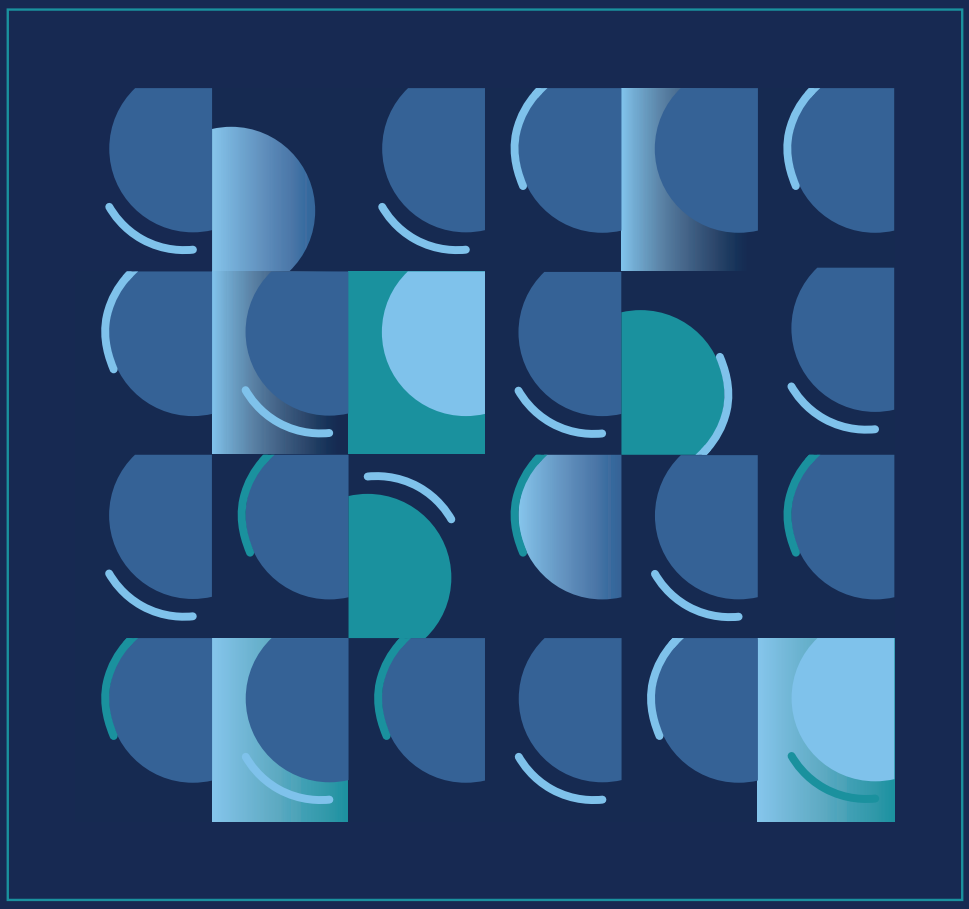


THE CAR T-CELL THERAPY CLINICAL TRIAL JOURNEY

A Guide for Patients and Caregivers

THE CAR T-CELL THERAPY PROCESS

1. ELIGIBILITY SCREENING

You will undergo a series of tests to make sure that this clinical trial is appropriate for you and that you are eligible to participate.

2. COLLECTION/TRANSPORT

Your white blood cells will be collected in a process called *leukapheresis*, and then sent to the manufacturing facility.

3. CAR T-CELL ENGINEERING

Through a series of steps in the laboratory at the manufacturing facility, your T cells are transformed into CAR T cells.

4. LYMPHODEPLETING CHEMOTHERAPY

You will be given chemotherapy over 3-5 days to prepare your body to receive your new CAR T cells.

5. CAR T-CELL INFUSION

Your CAR T cells are infused. This takes about 30 minutes. They can now begin to find and destroy your cancer cells.

6. MONITORING AND LONG-TERM FOLLOW-UP

You will be followed to see how the CAR T cells are affecting your body and if they are working to fight your cancer.

Each of these steps is further explained on the following pages

AT THE MANUFACTURING FACILITY

A. RECEIVED

The manufacturing facility receives your white blood cells and confirms they are correctly identified as yours.

B. SEPARATED

Your T cells are separated from the rest of your white blood cells.

C. ENGINEERED

The instructions to make a new CAR protein are inserted into your T cells. After it's made, the CAR is delivered to the surface of the T cell and becomes a T cell receptor. These cells are now called CAR T cells.

D. MULTIPLIED

Your new CAR T cells are multiplied until there are millions of them.

E. PURIFIED AND TESTED

The CAR T cells are purified, then tested to make sure they are of good quality.

F. TRANSPORTED

Under strict temperature controls, your CAR T cells are shipped back to the treatment center.

ACKNOWLEDGMENTS

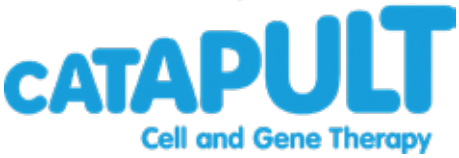
The ATTC network program is a UK system of Advanced Therapy Treatment Centres (ATTCs) operating within the NHS framework and coordinated by the Cell and Gene Therapy Catapult (CGT Catapult) to address the complex challenges of bringing advanced therapy medicinal products (ATMPs) to patients through three regional centers, one of which is the Northern Alliance Advanced Therapies Treatment Centre (NA-ATTC). The network is supported by the Industrial Challenge Strategy Fund delivered by UK Research and Innovation.

The NA-ATTC is pleased to offer *The CAR T-Cell Therapy Clinical Trial Journey — A Guide for Patients and Caregivers* in partnership with Autolus Therapeutics. These materials are available for download on the ATTC website https://www.theattcnetwork.co.uk/.

We are deeply grateful to all patients who have participated in CAR T-cell therapy clinical trials and especially for the guidance of the patients and caregivers in the CAR T Advisory Council. Without these contributions, this work would not have been possible.

Funded by

Coordinated by



WELCOME.

This Guide is intended for people who are either considering enrolling in or are already enrolled in a CAR T-cell therapy clinical trial. It contains information for both patients and those who care for them (caregivers). In these pages, you will find:

- General information about CAR T-cell therapy clinical trials
- An explanation of how CAR T-cell therapy works
- What you can expect during each step of the process
- Information about side effects
- Information specifically for caregivers
- Guidance on how and where to find support

You will learn from your clinical research team exactly what to expect in the clinical trial you are considering. The information and guidance provided here is not meant to replace that information. It should serve more like a reference for you – a place to start when you have questions to help prepare you for conversations with your healthcare team.

This Guide contains a lot of information and is not meant to be read in one sitting. Words or medical terms that might be unfamiliar to you are shown in *italics*. You'll find definitions in the **Glossary** on page 95, and a list of abbreviations on page 103. Don't hesitate to ask a member of your healthcare or clinical research team about anything you don't understand.

To help you navigate through the Guide, phrases like "information found on page X" have been included. You can click on the text and it will take you directly to the information. These links are blue and underlined to stand out.

Remember that CAR T-cell therapy is a newer therapy that is quickly changing as new discoveries are made. Always look first to the information and guidance given by your healthcare and clinical research teams for information specific to your clinical trial.

You, your caregiver, your loved ones, and your clinical research and healthcare teams are all partners on this CAR T-cell therapy journey. You all have the same goal: ensuring that you are well cared for and safe throughout this clinical trial. This Guide is meant to help you learn about the process so that you will know what questions to ask and what to expect.

TABLE OF CONTENTS

Click on any section to go directly to that page.

INTRODUCTION TO CLINICAL TRIALS

HOW CAR T-CELL THERAPY WORKS

TABLE OF CONTENTS, CONT.

Click on any section to go directly to that page.

THE CAR T-CELL THERAPY **PROCESS**

SIDE EFFECTS

TABLE OF CONTENTS, CONT.

Click on any section to go directly to that page.

SUPPORT ALONG THE JOURNEY

THE VITAL ROLE OF CAREGIVER

TABLE OF CONTENTS, CONT.

Click on any section to go directly to that page.

ADDITIONAL **RESOURCES**

GLOSSARY

INTRODUCTION TO CLINICAL TRIALS

Words that appear in *italics* are defined in the **Glossary** on page 95.

CLINICAL TRIAL OVERVIEW

Before a new drug treatment is available to patients it must be tested in a *clinical trial* to make sure it is safe and effective. *Safe* means that there are no unacceptable levels of unwanted effects of the treatment. *Effective* means that under certain conditions the treatment works. Every drug or medical treatment can have *side effects*, both known and unknown. A side effect is an unwanted effect of a treatment.

All clinical trials, including CAR T-cell therapy clinical trials, are carefully controlled to be sure the risk to *participants* is as low as possible. Many groups look out for the safety of clinical trial participants. Two of these are the *US Food and Drug Administration (FDA*) and *Institutional Review Boards (IRBs)*. The FDA will review information about the product to evaluate its safety before it can be used in a clinical trial. IRBs make sure that the rights, safety, dignity and well-being of clinical trial participants are protected.

The treatments used in clinical trials are experimental. It is not known whether you will benefit from a treatment used in a clinical trial. The experimental treatment is different than the standard-of-care treatment you would receive as a patient. You may be exposed to unknown risks. However, there may be other benefits of participating:

- ✓ You may receive tests and monitoring that patients outside of a clinical trial would not receive or may not be required to receive.
- ✓ You have a chance to receive a therapy that is not available to most patients outside of a clinical trial.
- ✓ Your participation will contribute to medical knowledge. This could make a difference for other people with your type of cancer.

Clinical trials are overseen by a trial *sponsor* and are conducted by *investigators*. Clinical trial investigators are usually specialist doctors with expertise in treating the disease being studied. A new drug or therapy usually must be studied in many clinical trials before it is approved to be marketed and used in patients. A clinical trial may be identified as a phase 0, 1, 2, 3 or 4 trial (sometimes called phase 0, I, II, III, or IV). Each phase is designed to answer specific questions about the new treatment.

ELIGIBILITY CRITERIA

Eligibility criteria define the population of patients that can or cannot participate in a particular trial and help protect the safety of trial participants.

Inclusion criteria are the factors that patients must have in order to participate in a particular clinical trial. Examples include age, the type and stage of cancer, health status and required prior therapies.

Exclusion criteria are the factors that prevent someone from participating in a particular clinical trial, even if they have the characteristics listed in the inclusion criteria. Examples may include pregnancy, therapies already received or participation in another clinical trial.

If you are found to be too unwell to participate in a clinical trial, ask your healthcare provider or the *clinical research team* if it may be possible to be reevaluated in the future if your health improves. You can learn more about the screening process on pages 35-38.

CAR T-CELL THERAPY CLINICAL TRIAL PHASES

	Why is it done?	What dose is given?	Things to know
PHASE 0 Phase 0	To learn about if and how a new CAR T-cell therapy affects the body.	Low	Usually the first time the CAR T cells are given to people.
PHASE 1 Is it safe?	To find the dose that will be used for phase 2. Usually the highest safe dose.	Starts low. There may be a *dose escalation*.	All participants will receive the CAR T cells.
PHASE 2 Does it work?	To learn more about whether and how the CAR T cells work.	The dose determined to be best in the phase 1 trial.	All participants will receive the CAR T cells.
PHASE 3 Is it better than what we have?	To find out if the new therapy is more effective or has fewer side effects than the current standard-of-care or an approved CAR T-cell therapy.	Most effective safe dose found in phase 2.	May be randomized such that half of the participants receive experimental CAR T cells and half receive another treatment.
PHASE 4 Are results similar when used after FDA approval?	To learn more about the long-term safety and effectiveness outside of a clinical trial setting after FDA approval.	The FDA-approved dose.	To learn more about the long-term safety and effectiveness outside of a clinical trial setting after FDA approval.

More information about each of these clinical trial phases can be found on the following pages.

Phase 0 or "First in human"

Phase 0 clinical trials are done to learn if and how the CAR T cells affect the body. They involve a very small number of participants. A phase 0 trial is the first time the CAR T cells have been given to people. Participants usually receive a smaller dose of cells than what investigators plan to use in later phase trials. Phase 0 clinical trials test whether the treatment reaches the cancer cells, how it acts in the human body, and if cancer cells respond to the treatment. These early trials are not meant to answer the question of whether the CAR T cells work to fight cancer (that will come in a later phase trial), but this information is recorded.

Is it safe?

Phase 1 clinical trials are done to find out if and how the CAR T cells can be given safely. They determine:

- ✓ The dose of CAR T cells that will be used for the phase 2 trial.
- ✓ How to best administer the CAR T cells.
- ✓ How the CAR T cells behave in the body, if this hasn't already been determined in a phase 0 trial.

A phase 1 clinical trial could be the first time the CAR T cells have been given to people, and might involve a *dose escalation*. This means that the first few participants are given a low dose of CAR T cells. If it is safe, the next group is given a slightly higher dose and so on until all of the planned doses have been tested.

How long the CAR T cells remain in the body and whether they fight cancer will also be studied.

A "dose" of CAR T cells is the number of CAR T cells given to you initially. These cells can multiply and increase in number once infused into your body.

Note: *All participants in a phase 1 clinical trial will receive the CAR T cells being studied.*

Does it work?

Phase 2 clinical trials are conducted to learn if the CAR T cells fight cancer. Like in every clinical trial, participants are watched carefully for side effects.

Participants receive a dose that was determined to be best based on the phase 1 trial. Because there are more participants in a phase 2 trial, there is a chance that less common side effects will be discovered.

Phase 1 and phase 2 clinical trials are sometimes combined into a phase 1/2 trial. In a combined trial, participants in the phase 2 portion of the trial receive a dose determined to be best during the phase 1 portion.

Note: *All participants in a phase 2 or phase 1/2 clinical trial will receive the CAR T cells being studied.*

Is it better than what we already have?

Phase 3 clinical trials are conducted to find out whether the experimental CAR T-cell product works better or is safer than the *standard-of-care treatment* or an already *approved* CAR T-cell product. Examples of standard-of-care treatments might include chemotherapy or stem cell transplant.

Phase 3 clinical trials may be *randomized*. This means that participants are divided into groups by random chance. Neither the physician nor the patient gets to decide which group the patient will be in. Patients assigned to the “treatment group” receive the CAR T-cell product being studied. Patients assigned to the “control group” will receive a different treatment. Depending on the clinical trial, this treatment could be either a standard-of-care treatment or an approved CAR T-cell product.

FDA review: Have safety and efficacy been proven?

The clinical trial sponsors will submit the trial results and other information to the FDA. There, a team of doctors, scientists, chemists and other experts will review all the submitted information. Sometimes, this team asks trial participants to tell them about what they experienced during or after their participation in the clinical trial.

This team will decide, among other things:

- If the benefits of the new CAR T-cell therapy are greater than the risks of the treatment.
- If the new therapy can be marketed and used in patients.

They will also make decisions about whether other clinical trials will be required after the product is approved. If the CAR T-cell therapy is approved, it is no longer considered an experimental treatment. It can now be marketed and prescribed to patients.

A Word About Placebos

Patients are sometimes worried that if they enroll in a cancer clinical trial, they might receive a placebo (an inactive treatment). Be assured that clinical trial participants with active disease are never given a placebo to treat their cancer.

In phase 1 or phase 2 CAR T-cell clinical trials, all participants receive the experimental CAR T-cell therapy. All participants in randomized phase 3 CAR T-cell trials receive treatment for their cancer. Some will receive the experimental CAR T-cell product and others will receive a different treatment. A placebo is never used.

PHASE 4

After FDA approval: What else can we learn?

Phase 4 clinical trials are conducted after a product has been approved and is marketed. These trials are often carried out to learn more about how long side effects last or about side effects that were not seen in earlier trials. They might also study how well the treatment continues to work over a long period of time.

Safety is always the top priority in clinical trials.

All clinical trials have risks, both known and unknown. It is helpful to know there are many individuals and groups looking out for your safety when you participate in a clinical research trial.

