Creating Hope:
The potential of CAR T for your patients

Consult early for CAR T,
and explore the possibilities

CAR T therapy is a personalized therapy that has become a recommended treatment option for certain hematologic cancers[1-7]

53% of HCPs have referred patients with various lymphoma types for CAR T therapy[8]*

Yet there may be additional opportunities to refer more eligible patients. Since 2017, 6 CAR T therapies have received FDA approval for over 10 indications.[9-14] With extensive clinical-trial and real-world experience, CAR T therapies have the potential to help more patients.[1-3,15-21]

Response rates in clinical trials†

	LBCL[15]	FL[16,17]	ALL[18]	MM[19]
ORR	**69%** (95% CI: 57-79)	**86%-95%**	NA	**77%** (95% CI: 68-85)
CR	**49%** (95% CI: 44-52)	**69%-80%**	**80%**	**37%** (95% CI: 26-50)

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend anti-CD19 CAR T therapy for second-line relapsed LBCL within 12 months or primary refractory disease.[4]

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ALL=acute lymphoblastic leukemia; CAR T=chimeric antigen receptor T cell; CD=cluster of differentiation; CI=confidence interval; CR=complete remission; FDA=Food and Drug Administration; FL=follicular lymphoma; HCP=healthcare provider; LBCL=large B-cell lymphoma; MM=multiple myeloma; NA=not available; ORR=objective response rate.

Efficacy in real-world studies

Across CAR T therapies in the real-world setting†

	LBCL[2,3,20,21‡§‖¶]	ALL[22#]	MM[23-25**††‡‡]
ORR	55%-82%	NA	32%-83%
CR	32%-64%	86% (95% CI: 80.6-89.7)	34%-35%
12-month PFS	32%-45%	NA	NA
12-month OS	54%-64%	NA	56%

CAR T therapy is bolstered by 10+ years of evidence.[26,27]

*In the preceding 6 months. Based on a 2021 US web-based survey of 371 oncologists.[8]
†The efficacy results shown are based on current available data. Not all indications have efficacy results available.
‡Based on a systemic review and meta-analysis of published RWE studies that included at least 2100 patients with R/R LBCL treated with CAR T therapy.[21]
§Based on a national, multicenter, retrospective study that evaluated the safety and efficacy of a CAR T therapy in a real-life setting in 75 patients with R/R LBCL who underwent leukapheresis with the intent to receive treatment at 10 European institutions.[3]
‖Based on a non-interventional, prospective, longitudinal study using CIBMTR registry data of 682 patients with DLBCL, HGBL, and transformed lymphoma.[20]
¶Based on a retrospective study of 298 patients with R/R LBCL who underwent leukapheresis with the intent to receive CAR T treatment at 17 US institutions.[2]
#Based on a non-interventional prospective study using CIBMTR registry data of 410 pediatric/young adult patients with R/R ALL or adult patients with R/R NHL.[22]
**Based on a single-center study in the US of 20 patients with R/R MM who received CAR T therapy after at least 4 lines of prior therapy.[23]
††Based on a national, multicenter, retrospective analysis of 108 patients with R/R MM after 4 prior lines of therapy from 10 US academic centers.[24]
‡‡Based on a global, noninterventional, retrospective study using real-world data of 190 patients with R/R MM.[25]
ALL=acute lymphoblastic leukemia; CAR T=chimeric antigen receptor T cell; CD=cluster of differentiation; CI=confidence interval; CIBMTR=Center for International Blood and Marrow Transplant Research; CR=complete remission; DLBCL=diffuse large B-cell lymphoma; FDA=Food and Drug Administration; FL=follicular lymphoma; HGBL=high-grade B-cell lymphoma; LBCL=large B-cell lymphoma; MM=multiple myeloma; NA=not available; NHL=non-Hodgkin lymphoma; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; R/R=relapsed/refractory; RWE=real-world evidence.

