emily whitehead foundation
activate the cure for childhood cancer

Catalyst Healthcare Consulting

Amplifying the Voice of CAR T-Cell Therapy Patients and Caregivers

Survey Results to Better Understand Patient Experiences with Long-Term Follow-Up Studies

About the Authors

Catalyst Healthcare Consulting

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Catalyst Healthcare Consulting is a dynamic, hands-on regulatory affairs partner to global innovators, advocates, payors, providers, investors, and trade organizations helping to speed innovative healthcare solutions to market to improve the lives of patients. The Catalyst team is comprised of experts in the fields of regulatory strategy, public policy, FDA dynamics, patient engagement, reimbursement and government programs, as well as scientific communication who bring vision, expertise, energy, and creative solutions to the table. The team works side-by-side with clients to efficiently obtain citical regulatory and policy objectives and help clients build collaborations and propel their cutting-edge technologies into the hands of patients.

To learn more about Catalyst, visit catalysthcc.com.

Emily Whitehead Foundation

George Eastwood

Emily Whitehead Foundation is a non-profit organization dedicated to advancing the fight against childhood cancer, with a particular focus on supporting CAR T cell therapy research. Founded in 2012 by the family of Emily Whitehead, the first pediatric patient to receive this CAR T therapy for leukemia, the foundation has become a leading advocate for innovative cancer therapies. Through fundraising, awareness campaigns, and partnerships with research institutions, the foundation helps accelerate the development of life-saving treatments and ensures that families facing cancer have access to the latest advancements. With a focus on hope, progress, and patient advocacy, the Emily Whitehead Foundation continues to make a profound impact on the future of pediatric cancer care.

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Key Findings

CAR T recipient participation in long-term follow-up (LTFU) studies diminishes over time

20% of survey respondents who received CAR T therapy >12 months ago have stopped participating in LTFU appointments

80% of survey respondents who have stopped participating in LTFU appointments stopped attending them at or after 5 years post-treatment

Under the current system, participation in annual follow-up visits for all 15 years may not be feasible

38% of survey respondents who were treated >12 months ago and still attend follow-up appointments do not see themselves attending for all 15 years

68% of these respondents anticipate attending follow-up appointments for only 3-9 years

CAR T recipients and caregivers identify travel-related challenges as primary hurdles to follow-up attendence

64% of survey respondents indicated distance to site as a challenge to attending follow-up appointments

73% of survey respondents live >1 hour away from the original treatment center

66% of respondents indicated that attending follow-up appointments is not easy

Many CAR T patients and caregivers lack sufficient understanding of important aspects of LTFU studies

44% of survey respondents indicated they were not told by their CAR T treatment team that they would have to attend follow-up appointments for 15 years

61% of respondents indicated they were not told by their CAR T treatment team that they could attend follow-up appointments at medical centers other than the original site

73% of respondents reported not being told that LTFU studies monitor for secondary malignancies potentially caused by CAR T therapy

The majority of patients and caregivers are comfortable with certain modifications to the existing LTFU data collection process

81% of survey respondents indicated they are comfortable with allowing CAR T manufacturers to access their EHRs to obtain data regarding health changes

Introduction

Since 2017, six chimeric antigen receptor (CAR) T-cell therapies have been approved in the United States as treatments for patients with relapsed and/or refractory B-cell lymphomas, B-cell acute lymphoblastic leukemia, and multiple myeloma. Because the viral vectors used to generate CAR T-cells function to integrate the CAR transgene into the genome of recipient cells, FDA required 15 years of long-term follow-up (LTFU) to assess long-term safety of the initial approvals of these novel therapies. Per subsequent draft FDA guidance issued in September 2018 and finalized in January 2020, CAR T manufacturers are expected to design and conduct 15-year LTFU studies on patients who have received CAR T therapy as part of a clinical trial or via commercial administration[1,2]. While FDA guidance is not legally binding, it describes the Agency's current thinking, and therefore its general expectations; the specific details of an LTFU plan, such as the number of subjects to be studied, are negotiated between FDA and a sponsor at the end of the product review process prior to market approval.

Despite FDA Center for Biologics Evaluation and Research (CBER)'s expectation of extensive LTFU studies of sponsors for certain gene therapy technologies that include CAR T cells, to our knowledge, the patient burden around these requirements has not been studied. Therefore, to tap into this important patient perspective, the Emily Whitehead Foundation partnered with Catalyst Healthcare Consulting to survey CAR T patients and their caregivers to better understand the patient experience throughout LTFU studies, with the intent to pinpoint any perceived challenges, and explore ways the current LTFU process could be made more patient-friendly.

In this white paper, we briefly summarize the current FDA requirements for LTFU studies for context as they relate to CAR T cell therapies and present the results of the patient experience survey, which evoked responses from nearly 100 CAR T patients and caregivers. The survey results highlight clear trends in LTFU participation and awareness that may warrant updated thinking to make LTFU studies more patient-friendly.

