Cell and Gene Therapy:
Patient and Caregiver Odyssey

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National Pharmaceutical Council®

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EXECUTIVE SUMMARY

Cell and gene therapies (CGTs) represent a new frontier in personalized medicine, offering potential cures or long-lasting benefits for severe conditions such as rare genetic diseases and certain cancers. The odyssey from diagnosis to treatment to recovery is often lengthy and challenging. Moreover, this landscape continually evolves as new therapies are approved each year to treat more conditions.

As integral stakeholders in the healthcare system, employers and payers should understand the challenges that patients and caregivers face along their treatment odyssey. Employers and payers are in a unique position to support and empower patients and caregivers by recognizing and understanding these challenges and making efforts to mitigate and overcome barriers to treatment. Similarly, as CGTs become available to treat more conditions, patients and caregivers need to understand these challenges and barriers to better navigate their potential treatment odyssey.

This white paper explores the patient and caregiver experience through five key stages:

1. **Awareness and Diagnosis:** Patients face long delays, misdiagnoses, and barriers, particularly for rare diseases, and it often takes years to receive a correct diagnosis.
2. **Initiation of Treatment:** Before starting CGT treatment, navigating treatment options, referrals, insurance approvals, and financial planning present significant challenges.
3. **CGT Treatment Administration:** The process of preparing and administering CGTs is complex. It often requires extended hospital stays and intensive monitoring, which create significant physical and emotional challenges.
4. **Post-Treatment Monitoring and Follow-up:** Patients undergo long-term monitoring for side effects and efficacy, with follow-up care lasting years in many cases.
5. **Ongoing Support and Survivorship:** Patients manage reintegration into daily life and potential long-term side effects, often aided by peer support.

After a brief introduction to CGTs, subsequent chapters explore each of these stages in detail and provide recommendations for addressing some of the key barriers that patients and caregivers face during each stage of their odyssey.

The path to CGT treatment is filled with significant emotional, physical, logistical, and financial challenges, requiring the coordinated efforts of caregivers, healthcare providers, insurance providers, therapy manufacturers, employers, and patient advocacy groups. These stakeholders must work together to further streamline processes, reduce barriers, and provide comprehensive support throughout the entire journey. As CGT treatment continues to evolve, addressing these challenges will be crucial to improving access and outcomes for future patients.

Every patient's journey through the continuum of care from diagnosis to treatment and beyond is as individual as they are. Cell and gene therapies (CGTs) represent a shift towards more personalized medicine, moving away from the traditional one-size-fits-all approach that often falls short in treating complex and rare conditions. CGT treatments hold tremendous promise to improve health and longevity and can bring tremendous hope to patients facing the threat of serious illness. The odyssey many patients face when going through CGT treatment, however, is filled with challenges and roadblocks along the way.

Figure 1 provides a high-level overview of this complex odyssey, highlighting key milestones and introducing the five core chapters of this white paper.

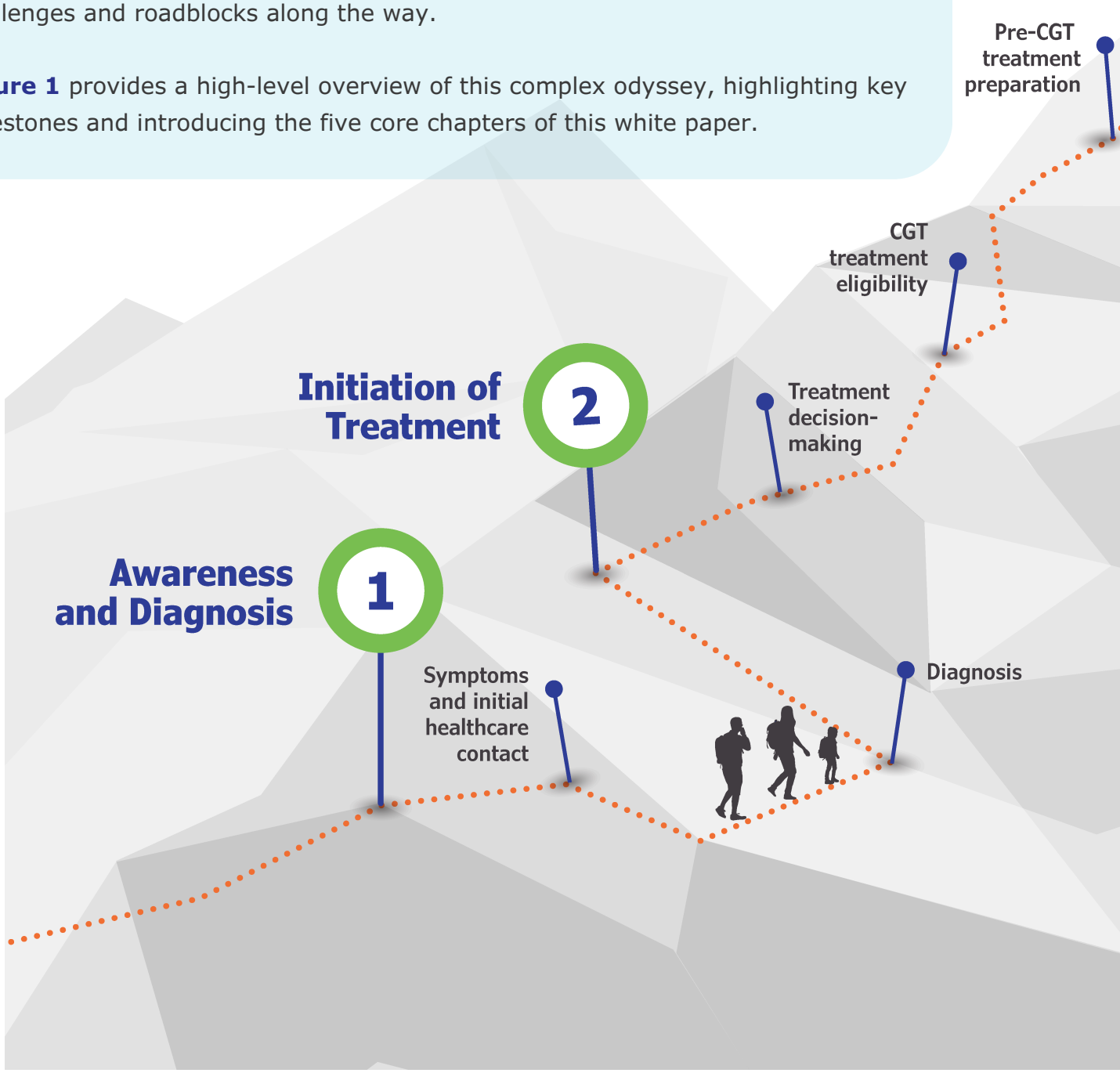
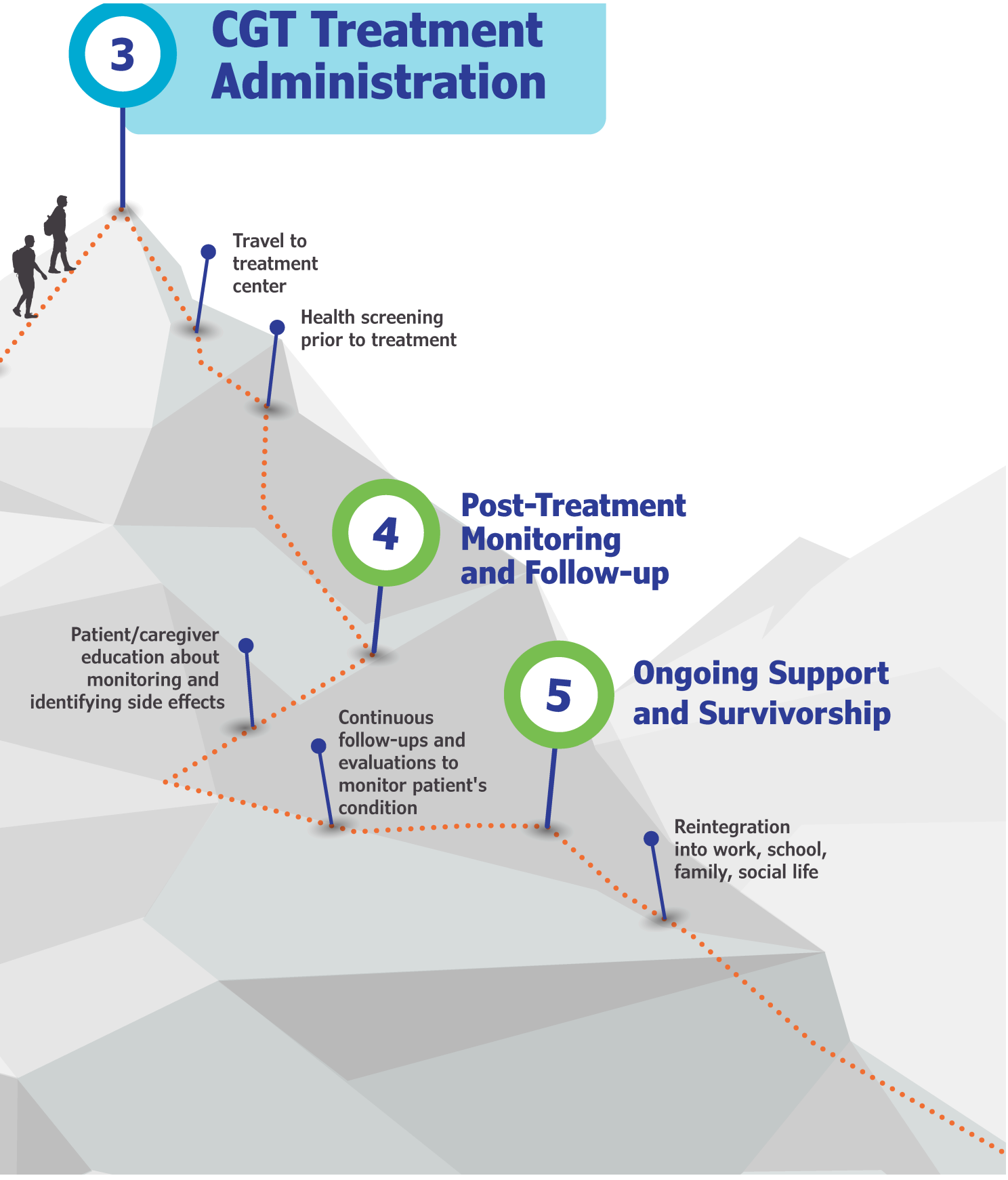


Figure 1. The Cell and Gene Therapy Patient Odyssey: Overview of Key Milestones



When a patient is diagnosed with the type of serious condition that may be eligible for CGT treatment, it is a time of great anxiety and uncertainty in their life and for their loved ones. Given that many CGT treatments have recently been approved, and patients may not be as familiar with them, both they and their caregivers typically have many initial questions, including:

What are cell and gene therapies?

