It takes a village: Using education to bridge the gap in CAR T cell therapy

Amy Corrao, MSN, NP-C
Scientific Director, US Medical Affairs, Cellular Therapy
Bristol Myers Squibb
Patient Journey Through CAR T Cell Therapy Requires Close Collaboration Between the Treating Site and Referring Providers

**Early collaboration may facilitate timely referral and eligibility evaluation**

- **Patient identification and referral**
  - Meet the CAR T cell therapy multidisciplinary team
  - Cells are collected by leukapheresis, then shipped for manufacturing

- **Consultation at CAR T treatment center**
  - Bridging therapy may be given to maintain disease control
  - Bridging therapy should be coordinated between the referring and CAR T cell therapy treating physicians

- **Apheresis**
  - LDC is administered prior to CAR T cell infusion to deplete endogenous T cells and create an environment for CAR T cell expansion

- **Bridging and lymphodepleting chemotherapy (LDC)**
  - Infusion occurs at a certified treatment center
  - After infusion, patients are closely monitored for at least 4 weeks at or near the CAR T treatment site
  - After at least 4 weeks, patients may be discharged back to the referring physician’s care

- **Infusion and monitoring**
  - Patients receive ongoing care to monitor and manage any persistent or delayed complications

- **Long-term follow-up**
  - Communication continues between the CAR T cell therapy treatment center and the primary hematologist/oncologist as patients are monitored long-term

**CAR T Academy**

CAR, chimeric antigen receptor.

Treatment and Management Requires Open Communication Between Non-CAR T Hematology Practitioners and Treating Institutions

Non CAR T Hematologist/Oncologist
The first point of contact, may be responsible for giving an overview of the CAR T process, refers patients for CAR T cell therapy, manages patient after return from CAR T treatment.

CAR T Specialist
The treating provider at a qualified treatment facility.

Nurses, APPs, and Pharmacy Staff
Have a critical role in care coordination (both clinical and logistical aspects), educating patients and caregivers, and managing side effects including potential long-term effects.

Continued collaboration through recommended 15-year data follow-up.

References:
Objectives for Collaboration Between CAR T Referrers and Academic Treaters to Help Address Challenges to CAR T Cell Therapy

Bring the latest in CAR T science/clinical experience to referrers and treaters

- Requires open communication around CAR T cell treatment, clinical trial data, and CAR T cell product selection

Support the seamless management and transfer of patients during and after CAR T treatment

- Requires close coordination (eg, transfer of patient treatment history) and direct communication between the referring doctor and treating oncologist for successful transitions of patient care

Improve the patient referral process/experience

- Requires developing professional relationships with direct lines of communications (eg, personal cell phone, emails) to facilitate transfer of patients between providers
- Requires good communication around referral timing, clinical indications, and impacts of prior treatments to help reduce challenges to patient referral for CAR T cell therapy

What Is CAR T Academy?

CAR T Academy is an online resource that provides treatment sites with CAR T education* reviewing concepts across the CAR T patient journey.

- Users can review each module and play each video individually, and log in to track their progress and the completion status of each module.

- The CAR T Academy modules can be directly accessed and are available for download at www.CAR-T-Academy.com

*Module completion is not a requirement by BMS, nor does it qualify towards any accreditation (eg, continuing medical education)
CAR T Cell Therapy Overview for Non-CAR T Hematology Practitioners
CAR T Academy: CAR T Cell Therapy Overview for Non-CAR T Hematology Practitioners

01 Introduction to CAR T Cell Therapy
02 Patient Journey and Clinical Considerations
03 CAR T Cell Therapy Side Effects and Long-term Follow-up
What is CAR T Cell Therapy?

- CAR T cell therapy is a type of immunotherapy that leverages the ability of T cells to detect and target specific antigen-expressing cells, including cancer cells.
- Gene transfer technology is used to express CARs on T cells, conferring antigen specificity.
  - CAR T cells can be directed to a specific surface antigen found on target cells.
  - CAR T cell therapy takes advantage of the cytotoxic potential of T cells by binding target cells in an antigen-dependent manner.

