genetic disease?

Session 1: Patient and Caregiver Safety Considerations in Decision-Making about Gene Therapy

Question 1: What information about risks (or uncertainties about risks) of gene therapy products did you consider or would you consider when determining whether to receive the gene therapy? Please select all that apply.

Question 2: Imagine there was another option to treat the disease or condition beyond managing the symptoms available now or in the near future. What do you think is most important to consider in making the decision to move forward with gene therapy versus the other option? Select up to 3 responses.

Question 3: What information about gene therapy risks were/would be most important to you when determining whether to receive the gene therapy? Please select up to 3 responses.

Session 2: Partnering With Patients and Caregivers on Long-Term Studies After Receiving a Gene Therapy

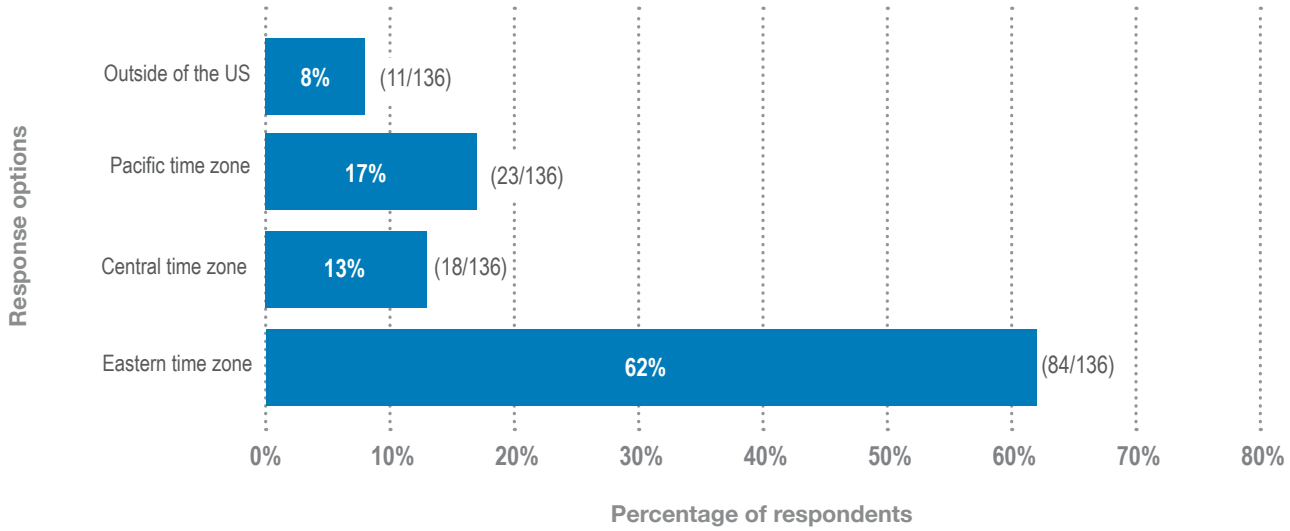
Question 1: What would motivate you to consider participating in a long-term registry or study after receiving a gene therapy product? Select up to 5 items most important to you.

Question 2: What concerns do you have about participation in a long-term registry or study after receiving a gene therapy product? Select up to 5 items most important to you.