- ✓ The FDA reviews information about the product before they allow a new drug or treatment to be used in a clinical trial.
- ✓ IRBs make sure that the rights, safety, dignity and well-being of clinical trial participants are protected.
- ✓ Some trials have a separate safety committee whose role is to monitor for side effects and make decisions about what actions to take to protect the safety of participants.
  - If serious side effects occur more often or are more severe than what was expected, the safety committee will temporarily or permanently stop or modify the trial.
- ✓ Trial investigators closely monitor you for side effects during the entire trial.

LONG-TERM FOLLOW-UP

CAR T-cell therapy is a type of *gene therapy* (see page 30). In CAR T-cell therapy, T cells are genetically modified to help them find and destroy cancer cells. This change is designed to be long-acting and may be permanent.

To learn more about possible unwanted long-term or delayed side effects, the FDA requires a 15-year monitoring period for anyone who has received CAR T-cell therapy. This is called a *"long-term follow-up" (LTFU) study*. At some point during your clinical trial, you may be asked to participate in a LTFU study. The study will begin after your CAR T-cell clinical trial ends.

The number of years you will be asked to participate in the LTFU study depends on the length of your initial CAR T-cell therapy clinical trial. For example, if your initial trial is for 2 years, you will be asked to take part in the LTFU study for 13 years (for a total of 15 years).

You may be asked to sign another informed consent form for the LTFU study (see page 18 for more about informed consenting).

INFORMED CONSENT INFORMATION

THE INFORMED CONSENTING PROCESS

It is important for you to understand exactly what the clinical trial involves before you agree to participate. During the informed consenting process you will be provided with information that will help you make this decision. Take full advantage of the time you are given to ask questions. The words used may be unfamiliar or hard to understand. If any information is not clear, ask that it be explained. The informed consent documents include:

1. ***Participant Information Sheet (PIS):*** Includes information about the purpose and plan of the research, what will be done to you, and any risks or discomforts you may experience.
2. ***Informed Consent Form (ICF):*** Records the signatures of both you and the person from the clinical research team who reviews the information with you. In some cases, a legal guardian and/or caregiver may also be asked to sign. This is an agreement between you and the researchers about what each of you agrees to do throughout the research process. Signing this document means that you understand the information contained in the PIS, that you have been given time to ask questions about it and that you agree to participate in the clinical trial.

- ✓ The ICF must be signed before you have any procedure or test related to the clinical trial (see page 19).
- ✓ Signing the ICF does not mean that you will be accepted into the clinical trial.
- ✓ The ICF is a legal document but it is not a contract. It requires that both parties follow what is outlined in the documents received during the informed consent process. However, signing it does not require you to continue to participate in the clinical trial and you may withdraw from the trial at any time, and for any reason.

MAKING THE INFORMED CONSENTING PROCESS EASIER

Your clinical research team wants you to have the information you need to make an informed decision about whether to participate in the clinical trial you are considering. Information may be provided in written form, verbally or even in video form. Here are some suggestions to help make the process easier:

Before your first visit

- ✓ A research nurse or coordinator might be able to answer some of your questions over the phone.
- ✓ Ask if the PIS can be sent by mail or email so you can prepare ahead of time.
- ✓ If you have a copy of the PIS, highlight or underline anything you have questions about.
- ✓ Ask a friend or family member to read the PIS too, and see if you both understand the information the same way.
- ✓ Make a list of questions you want to ask the clinical research team.
- ✓ Consider sending your questions ahead of time so the clinical research team can be well prepared to answer your questions.

At your first visit*

- ✓ If COVID-19 or other infection control restrictions allow, bring a friend or family member with you to take notes and make sure all of your questions are answered.
- ✓ If you are not allowed to bring someone with you, ask if they can join by speaker phone or a video call.
- ✓ Consider asking if you can record your visit.
- ✓ Give a copy of your questions to the clinical research team or ask them to make a copy of your questions before the meeting begins.

*Some patients might feel that members of the clinical research team are too busy to answer their questions. But it is very important that you understand information about the trial before you agree to participate. The team has set aside this time to answer your questions. If you do run out of time, schedule a follow-up call or visit to continue the discussion.

At the end of your visit:

- ✓ You may be asked to sign the ICF. If your questions have been answered and you want to participate, sign the form and ask for a copy.
- ✓ Screening tests may be scheduled after you sign the form.
- ✓ If you are not prepared to make a decision, you will be able to take the PIS home with you. Ask what the next step is. You may be able to ask follow-up questions over the phone, or another visit may be scheduled.

MAKING THE INFORMED CONSENTING PROCESS EASIER, CONT.

Additional questions for the clinical research team

About medical care unrelated to the clinical trial

- ✓ How will the healthcare team communicate with my local healthcare provider?
- ✓ Who will be in charge of my medical needs that are not related to the clinical trial?
- ✓ Will I be able to take my regular medications during the trial?

About hospital stays

- ✓ Will I have to be in the hospital to participate? For how long?
- ✓ Will my caregiver be able to visit or stay with me in the hospital?
- ✓ If COVID-19 or other infection control restrictions prevent my caregiver from visiting, are there other ways we can communicate with each other?

About insurance and out-of-pocket costs

- ✓ What costs will be covered by the trial sponsor?
- ✓ Who can I ask about the costs I will be responsible for?
- ✓ What is the contact information for the financial specialist or the person I should talk to if I have questions about charges or billing?

THE PARTICIPANT INFORMATION SHEET (PIS)

Every clinical trial is unique. The information contained in the PIS will be different for every trial. Ask your clinical research team if you don't see the information you are looking for. The following information will be included:

About the research

- What is the research question this trial is designed to answer? Examples are: Is it safe? Does it work? Does it work better than what is currently used?
- What is being tested? A drug? A device? A procedure?
- Detailed information about the specific drug or therapy being tested.
- The length of the trial.
- What the alternatives are if you choose not to participate.

Why you are being asked to participate in the clinical trial

- Information about which patients will be included or excluded from participating.

Your rights as a clinical trial participant

- A statement confirming that your participation is voluntary.
- Your right to withdraw from the trial at any time and for any reason.
- An explanation of how your privacy will be protected.

What will happen if you agree to participate

- Detailed information about the entire process will be provided. This may include a schedule of planned visits.
- Information about the tests, procedures, examinations and treatments you will have during the screening process (See pages 35-38 for more information about Eligibility screening).
- A description of the known risks of participation.
- A description of the possible benefits of participation.

Financial Information

- The costs you will be responsible for.
- What expenses may be reimbursed.
- More information on finances and clinical trials can be found below.

The PIS has a lot of information, and it may be too much to absorb in one sitting. There may be time for you to take the PIS home with you to read it again. If this is not convenient for you, take the time you need to have all of your questions answered before you sign the informed consent form.

FINANCES AND CLINICAL TRIALS

Costs and Insurance Coverage

Before agreeing to participate in a clinical trial it's important to understand costs you may be responsible for. Costs are divided into 3 basic categories:

Costs covered by the trial sponsor:

- ✓ The cost of the experimental therapy and its administration.
- ✓ The cost of any tests required by the trial that aren't considered to be the standard-of-care for your type of cancer. This includes things like laboratory or imaging tests and extra office visits.
- ✓ The trial sponsor may also contribute to the costs of travel and lodging. This depends on the particular clinical trial. Ask your clinical research team what costs the sponsor may cover.

Costs covered by your insurance:

- ✓ Costs of medical care that is considered to be the standard-of-care for your type of cancer. It includes things like laboratory and imaging tests, cancer treatments and hospital stays that are not related to the clinical trial.
- ✓ The amount of coverage depends on your insurance.
  - **Private health plans** usually cover these costs*.
  - **Medicare** usually covers these costs. Visit medicare.gov or call 1-800-Medicare (1-800-633-4227) to see if the trial you are considering meets Medicare's requirements.
  - **Medicaid** coverage varies by state. Check to see if your state covers routine care costs during your participation in a clinical trial.
- ✓ Possible exclusions by some insurance plans:
  - Some will not cover costs of standard-of-care therapy if you are enrolled in a phase 1 clinical trial.
  - Some exclude coverage for any trial taking place in a different state.
  - Some managed care plans will require you to have your lab and imaging tests performed at a facility within their network.
- ✓ Check with your insurance company about coverage for clinical trials. If you are denied coverage, consider filing an appeal. It sometimes requires several appeals to obtain coverage. If your appeals are not successful, patient advocacy groups may be able to help. (See the **Additional Resources** section on page 84).

Costs and Insurance Coverage, cont.

Information about private insurance, Medicare and Medicaid coverage while participating in a clinical trial can be found at ASCO.org.

The Leukemia & Lymphoma Society also offers a list of resources to help with insurance issues:

Costs you are responsible for:

- ✓ Co-pays, co-insurance, and deductibles.
- ✓ Travel expenses and parking for you and your caregiver.
- ✓ Food and lodging for your caregiver while you are at the treatment center.
- ✓ Food and lodging for both you and your caregiver if you are being treated as an outpatient.
- ✓ Childcare or eldercare, pet care, lost wages, etc.

Financial assistance for some of these costs is available from several patient organizations. A list can be found at Cancer.net.

Help with travel expenses, parking, food, and lodging are sometimes available from the trial sponsor or the treatment center where you are receiving care. If this help is not offered, ask if it is available.

During the informed consenting process you will be told about any costs that you will be responsible for. You will also be directed to someone to contact with questions about your bill. This is usually a financial specialist or a social worker.

In the best of circumstances, medical bills can be confusing. When participating in a clinical trial, figuring out whether you are responsible for a charge can be a challenge. Your clinical research team can tell you whether the trial you are participating in has funds to help with expenses like travel and lodging. They will direct you to financial specialists at your treatment center to help with questions about other charges.

Costs and Insurance Coverage, cont.

Multiple Appeals of Coverage Denial May Be Necessary

- ✓ Your private health insurer generally cannot refuse to let you participate in a clinical trial, but there are exceptions. It cannot deny coverage of routine costs and it cannot increase your costs because you are taking part in a trial. Talk directly with your insurance company to make sure you understand what is covered. If you don't already have a case manager, ask for one to be assigned to your case. Ask for a written explanation of your benefits. If you receive a denial, you should appeal, perhaps several times if needed.

- ✓ Your insurer is not required to cover care from out-of-network providers or hospitals. Many will make exceptions if there are no similar treatment options within their network. If coverage is denied for this reason, you can appeal. Speak to the financial specialists at your treatment center and your insurer to make sure you understand what is covered and how to appeal if necessary.

THE CLINICAL RESEARCH TEAM

You will see “the clinical research team” mentioned many times in this Guide. Team members at each treatment center will be different, but one thing will be the same: There are many people dedicated to your care and safety throughout the trial.

You may meet many members of the team:

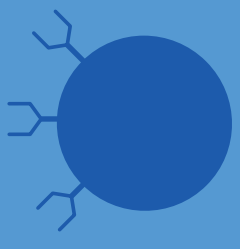
- The doctors and nurses who will explain the trial to you and answer your questions. The doctor is sometimes called an Investigator. The nurse is sometimes called a Research Nurse.
- The healthcare providers who will care for you at the treatment center and during any hospitalizations. These are often the same healthcare professionals that explained the trial to you.
- The social workers, pharmacists, physical therapists, nutritionists and others who will help meet your needs while you are participating in the trial.
- The coordinators who will help schedule appointments.
- The financial specialists who will help you with billing issues.

There are many other people working behind the scenes that you may not meet:

- The Principal Investigator who leads the team of Investigators at your treatment center.
- The investigators who oversee the trial and make sure the written research plan is followed.
- The scientists and researchers who developed the new therapy being tested.
- The trial sponsors who initiated and paid for the trial.
- The safety committee which monitors for side effects and decides whether it is safe to continue the trial.
- The Institutional Review Board (IRB) members who help to protect your rights and welfare as a clinical trial participant.
- The courier company that safely transports your cells to and from the manufacturing site.
- The team that manufactures your CAR T cells and makes sure they are of good quality.
- The many assistants and office workers who support each team.
- The other clinical trial participants who have had the experimental treatment before you.

As you can see, you might encounter dozens of people throughout your CAR T-cell therapy clinical trial journey. Don’t hesitate to ask those you meet what part they will play in your care.

HOW CAR T-CELL THERAPY WORKS



Words that appear in *italics* are defined in the **Glossary** on page 95.

CELLS, CANCER AND THE IMMUNE SYSTEM

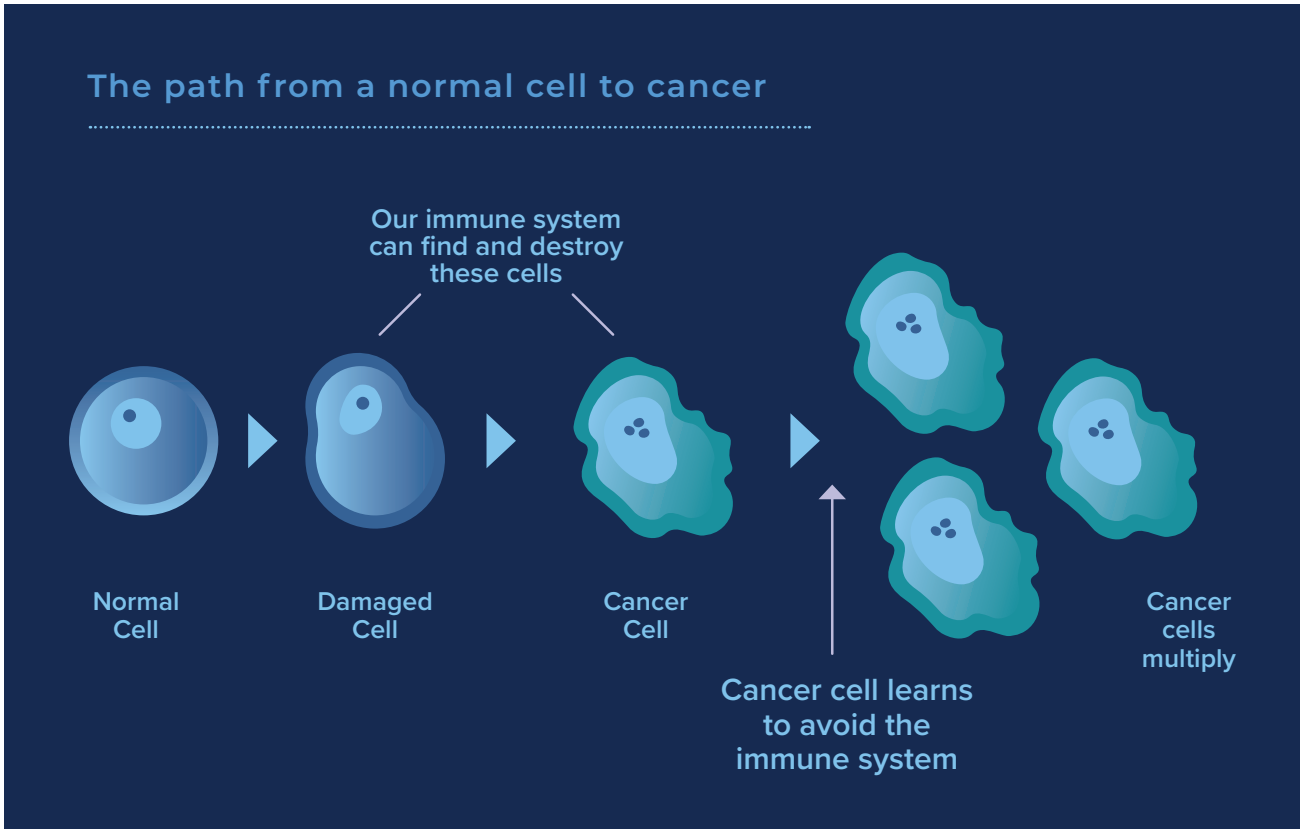
Our bodies are made up of trillions of *cells*. Cells provide structure, take in nutrients, produce energy, and carry out many other functions. Cells also carry our genetic material and make copies of themselves by dividing, or growing in number.