Given the accelerating pace of development and expanding indications of CAR T-cell therapy, which has sparked a growing FDA interest in exploring policy options for LTFU, the right time to examine patient views of these requirements and to reduce barriers to participation is now.

Introduction

FDA Guidance on LTFU Studies

2020: "Long Term Follow-up After Administration of Human Gene Therapy Products"

Outines a risk assessment framework for the inclusion of LTFU studies in the clinical protocol and post-licensure plans to monitor long-term safety of products that use gene therapy (GT). For GTs, including CAR T-cell therapies using integrating vectors, FDA recomends 15 years of LTFU.

2024: "Considerations for the Development of Chimeric Antigen Receptor (CAR) T Cell Products"

Confirms that for CAR T-cells with an integrating transgene, FDA recommends 15 years of LTFU.[2]

2024: FDA Safety Communication

Announces FDA's conclusion that the serious risk of T cell malignancies is applicable to all currently approved BCMA-directed and CD19-directed genetically modified autologous CAR T cell immunotherapies, and therefore patients and clinical trial participants receiving these therapies should be monitored life-long for secondary malignancies.[3]

What LTFU Studies Measure

FDA guidance highlights adverse events unique to human GT products that may be associated with delayed events, some of which apply to CAR T-cell products that are genetically engineered to carry the CAR transgene.[1,2] For CAR T-cells, the agency expects 15-year LTFU studies to measure the presence and/or degree of:

- Secondary malignancies caused by viral vector–mediated integration events in the genome or off-target genome modifications, which can arise from disruption of critical host genes or activation of proto-oncogene(s) near the integration site(s)
- Replication competent viral vectors that may result in latent or persistent infections
- CAR T-cell persistence determined via assays that test for the presence of CAR T cells/vectors and the activity of CAR T-cells (e.g., gene expression or biomarker changes)

Introduction

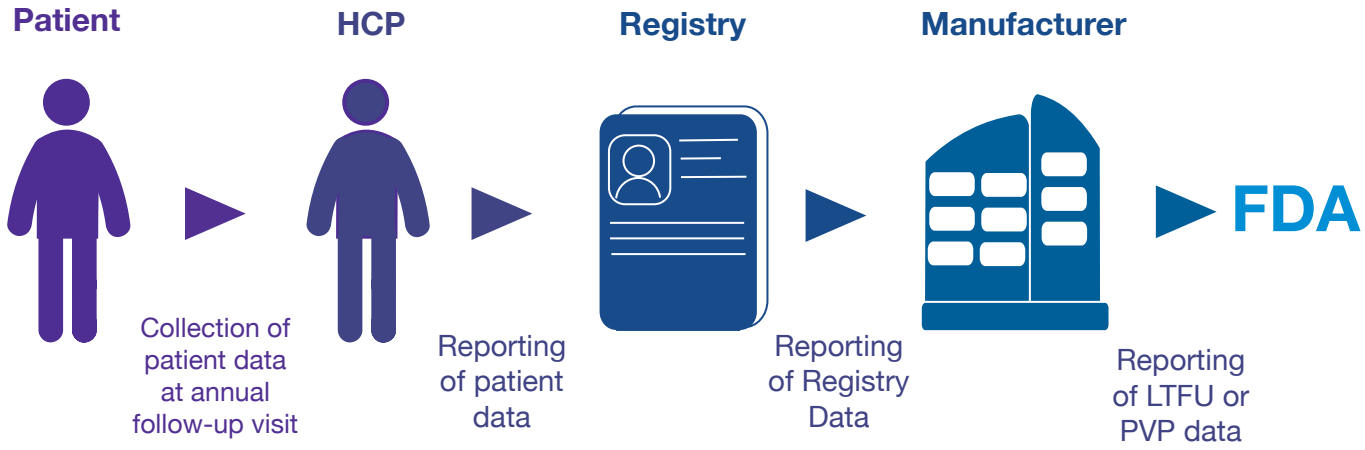
The LTFU Study Process

Per FDA guidance, sponsors should establish a dedicated clinical LTFU protocol and Pharmacovigilance Plan (PVP) to monitor investigational and commercial CAR T products, respectively.

The agency recommends these packages include plans for:

- Data collection, including patient visit schedules, a sampling plan (for patient test samples, such as blood), methods of monitoring tests, and clinical events of interest that will be monitored over the entire LTFU observation.
- Maintenance of adequate records for each subject that was administered the investigational product, which are obtained annually from health care professionals (HCPs) and reported to registries.
- Potential establishment of a registry or use of an existing patient registry to systematically capture pertinent data obtained via annual patient follow-up appointments, which FDA may recommend.