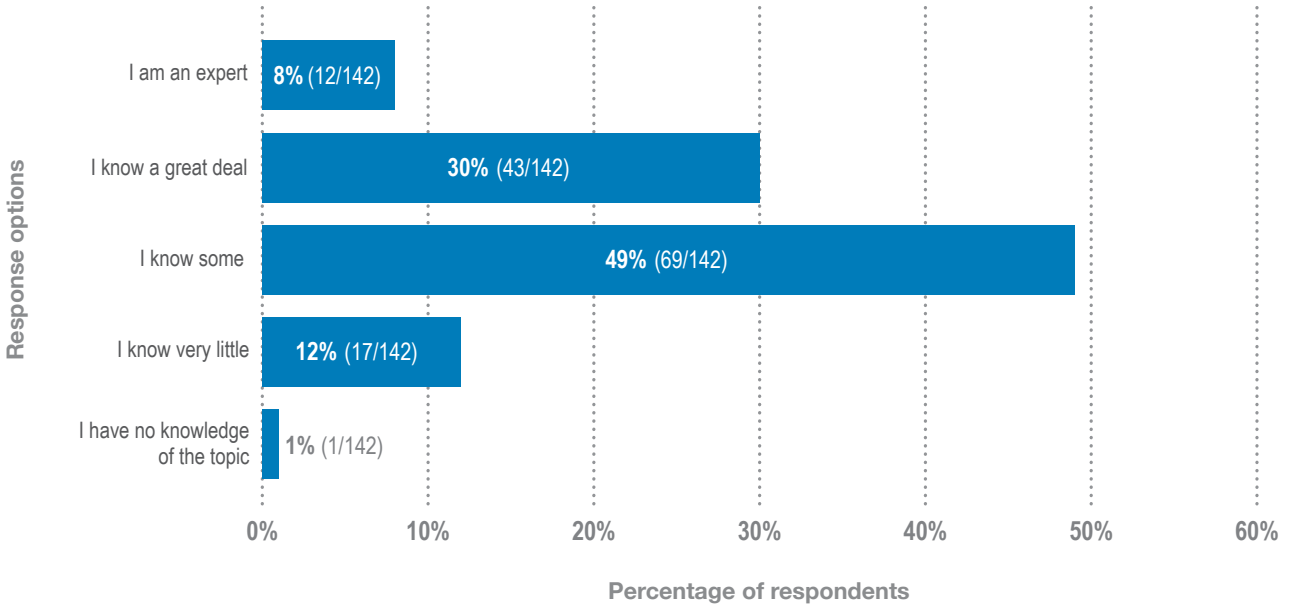
Question 3: What would you be willing to provide input on for a registry or long-term study? Select up to 3 items most important to you.

Demographic Questions

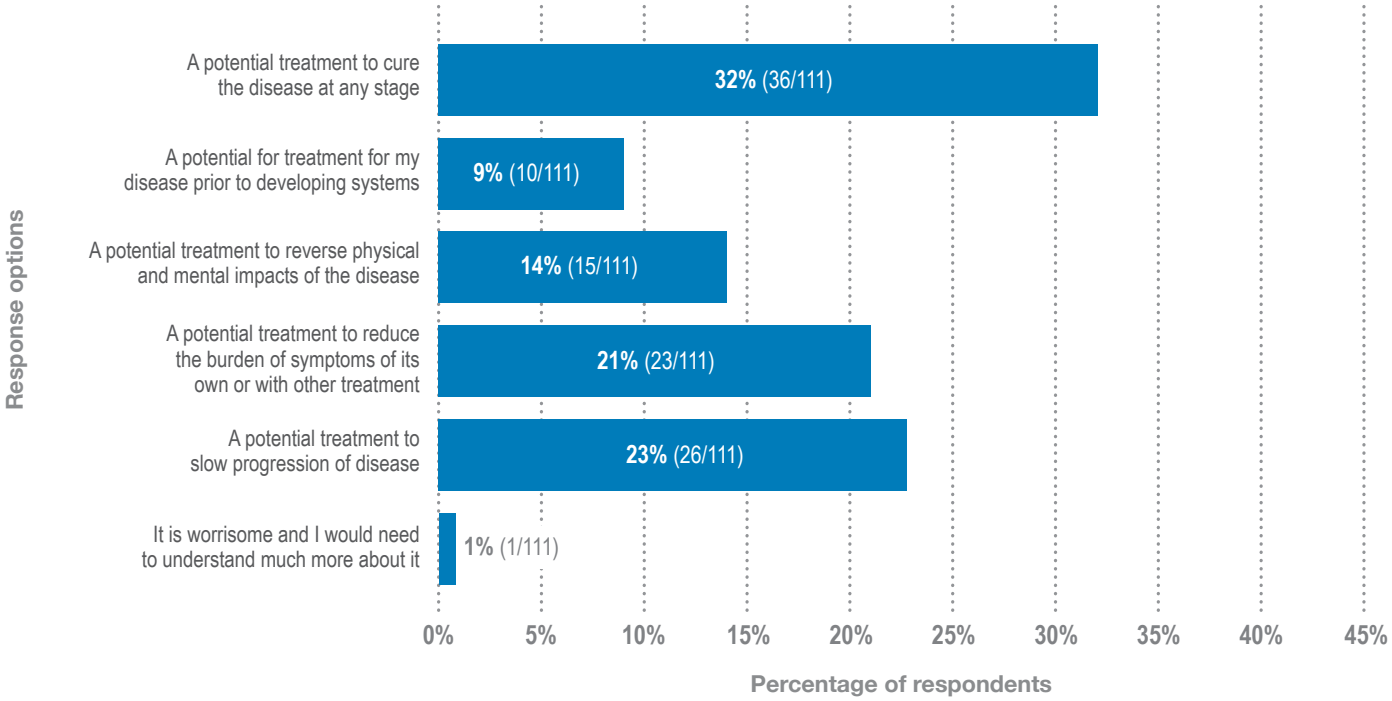
Question 1: Geographically, where do you live?