Cells get messages from nearby cells that tell them what to do. Cells may be instructed to grow and divide or to stop growing and die. Healthy cells can follow these instructions.

Cancer results when a cell is damaged and ignores the message to stop growing or to die. The process of a normal cell becoming a damaged cell and then a cancer cell can take a long time and can involve many changes (called *mutations*).

Our immune system normally does an excellent job of protecting us from most threats. This includes stopping damaged cells from growing and making more cells, or multiplying. Our immune system regularly protects us against cells that have developed into individual cancer cells.

Cancer results when a single cancer cell learns how to avoid or hide from the immune system. This allows that individual cell to divide and grow uncontrollably.



ONGOING CANCER SURVEILLANCE

Our immune system protects us from cancer with the help of *T cells*. T cells are white blood cells that travel through the bloodstream, searching for abnormal cells. T cells have a structure on their surface called a *receptor* that allows them to recognize, attach to and destroy abnormal cells.

T cells can recognize cancer cells as abnormal because cancer cells have a substance on their surface called an *antigen*. Receptors on T cells find antigens on cancer cells.

This ongoing process prevents a single cancer cell from making more cancer cells.

Our immune system can usually find and destroy individual cancer cells. However, cancer cells can learn to escape the immune system. Cancer cells learn how to avoid the immune system in different ways:

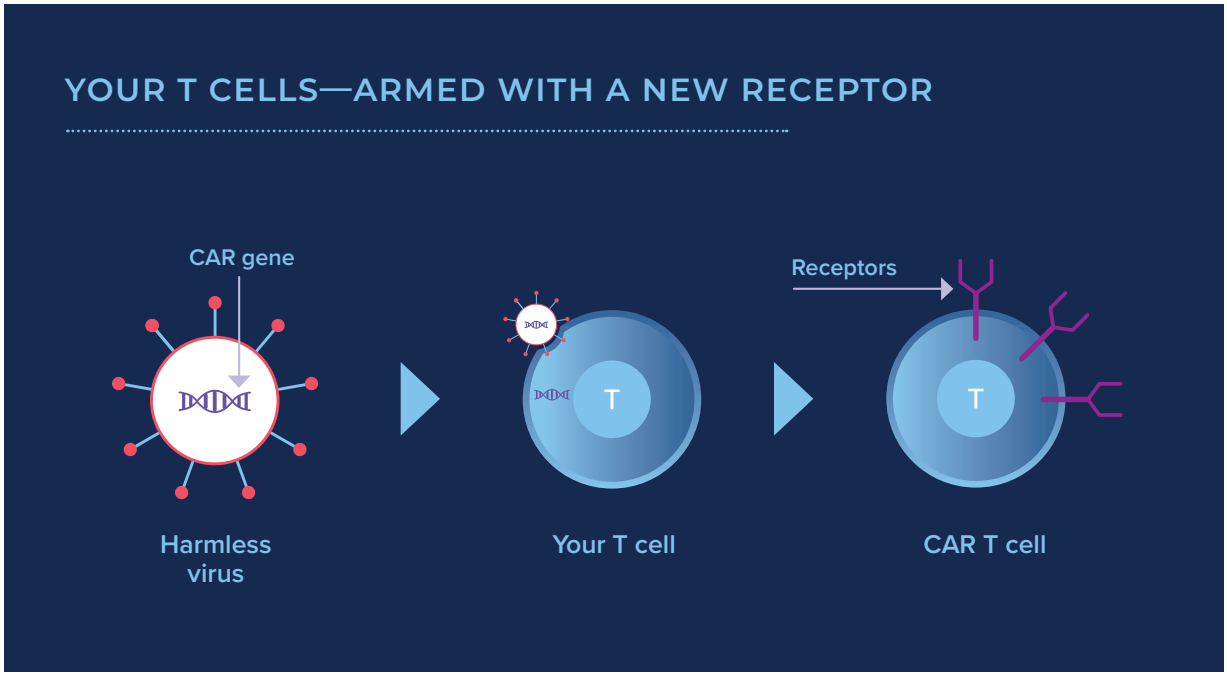
- Disguising themselves as “normal” so that T cells do not recognize them.
- Displaying so many antigens on their surface that T cells can’t respond.
- Producing chemicals that turn off the immune response.

This allows a single cancer cell to survive, divide uncontrollably and crowd out normal cells, leading to the symptoms of cancer.

Immunotherapy is a type of cancer treatment that helps our immune system recognize and attack cancer cells that have learned how to avoid our immune defenses.

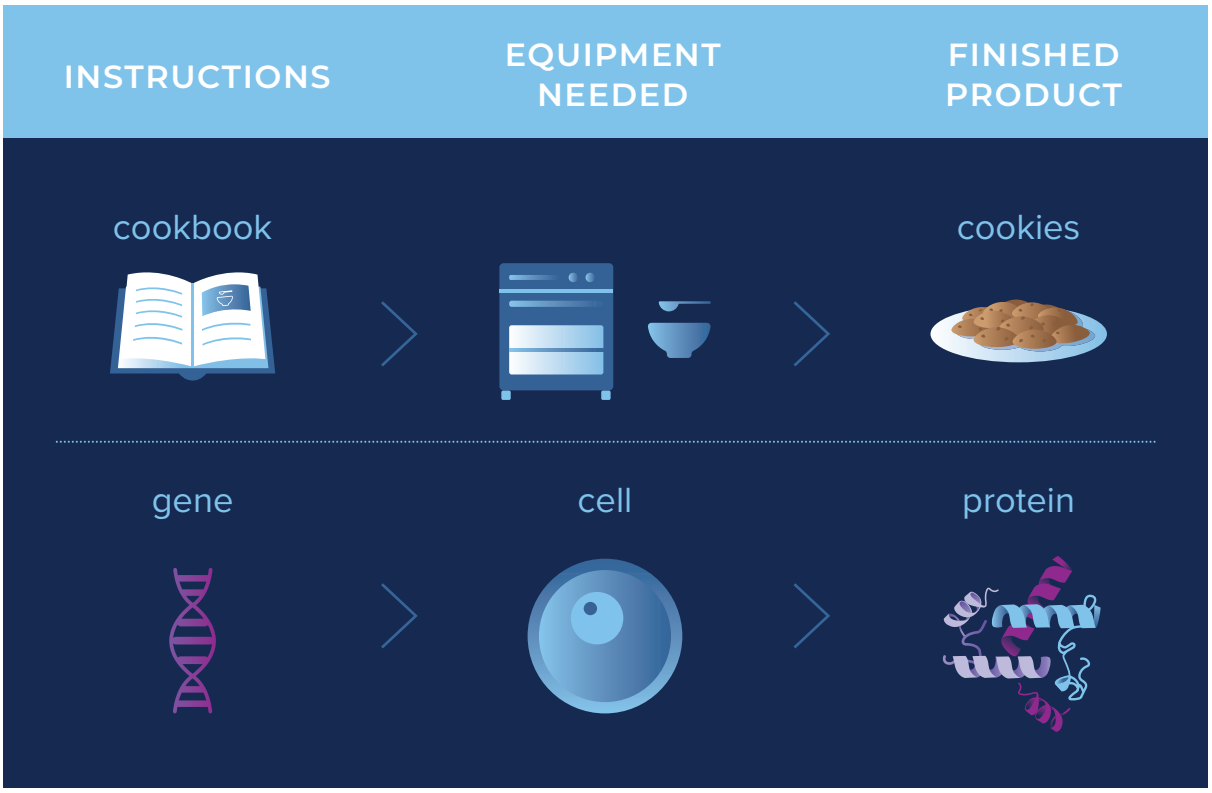
HOW CAR T CELLS WORK TO FIGHT CANCER

Chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy. The goal is to arm your own T cells with a new receptor that can recognize cancer cells as abnormal and help your T cells kill them.



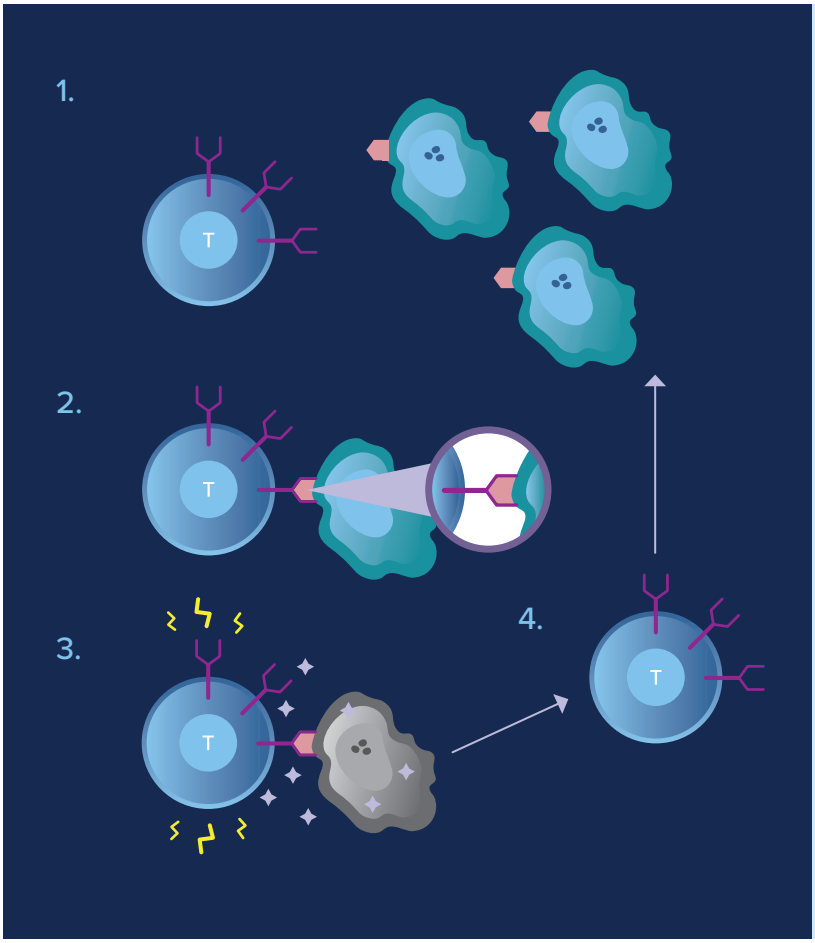
CAR T-CELL THERAPY IS *GENE THERAPY*

Genes carry the DNA instructions for the new CAR protein. Just as a cookbook carries a recipe or instructions on how to make a particular cookie, a gene carries the instructions for how to make a new protein.



The gene is inserted into your T cells in the laboratory at the manufacturing facility. They now have the instructions to make the new CAR protein.

HOW CAR T CELLS SEEK OUT AND KILL CANCER CELLS



1. CAR T cells circulate through the bloodstream, seeking out cancer cells that are hiding from the immune system.
2. The CAR recognizes and attaches to the antigen on the cancer cell.
3. The CAR T cell activates, multiplies, and releases chemicals called *cytokines* that kill the cancer cell.
4. The CAR T cell detaches from the killed cancer cell and seeks out more cancer cells.

= CAR = Cancer cell antigen = Cytokine

DIFFERENT TYPES OF CARS

The first approved CAR T-cell therapies targeted cells that have an antigen called "CD19" on their surface. CD19 is found on some leukemia and lymphoma cells and also on most normal *B cells*.

There are many more CARs being studied to treat cancer that can attach:

- to a different cancer antigen
- to more than one cancer antigen
- in different ways to the antigen, which can affect how the T cell is activated

You will learn from your clinical research team exactly what type of CAR will be used in the clinical trial you are considering.

Autologous vs Allogeneic CAR T Cells

CAR T cells can be made from a patient's own T cells (called "*autologous*") or from the T cells of a healthy donor (called "*allogeneic*"). Currently, the most common source of T cells used to create CAR T cells is the patient's own T cells.

While each clinical trial will be different, CAR T-cell therapy always involves a series of steps that are explained on the following pages. For an overview, see the **CAR T-Cell Therapy Process Journey Map** on page 34.

THE CAR T-CELL THERAPY **PROCESS**

THE CAR T-CELL THERAPY PROCESS

1. ELIGIBILITY SCREENING

You will undergo a series of tests to make sure that this clinical trial is appropriate for you and that you are eligible to participate.

2. COLLECTION/TRANSPORT

Your white blood cells will be collected in a process called *leukapheresis*, and then sent to the manufacturing facility.

3. CAR T-CELL ENGINEERING

Through a series of steps in the laboratory at the manufacturing facility, your T cells are transformed into CAR T cells.

4. LYMPHODEPLETING CHEMOTHERAPY

You will be given chemotherapy over 3-5 days to prepare your body to receive your new CAR T cells.

5. CAR T-CELL INFUSION

Your CAR T cells are infused. This takes about 30 minutes. They can now begin to find and destroy your cancer cells.

6. MONITORING AND LONG-TERM FOLLOW-UP

You will be followed to see how the CAR T cells are affecting your body and if they are working to fight your cancer.

AT THE MANUFACTURING FACILITY

A. RECEIVED

The manufacturing facility receives your white blood cells, and confirms they are correctly identified as yours.

B. SEPARATED

Your T cells are separated from the rest of your white blood cells.

C. ENGINEERED

The instructions to make a new CAR protein are inserted into your T cells. After it's made, the CAR is delivered to the surface of the T cell and becomes a T cell receptor. These cells are now called CAR T cells.

D. MULTIPLIED

Your new CAR T cells are multiplied until there are millions of them.

E. PURIFIED AND TESTED

The CAR T cells are purified, then tested to make sure they are of good quality.

F. TRANSPORTED

Under strict temperature controls, your CAR T cells are shipped back to the treatment center.

Each of these steps is further explained on the following pages

Words that appear in *italics* are defined in the **Glossary** on page 95.

INTRODUCTION

All CAR T-cell therapy involves these 6 steps:

1. Eligibility screening
2. Collection and transport
3. CAR T-cell engineering
4. Lymphodepleting chemotherapy
5. CAR T-cell infusion
6. Monitoring and long-term follow-up

We explain below what you can expect during each step. You can find a summary of what will be happening to you (steps 1-6) and what will be happening with your cells (steps A-F), on the **CAR T-Cell Therapy Process Journey Map** on page 34.

1. ELIGIBILITY SCREENING

Your healthcare team needs to make sure that participating in this clinical trial is appropriate for you. They will also need to verify that you are eligible to take part in the trial. After the clinical research team is certain that you understand what will be involved in the clinical trial and you have signed the ICF, you will be able to begin the screening process.

Screening is a series of medical tests and examinations. Your clinical research team will explain each one and help coordinate scheduling*. The tests needed for each trial and for each patient will be different. In general, the clinical research team needs to be sure that:

- ✓ You are well enough to participate.
- ✓ Your liver, heart, lungs and kidneys are functioning well.
- ✓ You don't have a serious heart, *neurological* (brain, spinal cord, and nerves) or immune system disorder.
- ✓ You don't have a serious infection.
- ✓ Your cancer cells have the antigen, or "marker," that will allow the CAR used in this trial to see them.

*Screening tests are usually performed at the treatment center.

To start, you should expect to receive a complete physical exam. There will also be tests to measure your neurological function. These might include tests for memory, language, and reaction time. Additional tests that might be needed are explained in the table below.