Well-characterized and manageable safety profile[15,16,18,28-32]

Toxicities are managed per industry-established guidance[33,34]

- The safety profile of CAR T therapies is well characterized, with no new unexpected serious adverse events or neurologic toxicities found in long-term follow-ups[15,18,37]

- Primary toxicities associated with CAR T therapy include CRS and neurologic toxicities[33]
  - Often, CRS and neurologic toxicities were low, Grade 1 or 2[15,18,36]
  - Most CRS and neurologic toxicities occur within the first few weeks and are treated at the CAR T treatment center[33,37,38]

Comparable safety outcomes seen in real-world and pivotal studies[20-22,24]

- Any grade CRS and neurologic toxicity incidence ranges from 45% to 93% and from 15% to 70% of patients, respectively[2,3,20-22,36,39,40]

The management of therapy-related toxicities has evolved with processes and strategies in place to address potential adverse events that may arise.[41,42]

CAR T=chimeric antigen receptor T cell; CRS=cytokine release syndrome.

CAR T treatment centers are well equipped to manage the most common AEs: CRS and NTs[33]

CRS and neurotoxicity: onset and duration[42-48]

	Day 1-3		Within Week 1
CRS	High fever is a common first sign and typically occurs before other more serious side effects	Median time to onset is 2 to 3 days and rarely later than 14 days after treatment	CRS usually occurs within the first week. Severe CRS can manifest as early as 1 day after infusion
	Common signs and symptoms include: Fever, tachycardia, hypotension, depressed cardiac function, dyspnea, and hypoxia. Additional constitutional symptoms may include fatigue, headache, and myalgia.		

	Week 1		Week 3-4
Neurotoxicity	Can occur concurrently with high fever and other CRS symptoms, but can also occur after CRS	Potentially more severe symptoms can occur after CRS symptoms subside, usually more than 5 days after CAR T treatment	In ~10% of patients, delayed neurotoxicity can arise 3 to 4 weeks after treatment or later
	Some of the earliest manifestations include: Tremors, dysgraphia, impaired attention, apraxia, and mild lethargy. Bradycardia, hypertension and respiratory depression, and coma can also occur.		

Incidence, onset, and duration of CRS and neurotoxicity vary among individual patients and can be longer than what is listed.

AE=adverse event; CAR T=chimeric antigen receptor T cell; CRS=cytokine release syndrome; NT=neurologic toxicity.

22,000+ patients with certain hematologic cancers have been treated with CAR T therapy globally[49,50]

A broader range of patients than those studied in clinical trials may benefit from CAR T therapy[20,22,39,51,52]

- Real-world evidence was generally consistent with the efficacy and safety results seen in clinical trials[20,22,39,51,52]
- Some patients who received CAR T in real-world studies had ECOG performance scores ≥2[53]
- Stem cell transplant has general age guidelines (<65 years of age), while CAR T does not, enabling greater eligibility for patients to receive CAR T therapy[54,55]
  - Patients who received CAR T in real-world studies ranged from **14** to **91** years of age[2,3,20,40,51]*

*Excludes pediatric ALL age ranges.

ALL=acute lymphoblastic leukemia; CAR T=chimeric antigen receptor T cell; ECOG=Eastern Cooperative Oncology Group.

Improve the rate of successful referral by identifying appropriate patients for CAR T

CAR T patient eligibility

Current inclusion criteria are less strict than those of the pivotal trials.[20,39,54]

Patients with aggressive R/R B-cell NHLs are historically associated with a poor prognosis and should be evaluated promptly for CAR T eligibility.[33,56]

Patients should be selected based on their ECOG performance status, adequate bone marrow and organ function, and lack of major cardiac and pulmonary toxicities.[54]