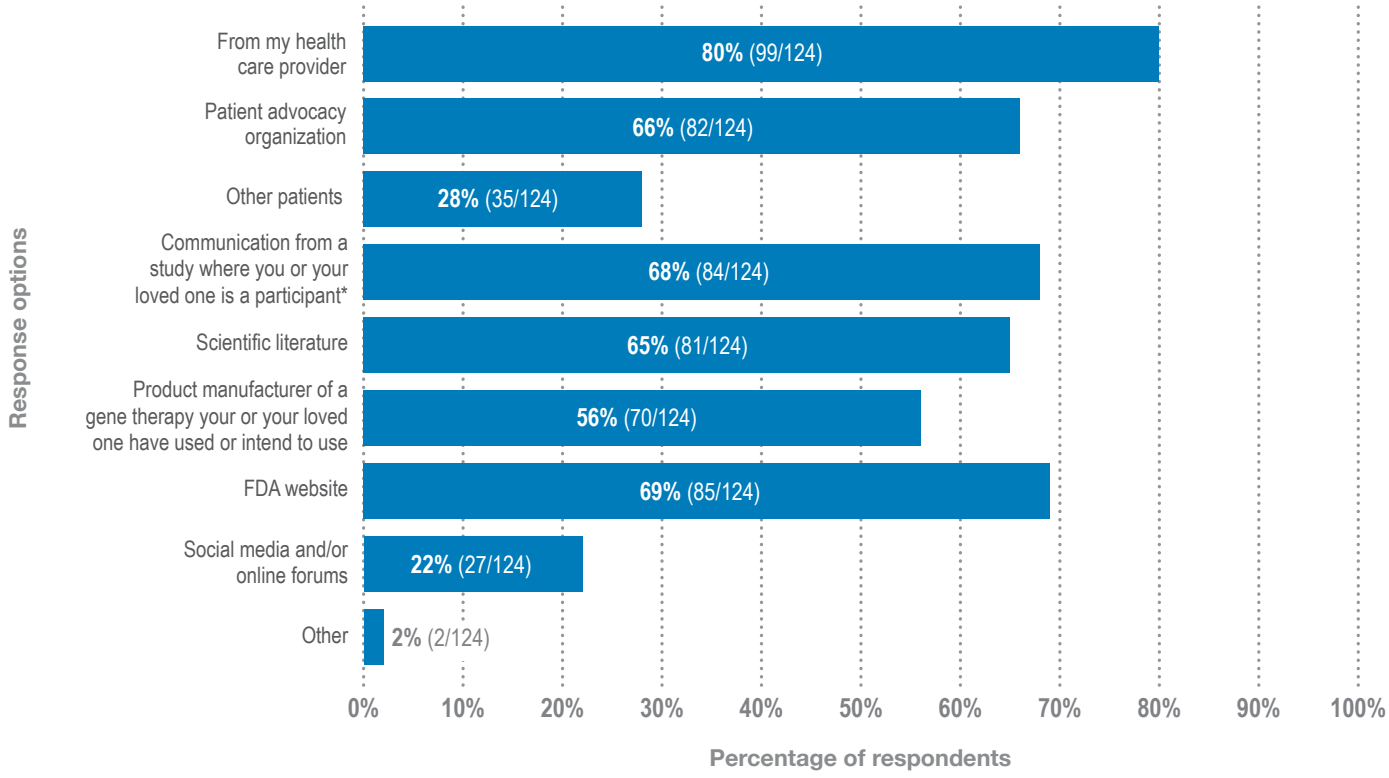
Question 2: How would you describe your level of knowledge of gene therapies?



Question 3: What does gene therapy mean to you as a patient or care partner? Please select the one option you can relate to the most.