**CAR T Cell Persistence**
- CAR T cells may also expand and persist, providing T cell memory for a period of time.
- Persistent CAR T cells consist of both effector (cytotoxic) and central memory T cells.

---

**References:**
Components of a CAR T Cell

Autologous CAR T cell therapy helps equip a patient’s T cells with the ability to detect and destroy target cells, including malignant cells, by combining the specificity of an antibody with the cytotoxic and memory capabilities of a T cell\(^1,2\)

![Diagram of CAR T cell components](image)

**Chimeric antigen receptor (CAR)**

1. **External targeting domain**
2. **Spacer hinge**
3. **Transmembrane domain**
4. **Intracellular co-stimulatory and signaling domains**

**CARs** consist of an extracellular domain, capable of binding tightly to a tumor antigen, which is fused to at least one intracellular costimulatory domain that transduces the key signal to initiate the signaling cascade\(^1,3\)

1. When a CAR binds to a specific antigen on the target cell, a signaling cascade is induced, leading to activation of the CAR T cell\(^1\)

2. Once activated, the T cell\(^1\):
   - Induces cytotoxic activities
   - Expresses proapoptotic-molecules (e.g., FasL and TRAIL) to induce apoptosis of the target cell
   - Secretes pro-inflammatory cytokines to activate other tumor-infiltrating immune cells

3. For hematologic malignancies, the target cells typically reside in the same locations as the migrating T cells, with none of the physical barriers or immunosuppressive microenvironments of solid tumors\(^2\)

References:
Overview of the CAR T Cell Therapy Process

The autologous CAR T cell therapy process generally involves1-3:

• Collecting a patient’s T cells via apheresis
• CAR T cell manufacturing  
  — Genetically engineering T cells to express the CAR  
  — Expanding CAR T cells to generate sufficient cell numbers for therapy  
  — During the manufacturing period, some patients may receive bridging therapy
• Infusion of CAR T cells to the patient after the patient has received preparative chemotherapy, or lymphodepleting chemotherapy
• Short- and long-term patient monitoring after infusion of CAR T cells

Autologous CAR T Cell Manufacturing Methods

Overview of the CAR T Cell Manufacturing Process\(^1,2\)

1. Leukapheresis
   - Patients undergo leukapheresis to collect PBMCs; the PBMCs are then shipped to a manufacturing facility
   - Collected apheresis products may be processed differently depending on the downstream procedures using one of several commercially available devices

2. Selection & Activation
   - Lymphocytes are isolated from the PBMCs and T cells are activated

3. Gene Transfer
   - Isolated patients T cells are transduced with a viral vector to insert the CAR genetic sequence

4. Cell Expansion
   - Engineered T cells are expanded to a therapeutic dose
   - Cellular product is concentrated and cryopreserved in container(s) before being shipped to the treatment site for infusion to the patient

CAR T cell total manufacturing time may range from ~2—5+ weeks, varying by product and manufacturer\(^3\)

PBMC, peripheral blood mononuclear cells.

CAR T Academy: CAR T Cell Therapy Overview for Non-CAR T Hematology Practitioners

01 Introduction to CAR T Cell Therapy

02 Patient Journey and Clinical Considerations

03 CAR T Cell Therapy Side Effects and Long-term Follow-up

Icon indicates areas of collaboration between the non-CAR T and CAR T treatment teams
Patient Journey Through the CAR T Cell Therapy Process

**Patient identification and referral**
- Patient identification begins with the referring hematologist/oncologist.
- Early collaboration may facilitate timely referral and eligibility evaluation.

**Consultation at CAR T cell therapy treatment center**
- Referred patients meet the CAR T cell therapy multidisciplinary team to determine if CAR T cell therapy is right for them.