Measurement	Type of evaluation test
Basic level of health	***ECOG performance score:*** A measurement of your ability to care for yourself and perform daily activities.
Kidney function	Blood tests.
Liver function	
Infection	
Lung function	***Pulmonary function tests (PFTs):*** Breathing tests to see how well your lungs are working.
Staging or extent of your disease	***Bone marrow biopsy:*** A sample of bone marrow is collected using a hollow needle inserted into the bone (usually the hip bone).
	Lumbar puncture (or spinal tap): A sample of the fluid surrounding the brain and spinal cord is collected using a needle inserted between 2 bones in the spine.
	Tumor biopsy: A sample of tumor tissue, if one has not already been taken recently.
	Scans, which might include: • ***CT scan:*** Uses a series of X-rays and a computer to create detailed images of the body. • ***PET scan:*** Uses a small amount of a radioactive tracer to be able to see cancer cells. • ***PET-CT scan:*** PET and CT scans are combined to create a 3-dimensional image. • ***MRI:*** Uses a strong magnetic field, radio waves and a computer to create detailed images of the body. • ***Angiography:*** An X-ray image of the blood vessels. A dye will be injected that will make the vessels visible. • ***Ultrasound scan:*** Sound waves are used to show deep structures of the body. • ***Skeletal survey:*** A series of X-rays to look for areas of bone that may be damaged.

Measurement	Type of evaluation test
Heart condition	Several different tests may be used, including: • ***ECHO:*** An ultrasound image of the heart. • ***MUGA scan:*** A small amount of a radioactive tracer is injected. A special video camera is then used to show how well the heart is pumping. • ***ECG:*** Records the electrical activity of your heart.
Pregnancy (if you are female and of childbearing age)	Blood or urine test.

Depending on your specific situation, you may not need all of these tests, or you may need other tests in addition to the ones listed here. Your clinical research team will explain the tests you need.

Screening tests are an important part of every clinical trial. An explanation of each test, the risks involved and any discomfort you may experience are explained in the PIS. If there is anything you don't understand, ask your healthcare provider or clinical research team.

If you are worried about any discomfort you may have during these tests, speak to your healthcare team. There may be steps that can be taken to lessen your discomfort.

Waiting to learn if you are eligible for a trial can be stressful. Ask your healthcare team when and how you will learn the results of the tests. Having an idea about timing can help reduce the anxiety as you wait. See pages 65-69 for ways to help cope with stress and anxiety.

Even if you are found to be eligible for the clinical trial, you may not be able to receive CAR T cells in these cases:

1. Your T cells may not grow well in the laboratory. This is rare and is sometimes the result of having very low blood counts at the time of leukapheresis. A second leukapheresis may be performed to collect more cells. See additional information about leukapheresis on page 39.
2. Your health may worsen such that your doctor believes CAR T-cell therapy may be unsafe for you.

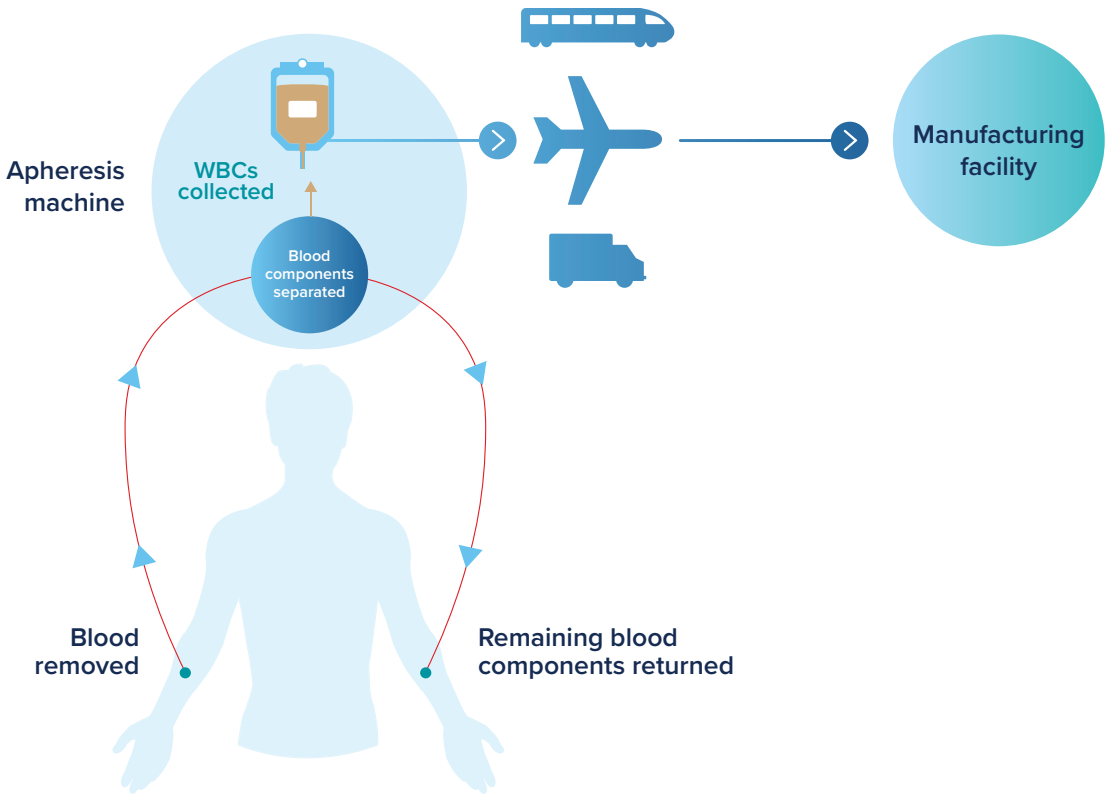
It can be disappointing to learn you are not eligible for a trial you wanted to take part in. Ask if there is a chance you could become eligible for this trial in the future or about other treatment options.

2. COLLECTION (LEUKAPHERESIS)/TRANSPORT

Leukapheresis (sometimes called *apheresis*) is the process used to collect your white blood cells. T cells are one type of white blood cell. They will be used to create your new CAR T cells.

An overview of the process:

1. Your blood is removed from one arm through a vein. It will go through a machine that separates and collects the white blood cells (WBCs).
2. The other parts of your blood (plasma, red blood cells and platelets) are given back to you through a vein in your other arm.
3. The bag containing your white blood cells is identified with a label that shows it is yours, and then is sealed to protect it.
4. Your cells are transported under strict temperature controls to the manufacturing facility.



Leukapheresis takes place in a special unit in treatment centers, hospitals or other centers of care. It usually takes between 2-4 hours. You may need to sign a separate consent form for leukapheresis. Ask questions about anything that is not clear.

Many factors can affect the timing of your leukapheresis appointment. Talk to your healthcare team if you have questions or concerns about when your leukapheresis procedure is scheduled.

What to expect

For a few days before leukapheresis you may be asked to drink plenty of fluids and to avoid caffeine and alcohol. You might also be asked to eat foods high in calcium like yogurt, milk, cheeses, or sesame seeds. This is to help prevent your calcium levels from falling too low during the procedure.

On the morning of the procedure you might be asked to limit how much fluid you drink. This is to help avoid the need for bathroom breaks. You will need to remain in a chair for several hours so be sure to ask to use the restroom just before the procedure starts.

Before leukapheresis, a blood test will be performed to check your blood cell counts. Your blood pressure, temperature, pulse and respiration rate will also be checked.

You will sit in a reclining chair or a bed with a blanket and pillows. Depending on infection control rules, a friend or family member may be able to sit with you. Once the procedure starts, you will not be able to get up until it is complete.

There are different ways to access your veins. Before your procedure, your veins will be examined to find the best way for you. If your veins aren't large enough, you may be scheduled for a *catheter* placement. For most methods, you will need to keep both arms straight for the entire procedure.

To make sure that your blood doesn't clot during the procedure, an anticoagulant (or blood thinner) will be injected into the intravenous (IV) line.

Heparin, a blood thinner you might have heard of, is usually not used during leukapheresis for patients undergoing CAR T-cell therapy. Instead, citric acid or sodium citrate is usually used. In addition to thinning your blood it may lower your blood calcium levels. Be sure to tell your nurse if you feel tingling or numbness. This can be a sign of low calcium. Calcium tablets can be given to help.

The machine will be turned on. Your blood will be removed from one arm and delivered to the apheresis machine. There, the blood is spun at high speeds to separate your white blood cells from the rest of your blood. Your white blood cells will be collected. The remaining blood components will be returned to you through your other arm.

Your nurse will be watching you closely. You should not feel any discomfort. If you feel any numbness or tingling, usually in your fingers, toes or lips, be sure to tell your nurse.

What to bring

- ✓ Wear comfortable clothes with short sleeves or sleeves that can easily be raised above your elbow.
- ✓ Slippers, if you are comfortable in them, or other comfortable shoes.
- ✓ Something to read, watch, or listen to, but remember you will need to keep your arms straight.

After leukapheresis

Your IV lines will be removed and dressings will be applied. These will need to be kept in place for at least 3-4 hours.

After the nurse has checked you and if you feel well, you can leave. It's a good idea to have someone drive you home. You should rest, drink extra fluids and eat well. Avoid exercise or any heavy lifting for the rest of the day.

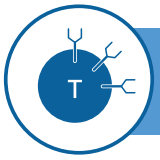
The bag containing your white blood cells is identified with a label that shows it is yours and then sealed to protect it. It is then transported under strict temperature controls to the manufacturing facility.

The secure chain of custody for your cells

Once they are removed from your body, great care is taken to make sure your cells are correctly identified as yours. Your cells will immediately be identified with a label after leukapheresis. You will notice that your identification and the identification on your bag of cells may be checked several times. Multiple levels of security are in place to track and verify the custody of your cells before and during the entire process:

- ✓ When your cells are shipped to the manufacturing facility.
- ✓ As your CAR T cells are manufactured in the laboratory.
- ✓ When your CAR T cells are shipped back to the hospital.
- ✓ When your CAR T cells are infused back into you.

- ✓ Leukapheresis is usually performed only once. However, it might be needed again if not enough T cells were collected the first time, or if they don't grow well in the laboratory. This might be caused by your disease process or by previous treatments.
- ✓ Ask your healthcare or clinical research team how long the manufacturing process usually takes. Ask them when and how you will learn about the progress of your cells in the laboratory.



3. CAR T-CELL ENGINEERING

Your T cells will be genetically modified to become CAR T cells in a specialized laboratory at the manufacturing facility. They are then multiplied until there are millions of them. While this is happening, you will be preparing to receive them.

Managing your care

Your healthcare team will keep in touch with the manufacturing facility about the progress of your cells. This will help them make decisions about caring for you during the wait.

You will be monitored closely to make sure your cancer does not advance significantly. If it does, you might be given treatment to lower your disease level. This is called *bridging therapy*. Bridging therapy may be given either at the treatment center or by your local healthcare provider. Talk to your healthcare team about whether you might receive bridging therapy and where it will be given.

Ask your healthcare team:

- ✓ About their plans to stay in touch with you and your local healthcare provider during this time.
- ✓ Whom you should contact if you have questions about the status of your cells.

Waiting for news about your cells can be stressful. Having a contact person who can answer your questions can help minimize stress.

When your cells are ready, the manufacturing facility will notify your healthcare team. You will be contacted to schedule the dates for your *lymphodepleting chemotherapy* (see page 45) and the CAR T-cell infusion (see page 46).

At the manufacturing facility

A. The manufacturing facility receives your white blood cells sent from the apheresis site or treatment center and confirms their identity.

B. Your T cells are separated from the rest of your white blood cells.

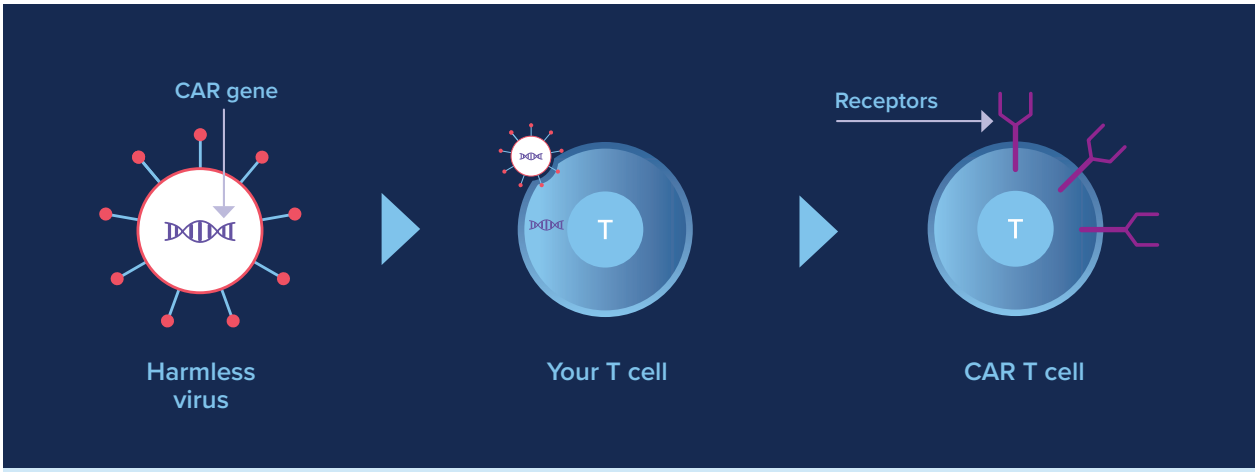
C. Your CAR T cells are engineered in a specialized laboratory.

- An inactive, harmless virus is used to carry the CAR gene into your T cells. The CAR gene contains the instructions for how to make the new CAR protein.
- The T cell uses the genetic instructions to make the new CAR protein.
- The CAR protein becomes a T cell receptor when it is delivered to the surface of the cell. These cells are now called CAR T cells.

D. Your CAR T cells are multiplied until there are millions of them.

E. Your CAR T cells are purified and tested to make sure they are of good quality.

F. Your CAR T cells are sent back to the treatment center under strict temperature controls.



1. A harmless virus is used to carry the CAR gene into your T cells.
2. Your T cells use the genetic instructions to make the new CAR protein.
3. The CAR is delivered to the surface of your T cells as a new T cell receptor. These cells are now called “CAR T cells.”

- ✓ The manufacturing process could take several weeks. Ask your healthcare team about how long it will take for the CAR T-cell product you will be receiving.
- ✓ Waiting for news about your CAR T cells can be stressful. To help you manage during the wait, use the support resources available to you. See page 61 and the **Additional Resources** on page 84 for more information.

4. LYMPHODEPLETING CHEMOTHERAPY

Once your CAR T cells have been sent back to the treatment center or hospital, your healthcare team will schedule your CAR T-cell infusion.

Before you receive your CAR T cells you will probably receive 3-5 days of chemotherapy. This usually involves 2 drugs, fludarabine and cyclophosphamide. You may receive different chemotherapy or have a different schedule depending on the clinical trial and your specific situation. Be sure to tell your healthcare team if you are particularly sensitive to side effects like nausea so they can adjust your pre-treatment medications.

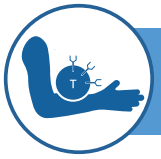
This chemotherapy is not meant to treat your cancer but to prepare your body to receive your new CAR T cells. This is called *lymphodepleting chemotherapy* because it lowers the number of white blood cells in your body, including your T cells. CAR T cells grow and multiply better when there are fewer of your own T cells present.

What to expect

This chemotherapy can be given at the hospital, in a treatment center or in an outpatient setting, depending on your particular situation. Your healthcare team will check to make sure you are well enough to receive the chemotherapy and your CAR T cells. You might receive:

- ✓ A complete physical exam.
- ✓ Tests for memory, language and reaction time to measure your neurological function.
- ✓ Blood tests to see if your liver and kidneys are working well, and to test for infection.
- ✓ Tests to see if your heart is functioning well.
- ✓ Tests or scans to check the extent of your cancer.
- ✓ A pregnancy test, if you are a female of childbearing age.

Your healthcare or clinical research team will explain the tests you will need.



5. CAR T-CELL INFUSION

Depending on your clinical trial, you may receive your CAR T cells in the hospital, at the treatment center or as an outpatient. Your healthcare team will check you to make sure you are well enough to receive them.

CAR T-cell infusion is the last step in the chain of custody for your cells (see page 42). Before receiving them, your identity and the label on your cells will again be checked and verified.

You may be given medications to keep you feeling well during the infusion. Your healthcare team will review these medications with you.

The infusion of your CAR T cells takes up to 30 minutes, and is usually uneventful. Don't be surprised if you notice an unusual taste in your mouth as the cells are infused. This is sometimes caused by a preservative used in the cell engineering process.