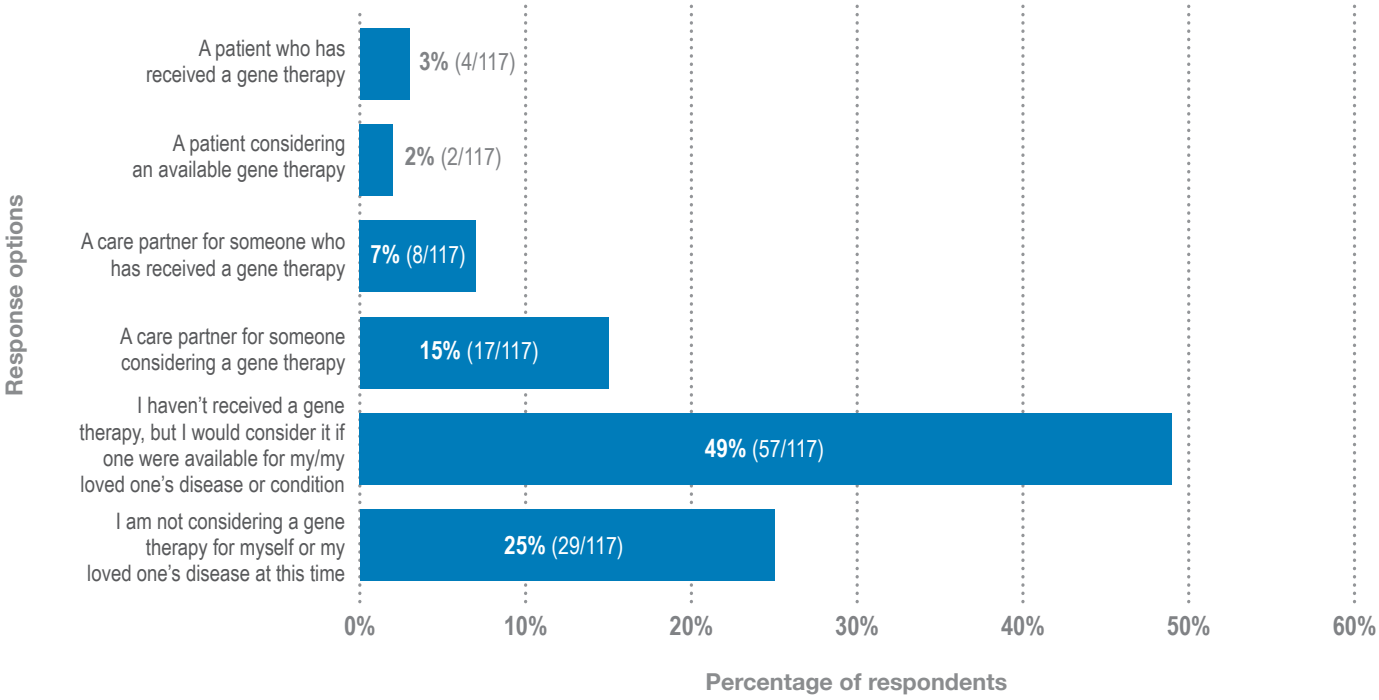


Question 4: How do you prefer to receive information about the risks of gene therapy? Please select as many as apply.