Our bodies are composed of trillions of individual cells, most of which perform specialized tasks to keep us functioning and healthy. Cells receive their instructions from the body's genetic code, DNA, which is like a blueprint that tells them what type of cell to become, which proteins to express, what function they should perform, and so on.

Genetic diseases occur when DNA has missing or damaged sections that prevent it from sending typical instructions to the cell. For example, in sickle cell disease (SCD), an individual inherits altered genes from both parents that affect how the body makes hemoglobin, a key component of red blood cells. The body cannot repair this variation on its own as the instructions, the DNA, are missing essential information. Gene therapies target specific sections of DNA to newly introduce or revise the genetic sequence, allowing the body's cells to function in a normal, healthy way.

In addition to inheriting missing or damaged genetic information, DNA can also be mutated over time. DNA mutation can happen naturally such as what occurs when DNA is copied during cell division, or it can be caused by environmental factors like UV light, smoking, or diet. Most of these changes are small and will go unnoticed, but if key cellular functioning areas of the DNA become mutated, this can lead to cancers or other types of illnesses. Cell therapies target these mutated groups of cells by introducing healthy cells to the body to regain the function lost.

What conditions are treated by cell and gene therapies?

In 2024, the U.S. Food & Drug Administration (FDA) reported 37 approved CGT products.[1] However, other reputable sources in the field typically cite lower numbers, ranging from 17 to 24 approved products in the U.S.[2,3] This variation stems from differences in how organizations define and categorize CGTs. Conditions treated by cell therapies include several types of cancer, including lymphoblastic leukemia, large B cell lymphoma, and multiple myeloma. Cell therapies for these conditions typically target patients who have not responded well to other treatments.

Currently approved gene therapy products treat a number of rare genetic diseases including spinal muscular atrophy (SMA) type 1, Duchenne muscular dystrophy (DMD), cerebral adrenoleukodystrophy (CALD), hemophilia A & B, beta-thalassemia, dystrophic epidermolysis bullosa (DEB), metachromatic leukodystrophy (MLD), Leber's congenital amaurosis (LCA), and sickle cell disease (SCD).

Individuals with these rare genetic diseases often begin presenting with symptoms during infancy or early childhood. They can cause serious complications ranging from blindness and the need for blood transfusions to the loss of motor abilities and death. Before the development of CGT products, most patients living with these conditions did not have effective treatment options. Today, thanks to CGT, children living with these rare genetic diseases have the opportunity to live healthy, fulfilling lives.

Beyond the currently approved therapies, many CGTs are in the development pipeline, and new conditions are being tested for currently approved products. One estimate puts the number of new CGT approvals at 66 by 2032.[4] Conditions currently being tested include numerous types of cancer, multiple sclerosis, cystic fibrosis, cardiovascular disease, Parkinson's disease, and osteoarthritis.[5,6]

How are cell and gene therapies made?

One important distinction from traditional therapies is how CGTs are produced. The manufacturing process is complex, as living materials are cultivated that will ultimately be given to the patient. In the case of cell therapies, this involves cultivating healthy cells. Cells used in treatments can come from a donor, known as allogeneic therapies, or from the patient themselves, referred to as autologous therapies. In autologous therapies, the patient's cells are harvested, transformed in a lab, and cultivated before treatment. Allogeneic therapies have the advantage of being produced in larger quantities, which allows for faster treatment of a greater number of patients. On the other hand, autologous therapies tend to be more effective and carry a lower risk of the body rejecting the treatment.

Similarly, for gene therapies, products can be produced either in vivo or ex vivo. In vivo therapies involve taking new genetic material created in a lab and inserting it directly into the patient's cells. Ex vivo therapies involve collecting cells from the patient, transforming the genetic material, and then reintroducing it to the patient's body. Both methods typically use a vector (usually a modified virus) to transport the genetic material. Like with cell therapies, ex vivo genetic therapies take substantially longer to produce as the patient's own genetic material must first be altered before treatment can begin.

What are the benefits and risks of treatment?

CGTs' main benefit is that they hold the potential to either cure patients or have a long-lasting (i.e., durable) positive impact on patients. And this oftentimes only involves one single administration of the treatment. For many treatments, it is not yet fully known how long the benefits will last. Clinical studies and follow-up studies are ongoing, however, and the data remain promising for many CGTs and patients.

Of course, there are risks to CGT treatment as well. For both cell and gene therapies, there is always the risk that treatment is not as effective as anticipated. For gene therapies, there are risks of having a strong immune system response, cells that were not the target receiving the genetic material, infections arising from the viral vector used to deliver the genetic material, or cancer developing as a result of DNA changes. Cell therapies also risk serious reactions, including strong immune responses, neurotoxicity, blood disorders, and infections due to a weakened immune system. The FDA weighs the risks and benefits of all CGTs and determines that the benefits outweigh the risks for all FDA-approved CGTs.

What support is available?

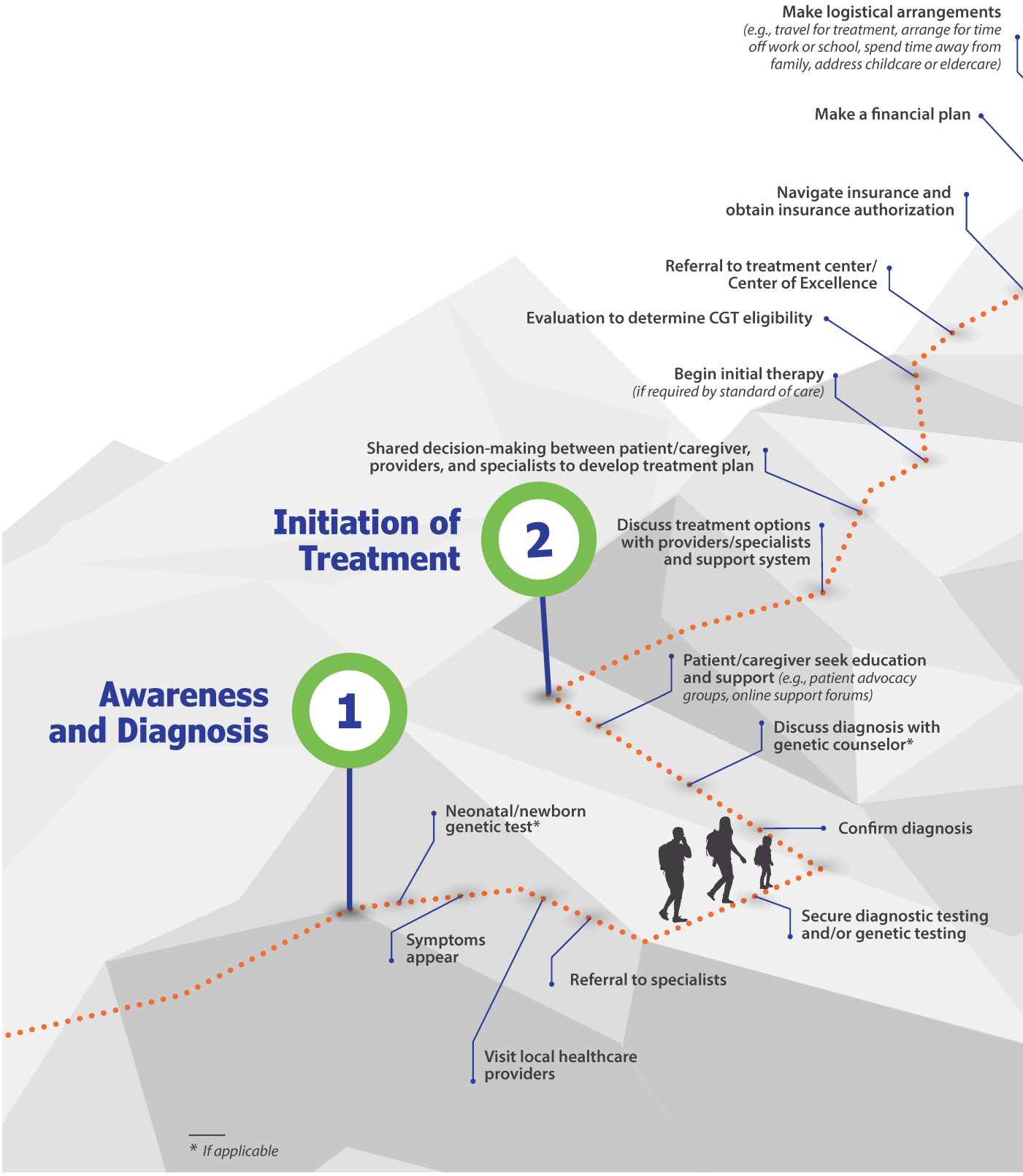
It is important to remember that no patient is on this odyssey alone. Family, friends, and caregivers are key pillars of support. Healthcare workers, including doctors, nurses, and administrative staff, are also important resources for receiving education, creating treatment plans, coordinating with insurers and billing departments, and helping to alleviate the concerns patients are feeling. Many patients also find emotional, financial, and logistical support from patient advocacy groups and other organizations. This support can help patients access essential resources and lighten the burden.

How long is the journey to receive a cell or gene therapy?

The journey to CGT treatment is often lengthy, typically spanning multiple years. Some patients or caregivers may spend multiple years becoming aware of their or their child's symptoms and obtaining a diagnosis. Further, due to insurance or other requirements, some patients must try several different treatments before they become eligible for a CGT.

Once diagnosed and eligible for treatment, the process can remain long and intense. Some therapies take months to produce and manufacture a precise, individual-specific medicine. Some therapies necessitate spending a month in the hospital after treatment for monitoring. Most therapies require significant follow-up to check for any reactions and to ensure the treatment is working. Throughout this process, many patients must travel to specialized treatment facilities hours away from home, requiring time and resources. For a more detailed understanding of the CGT odyssey, **Figure 2** presents a comprehensive, step-by-step breakdown, illustrating the numerous challenges and decision points that patients and caregivers navigate throughout their CGT experience.

Figure 2. Comprehensive Mapping of the Cell and Gene Therapy Patient and Caregiver Odyssey




3
CGT Treatment Administration
Patient/caregiver travel to treatment center
Onboarding and education about treatment procedure and possible side effects
Health screening prior to treatment
Patient's cells collected (for autologous/ex vivo therapies)
Informed consent (for clinical trials)
Cells modified in laboratory and transported back to treatment center*
Patient receives conditioning therapy*
Patient receives bridging therapy*
Inpatient monitoring for side effects*
Patient receives treatment via IV infusion or injection to target organ
4
Post-Treatment Monitoring and Follow-up
Patient closely monitored for post-treatment reactions
Patient/caregiver education about monitoring and identifying side effects
Discharge planning (for those receiving inpatient treatment)
5
Ongoing Support and Survivorship
Patient/caregiver receive information about self-care to manage recovery
Reintegration into work, school, family, social life
Transition from treatment healthcare team to local providers*
Continued learning about advancements in research and new treatments
Continuous follow-ups and evaluations to monitor patient's condition
Learning to manage long-term side effects*
Use of assessments and tools (such as patient reported outcomes) to understand patient's well-being post-treatment
Long-term follow-up
Education about new long-term effectiveness and safety as it is published
Ongoing care/survivorship care
Joining peer support and mentoring programs

AWARENESS AND DIAGNOSIS

For patients and their caregivers, the treatment odyssey typically begins when symptoms first appear. Naturally, there is wide variation in what symptoms appear depending on the condition and the individual involved. When young children or infants are the ones impacted, it can be quite challenging for their parents and caregivers to fully understand and explain these symptoms to a healthcare practitioner. Regardless of whether the impacted individual is a child or an adult and whether the condition in question is a rare genetic disease or cancer, the first point of contact with the healthcare system after symptoms appear is typically a local primary care provider.