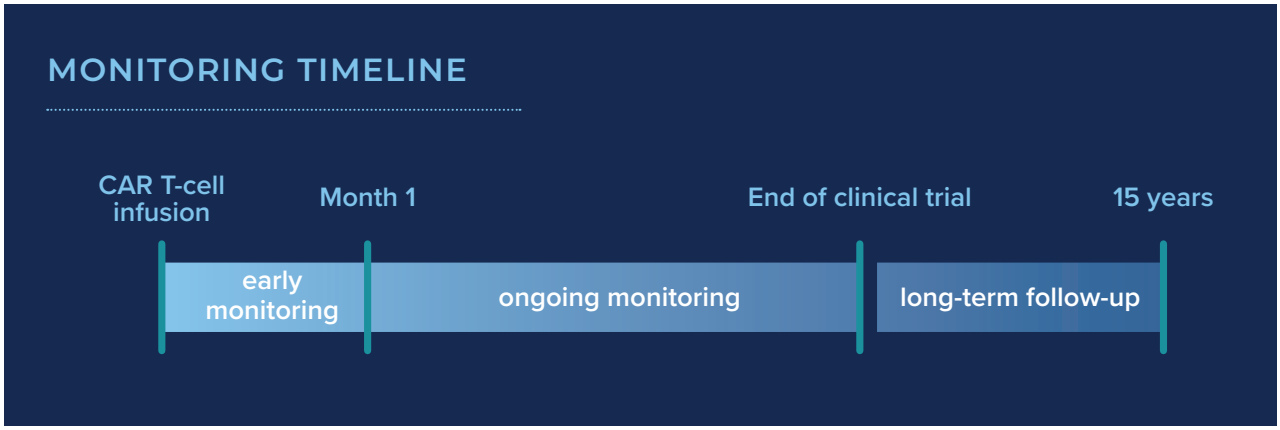
- ✓ Depending on the clinical trial and your specific situation, your CAR T cells may be given in 1 dose or in 2 doses on different days. You may have a different dosing schedule. Your healthcare team will explain your dosing schedule.

6. MONITORING

After you receive your CAR T cells, monitoring can be divided into 3 periods:

1. **EARLY MONITORING:** Usually from the day of CAR T-cell infusion to 4 weeks.
2. **ONGOING MONITORING:** Usually from 4 weeks to the end of the trial.
3. **LONG-TERM MONITORING:** CAR T-cell therapy is a type of gene therapy. As a result, after your clinical trial ends you may be asked to enroll in a long-term follow-up study. See page 17 for more information.

Your PIS has complete details about hospitalizations, treatment center visits, tests and procedures needed during this time. Your healthcare and clinical research teams will explain each test you will receive to monitor side effects and see how the CAR T cells are working to fight your cancer.



1. EARLY MONITORING: THE FIRST MONTH

The first 2 weeks

After your CAR T cells are infused, they will begin to find and destroy your cancer cells. Once they find your cancer cells, your CAR T cells will also begin to multiply. During the first few weeks you will be very closely monitored for any expected or unexpected ways your body might react to the actions of your CAR T cells.

The 2 most common side effects of CAR T-cell therapy are *cytokine release syndrome* (or *CRS*, sometimes called *cytokine storm*) and neurological side effects. *Neurological* means related to the brain, spine, or nerves. These neurological side effects are called *immune effector cell-associated neurotoxicity syndrome*, or *ICANS*. ICANS is sometimes called *neurotoxicity*.

If they occur, CRS and ICANS usually appear within the first month after CAR T-cell infusion. These physical responses to CAR T-cell infusion vary widely from none or mild to moderate or severe. The causes, timing and treatment of these and other side effects are addressed in more detail in the **Side Effects** section on page 53.

The length of this frequent monitoring period varies depending on the clinical trial and your needs. It usually lasts for 10 days to 2 weeks after receiving your cells. If you received your CAR T cells at the hospital, you may stay in the hospital for a portion of this early monitoring.

Whether you receive your cells in the hospital, in a treatment center or as an outpatient, you will need to stay close to the treatment center or hospital for at least the first 28 days. You will be required to have a caregiver with you at all times (24 hours a day, 7 days per week). They will help care for you and watch for side effects.

Your healthcare team want both you and your caregiver to feel confident about knowing what to do if you see certain side effects. Ask as many questions as you need to feel confident.

If you are not in the hospital during this time, you will usually return to the treatment center every day to see the healthcare team. You may have blood tests and other tests (see below). You may be admitted to the hospital if your doctor thinks it is needed.

If admitted to the hospital, you will be discharged when your healthcare team confirms you are well enough to leave. You will be given detailed instructions before you leave. Your healthcare team will allow plenty of time for any questions you have about their instructions. You will receive:

- ✓ Written *Discharge Instructions*. Sometimes these instructions are given verbally; if so, you may want to write them down.
- ✓ Information about whom to contact about your concerns, day or night, 24/7.
- ✓ An Emergency Wallet Card.

Carry the Emergency Wallet Card with you at all times. Give a copy of the Emergency Wallet Card to your caregiver. You can both create a "contact" in your smartphone with this information.

Weeks 2-4

About 2 weeks after receiving CAR T cells, most patients are able to leave the hospital or treatment center. You will need to remain fairly close by. Your healthcare team will continue to monitor you carefully. Your caregiver will need to stay with you at all times to help watch for symptoms. Depending on how you are doing, you may have appointments less often than daily.

What to expect

At each visit during the first month after you receive your cells, you will be carefully checked for side effects. You can expect to receive:

- ✓ A complete physical exam. Your temperature, pulse, blood pressure and weight will be taken.
- ✓ A neurological exam. Tests to monitor for ICANS might include your abilities to:
  - Name the year, month, city and hospital
  - Name 3 objects
  - Follow commands
  - Write a sentence
  - Count backwards from 100 by 10
- ✓ Blood tests to measure:
  - Blood cell counts
  - How well your liver and kidneys are working
  - Signs of inflammation
  - Signs of infection

Depending on the clinical trial and your specific situation, you may need other tests as well. The results of these tests help your healthcare team quickly identify and treat any side effects that arise.

2. ONGOING MONITORING

After the first month you will probably be able to visit the treatment center less often. For example, you might visit every 1-3 months for a period of time, and then less often until the end of the clinical trial. The schedule will vary depending on the clinical trial and your specific situation. Your schedule will be clearly explained to you by your healthcare team.

- ✓ Contact your healthcare team if you experience anything that concerns you, even if it is not included in the list of symptoms to watch for.
- ✓ Even though your treatment center visits will be less often as time passes, you will always have access to your healthcare team. Do not hesitate to contact them if you have any questions or concerns.

Often, beginning at month 1, your healthcare team will order tests and scans to see if your CAR T cells are working to fight cancer. This might involve:

- ✓ Blood tests. In addition to those listed above, they may include tests to measure how many CAR T cells are circulating in your bloodstream.
- ✓ Tests to evaluate your cancer. These could include:
  - Bone marrow biopsy
  - Lumbar puncture
  - Scans, which might include CT, PET-CT, MRI, angiography or ultrasound scans (see page 36)

Depending on your specific situation, you may receive other tests not listed here.

- ✓ It is important that you tell all your other healthcare providers (including emergency or urgent care centers) that you have received CAR T cells. It may affect decisions about your care.
- ✓ Share the contact information of your healthcare or clinical research team with all other healthcare providers you see apart from visits connected to your clinical trial.

  Note: Many healthcare providers are not yet fully familiar with CAR T-cell therapy. They may be uncertain of the steps they need to take to protect your CAR T cells. If your treatment need is not urgent, ask them to contact your healthcare or clinical research teams if they need information about your treatment.

LONG-TERM MONITORING

After your clinical trial is completed, you may be asked to participate in a long-term follow-up (LTFU) study. During this study, you will continue to be monitored for a period of up to 15 years after you receive your CAR T cells. Some of these visits may be at your local treatment center. See page 17 for more information about LTFU studies.

Visits during the LTFU study will be less often than during your initial clinical trial. You may be asked to sign another informed consent form to participate. The PIS will include scheduling and details about every test and procedure you may have. Ask your clinical research team if there is funding available to pay for your routine travel costs associated with these visits.

SIDE EFFECTS*

*This section explains some of the known side effects of CAR T-cell therapy. You may experience some or none of the side effects listed here. You may have side effects that are not listed here. Your healthcare team will tell you what signs and symptoms you need to watch for and tell them about. This information will also be contained in your Discharge Instructions. Make sure to ask about anything that is not clear or that you don't understand.


Words that appear in *italics* are defined in the **Glossary** on page 95.

TYPICAL CAR T-CELL THERAPY SIDE EFFECTS

Side Effect	Cause	Timing	Signs & Symptoms	Possible Treatments
Cytokine Release Syndrome (CRS)* *or cytokine storm	High levels of cytokines.	Starts 1 to 21 days after CAR T-cell infusion. Symptoms can last 1 to 2 weeks.	Fever, chills, headache, muscle aches, nausea, vomiting, fast heartbeat, having a hard time breathing, feeling dizzy/ light-headed.	Medications to decrease pain or nausea or increase blood pressure, giving oxygen, others. Tocilizumab (Actemra®) or a similar medication. Corticosteroids may be added in some cases.
Neurotoxicity* *immune effector cell-associated neurotoxicity syndrome, or ICANS	Unknown	Can start within 1-2 weeks after CAR T-cell infusion, or as long as 4-6 weeks afterwards. Usually resolves within 21 days but can last longer. Very rarely, can be fatal.	Headache, dizziness, shaking, hard time sleeping, anxiety, can't find words or inability to speak, confusion, hallucinations, difficulty writing. Severe symptoms can include seizures, brain swelling and coma.	Symptoms are treated. Anti-seizure medication may be given if you have a seizure. Corticosteroids may be used in some cases. If you also have CRS, tocilizumab or a similar medication may be used.
Tumor Lysis Syndrome	Cancer cells breaking apart and releasing their contents when destroyed by CAR T cells.	Up to a month after infusion.	High levels of certain minerals called electrolytes or waste products like uric acid in the blood.	IV fluids; allopurinol (which breaks down uric acid).
Cytopenias	Effect of CAR T cells and chemotherapy on the bone marrow, where blood cells are made.	May last for weeks or months following CAR T-cell infusion.	Feeling very tired (low red blood cell counts); frequent or severe infections (low white blood cell counts); bleeding (low platelet counts).	Growth factors (to stimulate bone marrow to produce more blood cells); transfusions of red blood cells or platelets; antibiotics or antifungal agents to prevent or treat infection.
B-cell aplasia	Direct action of CAR T cells on B cells (see above).	Immunoglobulin levels can fall 1-3 months after CAR T-cell infusion, and remain low for months or years.	Low B-cell counts, infections.	Antibiotics or antifungals to prevent or treat infection; intravenous immunoglobulin (IVIG) to replace antibodies.

WHY DO SIDE EFFECTS OCCUR?

All experimental therapies have both known and unknown side effects. There are known side effects of CAR T-cell therapy. Some are very common and some occur very rarely. You will learn about side effects that could occur in the clinical trial you are considering during the informed consenting process. They will be listed in the PIS, and the clinical research team will tell you about them. You will be given time to ask any questions you have about the information you are given.

You, your caregiver and your healthcare providers will be working together to watch for the signs and symptoms of side effects (see **Monitoring** on pages 46-51). The information contained in this section can help you prepare for a discussion about possible side effects of CAR T-cell therapy and the clinical trial you are considering.

Some side effects are the direct result of your CAR T cells doing what they were designed to do—kill your cancer cells:

- *Cytokines* are chemicals released when your CAR T cells find and attach to cancer cells. Cytokines help kill cancer cells (see page 31). However, very high levels of cytokines can be harmful and cause a group of symptoms called cytokine release syndrome (CRS) or cytokine storm.

- Low numbers of B cells, or *B cell aplasia*, can also happen after CAR T-cell therapy. This is because some CAR T cells are designed to destroy cells that have an *antigen* (or *marker*) called “CD19” on their surface. While some cancers of B cells have CD19, it is also found on normal B cells. B cells make antibodies, which protect us from bacteria and viruses. Low levels of B cells can lead to low antibody levels, which increases your risk of infection. If your antibodies are low due to B cell aplasia, treatments to help are available (see page 53).

The exact causes of other side effects are less well understood. The best example of this is a condition called *neurotoxicity*. This is also called *immune effector cell-associated neurotoxicity syndrome*, or *ICANS*. Neurotoxicity can be very mild, like a headache or mild confusion, or rarely can be extremely severe and life-threatening. This and other potential side effects will be explained during your informed consenting process.

There have been very rare reports of patients experiencing allergic reactions following CAR T-cell infusion. The healthcare team is prepared to treat you if you have an allergic reaction.

Whether or not the cause is understood, a great deal is now known about how to recognize and treat these side effects if they occur. Your healthcare and clinical research teams will be able to answer any questions you have about possible side effects and how they might be treated.

Signs and Symptoms of Treatment Side Effects:

- ✓ A *sign* is something that can be seen or measured. Blood pressure, temperature and pulse are examples of signs.
- ✓ A *symptom* is something that you feel or experience. For example, “I feel nauseous” or “I feel cold” are symptoms.

Your healthcare team will speak with you about the signs and symptoms you need to watch out for and tell them about. You will be given detailed information about whom to contact and when to contact them. If this information is not included in written Discharge Instructions, ask your team to write them down for you, or take the time to make notes before you leave.

SIGNS AND SYMPTOMS TO WATCH FOR

After you are discharged from the hospital or treatment center you will need to stay close by for a number of weeks (see pages 47-49). This will make it easier for you to get to your scheduled appointments. Staying nearby also allows you to return quickly to your treatment center, hospital or the emergency room if any of these things happen:

- ✓ Fever
- ✓ Having a hard time breathing
- ✓ Being lightheaded or dizzy
- ✓ Being confused or having a hard time talking or writing
- ✓ Anything that's not normal for you, like chills or shaking, severe nausea, vomiting or diarrhea

It's very common to have questions about exactly when you should call or return to the hospital or emergency room. If you are uncertain or unclear about any of the information, ask for more guidance. Your healthcare team wants you to have all your questions answered before you leave.

It is not always easy to know what causes a certain sign or symptom. A high temperature could be due to an infection, high levels of cytokines, or something else. You and your healthcare team are partners during the monitoring period. You will tell them about your signs and symptoms, and they will work to find the potential causes and the best way to treat them.

Trust yourself. If you are worried about anything you are experiencing, whether it's on the list or not, call the contact number or go to the emergency room.

Intravenous immunoglobulin (IVIG) is a medication often given to people who have received CAR T-cell therapy. IVIG provides extra antibodies and helps to prevent frequent infections until your B cells return to more normal levels.

- ✓ Look at your written Discharge Instructions and the information your healthcare team gave you to learn the signs and symptoms to watch for.
- ✓ Call your healthcare team whenever you are worried or have questions, even if it's not about something on the list of things to watch out for.

SUPPORT
ALONG THE JOURNEY

Words that appear in *italics* are defined in the **Glossary** on page 95.

INTRODUCTION

There have been many recent advances in cancer treatments. Using the body's own immune system to fight cancer is just one example of the remarkable progress that has been made in recent years.

However, the emotional impact of cancer and its treatment has changed very little. Patients tell us that the emotional impact of their cancer journey can be even harder to handle than the physical effects. Emotional reactions can surface at any time, beginning before diagnosis is made through treatment and beyond. The emotional challenges the CAR T-cell journey presents for all involved are no different.

We all have our ups and downs. But with cancer, even positive emotions can be stressful. A good scan brings relief, but thoughts may soon turn to uncertainty about the future. Sadness and joy, anxiety and relief, fear and excitement are just some of the emotions that patients and their loved ones might feel. Everyone deals with these feelings in different ways. Some people feel they should be able to handle these emotions on their own because they have been able to before.