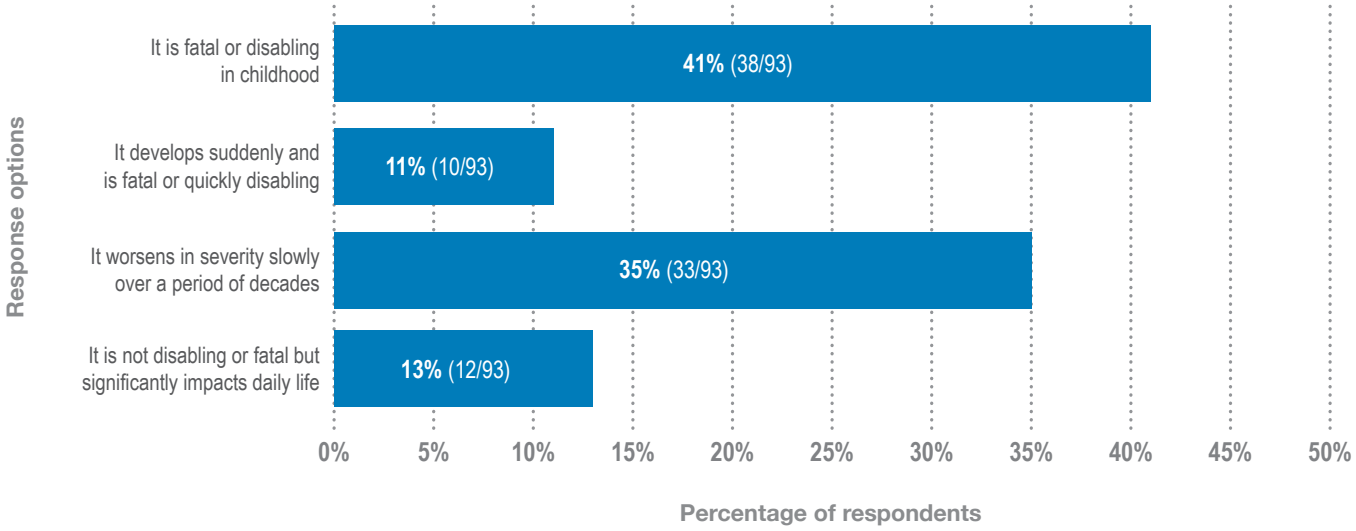


** for example, from the registry or study newsletter, study doctor, or research coordinator*

Question 5: We would like to know about the patients and care partners joining today's event. Please select the response that best describes you.

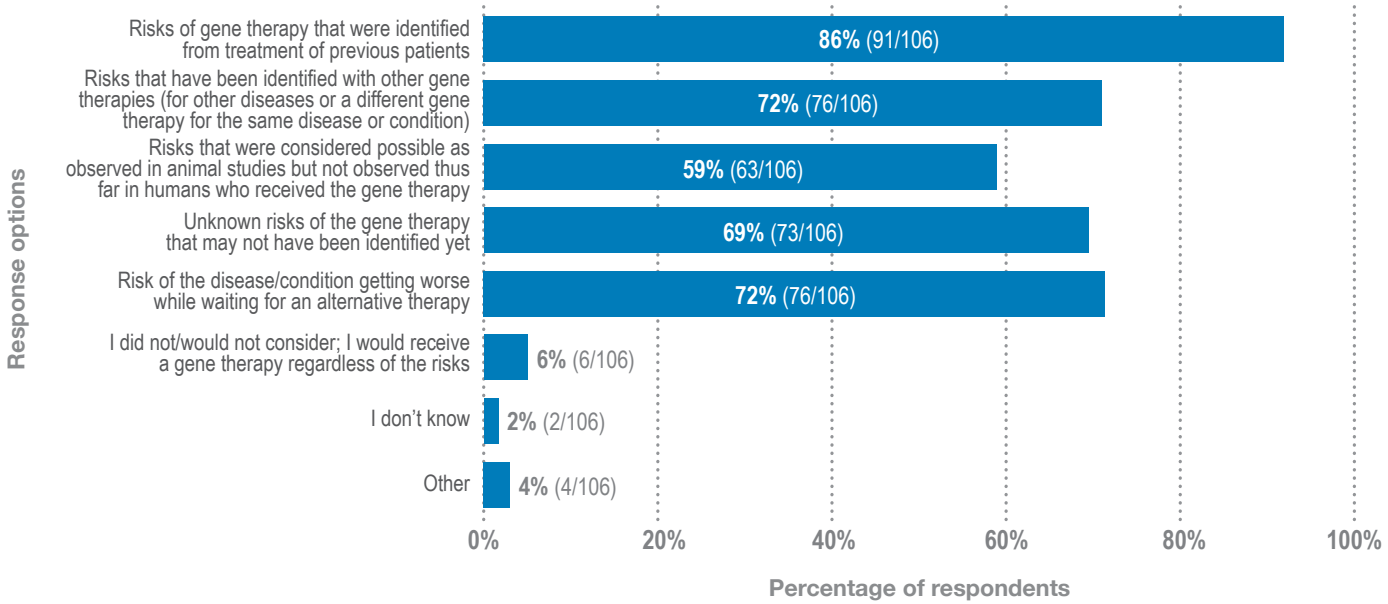


Question 6: How would you describe you or your loved one's genetic disease?