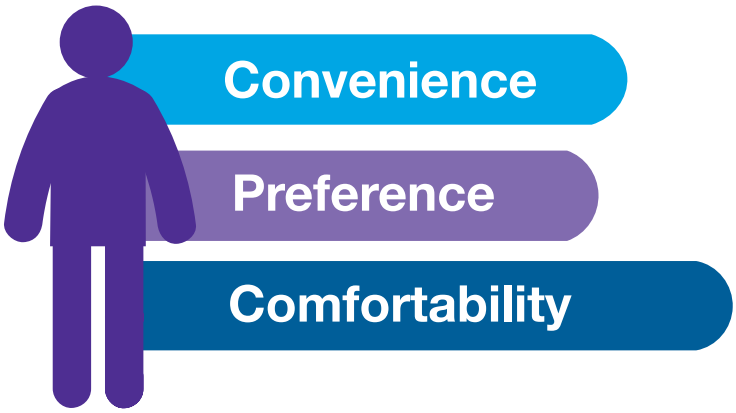
The typical LTFU process currently consists of the patient attending visits to a an HCP, which can occur at a site other than their clinical trial site or treatment center. The HCP obtains blood samples for analytical analysis per the clinical study protocol or PVP and is then responsible for reporting the analyzed data to the registry established or chosen by the sponsor. The CAR T manufacturer can directly access or request LTFU data from the registry for required reporting to the agency. If at any point a patient is diagnosed with a secondary malignancy, the HCP reports the data directly to the registry, the CAR T manufacturer, and the FDA Adverse Events Reporting System (FAERS).



Introduction

The Patient Perspective

Obtaining sufficient LTFU data is important to most accurately convey the long-term benefit–risk profile of CAR T therapies. A significant component of collecting robust long-term data is sufficient participation by patients in follow-up; therefore, patient convenience, preference, and comfortability are key elements affecting the adequacy of LTFU studies. To assess these key elements, the Emily Whitehead Foundation sought patient perspectives through a short online survey. The objective of the survey was to gain insight into the patient's experience with LTFU studies, including the level of patient engagement and awareness, and perceived or experienced barriers to patient participation in LTFU. Looking toward the future, the survey also asked for patient views of potential modifications to the current LTFU process to guide stakeholders toward informed, patient-focused solutions.



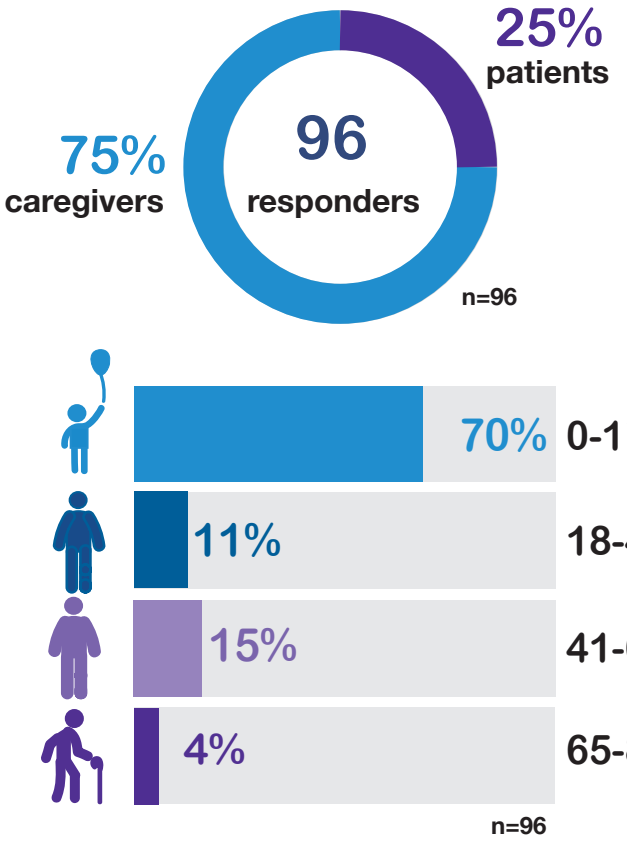
Methods

The Emily Whitehead Foundation worked with Catalyst Healthcare Consulting and with experienced survey conductor Andrea L. Paiva, Ph.D., ACPS, an Assistant Teaching Professor at University of Rhode Island Department of Psychology, to create a 10-minute online survey. The goal was to obtain insights from a diverse patient population that varied in features including age, location, and type (commercial or investigational) of CAR T product received. To do so, the team leveraged the EWF network, and several online channels leveraging numerous patient advocacy organizations and CAR T manufacturers to gain a wide distribution of the survey. The survey was conducted by Dr. Andrea Paiva and was initiated on August 12, 2024 and completed on September 13, 2024.