**Apheresis**
- Peripheral blood mononuclear cells (PBMC) are collected by leukapheresis, then shipped for manufacturing.
- Apheresis may occur at the treatment center or a qualified external apheresis center.

**Bridging and lymphodepleting chemotherapy (LDC)**
- Bridging therapy may be given to maintain disease control during CAR T cell manufacturing.
- Appropriate bridging therapy should be discussed and coordinated between the referring and CAR T cell therapy treating physicians.
- LDC is administered prior to CAR T cell infusion to deplete endogenous T cells and create an environment for CAR T cell expansion.

**Infusion and monitoring**
- Infusion occurs at a certified treatment center.
- After infusion, patients are closely monitored for at least 4 weeks at or near the CAR T cell therapy treatment site, and side effects are promptly managed.
- After at least 4 weeks, patients may be discharged back to the referring physician’s care.

**Long-term follow-up**
- Following treatment, patients receive ongoing care to monitor and manage any persistent or delayed complications of therapy.
- Communication continues between the CAR T cell therapy treatment center and the primary hematologist/oncologist as patients are monitored long-term.

References:
Considerations for CAR T Cell Therapy

General considerations for CAR T cell therapy:

- Have a disease as defined in commercial indication or in clinical trial\(^1\)
- Adequate marrow and organ function, as well as patient fitness and performance status\(^2,3\)
- Do not administer to patients with active infections or inflammatory disorders\(^3,4,a\)
- Absence of clinically relevant comorbidities (e.g., select cardiovascular, neurologic, or immune disorders)\(^3\)
- Cumulative chemotherapy exposure may adversely affect quality of circulating T cells\(^2\)
- Allogeneic stem cell transplant before CAR T cell therapy may increase the risk of GVHD\(^5\)

These considerations are typically part of the general workup conducted and do not necessarily disqualify patients from CAR T cell therapy.

Additional considerations:

- Socioeconomic factors\(^1\)
- Caregiver support\(^6\)
- Social work evaluation\(^7\)
- Stay in close proximity of treating institution for at least 4 weeks after CAR T cell infusion\(^6\)

Centers and manufacturers may have resources to assist eligible patients.

Precise criteria for eligibility vary by malignancy, treatment regimen or protocol, and CAR T cell product\(^3\)

* Including hepatitis B, hepatitis C, HIV, and CMV.

GVHD, graft-versus-host disease.

Patient workup may include:

Disease assessment and review of medical and treatment history\(^1,2\)
- May require confirmatory biopsy of disease if not recently completed or reviewed\(^2\)

Assessment of organ function, comorbidities, and performance status\(^1\)

Laboratory studies
- CRP\(^2\)
- Ferritin\(^2\)
- LDH\(^2\)
- CBC with differential\(^2\)
- Comprehensive metabolic panel\(^2\)
- Screening for infections including hepatitis B, hepatitis C, and HIV\(^3\)

Referring centers are often responsible for providing current patient records including\(^2\):
- Diagnostic scans
- Pathology reports
- Recent laboratory data
- Complete history and physical

CBC, complete blood count; CRP, C-reactive protein; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase.

• Apheresis is the removal of blood from a patient, and the subsequent separation into its components\(^1\)
  
  – Leukapheresis specifically refers to the collection of white blood cells\(^1\)

• Leukapheresis may be performed in the outpatient setting\(^2\)
  
  – Coordination across the multidisciplinary team can help achieve an efficient leukapheresis collection\(^2\)

PBMC, peripheral blood mononuclear cell.