But cancer and its treatment bring unique challenges. No two cancer journeys are the same, and no two individuals or families dealing with cancer are the same. Few people believe they should be able to treat their cancer without the guidance and support of specially trained healthcare professionals. Many believe, however, that they should be able to handle the many emotional, psychological, spiritual, social and financial stresses that come with a cancer diagnosis all on their own.

SUPPORTIVE CARE SERVICES

The good news is that help is available in many forms. A relatively new service offered in some cancer centers is called *Supportive Care*. In the past, patient support services to help in areas like pain and symptom management, and emotional and psychological needs were only offered to patients with advanced cancer.

In addition to helping patients undergoing active treatment, supportive care services are also directed to patients living with cancer as a long-term illness and to cancer survivors. Most patients and family members who take advantage of these services say their lives were greatly improved and that they were helped with issues they hadn't experienced before.

AVAILABLE SUPPORT

While every treatment center may not have a separate department called Supportive Care Services, these kinds of services are available on an individual basis in most centers. The goal of these services is to prevent or treat:

1. The symptoms of the disease.
2. The side effects of treatment.
3. The emotional, psychological, social, and spiritual problems that can arise with cancer and its treatment.

Not all treatment centers offer all services. If you can't find the service you are looking for at your treatment center, check with patient organizations like Cancercare® at cancercare.org, or the Cancer Support Community, at cancersupportcommunity.org. These and other organizations provide support and information for patients and families affected by cancer.

Below are some of the types of services offered by healthcare professionals within treatment centers or accessible through patient organizations:

- Figuring out how best to help with pain and symptoms (working with your treatment team).
- Emotional, psychological or spiritual support for you or your caregiver (for example, a staff psychologist, chaplain or oncology social worker).
- Helping you make difficult treatment choices and making sure those choices reflect your values and beliefs.
- Help with setting up a family meeting to explain what's going on with the disease and treatment process.
- Physical therapy, occupational therapy and recreational therapy.
- Integrative and complementary therapies (massage, acupuncture, meditation, yoga, music or art therapy).
- Advice on planning meals and good nutrition.
- Help in navigating the healthcare system.
- Planning for post-treatment care.

Complementary vs Alternative Treatments

- **Complementary treatments** are used along with medical treatments and are not meant to replace them. They may help ease some of the symptoms of cancer and its treatment.
- **Alternative treatments** are those that take the place of medical interventions. None of the services or treatments on the list above is meant to replace the treatments recommended by your healthcare team.
- **Always check with your healthcare team to learn if a particular complementary treatment is safe for you.**

Ask any member of your healthcare team if your treatment center has a Supportive Care department or offers supportive care services. If it does not, ask if some of these offerings may be offered by individual staff members within the center. Finally, contact patient organizations to learn about services to help support you on your journey.

STRESS AND DISTRESS

Stress responses are normal reactions to situations that make us feel frustrated, angry, or nervous—like a cancer diagnosis and its treatment.

Distress is always harmful and occurs when stress is severe, prolonged, or both.

Not all stress is bad—in fact, it can be motivating. The stress caused by thoughts of an upcoming exam might motivate us to study harder. The stress of finding out your weight is not what you expected could inspire us to change our diet. Being diagnosed with cancer can be stressful but reaching out for support can help us adapt to this new situation.

Stress does not need to define your cancer journey. Don't ignore or accept it but look for help to cope with it. Finding ways to cope with the stress and the emotional impact of cancer can save your energy to help you recover.

It's important to talk with your healthcare team if you have any of the symptoms of distress in the list below. There may be a physical cause that can be treated. For example, uncontrolled pain, heartburn or medications could affect your sleep, and these all can be helped. If a physical cause of your symptoms can't be found, there are other ways to help.

STRESS AND DISTRESS, CONT.

Listed below are some symptoms of distress. If you or your caregiver experiences any of these symptoms, let someone on your healthcare team know. They can guide you to the resources you need to address this important area of your cancer care.

- Sadness
- Fear, worry or helplessness
- Anger or feeling out of control
- Concerns about illness or treatment
- Worries about paying bills and the costs of living
- Questioning your faith, your purpose, the meaning of life
- Pulling away from too many people
- Concerns about taking care of others, such as a child or parent
- Poor sleep, appetite or concentration
- Depression, anxiety, panic
- Frequent thoughts of illness or death

UNCERTAINTY

One of the hardest things about cancer is dealing with the uncertainty it brings. You have probably felt uncertain about the future at many times in your life, including when you first found out you had cancer. You may feel uncertain again when the active phase of your clinical trial has ended.

These feelings are completely normal and understandable, and almost everyone has them. Hematologist Jerome Groopman, MD in his book "The Anatomy of Hope" explains that we can actually find hope in the uncertainty of a treatment or disease outcome. Because nothing is absolutely determined, there is not only reason to fear but also reason to hope.*

It's normal to have some worried thoughts. But if you have trouble concentrating or thinking about anything other than worry, or if you are nervous, restless or tense for more than a few days, it's time to reach out for help (see page 70).

*Groopman J. *The Anatomy of Hope: How People Prevail in the Face of Illness.* New York, NY. Penguin Random House. 2004.

A FEW WAYS TO MANAGE STRESS

Cancer is stressful for patients, caregivers and family members. Taking part in a clinical trial, especially one far from home, can also be demanding and stressful. Your healthcare team will suggest ways to help. Here are some things you can try on your own:

Mindfulness-Based Stress Reduction (MBSR)

Creative activities

Mindfulness meditation

Humor

Journaling/keeping a diary

Changing your focus

1. MINDFULNESS-BASED STRESS REDUCTION (MBSR)

MBSR is an 8-week program that can help you learn how to deal with stressful situations like cancer. People in an MBSR program learn that while they cannot always change the situation that's causing their stress, they can choose how they react to it. The program has been proven to work to reduce the symptoms of stress. It is offered in hundreds of hospitals, clinics and health centers around the world.

What is mindfulness?

Mindfulness is the practice of paying attention to the present moment with curiosity and non-judgment, instead of focusing on the past or worrying about the future.

Think about the difference between someone driving for the first time and someone who has driven for years. The new driver is paying complete attention to what they are doing, while the experienced driver's mind may not be focused on the "present moment" details of driving. Paying close attention to the experience of driving without much mind-wandering is an example of a mindful activity. Engaging in an activity in this way leaves little time for worrying about the past or future.

How might practicing mindfulness help?

Mindfulness is only one part of an MBSR program but it is probably the most important. We can cope better with a stressful situation if we stop thinking about the past or the future. These thoughts might be regrets about the past ("I should have gone to the doctor sooner"). They might be worries about the future ("My test results might not be good, and then..."). These types of thoughts make stress worse and do nothing to change or help the situation. The practice of mindfulness allows us to move our awareness away from these thoughts. The result is decreased stress.

A good example of the benefits of practicing mindfulness is found in the game of golf. Anyone trying to make a shot while angry at themselves for the last poor swing (the past) or worrying about the next difficult hole (the future) will probably perform poorly. Golfers understand the benefits of staying in the present moment!

Where can I find an MBSR program?

There are many MBSR programs available, both in-person and online. Ask your healthcare team if a program is offered at your treatment center. Some of these programs require a fee; some are free. To find free programs, search online for "free MBSR programs". Check to make sure the program is conducted by a trained mental health professional. See the **Additional Resources** section on page 84 for more information about finding a program.

2. MINDFULNESS MEDITATION*

Mindfulness meditation is a part of the MBSR program. It can also be done on its own. Mindfulness meditation is a type of meditation that has been studied a lot, but other kinds of meditation can also be helpful. If you're new to meditation, several apps are available that can help you get started. Most are free or are offered at a very low cost, such as:

- **Pause: Daily Mindfulness.** A variety of short sessions that help you relax and shift your focus away from distressing thoughts.
- **Insight Timer:** A free library of 60,000 meditations, music selections and inspirational talks. Paid services, including meditation courses, are also available.
- **Chillscape – Sonic Meditation:** A tool for quick bursts of mindfulness and anxiety relief. It can be used to relax, focus the mind or filter out unwanted distractions like pain or negative thoughts.
- **Headspace:** Loaded with meditation courses, sleep programs and movement practices. This is an expensive option, but their free trial may be useful as an introduction to mindfulness practices.
- **Mindshift CBT:** A free, scientifically based anxiety tool based on a type of therapy called Cognitive Behavioral Therapy (CBT). The interactive tool guides users to look at anxiety-producing thoughts in a healthier way.
- **Rebalance with Mindfulness:** A guided, 4 step process to combat stress by reconnecting the mind and body.

1. Diaphragmatic breathing†: A type of breathing exercise that reduces the stress response and brings your nervous system back into balance.
2. Mindful body scan: Emotions can appear as physical sensations. By developing an awareness of how your body feels, you can learn to regulate your emotions better.
3. Labeling emotions and sensations: Labeling emotions reduces their intensity. The app provides a logging system so that you can better understand your own emotions.
4. Allowing: The practice of allowing our sensations and emotions to exist without trying to change them or react to them. The app helps you choose how to respond to your emotions.

*Mindfulness meditation doesn't help everyone. Sometimes, it can even increase anxiety. If this happens to you, stop doing it and talk to a healthcare professional about what happened.

†Diaphragmatic breathing by itself can reduce stress. You can use this app to learn how, even if you don't continue with the other 3 practices.

3. JOURNALING/KEEPING A DIARY

Write or journal, just for you. This is a private way to express your thoughts, frustrations, and feelings safely and honestly. You can write about what's going on or use the following ideas to get you started:

- "What is the story I'm telling myself right now?" Halfway through, switch to: "What is a different way I can tell this story?"
- "What qualities am I grateful to have?"
- "What is one thing I can commit to today that my future self will thank me for?"
- "What is something I can do right now that my present self will thank me for?"
- "What is one past event that I saw as a failure and now see as a gift?"
- "My highest values in life are..."

National Public Radio StoryCorps is an excellent way to start writing. The website contains lists of questions for various roles. The list below is designed for adult children to ask their parents, but there are dozens of lists available on their website.

- Do you remember what was going through your head when you first saw me?
- How did you choose my name?
- What was I like as a baby? As a young child?
- Do you remember any of the songs you used to sing to me? Can you sing them now?
- What were my siblings like?
- What were the hardest moments you had when I was growing up?
- If you could do everything again, would you raise me differently?
- What advice would you give me about raising my own kids?
- What are your dreams for me?
- How did you meet mom/dad?
- Are you proud of me?

4. CREATIVE ACTIVITIES

Even if you've never drawn or painted before, try doing something creative. Creative activities help relax the part of the brain that is active when you feel stressed or scared. It's a way to change your focus. When was the last time you tried coloring? Search "meditative coloring pages" to find free, downloadable pages to get you started. Some treatment centers offer programs that feature art for healing. This may be a good time to master those new solos on the guitar or take it up for the first time.

5. HUMOR

Introduce positive humor. When was the last time you laughed so hard you cried? This may take some effort but ask your friends and family to help. Watch a comedy. Tell a joke. Laughing decreases cortisol, a stress hormone. It also releases endorphins, which have been shown to decrease pain.

6. CHANGING YOUR FOCUS

If you find yourself dwelling too long on unpleasant thoughts, get moving physically. If your doctor approves, go for a walk, do some stretching or gentle yoga or other activity you enjoy.

A WORD ABOUT GUILT

Guilt is an unhappy feeling that can arise because you have done something wrong or believe you have done something wrong. There are many reasons a person with cancer, their caregiver or their loved ones might feel guilty. It's important to understand that merely thinking something doesn't make it true. But ignoring the thoughts that cause guilt can lead to painful emotions that can drain your energy and lead to illness. For more information about this emotion see the **Vital Role of the Caregiver** section on page 73.

SPECIALISTS WHO UNDERSTAND THE CANCER JOURNEY

If you are having fears so great you are unable to sleep or eat well or have feelings of guilt, it might be time to seek help. A *psychosocial oncologist* is a person who specializes in the psychological, behavioral, emotional and social issues that arise for cancer patients and their loved ones. Licensed Clinical Social Workers (LCSW) and Licensed Professional Counselors (LPC) are just two of many other mental health professionals who may have expertise in cancer care. Your healthcare team may be able to suggest resources available at your treatment center. You can also ask for recommendations from friends, family members and your other healthcare providers. Other resources are in the **Additional Resources** section on page 84.

Caregivers

A cancer diagnosis touches everyone in the family, not only the person diagnosed with cancer. Being a caregiver of a person with cancer, especially one who is going through an intensive treatment experience, is considered to be a chronic stressor. Undergoing this chronic stress can have a negative impact on health and well-being. Caregivers don't often talk about the stress they experience because they don't want to move attention away from their loved one.

Caregivers, at least temporarily, take on multiple additional responsibilities and may not see the importance of looking after their own well-being. The recommendations for emotional support contained in this Guide are as important for the caregiver as the person diagnosed with cancer. See the **Vital Role of the Caregiver** section on page 73 for more information.

Talk to your healthcare team if either you or your caregiver is experiencing increased stress or have any of the signs of distress listed on page 63. You may also want to reach out to patient organizations that offer free telephone counseling services like Cancer Care® (https://www.cancercare.org/counseling). There is help available. You don't need to do this all on your own. See the **Additional Resources** section on page 84 for more information.

Personal Growth

While cancer and its treatment can bring high levels of stress, personal growth is often possible through these experiences. The idea of *post-traumatic growth* was first introduced by psychologists Richard Tedeschi, PhD and Lawrence Calhoun, PhD. It explains how those who struggle psychologically after going through a difficult experience often experience positive change.

An example of a positive change might be that, having survived this experience, you realize you are much stronger than you thought. This new awareness could lead to many positive changes. Not everyone will experience post-traumatic growth, but the suggestions contained in this section can help increase the chances that you will.

THE VITAL* ROLE OF CAREGIVER

*absolutely necessary, important, essential

Words that appear in *italics* are defined in the **Glossary** on page 95.

INTRODUCTION

This section is for caregivers. It has information about your important role caring for someone who is getting CAR T-cell therapy. We want you to know that while sometimes you may feel you are alone, many are ready to help. The entire clinical research team and other members of the healthcare team will be your partners to help care for your loved one. Your family, friends and many patient organizations are also available to support you.

As a caregiver for someone getting CAR T-cell therapy, you are your loved one's most important resource. You will have many responsibilities. If COVID-19 or other infection control policies allow, you will provide the companionship that is so critically important during this time. You will be there for practical needs like laundry or special food requests. Your presence can help assist or free up nursing staff. You will be an important extra set of eyes and ears to watch for symptoms of side effects following CAR T-cell infusion.

You may sometimes feel helpless in this situation that is mostly out of your control. Understanding the difference you can make may help ease these feelings.

Being a caregiver for someone getting CAR T-cell therapy is an essential role. It may be a good idea to have a “back-up” caregiver who could step in if you get sick or can’t be there.

If you get sick at any time during the process, tell someone on your loved one’s healthcare team. They will help you decide what you should do and whether your back-up caregiver may be needed.

YOUR RESPONSIBILITIES

1 UNDERSTAND THE PROCESS

CAR T-cell therapy involves many steps beginning with the *informed consenting process*. If infection control restrictions do not allow you to attend this visit, ask if you can attend by video or audio conference. If you ask ahead of time, you may even be able to record the visit so you and your loved one can review it again later.

It's a good idea for both you and your loved one to read the *Participant Information Sheet (PIS)* you will be given. Compare your understanding of the information and ask the clinical research team anything you have questions about. More information about the informed consenting process can be found in the **Introduction to Clinical Trials** section on page 10. An overview of the CAR T-cell therapy process can be found on page 34 and a more detailed explanation is found on pages 35-51. The PIS will have information that is very specific to the clinical trial you are considering.

2 WATCH FOR SIDE EFFECTS

When you leave the hospital or treatment center, you will be given information about exactly what to watch for. This information may also be given to you in the form of printed Discharge Instructions. Ask as many questions as you need to be confident about what to watch for. **Information about what you may be asked to watch for can be found in the Side Effects** section on page 53.