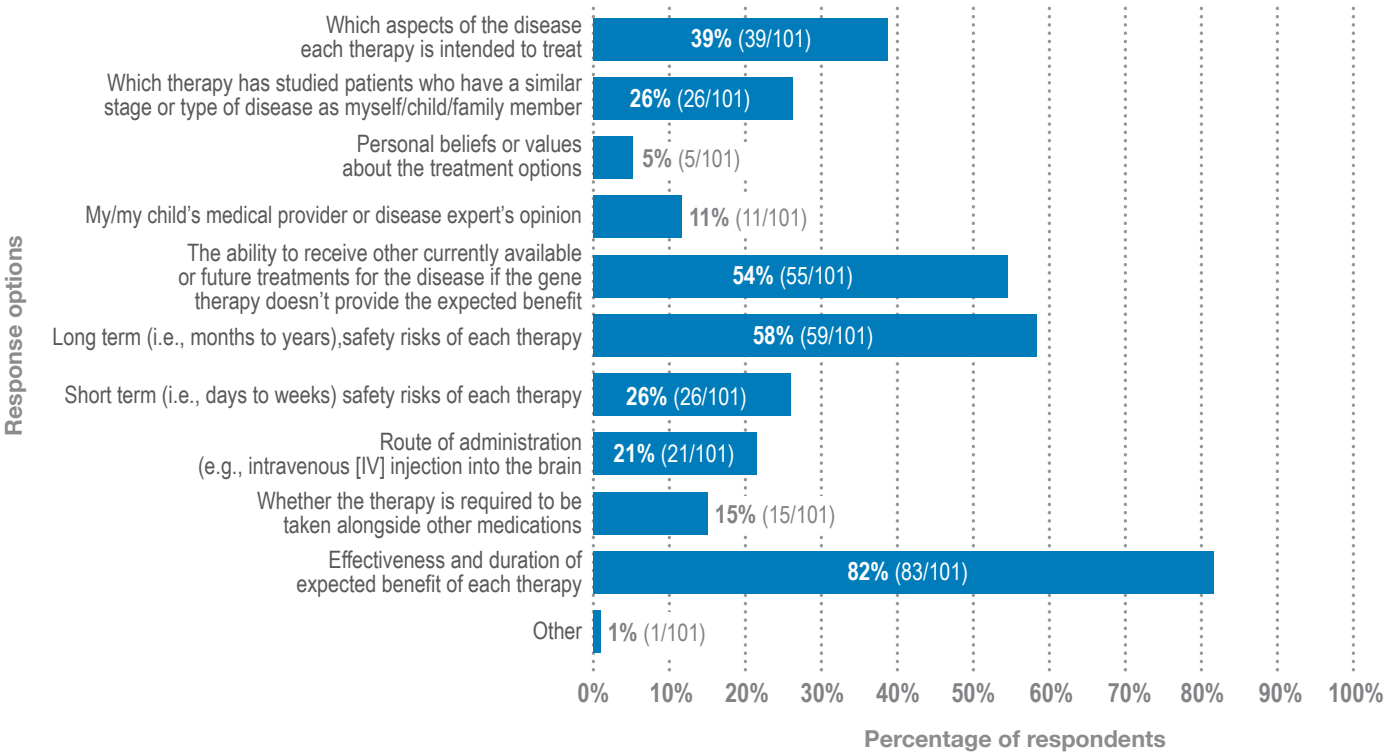


Session 1: Patient and Caregiver Safety Considerations in Decision-Making about Gene Therapy

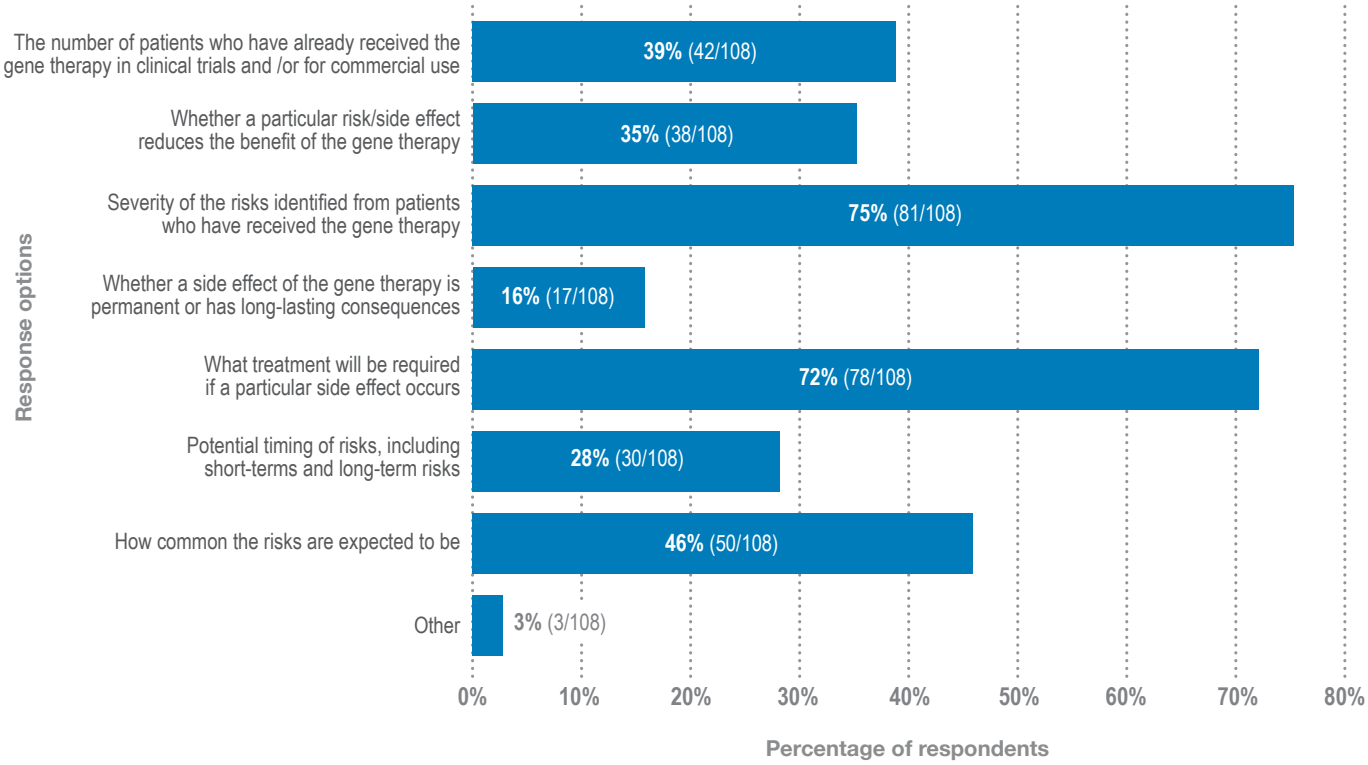
Question 1: What information about risks (or uncertainties about risks) of gene therapy products did you consider or would you consider when determining whether to receive the gene therapy? Please select all that apply.