As with the condition symptoms themselves, there is wide variability in primary care providers and an individual's ability to access timely, quality care. For some, their regular pediatrician or family care doctor can help in understanding changes to an individual's health and begin the process of obtaining a referral to a specialist for testing and diagnosis. For others, particularly those from historically marginalized populations and those with lower socioeconomic status, accessing primary care at this stage of the treatment odyssey can be a significant barrier.[7,8] Patients and caregivers may have to rely on local clinics, urgent care facilities, or the emergency room depending on what is available in their geographic area and their insurance status. Their concerns may not be taken as seriously as other patients[9,10] or their conditions may simply be stabilized before being discharged.

This variability in primary care has important implications for patients. Provider knowledge of rare and genetic diseases or and gene therapies (CGTs) may be limited. This often leads to delays in diagnosis or misdiagnoses. In fact, obtaining an accurate diagnosis for a rare disease can take up to seven years[11] and, in some cases, over a decade.[12] One study found that, on average, the cost to patients and their families with rare diseases and a delayed diagnosis exceeds $220,000 in avoidable medical bills and lost income.[13] Along this diagnostic odyssey, many patients find themselves visiting multiple primary care providers in search of second opinions or to locate a doctor who truly understands their condition and can serve as a trusted source of information. Having a reliable healthcare professional is crucial, as they can connect the patient with the appropriate care team, including specialists who focus on their specific conditions.

Obtaining a diagnosis for a rare disease can be a daunting task. There are more than 10,000 distinct rare diseases affecting 1 in 10 Americans,[14] making the challenge substantial. Of these rare diseases, 80% are genetic, and 95% do not have an FDA-approved treatment.[11] One of the best sources of obtaining an early diagnosis is through newborn screening.[13,15] Newborn screening has proven to be a highly successful public health program, significantly improving outcomes for various conditions associated with long-term disability and even death.[16] However, the system faces critical challenges due to its fragmented, state-by-state implementation and limited screening for diseases that involve genetic testing.[17] When a new genetic screening test is developed, it can take

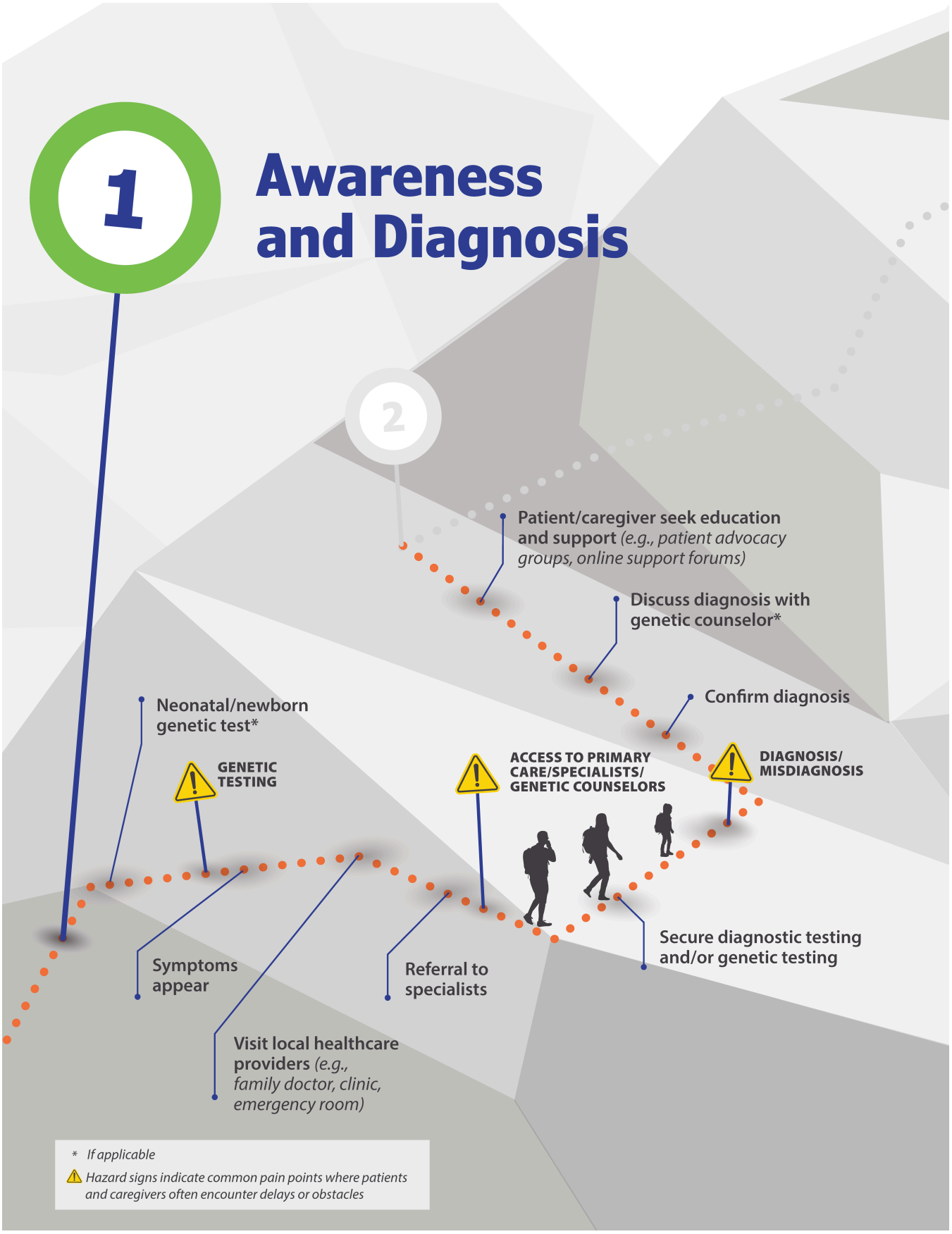
between 5-7 years from the time the test is recommended at the federal level to be incorporated by individual states into their screening regimen.[18] These delays, coupled with inconsistent adoption across states, can significantly impact the identification of children who would greatly benefit from earlier intervention.

For others, the diagnostic odyssey begins in earnest once the patient is referred to a specialist to begin testing. Depending on the condition, testing sites may be limited to a small number of Centers of Excellence (COE) spread across the country. These COEs are specialized healthcare facilities recognized for their exceptional expertise and resources in treating complex or rare conditions. This means that the patient and potentially a parent or caregiver need to take time off from work or school to travel for testing. It also means incurring not only travel and logistical costs but also substantial financial burdens. These can include copays, coinsurance, and deductible payments for those with insurance or potentially full out-of-pocket expenses for uninsured patients, depending on their specific situation. These costs, along with the anxiety and stress of not knowing exactly what is wrong, continue to build during this time. This step also represents a significant barrier for those from historically marginalized populations and those with lower socioeconomic status, for whom the cost of traveling and paying for testing can be prohibitively expensive or for whom trust in and knowledge of the medical system may be limited.

This stage of the odyssey may be especially difficult for pediatric patients with conditions that are not easily diagnosed. Some conditions have significant symptom overlap with other more prevalent conditions that should be ruled out and for which a misdiagnosis can occur. In addition to some type of genetic screening, there may also be a number of clinical tests, including biochemical tests, biopsies, MRIs, eye exams, as well as other neurological, cognitive, or physical examinations that specialists can administer before a diagnosis is confirmed. This process can, unfortunately, take months or even years if there are any delays or misdiagnoses. Such delays can lead to a significant deterioration in the child's condition, which can be distressing for everyone involved. Additionally, the opportunity for certain types of treatments may be missed due to the prolonged time it takes to obtain an accurate diagnosis.

Once a patient's diagnosis has been confirmed, there are many questions to ask and decisions that need to be made. Many find this step in the odyssey particularly overwhelming. This involves the need for communicating with family and friends as well as potentially one’s employer or school about their diagnosis, health condition, struggles with coping, and possible next steps for treatment. This also includes the need for finding information on treatment options and/or clinical trials as well as searching for the right doctor(s) and care team to create a treatment plan. This step may also involve genetic counseling based on the condition, and discussions on fertility preservation may occur depending on the available treatment options and their potential impact on future fertility.[19]

Figure 3. Steps and Barriers Within Awareness and Diagnosis



This initial phase of the patient and caregiver odyssey is often marked by emotional, financial, and logistical turmoil. The longer this phase persists before a diagnosis is confirmed and treatment begins, the more the patient's health is likely to decline, causing significant emotional strain on themselves, their friends, family, and caregivers. This accompanies the financial strain of continued doctor and/or hospital visits and the logistical strain of time off from work or school for patients and caregivers, as well as the need, in many cases, to regularly travel for testing and/or stabilizing treatment before receiving a confirmed diagnosis.

Support for patients and caregivers becomes vitally important during this time. They often initially look to doctors, nurses, hospital staff and administrators, and insurance providers for education and information about their condition and treatment options, along with understanding the costs and financial aspects of their condition. Additionally, patients and their caregivers may engage with patient advocacy organizations and therapy manufacturers themselves. These organizations can connect patients with support forums of those who have gone through or who are also going through this process, serve as navigators to help patients and caregivers understand the condition and treatment process, or even provide financial assistance for patient copays or travel and lodging expenses during treatment.[18] This support is critical for helping to make the treatment odyssey less burdensome for the patient, to ensure better treatment outcomes, and ultimately, to improve the patient's quality of life.

Did you know?

- It can take up to 7 years for an accurate diagnosis of a rare disease, and delayed diagnosis can cost patients $220,000 or more in avoidable medical bills and lost income.[11-13]
- While each rare disease affects a relatively small population, collectively, over 10,000 distinct rare diseases exist, impacting 10% of Americans.[14] Among these conditions, 80% are genetic in origin, and 95% currently have no FDA-approved treatment.[11]
- When a new genetic screening test is developed, it can take 5-7 years from the time it is recommended at the federal level to when individual states incorporate it into their testing regimen.[18]

Stakeholder Solutions

Early diagnosis and time to treatment have been shown to be key factors in preventing disease progression for those with genetic conditions.[20] Stakeholders should work together to expand newborn screening and develop and broaden the adoption of new genetic tests. This includes the creation of clear standards and frameworks for the incorporation of new tests in routine screening regimens and for eligibility requirements to obtain timely referrals for testing.