References:
Bridging Therapy May Help Control Disease Until CAR T Cells Are Ready for Infusion

- It can take several weeks before the CAR T cell product is manufactured and delivered to the patient\(^1,2\)

- Patients undergoing CAR T cell therapy may have active disease and may require bridging therapy during this period\(^1\)

Appropriate bridging therapy should be discussed and coordinated between the referring and CAR T cell therapy treating physicians\(^3\)

Bridging therapy goals\(^1\):
Maximize disease control
Minimize organ toxicity

References:
A washout period may be needed before leukapheresis to support the collection of a sufficient number of T cells for manufacturing\textsuperscript{1}

A washout period between bridging therapy and lymphodepletion may be needed to help avoid interference with CAR T cell activity\textsuperscript{1}

Washout periods should be discussed and coordinated between the referring and CAR T cell therapy treating physicians\textsuperscript{2}

Regimens are highly variable and depend on:

- Specific malignancy
- Disease burden
- Patient age
- Comorbidities
- Prior response to therapy

- Bridging therapy is carefully planned and selected with the aim to control disease and avoid patient harm or delay of CAR T cell infusion
- Patients are closely monitored for infections and other toxicities
- Bridging therapy delivery may take place at either the treating or referring center

Examples of bridging therapy:

Chemotherapy, immunomodulatory agents, radiation therapy, monoclonal antibodies, antibody-drug conjugates, corticosteroids, and lower-intensity regimens (as appropriate for certain patients)

References:
CAR T Cell Therapy Setting of Care Considerations

• Under certain circumstances, outpatient administration and monitoring may be appropriate per the CAR T cell therapy treating physician’s discretion or clinical trial protocol:
  – In these cases, patients are usually observed in the treating center for a few hours after CAR T cell therapy infusion to monitor for acute reactions; if none occur, they may be permitted to leave the treatment center.
  – Patients should stay within vicinity of the CAR T cell therapy treatment center for at least 4 weeks as directed by the CAR T cell therapy treating physician, or as indicated per clinical trial protocol.
  – Hospitalization may be necessary if toxicities develop.

Determining the setting for CAR T cell therapy infusion is based on several factors:

- Treatment center infrastructure
- Ability to provide patient coverage 24/7
- Anticipated onset and severity of AEs
- Training, education, and protocols for managing AEs
- CAR T cell product offered
- Availability of reliable caregiver(s)
- Patient and/or physician preference

01 Introduction to CAR T Cell Therapy

02 Patient Journey and Clinical Considerations

03 CAR T Cell Therapy Side Effects and Long-term Follow-up
Post-CAR T Cell Therapy Side Effects\textsuperscript{1-3}

Close monitoring after CAR T cell therapy infusion enables providers to help manage persistent and/or delayed complications and monitor disease status\textsuperscript{1}

Adverse reactions post-CAR T cell therapy may include\textsuperscript{2,3,a}:

**Short-term (<4 weeks)**
- Cytopenias
- Fatigue
- Infections
- Cytokine release syndrome
- Neurotoxicity

**Long-term (≥4 weeks)**
- Hypogammaglobulinemia
- Infections
- Prolonged cytopenias
- Fatigue
- Secondary malignancies
- Cytokine release syndrome
- Neurotoxicity

Because of the risk of delayed neurologic events, patients should not drive or operate machinery for 8 weeks after CAR T cell infusion\textsuperscript{4}

\textsuperscript{a} Note, other adverse reactions may occur that are not listed on slide.

CRS and Neurotoxicity Are Serious Adverse Effects of CAR T Cell Therapy

Following CAR T cell therapy, patients should be closely monitored for at least 4 weeks by the CAR T treatment center for cytokine release syndrome (CRS) and neurotoxicity.