Your loved one may feel completely well during this time. In that case, all you may need to do is remind them to write down the information that was asked for, and continue to watch for symptoms.

Some examples of symptoms you will be asked to watch out for include:

- Fever
- Having a hard time breathing
- Being lightheaded or dizzy
- Being confused or having a hard time talking or writing
- Anything that's not normal for your loved one, like chills or shaking, severe nausea, vomiting or diarrhea

The Discharge Instructions may include more or different symptoms to watch for.

Both you and your loved one should trust yourselves. If you are worried about anything your loved one is experiencing, whether it's on the list or not, or included in your Discharge Instructions or not, call the contact number you have been given or go to emergency room.

- ✓ You may notice some changes in your loved one more easily than they do. One example is “confusion.” You know what is normal for your loved one and you may notice a change before they do.
- ✓ Some instructions will be very clear, but others may not be. Ask as many questions as you need to feel confident about what to watch for and when and whom to call.

3 COMMUNICATE

...with each other

In many ways you and your loved one may function as one. You certainly share your hopes in terms of treatment outcomes. But keep in mind that while your goals may be the same, some of your concerns may be very different.

You might worry that you won't make the right decision about reaching out if a side effect occurs. This might cause you to ask so many questions that your loved one thinks you are "hovering".

Your loved one may worry they are "complaining" if they share too much. They might be concerned they are a burden to you.

These feelings are very common and understandable. Being open with each other about your feelings will help avoid misunderstandings. Ask them if it's OK to ask about how they are feeling – even if that is not what you would normally do.

...with your healthcare team

You will be told when and how to contact your healthcare team if certain symptoms appear. Some symptoms may require you to go immediately to the treatment center, hospital or emergency room (depending on the day and time the symptom appears). For others, you will be given one or more phone numbers to call. Here are some questions you may be asked. It will be helpful to write down the answers while you wait for your call to be returned:

- Do you want to come to the hospital? (If you would say "Yes," don't wait for the call back but go there right away.)
- What is the symptom? Fever? Pain? Confusion? Hard time breathing?
- Is it happening now?
- When did it begin?
- Is it getting worse?
- Does anything make it better?
- Has this ever happened before?
- What else do you want to tell me?

Your healthcare team will tell you that if you are not sure whether to make a call—just go ahead and call. They will reassure you and tell you what you should do next.

...with family and friends

By this time in your treatment journey you have probably found ways to let everyone know how things are going. A simple, low-tech way of doing this is to create an email distribution list. Enter email addresses in the blind-copy ("Bcc") field if you don't want to share other people's email addresses widely. Sending updates to this distribution list can help cut down on the need for multiple phone calls and emails.

If you are looking for a way to both update people and respond to offers of help, there are several organizations that will help you create a very simple website. Subscribers to your website will be notified when you post updates. You can also post errands and tasks you need help with, which can be very helpful if your treatment center is out of town and you need something done at home.

Family and friends want to help. You've no doubt heard, "let me know if there's anything I can do." While their offers are sincere, it can be hard for both you and them to identify exactly what you need help with and when. Using these services is helpful for everyone.

Here is a list of organizations that can help you set up a website.

- Cancer Care https://mycancercircle.net/
- Cancer Support Community https://www.cancersupportcommunity.org (select: MyLifeLine from the top menu bar)
- Caring Bridge https://www.caringbridge.org/

4 MANAGE THE DETAILS

At home

If the CAR T-cell therapy treatment center is not close to home, you will have many practical details to take care of while you are away. These can include arranging time away from work, establishing childcare or eldercare, maintaining your lawn or sidewalks, and bringing in the mail.

While it is hard to plan ahead for everything, setting up a website as mentioned above can be very helpful. Think about asking a friend or neighbor ahead of time if you can call them for unexpected needs. This may be the time to install a doorbell camera. Being able to see who is at the door from anywhere can be reassuring.

In temporary housing near the treatment center

Most of the tasks of daily living will fall to you while staying in your temporary housing. These will include safe food preparation, cleaning, keeping sick visitors away and managing medications, among others. Once you are settled in your temporary house and have a schedule of required visits to the treatment center, you will be able to set up a daily routine. This routine can help lower the stress of being in new surroundings, away from home and loved ones. For suggestions on where to get help finding temporary housing, see the **Additional Resources** section on page 84.

5 ARRANGE TRANSPORTATION

You will need a way to travel between your treatment center and your temporary housing for frequent visits. Sometimes, public transportation is a less stressful alternative to driving in an unfamiliar urban area.* Some treatment centers offer shuttle service between locations in their networks. Many have negotiated rates with taxi services. Patient transport services may be available. Ask if there is a patient liaison at your treatment center who can tell you what is available. When you have a plan for transportation, share it with your healthcare team. They will be able to tell you how to call for medical help in case of an emergency.

**When using any type of public transportation, it is a good idea to bring hand sanitizer or sanitizing wipes for infection control purposes.*

6 DEAL WITH INSURANCE AND FINANCIAL ISSUES

Medical bills can be confusing. You may have questions about who is responsible for a particular charge. Don't feel that you need to sort these questions out on your own. There are financial specialists available at each treatment center to help.

Some clinical trials include a payment (or "stipend") or will reimburse participants for travel expenses. Ask your clinical research team for information about expenses covered by the trial sponsor.

Also, check with patient organizations to see if they can provide financial help. See **Introduction to Clinical Trials** on page 10 for more information about costs and insurance coverage and the **Additional Resources** section on page 84 for a list of resources available to help with hospital bills and insurance issues.

7 GET EMOTIONAL SUPPORT

Taking part in a clinical trial, particularly one far from home, can be demanding and stressful for both you and your loved one. Healthcare providers know that stress can make physical recovery harder. Because of this, many providers often check on the psychological well-being of their patients.

It might surprise you to know that caregivers are just as likely, and sometimes even more likely, to be under chronic stress. Because caregivers don't often talk about the stress they experience, this may go unnoticed by the healthcare team. They don't want to draw attention away from their loved one. A common response to the question "How are you holding up?" is "Fine;hanging in there." even if the caregiver is having significant emotional discomfort.

Caregivers may have their own physical or emotional health challenges to deal with. These may take a back seat during the intensive period of care their loved one requires. There are the many added responsibilities. There is often a feeling of loneliness, especially if you're away from home. The physical absence of friends and family can contribute to a feeling of isolation. Caregivers may worry if the treatment will work well but don't want to talk about it for fear of upsetting their loved one.

It is important for the caregiver to be aware of the same signs of distress that their loved one may experience. See page 63 in the **Support Along the Journey** section for a list of symptoms that indicate that stress may have become more serious.

If you have any of these symptoms, it's very important that you talk to someone about it. When asked about how you are doing, it's OK to be honest. Simply sharing your feelings can greatly decrease stress.

If you have been seeing a counselor, make plans to hold video sessions or phone calls during your time away from home. If you don't already have a counselor there are many ways to find one. Some practices have counselors. Ask your primary care physician or nurse practitioner for a referral.

Your loved one's cancer center may have a list of counselors experienced in cancer care.

Patient organizations like Cancer Care® offer free counseling from licensed oncology social workers. Visit https://www.cancercare.org/counseling. See the **Additional Resources** section on page 84 for more information.

Reducing stress helps you both emotionally and physically. Taking good care of your own mental and physical health is essential–you must take care of yourself so you'll be able to take good care of your loved one.

A WORD ABOUT GUILT

Guilt is an unhappy feeling that can happen when you have done something wrong or *think* you have done something wrong. There are many reasons caregivers might have feelings of guilt. It's important to understand that merely thinking something doesn't make it true. But ignoring the thoughts that cause guilt can lead to painful emotions that can drain energy and lead to illness.

Consider the example of one family: Jack is in the hospital getting treatment for cancer. Joe and Anna are Jack's parents and Erin is his young wife. This is Joe's experience:

> *"Every night, Anna, Erin and I would stay in the hospital until Jack fell asleep. Then we would whisper 'I love you', and quietly sneak out of his room. We always felt guilty because we felt relieved to be able to leave the hospital, but Jack had to stay. It was really difficult to leave him there".*

Guilt is a clash between a strongly held value and our actions. For Joe, two strongly held values were in conflict: "I want to care for Jack" or "I need to stay healthy so that I can care for Jack." Either action taken can result in guilt, especially if Joe were to fall ill and not be able to care for Jack. Joe explained, *"We knew that if we were to wear ourselves out, it would have drastic results."*

Joe and his family received regular informal visits from a staff psychologist. Her simple question, "How are things going?" let him open up and talk to her. The psychologist helped Joe think about things in a different way. She suggested substituting the word "and" in place of "or": "I want to care for Jack AND I need to stay healthy so that I can care for Jack."

She explained that the strength of guilt indicates the importance we place on the value. If caring for Jack didn't matter as much as it obviously did, Joe wouldn't have any feelings about leaving the hospital. This allowed Joe to feel *good* about the strength of his value and appreciate the position he was in and the choice he had to make.

Dealing with these feelings is important. If you ignore them guilt can sometimes lead to depression, anxiety or even physical illness.

TIME TO RECHARGE

When your loved one is not staying in the hospital but is being monitored as an outpatient, you need to be with them 24 hours a day, 7 days a week. This can be demanding and stressful for both of you.

When your loved one is in the hospital for monitoring, you have a chance to take some time for yourself. Take a break whenever you can: get away from the hospital and enjoy a walk, get some fresh air, call a good friend. There will be many more options after COVID-19 restrictions are relaxed or lifted.

Taking a break will help you be refreshed when you and your loved one reconnect. Your health and well-being are vital for both you and your loved one.

More information about support for both you and your loved one can be found in the **Support Along the Journey** section on page 61 and the **Additional Resources** section on page 84.

ADDITIONAL **RESOURCES**

There are hundreds of free or discounted services for those being treated for cancer and their families. These pages offer only a few of them. We encourage you to reach out to patient organizations for help. Most list resources on their websites and all have helplines where you can ask for individual assistance.

PATIENT ORGANIZATIONS

Patient organizations provide a wide range of services for the cancer community. These include disease information in printed and digital form, videos, live webinars, in-person events (to resume post-COVID-19), assistance in finding a clinical trial, financial assistance, counseling services, research funding, policy advocacy efforts, professionally led online support groups, discussion boards, pet care support and more.

Cancer Care

Support Line: 800-813-HOPE (4673)

Email: info@cancercare.org

https://www.cancercare.org/

A national organization providing free, professional support services and information to help people manage the emotional, practical and financial challenges of cancer.

Cancer Support Community

Support Line: 888-793-9355

Email: info@cancersupportcommunity.org

Resource List: https://www.cancersupportcommunity.org/external-resources

https://www.cancersupportcommunity.org/

A worldwide nonprofit network of cancer support. 175 locations, including Cancer Support Community and Gilda's Club centers, hospital and clinic partnerships, and satellite locations.

PATIENT ORGANIZATIONS, CONT.

The Cutaneous Lymphoma Foundation

Support Line: 248-644-9014
Email: info@clfoundation.org
Resource List: https://www.clfoundation.org/patient-resources
https://www.clfoundation.org/

A non-profit patient advocacy organization dedicated to supporting every person affected by cutaneous lymphoma.

The Leukemia & Lymphoma Society

Support Line: (800) 955-4572
Clinical Trial Support Center: Request services through Help Line.
Resource List: https://www.lls.org/support/other-helpful-organizations
https://www.lls.org/

A North American patient organization that funds blood cancer research around the world, provides free information, support and clinical trial access services, and is the voice for all blood cancer patients seeking access to quality, affordable, coordinated care. Phone, live chat or email: https://www.lls.org/ (access live chat and email on home page).

Lymphoma Research Foundation

Support Line: 800-500-9976, or email: helpline@lymphoma.org
Email: LRF@lymphoma.org
https://lymphoma.org/

US-based nonprofit organization focused on lymphoma. Offers a wide range of support services, educational programs and free publications for people with lymphoma and their loved ones. Detailed information about lymphoma, ongoing support, help with long-term survivorship, financial support and other services.

The Multiple Myeloma Research Foundation

Patient Navigator: 1-888-841-MMRF (6673)
https://themmrf.org

Provides information about resources, disease and treatment education, healthcare provider referrals, assistance in identifying clinical trials, and connections to other patients and caregivers.

ACCOMMODATIONS AND HOUSING

NOTE: In response to the COVID-19 pandemic, some of the housing and transportation resources listed here may have temporarily suspended their offerings. Check with the service you are interested in to learn the current status of their offerings.

Airbnb and Cancer Support Community Partnership

CSC Airbnb Helpline: 877-793-0498

Airbnb is partnering with Cancer Support Community to provide free housing for cancer patients and caregivers who are traveling for treatment, provided they meet certain geographic and income criteria. Call the CSC Airbnb Helpline to learn more and to apply for the program.

The American Cancer Society's Hope Lodge

Support Line: 800-227-2345
https://www.cancer.org/treatment/support-programs-and-services/patient-lodging.html

Provides people with cancer and their caregivers a free place to stay while receiving treatment in another city. Currently, there are 30 Hope Lodge locations throughout the United States and Puerto Rico.

Healthcare Hospitality Network, Inc. (HHN)

https://www.hhnetwork.org/

If unable to find lodging, contact HHN's partner organization Joe's House (see contact information below).

Provides free or significantly reduced-cost lodging to patients and their families while receiving medical care away from home. Unlike a hotel, HHNs provide opportunities for those going through similar stressful situations to come together as a community where they can support one another. HHNs have shared kitchens, common living areas and private bedrooms just like a home, creating a warm and comfortable place far from home. HHNs help alleviate the financial burden often associated with medical crises and have been shown to reduce stress on both the patient and family members.

ACCOMMODATIONS AND HOUSING, CONT.

Joe's House

Support Line: 877-563-7468
Email: info@joeshouse.org
https://www.joeshouse.org/lodging

Website lists hundreds of places to stay across the country near hospitals and treatment centers that offer a discount for traveling patients and their loved ones. Some options are free.

- Users may search for accommodations by city or proximity to a cancer treatment center or hospitals.
- Works with hotels and other lodging facilities to centralize inventory and provide medical discounts to cancer patients.

Ronald McDonald House Charities

Support Line: 630-623-7048
https://www.rmhc.org/about-us

Offers rooms for families of pediatric patients younger than 21 years of age (some houses only serve families of those younger than 18 years of age). For most Ronald McDonald Houses, families may stay as long as their child remains in active treatment, although some Houses may establish a maximum length of stay.

Contact the social services department at the hospital your child will receive treatment. They will place your name on the waiting list for the day that you intend to arrive. Because each child's treatment is unique, a family's stay at the House is unpredictable. Therefore, most local RMHC Chapters are unable to confirm room reservations for your stay prior to your arrival.

TRAVEL ASSISTANCE

Air Charity Network™ (formerly Angel Flight America)

Support Line: 877-621-7177
http://aircharitynetwork.org/

Provides access for people in need who are seeking free air transportation to specialized healthcare facilities or distant destinations due to family, community, or national crisis.

Corporate Angels Network - Free Air Travel For Cancer Patients

Support Line: 914-328-1313
Email: info@corpangelnetwork.org
http://www.corpangelnetwork.org/#/home

Arranges free travel to treatment sites across the country for cancer patients, using empty seats on corporate jets.

Lifeline Pilots - Free Air Travel for Patients

Support Line: 1-800-822-7972
https://lifelinepilots.org/

Provides access to free air transportation on small (4-6 seat), private aircraft for distant health care and other needs. Missions are typically facilitated in: Illinois, Indiana, Iowa, Kentucky, Michigan, Minnesota, Missouri, Ohio, Tennessee, and Wisconsin.

Mercy Medical Angels

Email: info@mercymedical.org
https://www.mercymedical.org/

Provides information about charitable long-distance medically-related transportation. Refers to sources of help available in the national charitable medical transportation network.