Likewise, stakeholders should invest in further developing and harmonizing provider capabilities, workflows, and care networks. Currently, each new CGT typically requires its own specialized training and protocols, which may strain healthcare resources as more products gain approval and have specialized treatment requirements.[21] Developing standard treatment protocols for similar drug types and disease areas would strengthen provider capabilities and expand patient access.

INITIATION OF TREATMENT

After a patient's diagnosis is confirmed, the next stage in the patient and caregiver odyssey is to initiate treatment. Like the awareness and diagnosis stage, this stage also has considerable variability depending on the condition and the patient. Treatment availability varies significantly — while some conditions have multiple options, others may have very limited choices. Even when treatments exist, patients must first meet eligibility requirements to proceed with any therapy, including cell and gene therapy (CGT). For those who qualify and have multiple treatment options, the decision to use CGT involves carefully weighing the risks and benefits. For all patients and families, navigating their health insurance plan, the weight of potential financial burdens, and the challenges of coordinating treatment logistics represent significant barriers to patients when considering their course of treatment.

The first step in this part of the odyssey is to formulate a treatment plan. This typically involves the patient and caregivers meeting with their doctor and care team to discuss the patient's diagnosis, the patient's current health status, possible future progression of the condition, and treatment options. For some patients, this may be the first time they learn about CGT as a potential treatment option. Patients, caregivers, and their healthcare providers often engage in what is called shared decision-making to develop the treatment plan. Shared decision-making is a collaborative process in which the healthcare provider presents treatment options as well as evidence on the risks and benefits, and the patient explains their preferences, values, goals, and beliefs.

Even among patients who share the same rare disease, individual responses to treatment can vary substantially due to factors such as genetics, age, social determinants of health, and other characteristics.[22] Not only can these differences affect how patients respond to treatment, but they can also make the impact of treatment unique to each patient and difficult to predict with certainty. These variations underscore why the shared decision-making process is so crucial — it allows healthcare providers and patients to develop personalized treatment plans that account for individual patient circumstances and preferences. Together, the parties then agree on the best course of action to take for the patient's treatment. In some situations, healthcare providers may suggest a patient participate in a clinical study if the treatment for their condition is still under investigation and has not yet received FDA approval.

For many patients with rare genetic conditions, the decision to start CGT treatment, while still full of uncertainty and concerns regarding effectiveness and possible side effects, may be rather straightforward. Some conditions, particularly those impacting children, do not have alternative treatment options apart from CGTs. In these cases, the patient's family and caregivers likely have been fighting for months or years to obtain a diagnosis for their child to be able to start what might be the only effective treatment for their child's condition. While all treatment options need to be fully explored during this step, including understanding risks and benefits and agreeing to a treatment plan, time is of the essence

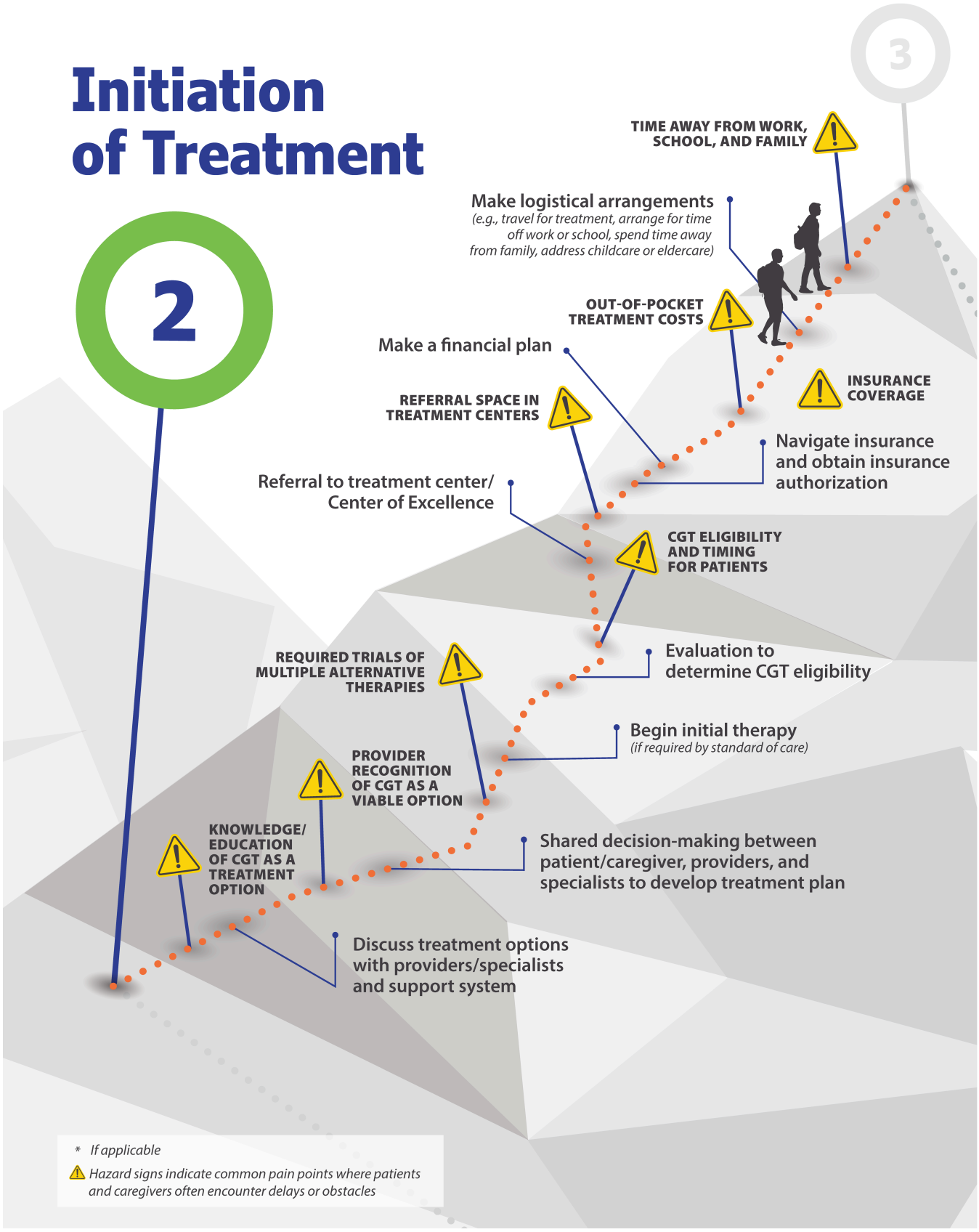
to begin treatment as soon as possible for many of these patients. CGTs may offer the potential to cure or prevent further progression of the condition, but in many cases, they must be administered early enough to achieve these desired outcomes.

For other patients, however, the road to CGT treatment at this stage is much more challenging. Conditions such as cancer have standards of established care, which include alternative therapies that patients are required to use before becoming eligible for CGT treatment. For cancers that have a CGT treatment available, patients often have to go through two to four lines of therapy before being eligible.[23] This means that the patient has to first be administered a treatment (e.g., chemotherapy or radiation) and have this treatment fail (i.e., this is called having a refractory cancer), or the treatment works initially but the cancer later returns (i.e., this is called having a relapsed cancer). These types of treatment failures can take months or even years to occur. Needing to go through this process multiple times means that the delay in becoming eligible for CGT treatment can be incredibly long for patients at this stage.

Did you know?

- For cancers that have a CGT treatment available, patients often must go through two to four lines of therapy before being eligible.[23]
- Patient cost-sharing encompasses several key insurance concepts that impact out-of-pocket expenses for CGT treatment and related care:
  - **Coinsurance** – The percentage of medical costs the patient pays, typically after meeting their deductible. For example, if the patient has 20% coinsurance, they pay 20% of the cost while insurance covers 80%.
  - **Copay** – A fixed amount the patient pays each time they receive a medical service, like a doctor's visit or lab test. This amount is set by the insurance plan and typically paid at the time of service.
  - **Deductible** – The amount the patient must pay for covered medical services each year before insurance starts paying. For example, with a $2,000 deductible, the patient pays the first $2,000 of covered services themselves.
  - **Out-of-Pocket Maximum** – The most the patient will have to pay for covered medical services in a plan year. After reaching this limit, the insurance plan pays 100% of covered services for the rest of the plan year.
  - **In-Network vs. Out-of-Network** – Refers to whether healthcare providers and facilities have contracted with the patient's insurance plan. In-network providers have agreements to provide services at negotiated rates, typically resulting in lower out-of-pocket costs. Out-of-network providers haven't contracted with the patient's insurance plan, which usually leads to higher out-of-pocket costs or may not be covered at all.

Figure 4. Steps and Barriers Within Initiation of Treatment



Once the decision to move forward with a CGT has finally been made, the patient's clinical eligibility for receiving treatment must be verified. This involves a comprehensive assessment of various factors, including the patient's condition status, age, overall health status, treatment and medication history, and the presence of antibodies that could interfere with treatment. The window for eligibility can be a challenge, as many of the treatments for pediatric genetic conditions, for example, are only approved for patients who fall within a narrow age range.[20] The timing for completing the evaluation at this stage is therefore critical to ensuring access to CGT treatments.

In many cases, the patient also needs a referral to a treatment center at this stage. For many conditions treated by CGTs, treatment is administered in what may be a limited number of specialized treatment centers of excellence (COEs) across the U.S. Sometimes, more patients are trying to reserve treatment spots than a COE has available.[24] This can be caused by provider capacity constraints, such as the number of trained staff and the availability of intensive care unit (ICU) or treatment beds, or it could be caused by the therapy manufacturer's availability to process samples.[18,25-27] Additionally, as most COEs are located in urban areas,[28] this represents a heightened barrier for rural patients who are required to travel long distances for treatment. On average, the time from referral to the decision to start treatment is around two months.[18]

Once the patient's eligibility to receive a CGT is confirmed and a place in a treatment center is secured, the next hurdle before treatment can begin involves obtaining authorization from the patient's insurance provider. Navigating insurance benefits can be complicated for routine procedures and services, making it even more challenging to obtain approval for costly treatments like CGTs. Patients and their caregivers must navigate a complex system in which the insurance provider may request more information, additional testing, or require the patient to try a different treatment first.

Some patients have their request for authorization denied and must work closely with their doctor, care team, and hospital staff to provide paperwork to appeal such decisions or to seek exemptions to the insurer's policies. To navigate the complexities of the healthcare system effectively, patients and caregivers can benefit greatly from learning about available resources and support services. Understanding these aspects can empower them to make informed decisions and access the care they need. It's important to note here that insurance authorization for those with commercial insurance will differ from those on Medicaid or Medicare. Whereas authorization for a patient with commercial insurance could take days or weeks, authorization from a state Medicaid agency could take months.[27]

This is also an opportunity for patients to finalize important pre-treatment health-related decisions, including fertility preservation, if applicable. While some states mandate coverage for fertility preservation services for a medical procedure such as CGT administration, which could affect future fertility, coverage may vary based on insurance type.[19] Patients should discuss with their insurer what specific services are covered (such as egg freezing, medications, ultrasounds, and medical procedures) and understand potential out-of-pocket costs.