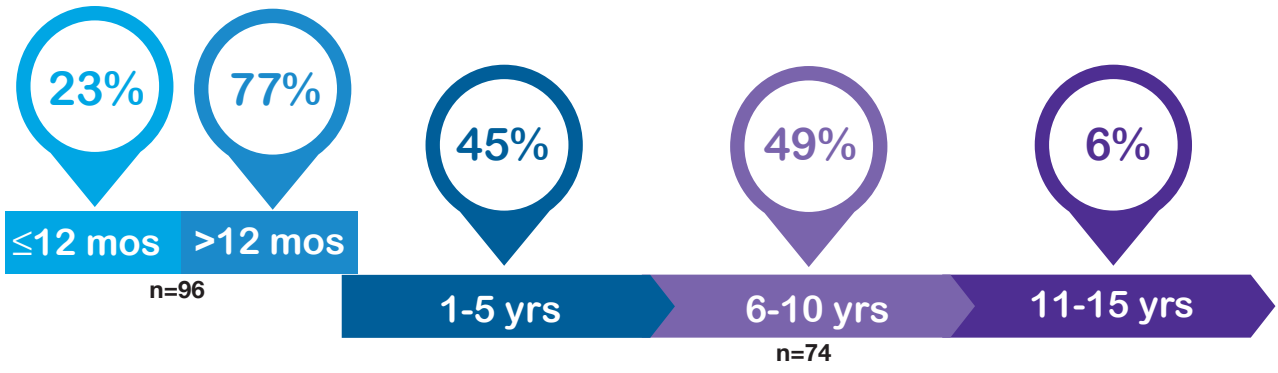
Results

Demographics

In total, there were 96 survey participants, 25% of which were CAR T patients and 75% of which were caregivers to a CAR T patient. This large caregiver population indirectly reflects the 70% of respondents who were aged 0-17 at the time of CAR T therapy receipt. This pediatric majority was expected given the selection bias for respondents who received CAR T therapy approved for pediatric indications. Moreover, 11% received CAR T therapy at the ages of 18-40, 15% at the ages of 41-64, and 4% at the ages of 65-81.



In addition to age group, the time since receiving CAR T therapies also varied between survey respondents, with 23% of patients receiving CAR T therapy within the last 12 months. Of the patients who received CAR T more than 12 months ago, 45% received CAR T within the last 5 years, 49% received CAR T within the last 6-10 years, and 6% received CAR T over 10 years ago.



Results

Demographics (cont.)

Both clinical trial and commercial settings were represented in the data, with 55% of respondents receiving an investigational CAR T treatment and the remaining 45% receiving one of four marketed treatments represented in the dataset. When asked where patients lived at the time of CAR T treatment, 22% lived in rural communities and 78% lived in urban communities (where large medical centers tend to be localized).

55%
of respondents received CAR T as part of a clinical trial

22%
of respondents lived in rural communities at time of treatment

45%
of respondents received CAR T commercially

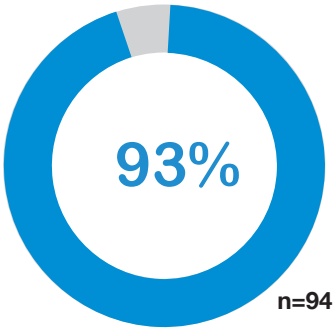
78%
of respondents lived in urban communities at time of treatment

n=96

Participation

Following the collection of demographic information, the survey was designed to ascertain actual and anticipated patient participation in common follow-up (FU) activities, expected of all patients from clinical trials and marketed CAR T cell therapies.

According to the survey data, 93% of respondents have obtained their recommended blood tests, which are typically conducted within the first 1-3 years after CAR T administration, suggesting that patients consistently meet at least one early FU recommendation.



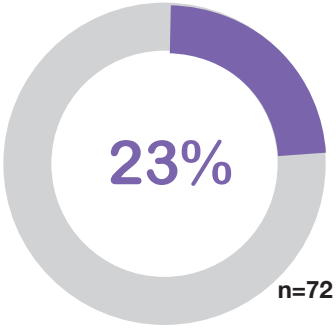
n=94

of respondents have obtained their recommended blood tests

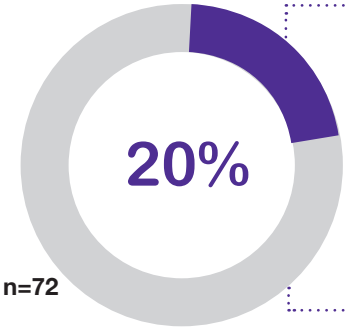
Results

Participation

Though early FU requirements were largely met, when looking at a longer-term scale, the survey data indicates a significant portion of patients are missing FU appointments or stopping their participation in LTFU altogether. In fact, 23% of survey respondents who were more than a year post-treatment reported they have missed a follow-up appointment and 20% of the same group have stopped participating in FU visits altogether. Of the respondents who have stopped participating in LTFU, 20% stopped within 2 years of treatment and 80% stopped attending appointments at or after 5 years post-treatment. Together, these data suggest that significant patient attrition occurs after 5 years post-administration and participation generally wanes over time.