TRAVEL ASSISTANCE, CONT.

Patient AirLift Services (PALS)

Support Line: 888-818-1231 or 631-694-PALS (7257)
Email: info@palservices.org
https://www.palservices.org

Arranges free air transportation services for people in need. PALS volunteer pilots bear all costs of each medical flight, including fuel, oil, landing fees, ramp fees and other expenses. Patients are not responsible for any air transportation costs.

Patients must typically arrange for and pay for local ground transportation at both destination and departure locations.

CLINICAL TRIAL PARTICIPATION FINANCIAL SUPPORT

Lazarex Cancer Foundation

Support Line: 877-866-9523 or 925-820-4517
Email: info@lazarex.org
https://lazarex.org/

Promotes early stage cancer diagnosis to increase survival, especially for the medically underserved. Helps remove barriers to clinical trial participation for advanced stage patients in FDA clinical trials. Offers financial assistance for lodging and transportation costs for participation in FDA-approved clinical trials.

LEGAL AND FINANCIAL ISSUES AROUND THE CANCER EXPERIENCE

Cancer Financial Assistance Coalition (CFAC)

https://www.cancerfac.org/

A coalition of financial assistance organizations joining forces to help cancer patients experience better health and well-being by limiting financial challenges. Their site can be searched by diagnosis, type of assistance, age or geography.

Family Reach

Support Line: 973-394-1411 or 857-233-2764
https://familyreach.org/

Dedicated to removing the financial barriers that come with a cancer diagnosis. Works with patients and healthcare professionals at more than 400 top-tier hospitals and cancer scenters, striving to reach more families before they hit critical financial breaking points. Resource navigators are available to assist.

Triage Cancer

Support Line: 424-258-4628
https://triagecancer.org/cancer-finances

A national nonprofit organization that provides education on the practical and legal issues that may impact individuals diagnosed with cancer and their caregivers.

BUILD A CARING COMMUNITY

Here is a list of organizations that can help you set up a website.

- Cancer Care: https://mycancercircle.net/
- Caring Bridge: https://www.caringbridge.org/
- My Lifeline/Cancer Support: www.cancersupportcommunity.org/mylifeline

GENERAL INFORMATION ABOUT CLINICAL TRIALS

Additional information about participating in or supporting a loved one during a clinical trial is available at:

The American Cancer Society (ACS)

https://www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

The Center for Information and Study on Clinical Research Participants (CISCRP)

www.ciscrp.org

The Leukemia and Lymphoma Society (LLS)

https://www.lls.org/treatment/types-of-treatment/clinical-trials

National Institutes of Health (NIH)

https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics

CAR T-CELL THERAPY PROCESS VIDEOS

These short videos about the CAR T-cell therapy process explain exactly how the treatment works:

CAR T-Cell Therapy: How Does It Work?

Dana-Farber Cancer Institute

https://www.youtube.com/watch?v=OadAW99s4Ik

The 8 Steps of CAR T-Cell Therapy

Dana-Farber Cancer Institute

https://www.youtube.com/watch?v=WN6TfgDMdFc

CAR T-Cell Therapy for Cancer Treatment: How It Works

MD Anderson Cancer Center

https://www.youtube.com/watch?v=UZpHu0gl6LU

CAR T-Cell Therapy

The Leukemia and Lymphoma Society (LLS)

https://www.youtube.com/watch?v=uC16iDy2XoI

CAR T-Cell Therapy: Side Effects

The Leukemia and Lymphoma Society (LLS)

https://www.youtube.com/watch?v=rIPlBrmMnoA

How to Biohack Your Cells to Treat Cancer (TedEd YouTube Video)

The science of biohacking, where biologists go into a patient's genetic code and reprogram their immune system to recognize and fight cancer cells.

https://youtu.be/Mt5C5fhuU_0

APPS PROVIDING HELP ALONG THE JOURNEY

These apps are available on the App Store or Google Play.

- **Calm**

  Calm is the #1 app for sleep and meditation. Join the millions experiencing better sleep, lower stress and less anxiety.

- **Chillscape**

  Sonic Meditation: A tool for quick bursts of mindfulness and anxiety relief. It can be used to relax, focus the mind or filter out unwanted distractions like pain or negative thoughts.

- **Headspace**

  Loaded with meditation courses, sleep programs and movement practices. This is an expensive option, but their free trial may be useful as an introduction to mindfulness practices.

- **Insight Timer**

  A free library of 60,000 meditations, music selections and inspirational talks. Paid services, including meditation courses, are also available.

- **MindShift CBT**

  A free, scientifically based anxiety tool based on a type of therapy called Cognitive Behavioral Therapy (CBT). The interactive tool guides users to look at anxiety-producing thoughts in a healthier way.

- **Pause: Daily Mindfulness**

  A variety of short sessions that help you relax and shift your focus away from distressing thoughts.

- **Rebalance with Mindfulness**

  A guided, 4 step process to combat stress by reconnecting the mind and body.

  1. Diaphragmatic breathing*: A type of breathing exercise that reduces the stress response and brings your nervous system back into balance.
  2. Mindful body scan: Emotions can appear as physical sensations. By developing an awareness of how your body feels, you can learn to regulate your emotions better.
  3. Labelling emotions and sensations: Labelling emotions reduces their intensity.
  4. Allowing: The practice of allowing our sensations and emotions to exist without trying to change them or react to them. The app helps you choose how to respond to your emotions.

  *Diaphragmatic breathing by itself can reduce stress. You can use this app to learn how, even if you don't continue with the other 3 practices.

GLOSSARY

Allogeneic: Allo means “other”. Allogeneic means that the cells or tissue given to a patient come from someone other than the patient.

Angiography: An X-ray image of blood vessels that uses a dye so that the blood vessels can be seen.

Anticoagulant: A substance used to prevent the formation of blood clots or break up existing blood clots.

Antigen: An antigen is anything that can be “seen” by the immune system. There are many different types of antigens. In CAR T-cell therapy, antigens are a substance (or marker) on the outside of a cell that is recognized by the CAR T cell and “marks” the cell for destruction. An example of an antigen (or *marker*) in CAR T-cell therapy is CD19, found on the outside of both normal and cancerous B cells.

Apheresis: The process of removing whole blood from a patient, processing the blood in a machine that separates out one component and then returning the remainder of the blood components to the patient. There are several kinds of apheresis procedures, each named after the component of blood that is extracted. When white blood cells are extracted, the process is called *leukapheresis*.

Approved: Indicates that a drug or therapy has been fully tested in clinical trials to ensure it is safe and effective and has been approved for use outside of a clinical trial by the FDA.

Autologous: Auto means “self”. Autologous means that the cells or tissue given to a patient come from that same individual.

B cell: A type of white blood cell (or lymphocyte) that makes antibodies to fight infection. Like all other cells in the body, B cells can become cancerous.

B-cell aplasia: Low numbers of B cells. B-cell aplasia is one of the expected results of successful anti-CD19 targeted therapy.

Bone marrow biopsy: A procedure that takes a sample of bone marrow by inserting a hollow needle through the bone (usually the hip bone) and into the bone marrow.

Bridging therapy: Therapy that is meant to control cancer during the time between leukapheresis and CAR T-cell infusion.

Cannula: A small tube inserted into a vessel, cavity or duct to allow flow of substances (usually fluids).

CAR: See *Chimeric antigen receptor (CAR)*.

Catheter: A thin tube used to deliver blood, fluids or medications into a vein.

CD19: An antigen, or "marker" found on the surface of B cells. See "antigens".

Cell: The basic membrane-bound unit of life that composes all living things.

Chimeric antigen receptor (CAR): A protein created in a laboratory that is designed to recognize an antigen (or marker) on cancer cells. When added to T cells, CARs give T cells (now called "CAR T cells") the ability to identify and destroy cancer cells.

Chronic stressor: Stress resulting from repeated exposure to situations that lead to the release of stress hormones. This type of stress can cause wear and tear on your mind and body.

Clinical trial: Research that involves human participants, carried out to learn if a treatment is safe and/or works.

Clinical Research Team: A group of professionals involved in all aspects of running a clinical trial. Team members can include investigators, research nurses and coordinators, data managers, staff nurses and doctors. In some centers, team members may also serve as the healthcare providers for trial participants.

CT or CAT scan: Uses a group of X-rays taken at different angles around the body and a computer to create detailed cross-sectional images.

Cytokines: Small proteins that regulate the immune system. Cytokines are released by certain immune system cells. They can stimulate the immune system to attack cancer and also cause the production of more cytokines.

Cytokine release syndrome (CRS): A common side effect of CAR T-cell therapy. CRS occurs when many cytokines are released by immune cells during immunotherapy. Some symptoms are nausea, fever, headache, rapid heartbeat, low blood pressure, rash and trouble breathing. CRS can be mild or moderate. CRS can feel like a very bad case of the flu, but in rare cases it can be severe or life-threatening.

Cytokine storm: See *Cytokine Release Syndrome*.

Cytopenias: Low blood cell counts, including red blood cells, white blood cells, and platelets.

D

Discharge instructions: Instructions given to a patient when discharged from the hospital, usually by a nurse. They include important information for patients and caregivers to manage their own care when outside of a hospital or treatment center. These instructions can be given in written or verbal form.

Distress: Emotional, social, spiritual or physical pain or suffering that may cause a person to feel sad, afraid, depressed, anxious or lonely. People in distress may also feel that they are not able to manage or cope with changes caused by normal life activities or by having a disease, such as cancer.

Dose escalation: A study design in which a very small dose of a treatment is given to a small number of patients. If it is found to be safe, the next group receives a higher dose. This continues until all the planned doses have been tested.

E

ECG: Electrocardiogram, electrocardiograph. Records the electrical activity of your heart.

ECHO (echocardiogram): An ultrasound image of the heart.

ECOG performance score: A questionnaire that measures the ability to care for oneself and perform daily activities and physical functions (like walking, working, etc.).

Effective: How well a treatment works under “real-world” conditions.

Efficacy: How well a treatment works under ideal and controlled circumstances, as in a clinical trial.

Eligibility criteria: Factors that define the population of patients that will be allowed to participate in a particular trial.

Emergency Wallet Card: A card with information about the CAR T-cell therapy you have received and contact information for your clinical research and healthcare teams.

Exclusion criteria: Factors that disqualify a patient from participating in a particular clinical trial.

Genes: Stretches of DNA that serve as the “instructions” or blueprints for cells to make proteins.

Gene therapy: A therapy that uses genes to treat or prevent disease. In CAR T-cell therapy, a gene carrying instructions to make a new protein receptor is inserted into T cells.

Hypogammaglobulinemia: Low levels of antibodies, or immunoglobulins.

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS, or neurotoxicity): A severe side effect of CAR T-cell therapy in which the immune response can produce a toxic effect on the nervous system. Patients may suffer headaches, confusion, seizures, loss of speech and loss of motor skills. ICANS can range from very mild to quite severe and life-threatening.

Immunotherapy: A type of treatment that uses the immune system to treat disease (including cancer).

Inclusion criteria: Factors that a patient must have in order to participate in a particular clinical trial.

Informed consent: See *Participant Information Sheet*.

Informed consenting process: A process that makes sure clinical trial participants are fully informed about and understand all the details of a clinical trial before agreeing to participate.

Intravenous immunoglobulin (IVIG): A treatment often given to people who have received CAR T-cell therapy. IVIG provides extra antibodies and helps to prevent frequent infections until B cells return to more normal levels.

Investigator: A person responsible for the conduct of a clinical trial at the clinical research site. If there is more than one investigator at a site, the leader is called the “Principal Investigator”.

Institutional Review Board (IRB): A group of doctors, nurses, scientists and community members that protects the rights and welfare of anyone participating in a clinical trial. The IRB will review and monitor any research at their institution that has human participants.

Leukapheresis: A procedure that involves removing blood from the body, delivering it to a machine that separates and collects white blood cells and then returning the remaining blood components to the body.

Long-term follow-up study (LTFU): A study in which patients in a clinical trial are monitored for an extended period of time to learn about possible delayed side effects.

Lumbar puncture (spinal tap): A procedure that takes a sample of cerebrospinal fluid (liquid that surrounds the brain and spinal cord). This is done by inserting a needle between two vertebrae (bones in the spine).

Lymphocytes: White blood cells that play an important role in the immune system. There are three types: B cells, T cells and Natural Killer (NK) cells.

Lymphodepleting chemotherapy: Chemotherapy given before CAR-T cell infusion in order to decrease the number of white blood cells (including T cells) in the body. CAR T cells grow and expand better if there are not as many of the patient's own T-cells present.

Marker: See *antigens.*

MRI (magnetic resonance imaging): A procedure that uses a strong magnetic field, radio waves, and a computer to make detailed pictures of the body.

MUGA (multiple gated acquisition): A type of heart scan that uses a small amount of a radioactive tracer and a special video camera to see how well the heart is pumping.

Mutation: A change that occurs in the DNA sequence. Certain mutations may lead to cancer or other diseases.

Neurological: Related to the brain, spine, or nerves.

Neurotoxicity: Producing a toxic effect on the nervous system. See *Immune Effector Cell-Associated Neurotoxicity Syndrome.*

Participant: An individual who participates in a clinical trial.

Participant Information Sheet (PIS): A document that provides potential clinical trial participants with enough information about the clinical trial to allow them to make an informed decision about whether to participate. This is sometimes called an Informed Consent document.

PET-CT scan (Positron Emission Tomography/Computed Tomography): A type of scan that uses a small amount of a radioactive tracer to light up active cells. Cancer cells show up as bright spots on a PET scan.

PFT (pulmonary function tests): Breathing tests to see how well the lungs are working.

Placebo: An inactive treatment, used in some studies to compare to an experimental treatment.

Platelets: Blood cells that help blood to clot to stop bleeding.

Post-traumatic growth: Positive life changes that develop through a stressful, frightening experience.

Principal Investigator: The person in charge of all aspects of a clinical trial.

Protocol: A detailed, written plan and set of instructions. In a clinical trial, all aspects of patient care and all procedures are done according to the clinical trial protocol.

Psychosocial Oncologist: A person who specializes in the psychological, behavioral, emotional and social issues that arise for cancer patients and their loved ones.

Randomized: A clinical study design that randomly assigns participants to different groups to compare different treatments.

Receptor: A protein on the surface of a cell that can recognize and attach to an antigen.

Safe: There are not unacceptable levels of unwanted effects of the treatment.

Side effect: Any unwanted effects of a treatment.

Sign: Something that can be seen or measured.

Skeletal survey: A series of X-rays to look for areas of bone that may be damaged.

Sponsor: The person, company, group or organization that pays for and oversees a clinical trial. The sponsor collects and analyzes data from the trial.

Standard-of-care Treatment: The best (or generally accepted) treatment for a specific disease.

Stress responses: Normal reactions to situations that make us feel frustrated, angry or nervous—like a cancer diagnosis and its treatment.

Supportive Care Services: Services aimed at preventing or treating symptoms of cancer as early as possible. This includes helping with side effects caused by treatment and psychological, social and spiritual problems related to a cancer diagnosis or its treatment.

Symptom: Something the patient feels or experiences.

T

T cell: A type of white blood cell that travels throughout the body and destroys damaged or infected cells.

Tumor biopsy: A sample of tumor tissue.

Tumor lysis syndrome: Condition that can occur when a large number of cancer cells die within a short period of time, releasing their contents into the blood.

U

Ultrasonography: An imaging procedure that uses sound waves to create pictures of structures deep within the body.

LIST OF ABBREVIATIONS

CAR	Chimeric Antigen Receptor
CRS	Cytokine Release Syndrome
FDA	Food and Drug Administration
ICANS	Immune Effector Cell-Associated Neurotoxicity Syndrome
ICF	Informed Consent Form
IRB	Institutional Review Board
IVIG	Intravenous Immunoglobulin
LTFU	Long-term Follow-Up (study)
MBSR	Mindfulness-Based Stress Reduction
PIS	Participant Information Sheet