**CRS**
- Typical time to onset: 1-7 days (range: 1-63)\(^2\)\(^-\)\(^7\)
- Typical duration: 4-10 days (range: 1-63)\(^2\)\(^-\)\(^7\)
- Signs and symptoms of CRS may include fever, hypotension, tachycardia, hypoxia and chills\(^8\)

**Neurotoxicity**
- Typical time to onset: 2–8 days (range: 1-368)\(^2\)\(^-\)\(^7\)
- Typical duration: 7–21 days (range: 1-578)\(^2\)\(^-\)\(^7\)
- Signs and symptoms of CAR T neurotoxicity may include dizziness, delirium, anxiety, tremors, encephalopathy, insomnia, impaired attention, ataxia, aphasia, and lethargy\(^8\)

It is important to watch for signs as both of these events may require hospitalization\(^8\)

In some instances, delayed onset of CRS and/or neurotoxicity may occur. Notify the CAR T treatment center if CRS or neurotoxicity is suspected\(^1\)

---

\(^a\) For more details on CRS and neurotoxicity, please refer to CAR T Academy Module 5 - Acute Management.

References:

---

03: Side Effects and Long-term Follow-up
Long-term Monitoring Post-CAR T Cell Therapy

After at least 4 weeks, or when toxicities resolve, patients can be transferred back to their primary hematologist/oncologist. Long-term follow-up may be conducted by a multidisciplinary team to monitor disease status and long-term side effects.

Close communication between the non-CAR T hematologist and the treatment site is needed for ongoing patient follow-up.

- Follow-up with non-CAR T practitioners is personalized and may vary on a case-by-case basis.
- The long-term follow-up phase occurs up to 15 years post-infusion, as recommended by the FDA. Patients should also be monitored life-long for secondary malignancies.

Elements of long-term follow-up can include:
- Managing persistent and/or delayed complications
- Monitoring disease status and for occurrence of secondary malignancies

References:
Considerations for Management of Prolonged Cytopenias

Patients may exhibit cytopenias for weeks to months following lymphodepleting chemotherapy and CAR T cell therapy infusion.

- Incidence, duration, and severity of cytopenias varies between products and indications. Incidence of Grade 3-4 cytopenias 28+ days after CAR T cell infusion has been reported to range from 12-41% for neutropenia and 13-49% for thrombocytopenia. While less frequent, prolonged anemia may also occur.

- While cytopenias often recover within a few months post-CAR T cell infusion, cytopenias have been observed in patients up to 24 months following CAR T cell infusion.

Consider supportive care, growth factors, and/or corticosteroids to support patients with severe cytopenias, when appropriate.

Physicians should consult product-specific information and/or clinical trial information, and/or their institutional guidelines.

References:
Considerations for Management of Hypogammaglobulinemia and Infections

- Hypogammaglobulinemia develops in approximately 50% of patients that receive CAR T cell therapy.
- For these patients, as well as immunologically-immature pediatric patients, intravenous immunoglobulin (IVIG) replacement is routine.
- Consider IVIG treatment monthly for select patients until reaching a steady state.

- Infections following CAR T cell therapy are common, and have been reported in up to 70% of patients.
- Most early infections are bacterial or respiratory viral infections.
- Beyond 30 days, viral infections predominate, and long-term antiviral prophylaxis may be considered.
- When eligible, vaccination may also reduce infection rates.
- Consider inactivated vaccines ≥6 months after CAR T cell therapy and ≥2 months after IVIG.
- Consider live vaccines ≥6-12 months after CAR T cell therapy and immune reconstitution.

References:
1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Management of Immunotherapy-Related Toxicities V.1.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed June 15, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
Because genetic alteration is used to create CAR T cells, there is a possibility that these products can cause insertional mutagenesis, resulting in secondary malignancies. In a small cohort of patients followed up to 5.25 years, 15% developed subsequent malignancies including nonmelanoma skin cancer, myelodysplastic syndromes, melanoma, bladder cancer, and multiple myeloma. The median time from first infusion to diagnosis for subsequent malignancies was 2 to 16 mo, depending on the type of malignancy. Secondary malignancies should be treated per disease-specific protocols.

Fatigue can be a common and difficult-to-manage side effect of CAR T cell therapy with incidence ranging from 23-52% in clinical trials. Consider ruling out any possible contributing factors, such as anemia and hypothyroidism. Consider avoiding steroid use due to potential T cell suppression that may limit activity of CAR T cells. Consider nonpharmacologic interventions including exercise, yoga, and meditation.