of respondents who were treated >12 months ago have missed a FU appointment

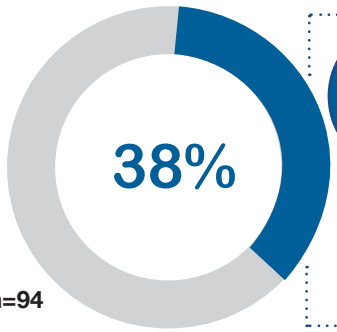


of respondents who were treated >12 months ago have stopped participating in LTFU

stopped attending FU appointments within 2 years post-treatment

stopped attending FU appointments at or after 5 years post-treatment

Illuminating intentions for future participation, 38% of all survey respondents treated >12 months ago who still attend FU appointments indicated they don't envision themselves attending for all 15 years. Of the respondents who don't envision themselves going to FU for all 15 years, 50% received CAR T cells ≤2 years ago. On the other hand, only 17% of respondents who received CAR T ≥10 years ago don't see themselves completing LTFU studies, likely because they are already nearing the 15-year mark and were pioneering CAR T patients. Moreover, of the respondents who don't envision themselves going to FU for all 15 years, 32% envision themselves attending FU appointments for 3-5 years and 36% see themselves attending FU for 6-9 years, suggesting that passive safety monitoring for major health events may be more realistic beyond a certain timepoint.



of respondents treated >12 months ago who still attend FU appointments do not see themselves attending for all 15 years

of these respondents received CAR T within the last 2 years

of these respondents received CAR T 10 or more years ago

of these respondents see themselves attending FU appointments for 3-5 years

of these respondents see themselves attending FU appointments for 6-9 years

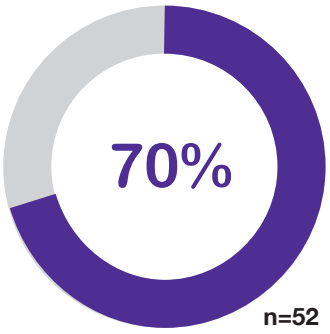
Results

Participation (cont.)

Challenges

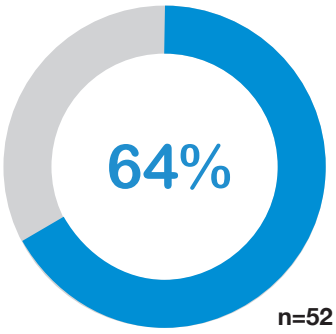
For survey respondents who indicated they were not attending FU appointments or did not plan on completing the full 15 years of LTFU, the survey was designed to explore why and potential barriers.

In general, 70% of respondents traveled to their LTFU appointments by car. When CAR T patients and caregivers were asked to select from a list of 15 options the top reasons for missing a FU appointment or top perceived challenges that could make attending a FU appointment difficult, most question respondents (64%) selected “distance to site” as the main experienced or perceived challenge. Moreover, when asked how burdensome respondents find attending FU appointments, 66% of survey respondents did not select “easy” or “very easy”



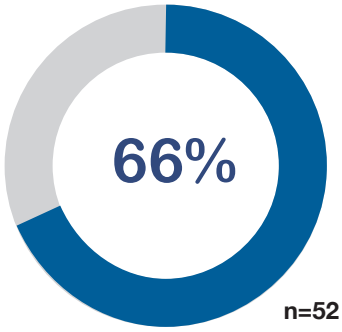
n=52

of respondents travel to FU appointments by car



n=52

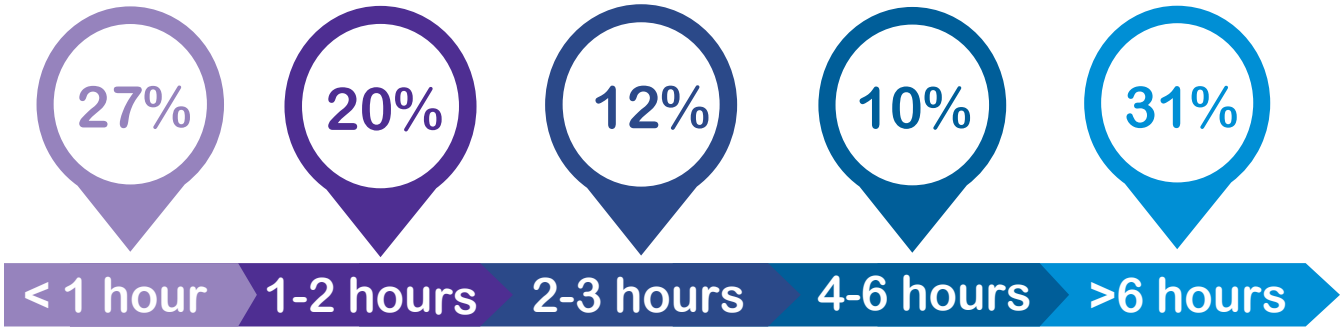
of question respondents selected “distance to site” as a major challenge



n=52

of survey respondents did not find traveling to FU appointments to be easy

When asked how far from the original treatment centers patients live, 31% of respondents indicated they live more than 6 hours away from the original site of treatment, while only 27% live within an hour of the original site.