Another hurdle that patients and caregivers must face before initiating treatment is that of making logistical arrangements for the duration of treatment. This often includes arranging travel to and booking accommodations near the treatment center, managing time off from work or school, and, if applicable, securing childcare and pet care. Arranging travel and accommodations can be particularly challenging if the patient's health condition is poor, potentially adding strain or creating apprehension about being treated in the first place.

A final hurdle before treatment begins, and one that patients and caregivers indicate as being one of the most significant hurdles in the entire treatment odyssey, revolves around the finances of treatment.[29,30] CGTs are generally considered valuable, while also being known for their high costs. Unlike traditional therapies that require repeated doses over an extended period of time (or over a lifetime for some chronic conditions), CGTs typically only have one administration. Instead of costs being spread out over the years for insurance providers and patients, they can occur all at once, increasing financial strain for payers and patients alike. Traditional insurance benefit designs are not well equipped to minimize the costs to patients who decide to initiate a CGT.

For patients, cost-sharing usually comes in the form of copays, coinsurance, and/or annual deductible payments. Copays are paid each time the patient visits their doctor, has lab work done, or goes to the hospital, for example. Coinsurance is usually a percentage of costs the patient is responsible for paying themselves. This could be as high as 20-40% and represents substantial costs, considering not only the CGT itself but also the hospital stays, evaluations, testing, and associated care that accompany it.[31] Coinsurance typically is applicable after the patient pays their deductible for the year. This can vary greatly by health insurance plan, but estimates suggest the average deductible for single employer-sponsored coverage is approximately $2,000, while for family coverage it is nearly $4,000.[32]

Fortunately, health insurance plans have an out-of-pocket maximum that protects patients from being responsible for paying exorbitant costs due to catastrophic incidents, such as treatment for serious conditions. For 2024 ACA Marketplace plans, the maximum out-of-pocket limit for single coverage is $9,450, and for family coverage is $18,900.[33] Unfortunately, this only applies to in-network care and services or procedures covered by the insurance plan. One significant barrier to CGT treatment is that even though the CGT itself may be covered by the insurer, the treatment facility or doctors providing treatment could be out of network. In this case, the patient would be responsible for cost-sharing above and beyond their plan's out-of-pocket maximum.[34]

These costs also come at a time for patients and caregivers when many are experiencing lost income from not being able to work either due to their illness progressing or due to the time it takes to travel for medical evaluations, testing, and treatment. It is important at this stage for patients and caregivers to explore all the financial assistance programs and resources at their disposal. This can include, as mentioned previously, repeated attempts to work with the insurance provider to obtain coverage for a specific item, appealing denials of coverage, or seeking case-by-case exemptions.

Many hospitals and healthcare providers will work with patients in the case that insurance denies coverage by discounting their charged amount, creating a payment plan, or by providing some amount of charity care. Finally, as mentioned in the previous chapter, there are also patient support groups and therapy manufacturer assistance programs designed specifically to provide financial and logistical support to patients so that they can better afford their treatment. Patients and their caregivers should identify these programs as early as possible to ensure they know what type of assistance they are eligible for and at which stage of the treatment odyssey. Once the finances are worked out, the patient and their caregivers are finally ready for CGT treatment, coming after months or years of waiting and hoping.

Stakeholder Solutions

The financing of CGTs remains one of the largest challenges not only for patients, but also for payers, providers, employers, and therapy manufacturers all throughout the healthcare ecosystem. New or innovative payment models could be one way to better align incentives toward promoting the benefits of treatment and encouraging appropriate adoption of CGTs.[35] Some new models[36] being tested include:

- **Annuity-Based Payments** – Where a payer pays a fixed price for the therapy at regular installments, spreading the costs out over time instead of paying all at once.
- **Outcomes-Based Payments** – Where a payer pays a portion of the therapy's price up front and only pays the remainder if predetermined outcomes are met.
- **Outcomes-Based Rebates** – Where a payer pays the full price of the therapy up front but will have some amount of that rebated if the therapy does not meet predetermined outcomes.
- **Outcomes-Based Annuities** – Where a payer pays a fixed price for the therapy at regular installments, but only if the therapy continues to meet its predetermined outcomes.

CGT TREATMENT ADMINISTRATION

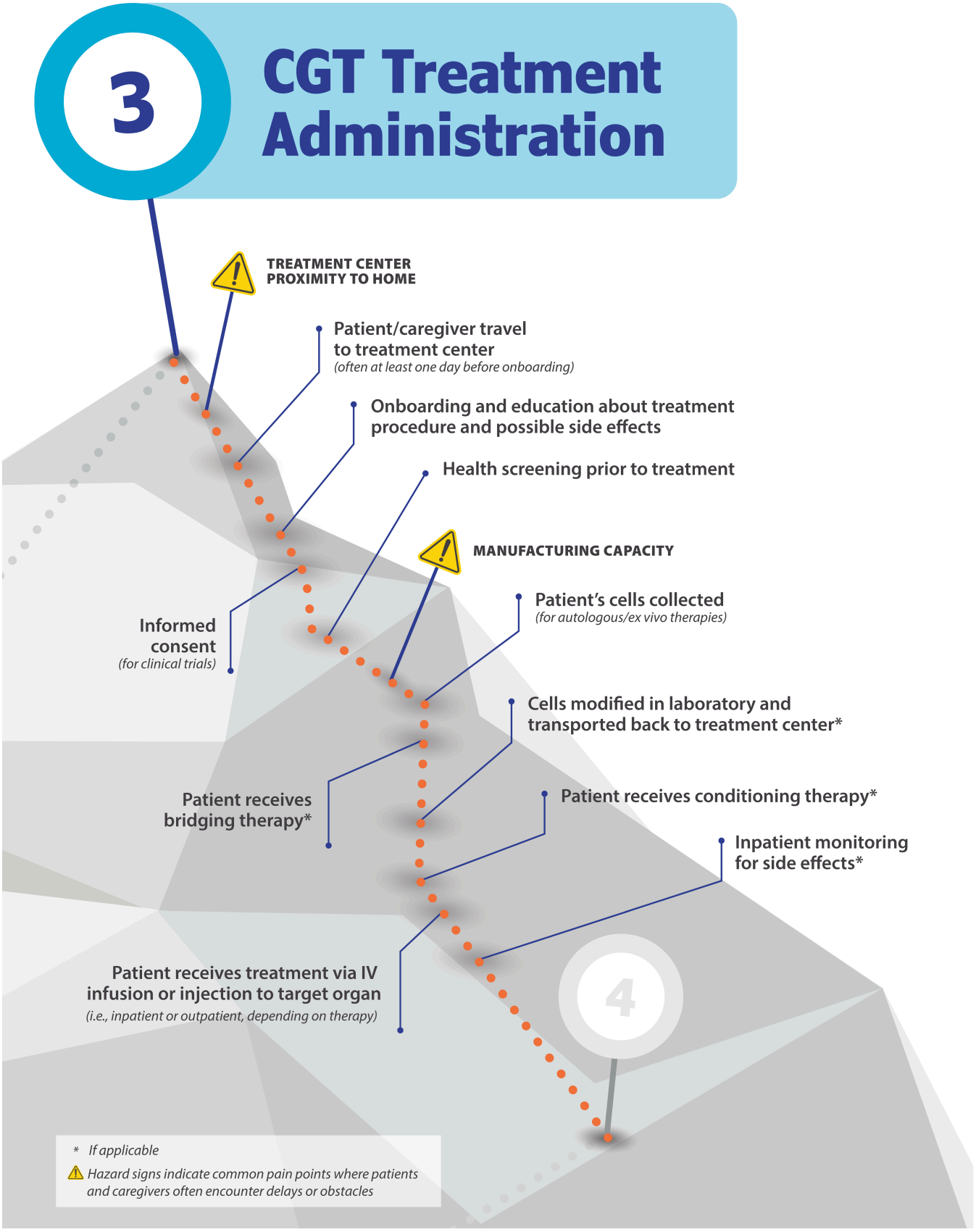
The third stage of the patient and caregiver odyssey represents the culmination of months or years. Patients and their caregivers have experienced anxiety, fear, and hope alongside condition-specific symptoms from first receiving a diagnosis. They then learned about cell and gene therapy (CGT) as a treatment option and made decisions about their care plan. Finally, they navigated clinical eligibility, insurance, financial, and logistical barriers to be ready for treatment. This stage represents a change in the patient and caregiver odyssey from that of hoping for and desiring a treatment that will improve their condition to one of finally receiving that treatment and believing that they are on the road to improvement and a healthy life.

This stage of the treatment odyssey begins in many cases with traveling to a specialized treatment center. As mentioned in the previous chapter, many CGTs are currently only administered in specialized centers of excellence (COEs), requiring patients and their caregivers to schedule treatment in advance and to make corresponding travel and accommodation plans. For patients and their caregivers, it often means being without resources or support from home for a prolonged period. Once the patient arrives at the treatment center, they undergo onboarding with the facility's care team, and they may go through the informed consent process in the case that treatment is part of a clinical trial.[37]

This can be challenging for patients who may have concerns about being in an unfamiliar environment or having a new care team around them. This comes along with a declining health condition for many patients. There may also be an inundation of treatment information as part of onboarding and informed consent, much of which may be technical or loaded with complex medical information.[37] This leads many patients and caregivers to fear the possibility of side effects and adverse events, which are typically a point of emphasis in this information exchange. Families also may not realize that receiving a CGT may limit future treatment options. After a patient receives a CGT, their body often develops antibodies in response to the therapy's delivery method, typically a viral vector. These antibodies could prevent the patient from receiving another CGT in the future, even if new treatments become available.[38,39]

Next, the patient undergoes evaluation once again to ensure that their health condition is sufficient for CGT treatment. Even though the patient's clinical eligibility was confirmed previously, their health status can change rapidly during the time it takes from being referred to the treatment being administered. Provider surveys have indicated low rates of cell therapy access for referred cancer patients in the U.S., with one survey reporting only 38% of patients were able to receive the treatment,[18] while other studies found an even lower rate of 30%[25] and 25%.[40] The two biggest reasons for non-treatment included the patient's disease progressing (indicated by 55% of respondents) and the patient's health condition being too poor (indicated by 45% of respondents).[18] These figures highlight a significant barrier at this stage in being able to start treatment quickly enough to ensure patients are healthy enough to receive the treatment they need.

Figure 5. Steps and Barriers Within CGT Treatment Administration



Did you know?