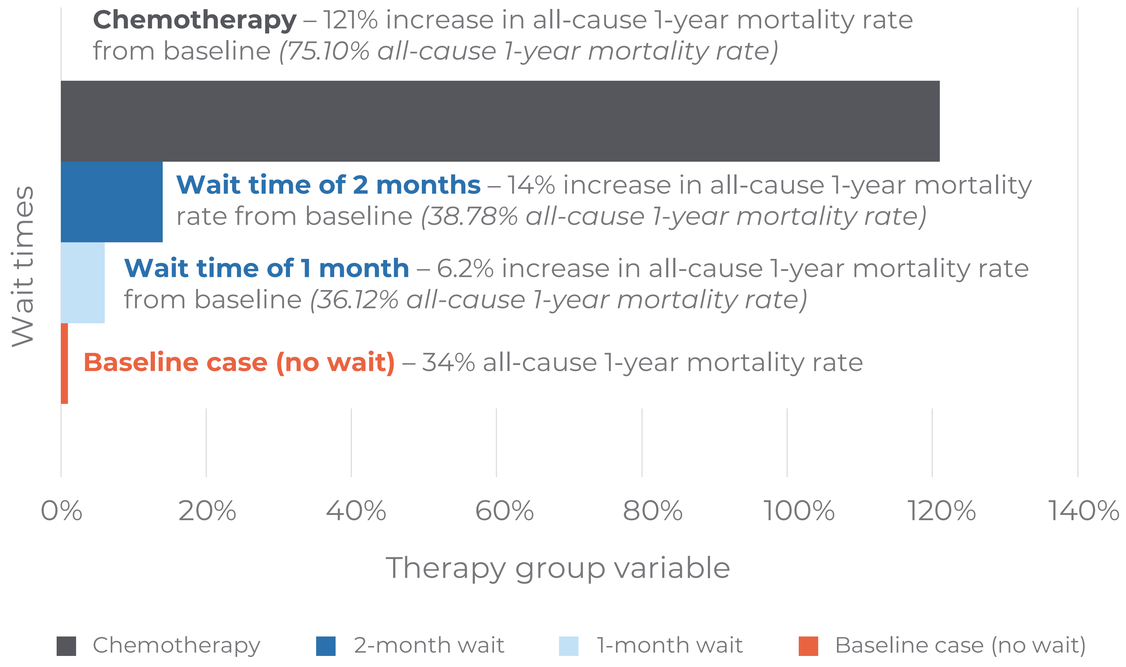
Evaluating patients with hematologic cancers for CAR T eligibility **upon treatment failure** may help accelerate the time to treatment initiation.[33,52,57]

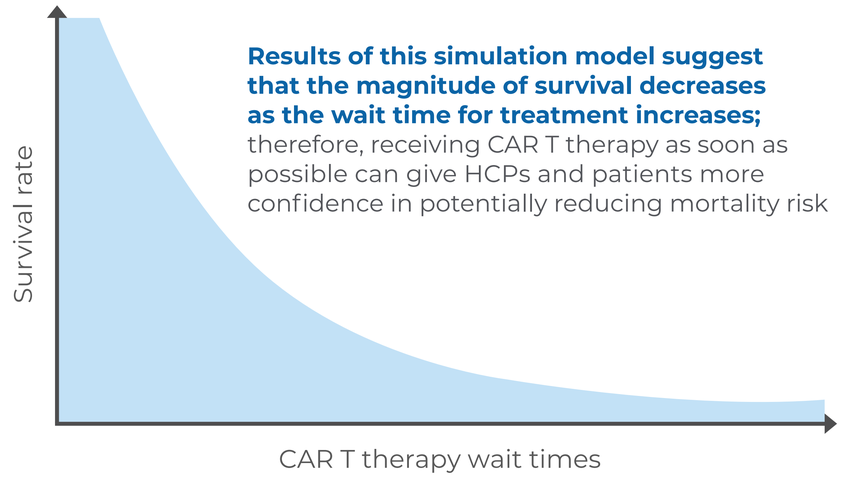
More of your patients may be eligible to receive CAR T therapy than you think. Consult with a CAR T treater early in the process to get more information.

CAR T=chimeric antigen receptor T cell; ECOG=Eastern Cooperative Oncology Group; NHL=non-Hodgkin lymphoma; R/R=relapsed/refractory.

The largest cause of mortality of patients receiving CAR T-cell therapy is wait times[58]*

Increase in all-cause 1-year mortality rate relative to the baseline 1-year mortality rate of 34.0%





Results of this simulation model suggest that the magnitude of survival decreases as the wait time for treatment increases; therefore, receiving CAR T therapy as soon as possible can give HCPs and patients more confidence in potentially reducing mortality risk

Graph is an artistic representation of data trends.

Increasing the wait time for CAR T-cell therapy from 1 to 9 months increased the predicted 1-year mortality rate from **36.1%** to **76.3%**[58]

Survival rates decrease as the wait times for CAR T-cell therapy increase[58]

*Information presented is based on a system-level microsimulated discrete event simulation model to project the potential impact of wait times on CAR T-cell therapy for patients with relapsed/refractory DLBCL.[58]

CAR=chimeric antigen receptor; CAR T=chimeric antigen receptor T cell; DLBCL=diffuse large B-cell lymphoma; HCP=healthcare provider.