n=71

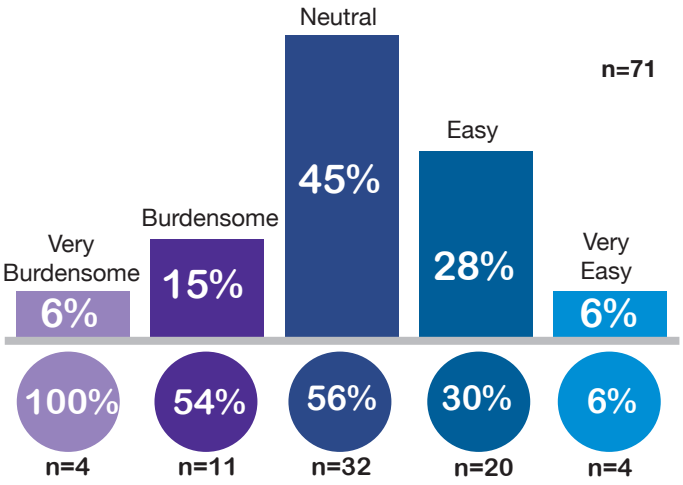
Participation (cont.)

Challenges

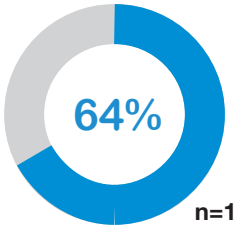
When asked how burdensome respondents found traveling to FU appointments, the 6% of respondents who indicated it was very burdensome all lived ≥2 hours away from the original treatment site. On the other hand, 94% of the 6% of respondents who found traveling to FU appointments to be very easy lived within 2 hours of the treatment site.

From the results, traveling to the site seemed to influence whether patients participated in LTFU, since 64% of the respondents who indicated they have stopped attending FU appointments lived ≥6 hours away and 79% lived ≥2 hours away from the original treatment center.

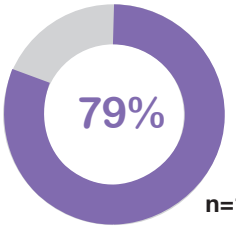
Reported difficulty level of attending FU appointments



Percentage of respondents in each difficulty level group that live ≥2 hours away



of survey respondents who no longer participate in LTFU live ≥6 hours away

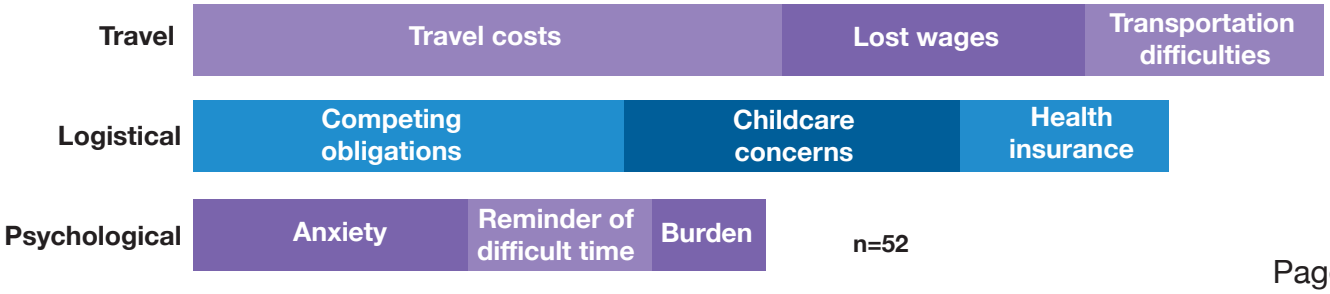


of survey respondents who no longer participate in LTFU live ≥2 hours away

In a question where respondents could select multiple options from a provided list of 15 challenges, other travel-related challenges identified included travel costs (30% of question respondents), costs associated with lost wages (18% of question respondents), and general transportation difficulties (16% of question respondents).

Beyond travel-related challenges, patients also experienced or perceived other logistical challenges, such as competing obligations (23% of question respondents), childcare concerns (18% of question respondents), and health insurance coverage (10% of question respondents).

From the list of perceived or experienced psychological challenges, 16% of question respondents indicated anxiety, 11% indicated that attending FU reminds them of a difficult time in their life, and 5% indicated the general burden of continuous monitoring as reasons for or challenges to missed LTFU appointments.

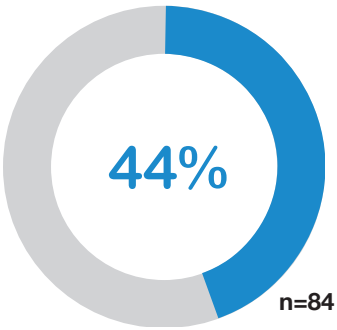


Results

Understanding of LTFU Expectations

Education shortfalls

When respondents were asked to report what their CAR T cell treatment team told them, 44% reported they were not told they would have to attend FU appointments for 15 years. Of these respondents who were not told about 15-year FU, 60% live in rural communities and 40% live in urban communities. Further, of these respondents, 64% received marketed CAR T products compared to 36% who received investigational CAR T products as part of a clinical trial.



of respondents reported they were not told by their CAR T treatment team that they would have to attend FU appointments for 15 years