- One provider survey indicated that only 38% of cancer patients in the U.S. referred to receive a CGT were able to receive it.[18] The two biggest reasons for non-treatment included the patient's disease progressing (indicated by 55% of respondents), and the patient's health condition being too poor (indicated by 45% of respondents).[18]
- CGTs can be manufactured in different ways, with key distinctions in source material and production approach that impact manufacturing timelines, treatment administration, and patient recovery:
  - **Autologous vs. Allogeneic:** Treatments can use either the patient's own cells (autologous), which takes longer but has better outcomes and lower rejection risk, or donor cells (allogeneic), which enables faster production and treatment of more patients but may have higher rejection risk.
  - **Ex vivo vs. In vivo:** Genetic modification can occur outside the body (ex vivo), where cells are collected, modified in a lab, and returned to the patient, or inside the body (in vivo), where genetic material is delivered directly into the patient.

The timing to begin treatment administration is also significantly impacted by the type of therapy at this stage. For cell therapies, there is an important distinction between autologous and allogeneic therapies. For gene therapies, there is an important distinction between ex vivo and in vivo therapies. Autologous cell therapies and ex vivo gene therapies use the patient's own cellular/genetic material that is collected, modified, and then reintroduced to the patient's body. This differs from allogeneic cell therapies and in vivo gene therapies, which typically use donor material and can be prepared and manufactured in advance of a patient requiring treatment. These therapies are sometimes referred to as off-the-shelf therapies as they are ready to be administered as soon as the patient is diagnosed and eligibility for treatment is confirmed.

Creating autologous cell therapies and ex vivo gene therapies can be an extremely lengthy process. First, patients go through a process called apheresis, where blood is collected and separated into different components; some components are collected, and the rest of the blood is returned to the patient. Next, the collected components are sent off to a laboratory in cryogenic and temperature-controlled shippers,[41] where upon receipt, a team modifies the cellular structure and/or genetic material, preparing it for treatment. For ex vivo gene therapies, the modified genetic material is typically placed in a vector, such as a deactivated virus, which helps to transport it back into the patient's cells, delivering the treatment. The process of collecting, processing, transforming, and manufacturing an autologous cell therapy or ex vivo gene therapy can take anywhere from several weeks to up to six months of processing time for some therapies.[24,42]

During the therapy's processing period, preventing the patient's health from declining is of the utmost importance. Many patients receive some type of stabilizing care or treatment during this waiting period. For cancer patients, they are likely to be given a bridging therapy, which could include standard chemotherapy, immunotherapy, and/or radiotherapy. In addition to stabilizing the patient's condition and controlling symptoms, these therapies, also called conditioning therapies, can be used to suppress the patient's immune system prior to treatment or to create space in the patient's bone marrow for the treatment to take hold.[43,44] Patients undergoing bridging and conditioning therapies must be monitored, as these treatments carry risks of adverse events separate from the CGT administration.

Once the therapies have been prepared and delivered to the treatment center, it is finally time for CGT administration. This involves the patient receiving an IV infusion or injection into a target organ or tissue, which is usually completed within a couple of hours. Administration can be done in either an inpatient or outpatient setting, depending on the specific therapy. For therapies that are administered in an inpatient setting, patients are sometimes required to remain in the hospital for up to one month to monitor adverse events and to manage any side effects.[45] One COE recommends that patients receiving CAR-T remain within two hours of the treatment center for 30 days post-administration, with a caregiver constantly present to monitor for fever, infection, and neurological difficulties.[23] Once the patient is discharged from the hospital, they will transition to outpatient visits for check-ups and monitoring. At this stage, it is critical for clear coordination and communication between the treatment center, specialists, and local healthcare providers to ensure any complications from CGT treatment are identified and addressed as quickly as possible.

The caregiver also has several key responsibilities throughout the treatment administration phase, with providing emotional and practical support being paramount. This aligns with survey findings where most patients reported that family offered pivotal moral support and reassurance during their decision-making process.[37] These supportive functions are especially important as patients navigate what can be a very difficult treatment process. Additionally, many patients need considerable support managing the number of medications they are taking and tracking symptoms to provide regular reports to the patient's healthcare providers. The caregiver is also vital in handling communications with the various healthcare teams, especially when coordinating the patient's care and transition from the treatment center back home to their local provider and care team. This often involves working with the patient's insurance provider as well as beginning to process bills and the financial aftermath of treatment.

At the end of this stage, patients and caregivers are typically exhausted from fighting a serious illness and grueling treatment regimen, and most have a long road to recovery in front of them. Many individuals are likely to feel that their future holds the promise of healing and improvement rather than being clouded by fear and anxiety about their condition.

Stakeholder Solutions

Infrastructure offers a key opportunity for stakeholder engagement and, ultimately, improved patient access.[21] One key treatment bottleneck stems from the limited number and geographic distribution of specialized treatment centers, including COEs.

One solution is a "hub-and-spoke" model that links community healthcare practices with COEs or other specialized treatment centers.[20] This network approach may help to optimize resource-sharing (such as diagnostic testing), improve cost efficiency, and streamline care delivery. To scale this model, policies are needed to standardize care models, support qualified COEs, and ensure reimbursement.

Additionally, expanding manufacturing capacity is essential. Manufacturing efficiency is key to broadening the availability of CGTs.[35,46] By leveraging available platform technologies — standardized processes and equipment that can be utilized across approved therapies and those still in development — manufacturers can increase production and improve access to new therapies.

POST-TREATMENT MONITORING AND FOLLOW-UP

After a long odyssey, the patient was finally able to receive a cell and gene therapy (CGT) to treat their condition. Following the treatment, the recovery process can be lengthy. It is essential for patients and their caregivers to maintain close communication with their healthcare providers to monitor the effectiveness of the treatment and any side effects that may arise. This stage of the patient and caregiver odyssey is characterized by cautious optimism. While there is hope that the CGT has been successful, there remains a recognition that serious side effects may still occur, potentially impacting the patient's quality of life. It is a stage marked by continuous evaluations, doctor visits, and reports on the patient's physical and emotional well-being.

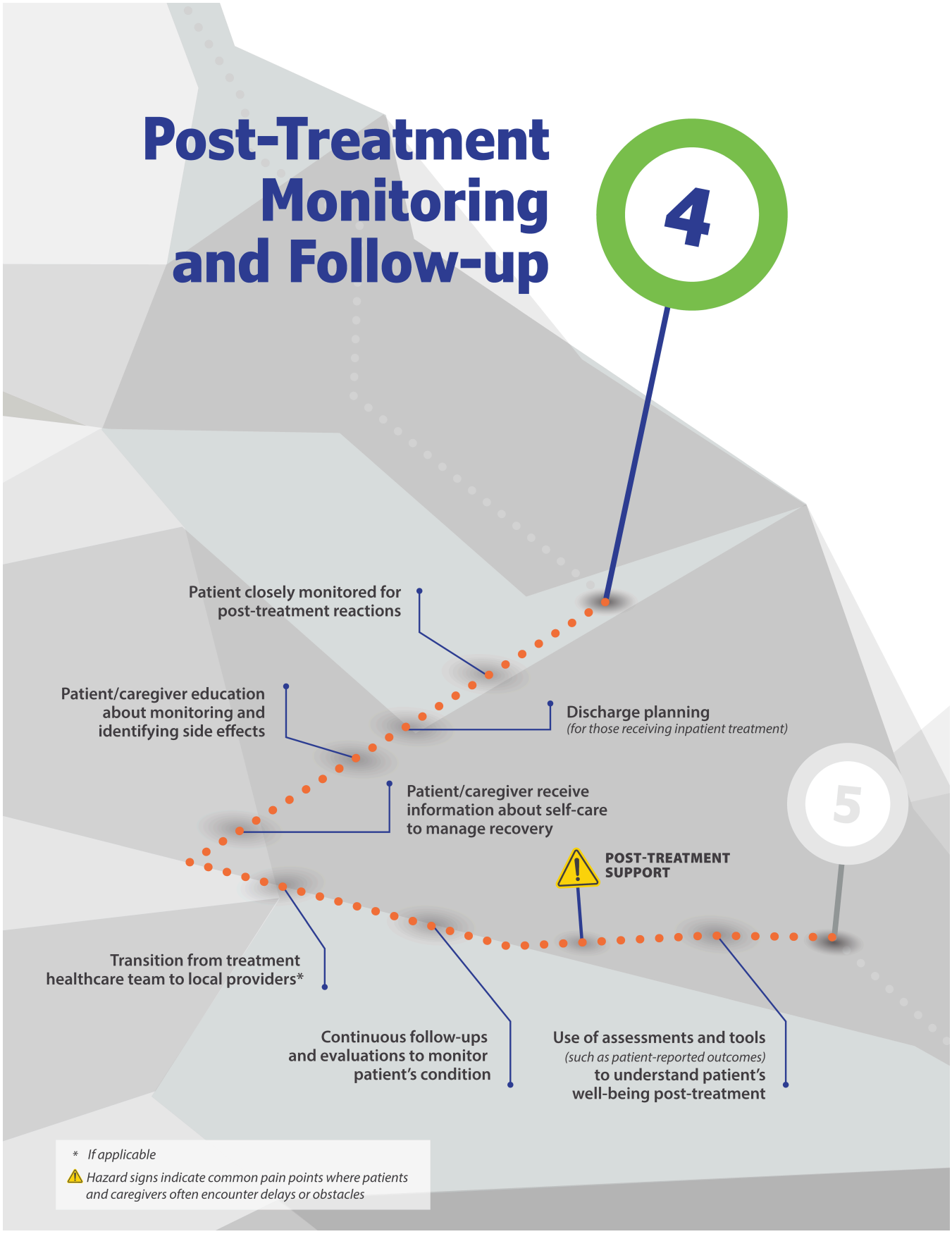
Did you know?

For many patients, follow-up evaluations can continue for up to 15 years to assess treatment effectiveness and monitor for side effects and complications.[47] For some patients, such as those who received cell therapies to treat cancer, the FDA recommends life-long monitoring as there is a higher risk of secondary cancers occurring after treatment.

The monitoring and evaluations begin immediately after the administration of the CGT. As mentioned in the previous chapter, some therapies require patients to stay in the hospital for up to a month post-treatment, during which time they often experience severe illness due to the effects of intense chemotherapy.[45] For cell therapies, patients are closely monitored for immune responses to treatment. One potential response is cytokine release syndrome (CRS), where the immune system overreacts — leading to potentially life-threatening symptoms. Another serious concern is neurotoxicity, where the immune system attacks the nervous system. Patients can also develop blood disorders such as anemia and are prone to serious infections due to having a weakened immune system.[48]

For gene therapies, patients are monitored in case there is a negative immune system reaction, complications in the case the wrong cells were accidentally targeted, side effects stemming from the newly inserted genetic material, or unexpected gene expression.[49] Typically, ex vivo gene therapies have reduced risk of off-target effects or immune responses as treatment involves the patient's own cellular material, which was modified in a controlled environment. With in vivo gene therapies, it can be harder to know beforehand how much of the injected or infused genetic material reaches the target or is taken up by non-target cells.