Question 2: Imagine there was another option to treat the disease or condition beyond managing the symptoms available now or in the near future. What do you think is most important to consider in making the decision to move forward with gene therapy versus the other option? Select up to 3 responses.

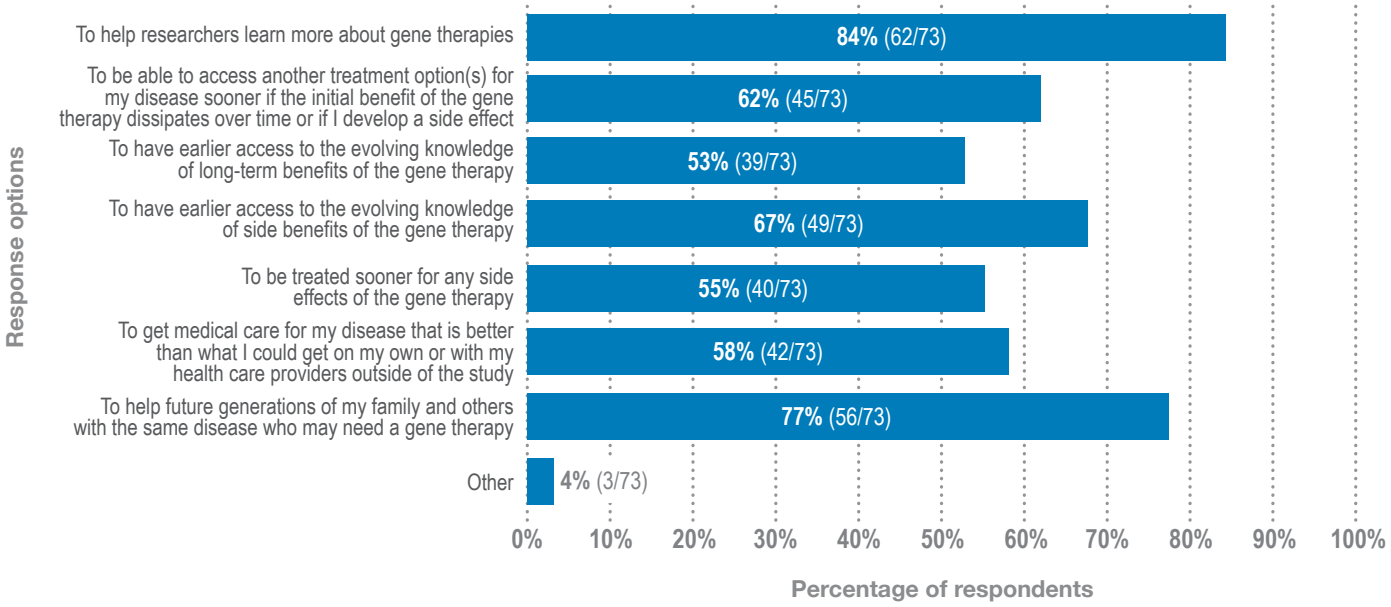


Question 3: What information about gene therapy risks were/would be most important to you when determining whether to receive the gene therapy? Please select up to 3 responses.