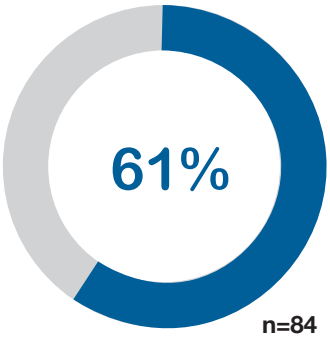
60%
of respondents who were not told they would have to attend FU appointments for 15 years live in rural communities

40%
of respondents who were not told they would have to attend FU appointments for 15 years live in urban communities

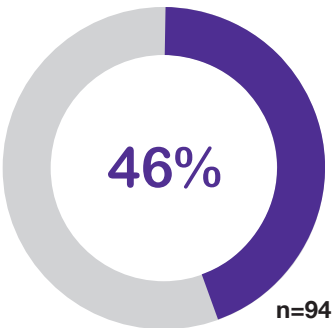
64%
of respondents who were not told they would have to attend FU appointments for 15 years received marketed CAR T products

36%
of respondents who were not told they would have to attend FU appointments for 15 years received investigational CAR T products

Given that the traveling distance to the original site of treatment is a major challenge limiting LTFU participation, the survey asked whether respondents were aware they could complete FU studies at medical centers other than the original site of CAR T-cell administration. The survey found that 61% of respondents reported they were not told by their CAR T treatment team that they could attend FU appointments at a location other than their original treatment center or trial site. However, some respondents seem to have obtained the information elsewhere since 46% of total respondents reported they have gone to FU appointments at local centers.



of respondents reported they were not told by their CAR T treatment team that they could attend FU appointments at medical centers other than the original treatment site.

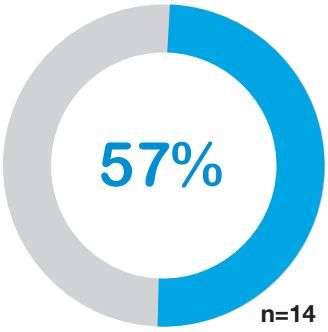


of respondents reported they have gone to FU appointments at local medical centers.

Results

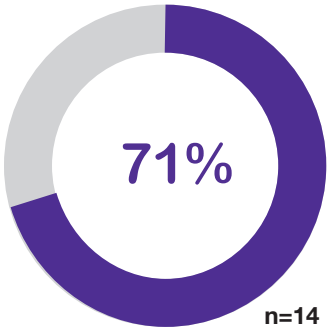
Understanding of LTFU

The survey data suggests that awareness can predict compliance. Of the respondents who indicated they have stopped attending LTFU studies, 57% reported their CAR T treatment team did not tell them about the 15–year LTFU requirement and 71% reported their CAR T treatment team did not provide information on attending FU appointments at local treatment centers.



of respondents who have stopped participating in LTFU reported not being told about the 15-year LTFU requirement

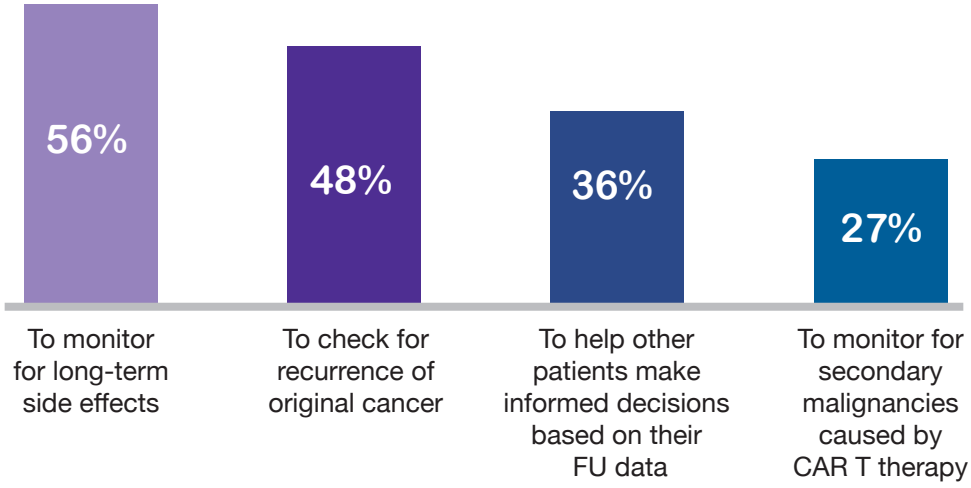
n=14



of respondents who have stopped participating in LTFU reported not being told they could attend FU appointments at local centers

n=14

To gauge patient understanding of the purpose of LTFU studies, the survey presented a number of options and asked responder to identify the reasons behind LTFU studies that have been communicated to them. Of the respondents, 56% reported being told LTFU studies monitor for long-term side effects, 48% have been told LTFU studies check for recurrence of the original cancer, 36% have been told LTFU studies help other patients make informed decisions based on what their FU data can provide to the medical field, and only 27% have been told LTFU studies monitor for secondary cancers caused by the CAR T therapy.