Figure 6. Steps and Barriers Within Post-Treatment Monitoring and Follow-up



After the initial follow-up period, patients, their caregivers, and the healthcare team agree on a discharge plan, including provisions for any necessary monitoring or complications that may arise. All patients and caregivers will be educated about possible side effects and adverse events that could occur after going home. This educational material will include how to monitor and identify these issues and what to do if one were to occur. Patients will also receive information on self-care for managing their recovery as they transition back home and to their local healthcare providers.

Recovery is often a lengthy process for many patients. Battling their illness and navigating the highs and lows of the CGT treatment odyssey, along with any other treatments they may have received, takes a toll on patients physically and mentally. At this stage, it is hoped that the CGT treatment is effective and starts showing signs of reversing or slowing down the patient's condition. Side effects from treatment can persist in the time after treatment, however, which can be a source of continued frustration and anxiety. Follow-up evaluations typically continue for up to 15 years for many patients to assess treatment effectiveness and to continue monitoring for side effects and complications.[47] For some patients, such as those who received cell therapies to treat cancer, the FDA recommends life-long monitoring as there is a higher risk of secondary cancers occurring after treatment.[18]

Many patients face challenges regarding care coordination during this stage of their odyssey. Effective communication and collaboration are essential when patients transition from specialists to their local healthcare providers. This ensures proper monitoring of the patient and allows for timely assessment of any side effects that may develop. Of course, as discussed in previous chapters, there is wide variability in patients' healthcare providers. Local specialists and primary care providers may effectively collaborate with treatment specialists from Centers of Excellence (COEs) to assist patients and their caregivers in managing ongoing monitoring and follow-up appointments. However, some providers may lack knowledge about the recovery process and potential side effects of treatments. Additionally, certain patients might struggle to access consistent, high-quality care due to health equity issues.

Ultimately, the patient's quality of life is the primary focus during this stage of the treatment odyssey. It is essential to help the patient return to the life they desire to live. An integral part of the recovery process is regular quality of life assessments from the patient's healthcare provider. Monitoring the physical, emotional, and social well-being of the patient is essential for ensuring recovery progresses well and for early identification of issues as they arise. For patients, recovery is about more than just their body's physical healing; it is about reconnecting with their daily lives and receiving the support and care to help them achieve a sense of normalcy. Important tools to aid providers in understanding patients in their recovery are patient-reported outcomes. These can be in the form of measures that patients themselves have identified as being important to their health and well-being or they can be how patients subjectively perceive their health status or quality of treatment. Studies have shown better outcomes for patients whose care and recovery journey include patient-reported outcomes.[50,51] By integrating patient-reported outcomes into post-treatment care, not only is the quality of follow-up enhanced, but it can empower patients in their recovery journey, ultimately leading to increased patient satisfaction.[52]

Stakeholder Solutions

Having the right patient support program in place before, during, and after treatment is essential during a difficult treatment odyssey. While many patients do find support from therapy manufacturers, patient advocacy groups, or others, having more coordinated and comprehensive support programs would go a long way to mitigating many of the biggest barriers patients face.

Stakeholders, including payers, employers, and providers, have numerous options to include as a part of a patient support program,[53,54] including:

- Establishing personal relationships with patients and caregivers early in the process to create a base of trust to better provide education, alleviate fears, etc.
- Offering a travel benefit to preferred, high-value providers for testing and treatment to help overcome travel and other logistical barriers to accessing care.
- Creating and strengthening programs to assist patients with financial and healthcare decision-making, including cancer care navigation, expert medical opinions, and decision-making support services.
- Providing ongoing support to help identify new clinical trials which individuals may be eligible for.

ONGOING SUPPORT AND SURVIVORSHIP

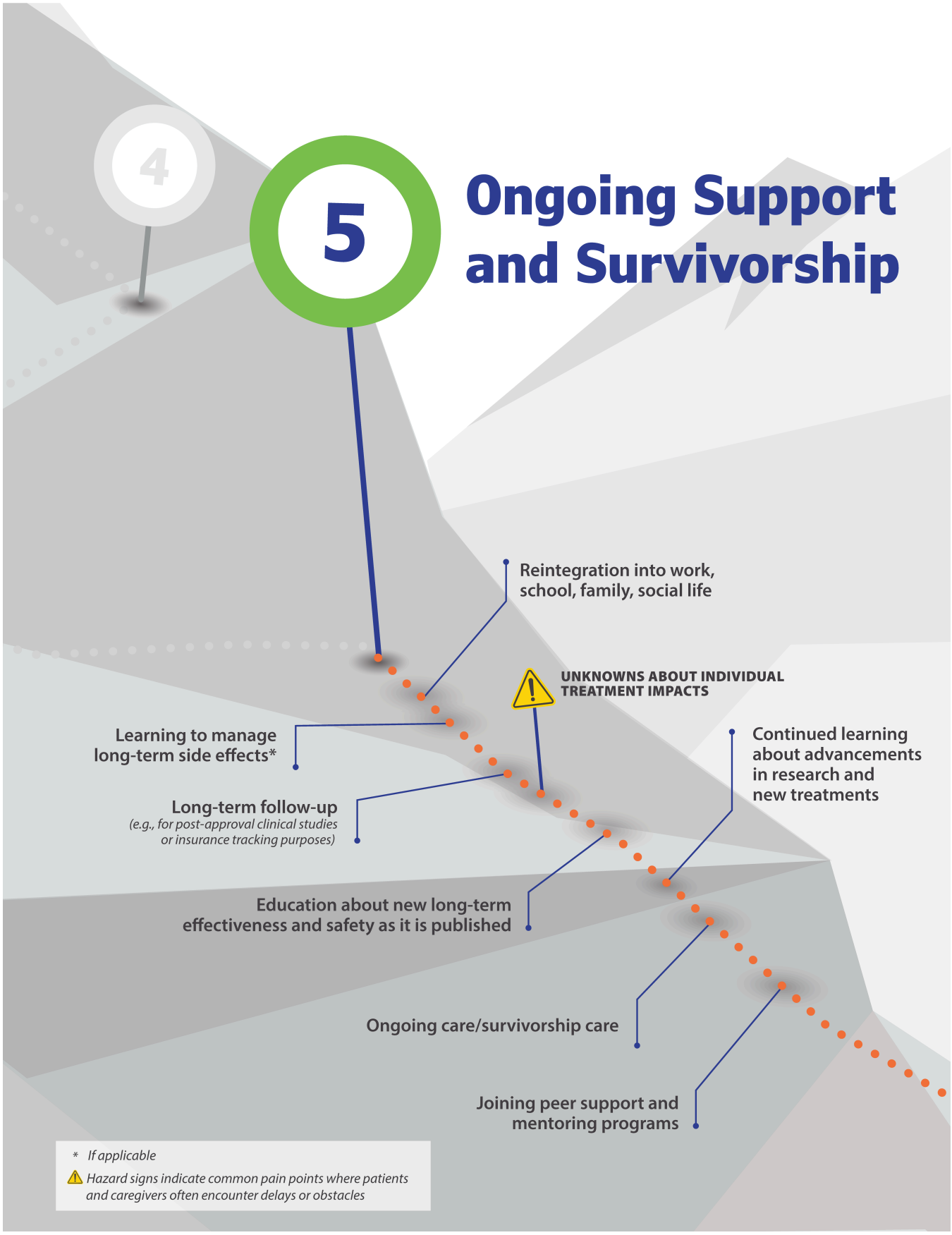
This is it. The patient and their caregivers have finally made it to the end of this long treatment odyssey. They have faced years of illness, uncertainty, financial pressure, taxing treatments, and a recovery process. But now, that is behind them, and hopefully, they are well on their way along to healing with their cell and gene (CGT) therapy being effective in curing or halting the progression of their condition. The question that guides this period remains — what's next? As patients transition into the role of survivors, they face new challenges and questions. How do they reintegrate into their lives while managing their ongoing health needs? Will treatment benefits last, and how long will side effects persist? How can these survivors access support networks, not only for their own continuing care, but also to support others on similar journeys? This new phase of the odyssey brings a shift in perspective, where patient experiences evolve into a lifelong journey of survivorship, with its own unique set of experiences and responsibilities.

One of the most challenging issues that survivors face after recovery is reintegration. So much time and energy has been spent combatting their illness that many feel distant and apprehensive about their return to work or school or even to their social life. They may feel different after going through their illness and treatment, and others may treat them differently. Many survivors need assistance at this stage which too can cause discomfort. The financial strain of treatment insurance benefit design means many families need long-term financial planning and assistance. This can impact how they live day-to-day and the decisions they make if there is still a cloud of medical debt persisting long after treatment is complete. Additionally, survivors may need accommodations from their employer or school, or they may need support navigating disability benefits. Some survivors have long-term side effects or complications and should utilize healthcare resources to aid in their reintegration.

The question of treatment benefits continues throughout this stage. While the major promise of CGTs is that they have the potential to be curative or have long-lasting, durable effects, many of these therapies are relatively new, and the 10-, 20-year, or longer outcomes are not yet known. It is possible that durability could fade at some point in the future considering the lifespan of the target cells or immune system response to the transplanted gene.[55] If the treatment effect diminishes over time, there may be a need for additional therapy. If a subsequent CGT is not feasible, a return to alternative therapies might be necessary to help manage the condition.

Because of this future risk, survivors and their caregivers should continually learn about their condition as well as any advances in research and new treatments. Most CGTs have long-term follow-up studies being conducted to monitor treatment effectiveness and side effects. There are also hundreds of ongoing clinical trials, as well as many therapeutics in early development, that could potentially benefit survivors in the future.[4]

Figure 7. Steps and Barriers Within Ongoing Support and Survivorship



This is particularly important if their treatment benefits decline or some other aftereffect occurs (e.g., a secondary malignancy developing). Ongoing education and access to resources serve a dual purpose for survivors. These tools not only help manage anxiety about potential recurrence but also equip survivors with knowledge and preparedness should they face future health challenges.