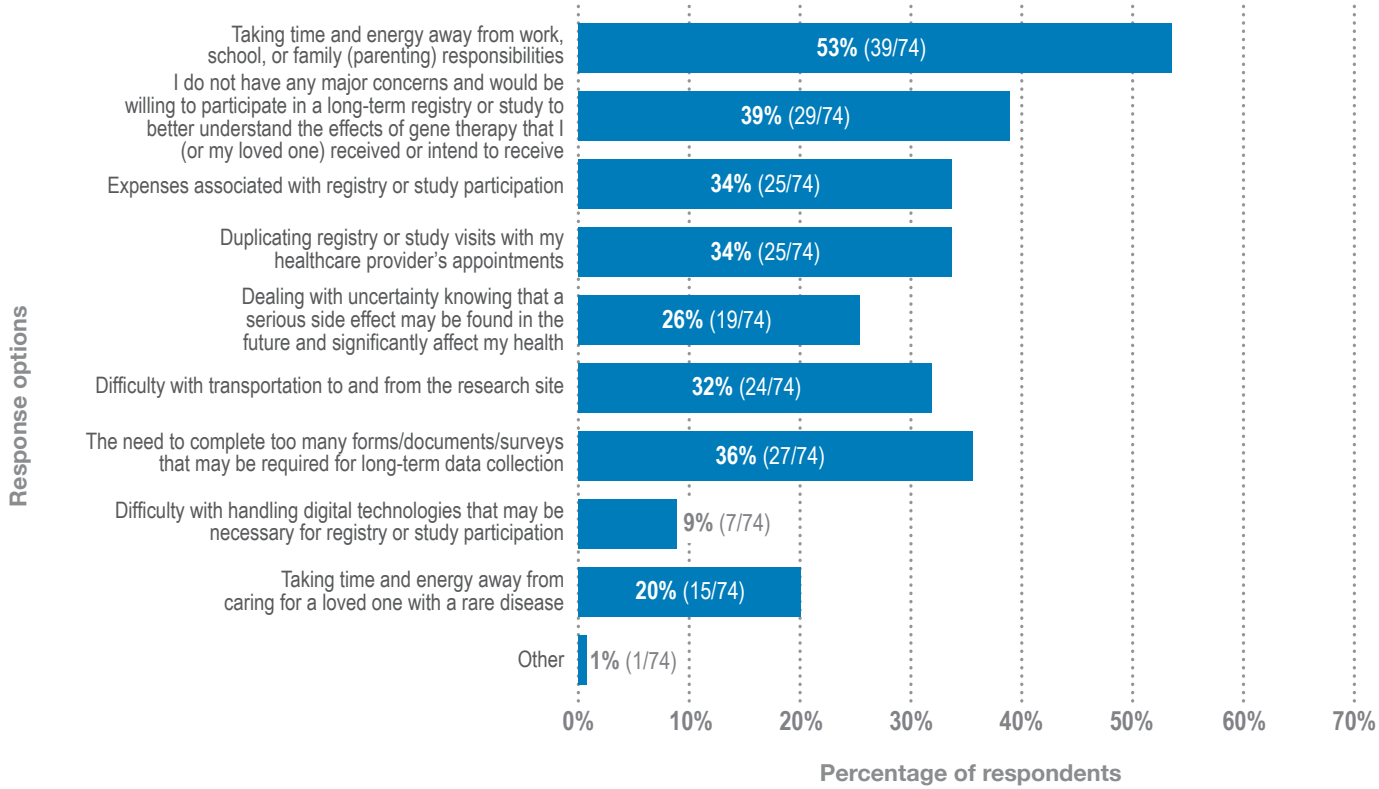


Session 2: Partnering With Patients and Caregivers on Long-Term Studies After Receiving a Gene Therapy

Question 1: What would motivate you to consider participating in a long-term registry or study after receiving a gene therapy product? Select up to 5 items most important to you.



Question 2: What concerns do you have about participation in a long-term registry or study after receiving a gene therapy product? Select up to 5 items most important to you.



Question 3: What would you be willing to provide input on for a registry or long-term study? Select up to 3 items most important to you.