References:
Example Clinical Testing in the First Year Post-CAR T Cell Therapy

Long-term

Day +28 to 1 year
Day +100 to 1 year
1-2 years
2-15 years

Example Clinical Testing Panel and Frequency per EBMT/EHA

<table>
<thead>
<tr>
<th>Tests</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemistry blood panels</td>
<td>Assess bone marrow recovery, organ health, and supportive care needs</td>
</tr>
<tr>
<td>Viral presence</td>
<td>Infection/ viral reactivation</td>
</tr>
<tr>
<td>Immunoglobulin or serum protein testing</td>
<td>Immune reconstitution</td>
</tr>
<tr>
<td>Peripheral blood immunophenotyping</td>
<td>Immune recovery</td>
</tr>
<tr>
<td>CAR T cell monitoring</td>
<td>CAR T cell persistence</td>
</tr>
</tbody>
</table>

- Additional tests and imaging should be carried out as clinically indicated and/or per institutional guidelines

Collaboration between the CAR T cell therapy treatment site and the non-CAR T hematology practitioner is important for monitoring and management of patients after CAR T cell therapy

- The frequency and timing for testing should be determined in collaboration between the CAR T cell therapy treatment team and the non-CAR T hematology practitioner

Delayed and prolonged events can occur, therefore more frequent testing should be considered in collaboration with treating physician to monitor for the onset of complications

a Physicians should consult product-specific information and/or clinical trial information, and/or their institutional guidelines.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CMV, cytomegalovirus; CRP, C-reactive protein; EBMT, European Society for Blood and Marrow Transplantation; EBV, Epstein-Barr virus; EHA, European Hematology Association; FBC, full blood count; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase.

Possible Frequency of Clinic Visits for Patients Through the LTFU

• CAR T cells may persist in some patients, underscoring the need for long-term monitoring for late effects of treatment\(^1,2\)

• The FDA recommends 15 years of observation for patients who receive CAR T cell therapies\(^3,4\)

After CAR T cell therapy, referring physicians remain in ongoing communication with the treatment site to report patient data during the long-term follow-up period\(^5\)

• This data may then be reported to the CIBMTR registry, and/or to the FDA, who capture long-term follow-up data for patients that received CAR T cell therapies\(^3,6\)

• To report SUSPECTED ADVERSE REACTIONS, contact the product manufacturer or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

CIBMTR, Center for International Blood & Marrow Transplant Research; FDA, Food and Drug Administration.

\(^a\) Physicians should consult product-specific information and/or clinical trial information, and/or their institutional guidelines.

\(^b\) Some patients may warrant more frequent or closer monitoring depending on prognosis, disease characteristics, and/or patient characteristics.

Patient Registry and Data Capture

The CIBMTR Cellular Therapy Registry:

- Offers a platform for standardized, comprehensive data collection
  - After CAR T cell therapy infusion, data is captured at 100 days, at 6 months, annually until year 6, and biannually after that until death

- Aligns with FDA regulatory guidelines for capturing relevant CAR T cell-associated toxicities
  - Specific outcomes captured include CRS, neurotoxicities, neutrophil and platelet recovery, hypogammaglobulinemia, severe infections, nonhematologic grade 4 toxicities, death from any cause
  - Event-driven forms can be used to report subsequent neoplasms and pregnancies

CIBMTR, Center for International Blood and Marrow Transplant Research; CRS, cytokine release syndrome; FDA, US Food and Drug Administration.
Patients will be co-managed by the primary hematologist and CAR T specialist leading up to infusion and following the initial post-infusion monitoring period. Care can then be transitioned back to the primary hematologist.1

Example topics of discussion for referring physicians and CAR T cell treatment sites when coordinating patient care:

- Appropriate bridging therapy
- Washout periods pre-apheresis and pre-lymphodepletion
- Timing and coordination of patient care at each institution after CAR T cell infusion
- Methods of efficient communication between practices

Non CAR T Hematologist/Oncologist
Refers patients for CAR T cell therapy1

CAR T Specialist
The treating provider at a qualified treatment facility1

Nurses, APPs, and Pharmacy Staff
Have a critical role in care coordination, educating patients and caregivers, and managing side effects including potential long-term effects2-4

Thank you for completing this module of CAR T Academy

We hope you found it informative and educational

• Follow this link to download a printable acknowledgment of completion:

  – NOTE: Completion of CAR T Academy modules does not qualify as CME or any other type of accreditation

• For more information and access to other CAR T Academy modules, please visit:
  https://www.car-t-academy.com
CAR T Academy Overview & Engagement
CAR T Academy Site Capabilities

Click to access downloadable PDF of module

Each module concludes with the option to download a printable acknowledgment of completion for personal records

Click to watch narrated video of module

Informational modules for US healthcare providers

The 10 modules comprising the CAR T Academy site seek to enhance the understanding of CAR T cell therapies for US healthcare providers. They are designed as an educational complement to enhance your understanding of the CAR T process and related clinical topics. The modules are accessible online, allowing you to review them in a convenient and self-paced format.

Following the summary at the end of each module PDF, there is an acknowledgment of completion that will provide you with a Q&A for review.

Bristol Myers Squibb | CAR T Academy
CAR T Academy Content Focuses on CAR T Therapy as A Product Class and Is Not Product or Disease State-Specific

CAR T Academy comprises 13 total modules:
- 12 content modules (with BMS cell therapy expert-presented videos)
- 1 case simulator (including a Q&A for review)

NEW

<table>
<thead>
<tr>
<th>Module</th>
<th>Overview</th>
<th>Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAR T 101</td>
<td>Overview of Immunity and Hematologic Malignancies</td>
<td>CAR T Cell Science</td>
</tr>
<tr>
<td></td>
<td>• Introduction to CAR T Cell Science</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CAR T Cell Targets</td>
<td></td>
</tr>
<tr>
<td>CAR T 102</td>
<td>• Overview of Journey through CAR T Cell Therapy Process</td>
<td></td>
</tr>
<tr>
<td>Patient Considerations</td>
<td>• Patient Evaluation for CAR T Cell Therapy</td>
<td>Patient Characteristics and Outcomes</td>
</tr>
<tr>
<td></td>
<td>• Considerations around CAR T Cell Infusion</td>
<td>Effect of Bridging and Additional Therapies on CAR T Cell Therapy</td>
</tr>
<tr>
<td>Apheresis</td>
<td>• Procedure Overview</td>
<td>Technical Considerations</td>
</tr>
<tr>
<td></td>
<td>• Cell Collection Considerations</td>
<td>Scheduling and Shipping</td>
</tr>
<tr>
<td>Bridging and Lymphodepletion</td>
<td>• Bridging Therapy</td>
<td>Lymphodepletion</td>
</tr>
<tr>
<td>CAR T Infusion</td>
<td>• Handling Guidelines</td>
<td>Product Guidelines</td>
</tr>
<tr>
<td></td>
<td>• Patient Preparation</td>
<td>Multidisciplinary Team Coordination</td>
</tr>
<tr>
<td></td>
<td>• Product Preparation</td>
<td></td>
</tr>
<tr>
<td>Acute Management</td>
<td>• Cytokine Release Syndrome (CRS)</td>
<td>Neurotoxicity</td>
</tr>
</tbody>
</table>

CAR T Academy comprises 13 total modules:
- 12 content modules (with BMS cell therapy expert-presented videos)
- 1 case simulator (including a Q&A for review)
CAR T Academy Content Focuses on CAR T Therapy as A Product Class and Is Not Product or Disease State-Specific

CAR T Academy comprises 13 total modules:
- 12 content modules (with BMS cell therapy expert-presented videos)
- 1 case simulator (including a Q&A for review)