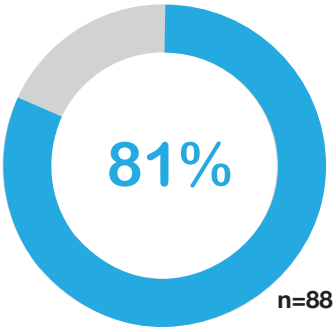
n=96

Results

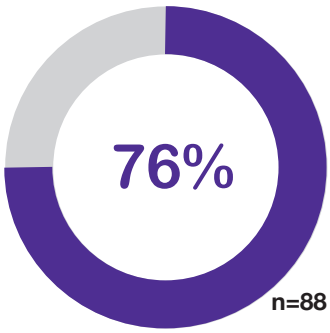
Comfortability

To understand how patients view potential modifications or alternatives to the current LTFU data collection process, the survey asked respondents to rate their level of comfortability with a series of proposed options.

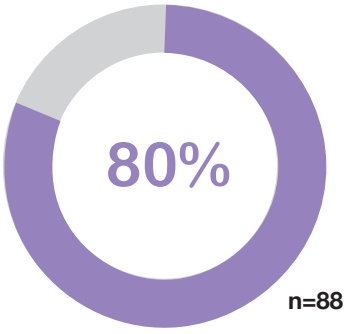
Of these proposed options, 81% of respondents indicated they would be comfortable with allowing CAR T manufacturers to access their electronic health records (EHRs), with 76% indicating they would be willing to grant CAR T manufacturers access to their EHRs for LTFU studies. Similarly, 80% of respondents indicated they are comfortable with attending appointments via telehealth and 77% indicated they are comfortable with entering their own health information in an online form or mobile app. On the other hand, only 48% of respondents indicated they would be comfortable with allowing a third party to use AI tools to monitor their EHRs to share data with CAR T manufacturers.



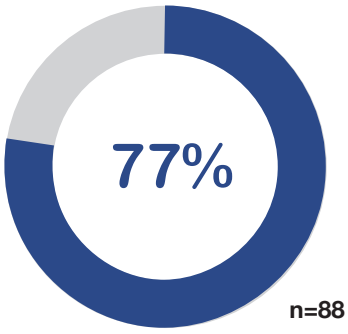
of respondents indicated they are comfortable with allowing CAR T manufacturers to access their electronic health records (EHRs)



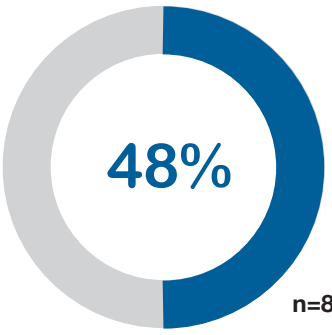
of respondents reported they would be willing to grant CAR T manufacturers access to their EHRs for LTFU studies



of respondents indicated they are comfortable with completeing appointments through telehealth



of respondents indicated they are comfortable with entering their own health information in an online form or mobile app



of respondents indicated they are comfortable with allowing a third party to use AI tools to monitor their EHRs to share data with CAR T manufacturers

Discussion

In light of the expanding development of CAR T-cell therapies, the growing patient populations they serve, and the increasing depth of experience with LTFU studies, this survey was conducted to explore patient experiences with LTFU requirements.

The findings were quite sobering and indicate that certain aspects of LTFU study designs should be re-evaluated with a stronger focus on patient convenience, preference, and comfortability.

The survey results presented herein may serve as a warning signal to regulators and sponsors around the need to review the current LTFU system and process and make it more patient-friendly.

Without consistent patient participation, LTFU data will be unlikely to accurately or significantly reflect safety outcomes of CAR T treatment, which remains a major overarching goal of regulators, sponsors, and patients.

Informing patients of the relative benefits and risks of CAR T-cell therapy is dependent on the collection of robust data in the post-market setting. However, various factors surrounding the current data collection process pose challenges to achieving more comprehensive data collection, including patient loss to follow-up.

The survey found travel-related barriers to be the most prevalent underlying cause of high LTFU drop-off rates. The survey also indicated that there is insufficient awareness that FU studies can be done locally. It may therefore be pertinent to revisit when, how, and how often patients are educated about LTFU expectations. Moreover, encouraging follow-up closer to home or within community centers may increase participation due to reducing the primary burden of long travel distances to treatment centers. There may also be a need for a concomitant increase in education of local providers around the regulatory recommendations for data collection as well as new tools to reduce the labor-intensive step of providing patient information to registries.

The survey results show that many patients are open to leveraging new tools, like EHRs, mobile apps, and telehealth to make LTFU more patient friendly. However, patients are not as comfortable with third parties leveraging AI to analyze EHRs, which suggests this solution may require providing additional information regarding intent and data security.

This patient experience survey is a first step to understanding patient perspectives regarding LTFU study requirements, challenges, and potential patient-friendly tools. FDA has demonstrated an interest in examining the LTFU process, which has led them to host a recent patient listening workshop. Based on the discussions during the session and the results of this survey, there is a need for more discussions, realistic expectations, and process improvements to the current LTFU system.

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Contact Information

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