Many survivors also find themselves taking part in a long-term follow-up study or are continuing to be tracked for insurance purposes well into this stage. This is quite important, both for better understanding the long-term effects of treatment as mentioned before, but also because of how some of these therapies are paid for between the insurance provider and therapy manufacturer. In certain situations, insurance providers and therapy manufacturers have entered into what is called an outcomes-based contract where some or all of the treatment cost can be returned to the insurance provider if the treatment does not work as expected. Long-term tracking for the purpose of these contracts can present a number of challenges for the survivor. Individuals can change insurance providers frequently, and continuing to pay for doctor's visits, evaluations, or tracking and submitting questionnaires and health information can be costly and burdensome. These can be partially mediated by the use of home-based approaches like televisits and electronic patient-reported outcomes, but insurance providers and therapy manufacturers should work together to make this process as simple and streamlined as possible to encourage survivors to remain engaged.[56]

The other side of the coin to the treatment benefits question is related to side effects. Both the condition itself and the course of treatment can leave survivors with long-term mental and physical health conditions that need ongoing monitoring and management. These can range from heart, liver, kidney, and bone issues to anxiety, depression, and post-traumatic stress disorder (PTSD) to infertility or sexual health problems.[19,57-59] Our knowledge about these issues is constantly evolving, and we're continuing to find new ways to prevent or manage them. As mentioned in a previous chapter, fertility preservation is an important topic for certain patients to discuss prior to using a CGT for many conditions like sickle cell disease (SCD). There is an ongoing legal fight about whether the therapy manufacturer can include fertility preservation as part of treatment, given that the risk of infertility is very high.[60] This is another area in which survivors and caregivers need to remain engaged in order to not only understand updates to the scientific understanding of their condition, but also the legal, regulatory, or legislative changes that could impact them or their friends, family, and other patients.

One barrier many survivors face during this phase of the odyssey is ongoing care. They may feel as though their healthcare provider is not necessarily equipped or knowledgeable about long-term complications that could arise after CGT treatment. This can be even more challenging for pediatric populations who were treated at a very young age and are dealing with new complications years later as adults. It is important to plan transitions of care as much as possible prior to this stage. Some of these transitions will be known in advance (e.g., a pediatric patient growing up and transitioning to adult care), but some are unforeseen (e.g., having an unexpected move or changing jobs and insurance carriers who do not cover a previous provider). It can also be helpful for survivors to seek out survivorship organizations that focus specifically on the long-term physical and mental aftereffects of serious conditions.

Finally, many survivors and caregivers join peer support and mentoring programs. Not only is this a way for survivors to discuss any issues they are facing, but some also find it therapeutic to guide and mentor those in the early stages of their own patient and caregiver odyssey.[61] Survivors can draw upon their own experiences and knowledge to help educate others. Fostering social connections and being active in the patient community is also important for building the resources and support that those early on in their treatment journey rely heavily upon. In this way, survivors and caregivers who have made it to the end of this challenging treatment odyssey can help smooth the path for future patients. Their insights can fill in knowledge gaps and lower hurdles, making the trek less daunting for those who may have their own odyssey in the future.

Stakeholder Solutions

Long-term efficacy and safety monitoring is essential for understanding CGT treatment outcomes. While current follow-up protocols can extend to 15 years post-treatment,[47] the healthcare system faces several logistical challenges in data collection and assessment.

Patient mobility across a fragmented and siloed healthcare system presents tracking challenges, as patients move, change jobs, and switch insurance carriers over time. Multiple stakeholders, including manufacturers, providers, and payers, currently collect different types of outcomes data, often independently.

A common barrier to innovative payment models is the need for specialized data infrastructure and personnel skilled in clinical analytics for outcomes tracking.[62] Determining data collection responsibilities remains a key point of negotiation between parties entering these arrangements. Where appropriate, stakeholders should align on coordinated approaches that establish clear accountability, standardized requirements, and sustainable monitoring processes supported by adequate technology infrastructure.

CONCLUSION

Cell and gene therapies (CGTs) offer transformative potential for patients and their caregivers with serious conditions, often requiring just a single administration. However, the odyssey to accessing these treatments can be lengthy and complex, marked by numerous barriers from diagnosis to recovery. Patients face delays in diagnosis due to misdiagnoses or varying provider expertise, and health equity concerns further exacerbate access challenges. Once diagnosed, patients must navigate eligibility criteria, financial burdens, and logistical challenges before receiving treatment. These hurdles can be overwhelming, and patients frequently rely on caregivers, healthcare providers, and insurers to guide them through the process.

The treatment itself, while promising, can involve prolonged procedures, particularly for autologous therapies, where patients may require bridging or conditioning therapies before treatment can be administered. Even post-treatment, patients and caregivers face ongoing challenges such as managing side effects, coordinating care, and transitioning back to everyday life. Long-term complications and the need for continuous follow-up care add further complexity. Nonetheless, peer support networks and community resources provide valuable guidance for survivors and new patients alike.

To fully realize the potential of CGTs, stakeholders across the healthcare system must work together to address the barriers patients and their caregivers face, ultimately improving treatment pathways. Healthcare providers, policymakers, and therapy manufacturers should work to build and standardize the capabilities and workflows needed to identify, refer, and treat patients more efficiently and closer to their homes. Insurance providers, employers, therapy manufacturers, and policymakers should collaborate to eliminate financial barriers to care, whether through innovative financial solutions like outcomes-based contracting and warranty models or through enhanced coverage options. These enhanced benefits could include travel support to preferred providers, care navigation assistance, decision-making support, and comprehensive post-treatment and survivorship services.

CGTs offer unprecedented hope for patients and their caregivers who may otherwise have no treatment options. However, realizing this potential requires addressing gaps throughout the entire patient odyssey, not just during treatment. The onus is on all stakeholders in the healthcare system to remove barriers and facilitate access to these innovative therapies for patients in need.

GLOSSARY OF KEY TERMS

ACA – Affordable Care Act, also known as "Obamacare" — a law that helps ensure Americans have access to health insurance and medical care.

Allogeneic – A type of cell therapy where the therapeutic cells come from a donor rather than the patient. While these treatments can be produced more quickly and treat more patients, they may carry a higher risk of the body rejecting the treatment.

Autologous – A type of cell therapy where the therapeutic cells come from the patient's own body. While these treatments take longer to produce, they tend to be more effective and have a lower risk of rejection since they use the patient's own cells.

Beta Thalassemia – A genetic blood disorder that reduces the production of hemoglobin, leading to severe anemia and requiring regular blood transfusions.

CALD – Cerebral Adrenoleukodystrophy, a rare genetic condition that affects the brain and nervous system, primarily in young boys.

Cancer, Relapsed – Cancer that returns after a period of improvement or remission following initial treatment. The cancer may come back in the same location or a different part of the body.

Cancer, Refractory – Cancer that does not respond to or has stopped responding to standard treatments. Also known as resistant cancer, these cases often require alternative or more aggressive treatment approaches.

CAR-T – Chimeric Antigen Receptor T-cell therapy, a type of cell therapy that modifies a patient's immune cells to fight certain types of cancer.

Cell and Gene Therapies (CGTs) – Advanced medical treatments that use cells and/or genetic material to treat disease by transferring or altering cells or genes in the body. These precision medicines are tailored to treat specific genetic conditions or cancers, often providing long-lasting therapeutic effects.

Center of Excellence (COE) – A healthcare facility recognized for providing high-quality, specialized care for specific conditions, including cell and gene therapies.

Chemotherapy – A type of cancer treatment that uses drugs to kill cancer cells or stop them from growing and dividing. While effective against cancer cells, chemotherapy can also affect healthy cells, leading to side effects such as fatigue, nausea, and hair loss.

Coinsurance – The percentage of medical costs a patient pays, typically after meeting their deductible. For example, if a patient has 20% coinsurance, they pay 20% of the cost while insurance covers 80%.

Copay – A fixed amount a patient pays each time they receive a medical service, like a doctor's visit or lab test. This amount is set by their insurance plan and typically paid at the time of service.

CRS – Cytokine Release Syndrome, a possible side effect of some cell therapies where the immune system becomes highly activated. The condition can cause symptoms like fever and inflammation.

DEB – Dystrophic Epidermolysis Bullosa, a genetic condition that causes extremely fragile skin that can blister and tear easily.

Deductible – The amount a patient must pay for covered medical services each year before their insurance starts paying. For example, with a $2,000 deductible, the patient pays the first $2,000 of covered services themselves.

DMD – Duchenne Muscular Dystrophy, a genetic condition that causes progressive muscle weakness, primarily affecting young boys.

DNA – Deoxyribonucleic Acid, the genetic material present in cells that carry instructions for how our bodies grow, develop, and function. Changes in DNA can cause genetic diseases.

Ex-vivo – Latin for "outside the body," this refers to a type of cell or gene therapy in which cells are taken from the patient's body, modified in a laboratory, and then returned to the patient. This is similar to taking blood for testing, but instead of testing, the cells are changed to help fight disease.

FDA – The Food and Drug Administration, a U.S. government agency that ensures medicines, including cell and gene therapies, are safe and effective before they can be used to treat patients.

GVHD – Graft Versus Host Disease, a side effect where donated cells treat the patient's body as foreign and attack it. The condition causes symptoms like skin rashes and stomach problems that require medical monitoring.

Hemophilia A and B – Rare genetic bleeding disorders where blood doesn't clot properly. Type A is caused by low levels of clotting factor VIII, while Type B is caused by low levels of factor IX.

ICU – Intensive Care Unit, a specialized hospital unit providing continuous monitoring and advanced medical care for critically ill patients.

In-Network – Healthcare providers and facilities that have contracted with the patient’s insurance plan to provide services at negotiated rates. Using in-network providers typically results in lower out-of-pocket costs.

In-vivo – Latin for "inside the body," this refers to cell or gene therapy that is delivered directly into the patient's body, often through an injection or infusion, where it works to treat the disease from within.

IV – Intravenous, a method of giving medicine or fluids directly into a vein through a needle or tube, allowing treatments to enter the bloodstream quickly.

LCA – Leber's Congenital Amaurosis, a rare genetic eye disorder that causes severe vision loss or blindness from birth or early childhood.

Medicaid – A joint U.S. federal and state health insurance program that helps cover medical costs for people with limited income and resources. Benefits and eligibility requirements vary by state, though all state programs must follow general federal guidelines.

Medicare – A U.S. federal health insurance program primarily for people aged 65 or older, as well as certain younger people with disabilities or specific health conditions.

MLD – Metachromatic Leukodystrophy, a rare genetic disorder that affects the nervous system and causes progressive loss of physical and mental abilities.

Out-of-Network – Healthcare providers and facilities that haven't contracted with the patient’s insurance plan. Using these providers typically results in higher out-of-pocket costs for the patient or may not be covered at all.

Out-of-Pocket Maximum – The most a patient will have to pay for covered medical services in a plan year. After reaching this limit, their insurance plan pays 100% of covered services for the rest of the plan year.

PTSD – Post-Traumatic Stress Disorder, a mental health condition that can develop after experiencing traumatic events, affecting how patients and caregivers process and cope with their medical journey.

Radiation – A cancer treatment that uses high-energy beams, such as X-rays or protons, to destroy or damage cancer cells. Radiation can be delivered externally (from outside the body) or internally (using radioactive materials placed inside the body), and is often used alongside other treatments like chemotherapy or surgery.

SCD – Sickle Cell Disease, a genetic blood disorder where red blood cells become crescent-shaped (like a sickle) instead of round, causing them to break down quickly and get stuck in blood vessels. This can cause severe pain, organ damage, and other serious health problems.

SMA – Spinal Muscular Atrophy, a rare genetic condition that affects muscle strength and movement, particularly in young children.

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