<table>
<thead>
<tr>
<th>Module</th>
<th>Content</th>
</tr>
</thead>
</table>
| Long-term Follow-up | • Post-treatment Complications  
• Relapse  
• Psychosocial Factors  
• Logistical Considerations  
• Registry |
| Program Setup | • Program Oversight  
• Healthcare Professional Considerations  
• Logistical Considerations |
| Outpatient Monitoring | • Patient Experience  
• Importance of a Caregiver |
| Overview for Non-CAR T Treaters | • Introduction to CAR T Cell Therapy  
• CAR T Patient Journey  
• Clinical Considerations  
• Side Effects and Long-Term Follow-Up |
| CAR T for Referrers in Autoimmune Disease | • Introduction to CAR T Cell Therapy  
• CAR T Patient Journey and Joint Care Model in Autoimmune Disease |
| Case Simulator | • Interactive Patient Case Simulator  
• Multiple Choice Management Questions |
CAR T Academy Content Focuses on CAR T Therapy as A Product Class and Is Not Product or Disease State-Specific

CAR T Academy comprises 13 total modules:
- 12 content modules (with BMS cell therapy expert-presented videos)
- 1 case simulator (including a Q&A for review)

Overview for Non-CAR T Treaters
- Introduction to CAR T Cell Therapy
- CAR T Patient Journey

NEW
- Clinical Considerations
- Side Effects and Long-Term Follow-Up

The new CAR T Academy module ‘CAR T Cell Therapy Overview for Non-CAR T Hematology Practitioners’ provides a high-level overview of CAR T cell therapy for practitioners at non-CAR T cell treatment centers.

‘Collaboration’ icons throughout the module highlight areas of collaboration between the non-CAR T and CAR T treatment teams.

NEW
- Introduction to CAR T Cell Therapy
- CAR T Patient Journey and Joint Care Model in Autoimmune Disease

Case Simulator
- Interactive Patient Case Simulator
- Multiple Choice Management Questions
Topics Covered in the New ‘Non-CAR T Treater’ Module Are Also Expanded Upon in Greater Depth in the Other CAR T Academy Modules and Are Available as Videos
How Can CAR T Academy Be Used At Your Institution?

CAR T Academy has been described as a valuable, ready-to-use educational resource that provides a deeper dive into CAR T cell therapy, and can be used to supplement existing institutional materials.

CAR T Academy can be used to help referring health care providers learn about the CAR T process and better understand the patient journey, timeline, areas of collaboration between centers, and areas of considerations when patients return to their care post-CAR T treatment.

Users have reported that their centers have used CAR T Academy as part of the orientation process for their new hires.

Note: CAR T Academy must not be used as a replacement of any institutional internal training.
Interest in Quality CAR T Educational Support

Between September and December 2023, a social media campaign was launched to increase awareness of CAR T Academy

11K+
Total clicks
CAR T Academy garnered over 11K total clicks on LinkedIn from both CAR T treaters and non-CAR T treaters

48%
Non-CAR T treaters
Non-CAR T treaters were the most engaged audience, delivering the highest clickthrough rate
CAR T treaters drove the highest click volume overall at 52%

69%
Nursing professionals
Across both CAR T treater and non-CAR T treater audiences, the highest number of clicks (69%) were generated by nurses, including registered nurses and nurse practitioners
Summary

• CAR T cell therapy is a complex, multi-step process that requires close collaboration and open communication across multiple stakeholders
  – Having educational CAR T resources to support provider collaboration is essential to successful treatment

• CAR T Academy is an online resource that provides treatment sites with CAR T education reviewing concepts across the CAR T patient journey
  – Content focuses on CAR T therapy as a product class and is not product or disease state-specific

• Resources, like CAR T Academy, can help to support education, introduce important cell therapy concepts, and provide support to both treatment and non-treatment centers