Start communication with patients and CAR T treatment centers before disease recurrence[33,52,57]

Patient consultation for CAR T therapy should occur **upon treatment failure** to help streamline the referral process and reduce wait times for treatment initiation.[33,52,57]

Referral tips for CAR T therapy

1

The first step in the process is to **request a consultation for your patient**.[33]

2

Refer patients directly to CAR T treaters to discuss CAR T in further detail.

3

Get to know the CAR T treatment center coordinators. They offer support throughout the entire referral process, including financial, transportation, and housing assistance.[37]

4

Consultations can be made easier by[33,38]:

- **Having the cellphone number of a verified CAR T treater**
- Considering telemedicine appointments
- Utilizing EHR systems

5

Organizations, such as The Leukemia & Lymphoma Society,* are valuable resources that are eager to become an extension of your clinical team.

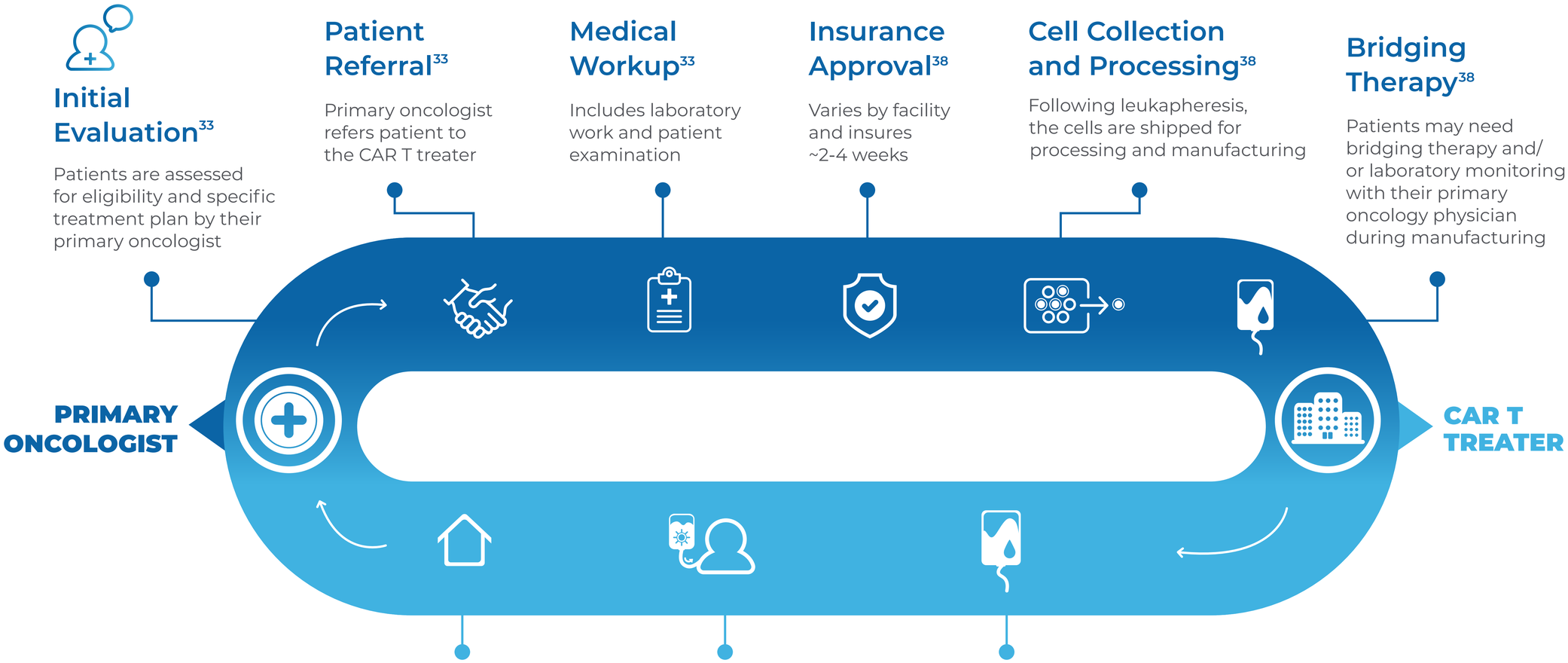
- They can also help navigate referral, financial, and logistical issues **(www.lls.org)**

*These resources are not operated or controlled by Kite. Eligibility requirements may vary and are established solely by each independent organization.

CAR T=chimeric antigen receptor T cell; EHR=electronic health record.

Collaboration and communication are key throughout the CAR T journey

Close collaboration between the primary oncologist, CAR T treater, and patient provides continuous insight and informed treatment decisions regarding overall continuity of patient care.



Initial Evaluation[33]

Patients are assessed for eligibility and specific treatment plan by their primary oncologist

Patient Referral[33]

Primary oncologist refers patient to the CAR T treater

Medical Workup[33]

Includes laboratory work and patient examination

Insurance Approval[38]

Varies by facility and insures ~2-4 weeks

Cell Collection and Processing[38]

Following leukapheresis, the cells are shipped for processing and manufacturing

Bridging Therapy[38]

Patients may need bridging therapy and/or laboratory monitoring with their primary oncology physician during manufacturing

Return Home[38]

When patients are medically stable, the CAR T treater can transition care back to the referring provider

CAR T Infusion[38]

CAR T-cell infusion administered by the CAR T treater 2-7 days following lymphodepletion

Lymphodepleting Chemotherapy[38]

Prior to infusion, the patient is reevaluated to ensure eligibility. Eligible patients then receive lymphodepleting chemotherapy

CAR T=chimeric antigen receptor T cell.

Stay connected with your patient's care every step of the way

Important considerations

BEFORE TREATMENT[57]

Educate patients on CAR T as an option in the event of relapse or refractory disease.

Help patients understand the breadth of clinical experience and adverse event management expertise of their multidisciplinary care team.

Encourage patients to visit **LetsChatCART.com**—a patient website that provides educational information on how CAR T works, what to expect when receiving CAR T, resources for caregivers, and where to find additional support.

DURING TREATMENT[33,45,48]

Patients will be at, or near, the CAR T treatment center for approximately 28 days for treatment and monitoring.

Most acute AEs occur within this time frame and are managed at the CAR T treatment center. CRS and neurologic toxicities post 28 days are rare.

AFTER TREATMENT[33,38,45,48]

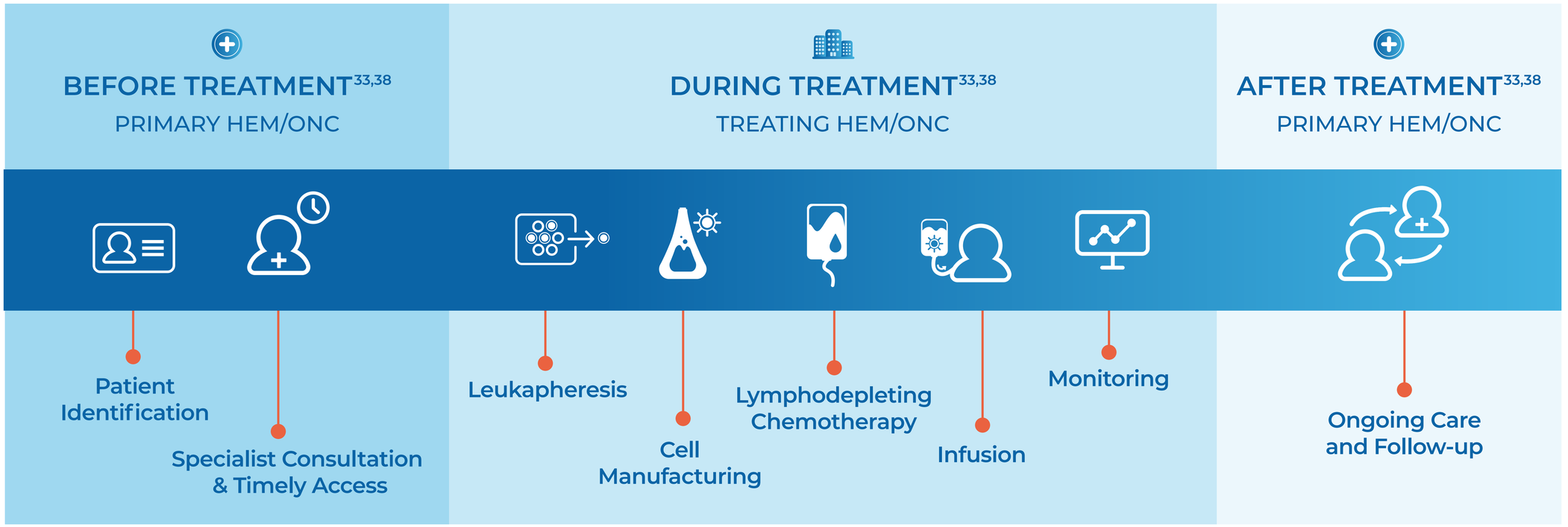
Primary oncologists typically do not need to manage acute adverse events.

Request a discharge summary and closely monitor patients based on report (ie, follow-up-visit, labs to be monitored, disease assessment, and infection prophylaxis recommendations, if needed).

Monitor for late toxicities (ie, cytopenias, hypogammaglobulinemia, and secondary malignancies).

AE=adverse event; CAR T=chimeric antigen receptor T cell; CRS=cytokine release syndrome.

The CAR T manufacturing process continues to be enhanced and standardized, with manufacturing success rates of 91% to 100% in clinical trials[17,28-32,38,59-61]



- CAR T-cell manufacturing involves leukocyte apheresis, processing, manufacturing of cells, and shipping[38]
- Bridging therapy can also be introduced, which can include chemotherapy, corticosteroids, or other therapies deemed appropriate to stabilize the patient during CAR T-cell manufacturing[33,38,52]

Once a patient is identified as eligible to receive CAR T, the treatment process can be completed in as little as 3 weeks.[33,38]

CAR=chimeric antigen receptor; CAR T=chimeric antigen receptor T cell.

Kite manufacturing is committed to predictable, reliable, and flexible delivery

Although turnaround times and product specifications vary across CAR T therapies, manufacturers strive to achieve fast turnaround times, in-spec target doses, and convenient apheresis date options to ensure timely administration.

7 DAYS A WEEK

Services provided every day, including Saturdays and Sundays, with multiple apheresis dates[62]

96% SUCCESS*

in manufacturing CAR T cells[63]

16-DAY MEDIAN TIME*

from leukapheresis to product release[64]

*Based on commercial manufacturing data as of October 2022.[63,64]

CAR=chimeric antigen receptor; CAR T=chimeric antigen receptor T cell.

Dedicated support throughout the treatment journey

Kite Konnect®

Kite Konnect can help with finding a CAR T treatment center and provide information about the support resources that may be available to your patient.

1-844-454-KITE [5483], Monday–Friday, 5 AM–6 PM PT.

CAR T treatment centers are independent treatment facilities certified to dispense Kite CAR T therapies. Choice of a CAR T treatment center is within the sole discretion of the physician and patient. Kite does not endorse any individual treatment center.

Resources may include referrals to independent third-party nonprofit patient assistance programs. These programs are not operated or controlled by Kite. Nonprofit patient assistance program eligibility requirements may vary and are established solely by each independent organization. Kite makes no guarantee with respect to reimbursement or copay assistance for any item or service.

Cell therapy patient programs are for eligible prescribed patients.

CAR T=chimeric antigen receptor T cell.

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Creating hope with CAR T: A promising treatment option for your patients

- CAR T therapy is a **proven, personalized therapy with clinical trial and real-world evidence**[1-3,15-22*]
- CAR T therapy's safety profile is **well characterized and managed** per established guidance[15,18,34]
- Evaluate patients for CAR T eligibility **upon treatment failure**[33,40,52]
- Refer patients directly to CAR T treaters to **reduce time to treatment initiation**[33]
- CAR T therapies have **high manufacturing success rates in clinical trials** (91% to 100%)[17,28-32,59-61]
- **Logistics and support are available** throughout the CAR T treatment journey[37]

Refer for CAR T consultation early to give your patients hope.

*Real-world evidence is based on Iacoboni et al 2020, Nastoupil et al 2020, Pasquini et al 2020, Landsburg et al 2021, and Jacobson et al 2022.

CAR T=chimeric antigen receptor T cell.

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