Bristol Myers Squibb®

CAR T Cell Therapy Case Simulator

PATIENT CASE

Catherine: Patient History[a]

- **Age:** 64-year-old woman
- **Social History:** Married with 2 adult children, retired schoolteacher
- **Treatment History:** Refractory disease after 2 prior lines of treatment
- **Evaluation:** Eligible for CAR T cell therapy based on evaluation by her oncology team

[a]Patient depicted is hypothetical.

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]
- Prior 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 graft-versus-host disease (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 2 weeks after CAR T cell infusion[8]

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]

[a] Including hepatitis B, hepatitis C, HIV, and CMV.
CMV, cytomegalovirus; HIV, human immunodeficiency virus.

References: 1. Taylor L, et al. *Clin J Oncol Nurs.* 2019;23:20-26. **2.** Yakoub-Agha I, et al. *Haematologica.* 2020;105(2):297-316. **3.** Leukemia & Lymphoma Society. Facts about chimeric antigen receptor (CAR) T-cell therapy. 2022. **4.** Hill JA, Seo SK. *Blood* 2020;136(8):925-935. **5.** Wall DA, Krueger J. *Curr Oncol.* 2020;27(suppl 2):S115-S123. **6.** Beaupierre A, et al. *J Adv Pract Oncol.* 2019;10(Suppl 3):29-40. **7.** Perica K, et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. **8.** US Food and Drug Administration. Accessed June 27, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor

PATIENT CASE

Catherine[a]: Prior to Infusion

Patient identification | **Apheresis** | **Bridging[b]** | **LDC and Infusion** | **Monitoring and long-term follow-up**

Patient Notes:

- Eligible for CAR T cell therapy based on evaluation by her oncology team
- Patient decides to proceed with CAR T

- Completed without incident and cells sent to manufacturer

- Completed 16 days prior to lymphodepleting chemotherapy (LDC)

- LDC regimen: fludarabine + cyclophosphamide over 3 days

[a]Patient depicted is hypothetical. [b]Not all approved CAR T cell therapies require bridging therapy; bridging therapy may be optional per physician's discretion.
LDC, lymphodepleting chemotherapy.

Management Question 1

A couple of days before Catherine is scheduled to receive LDC, she tests positive for an active infection. What should happen next?

A. Proceed with LDC as planned

B. Delay LDC until the infection has been treated or resolved

LDC, lymphodepleting chemotherapy.

Management Question 1

A couple of days before Catherine is scheduled to receive LDC, she tests positive for an active infection. What should happen next?

A. Proceed with LDC as planned

B. Delay LDC until the infection has been treated or resolved

The correct answer is B.

LDC, lymphodepleting chemotherapy.

Delivery of LD Chemo

- Patients are treated with LD chemo several days before CAR T cells are infused[1]
- Coordinated by the treating facility, and can be delivered in the inpatient or outpatient setting[2]
- Active infection must be excluded or under control prior to the start of LD chemo[3]

Patients should have a caregiver that meets certain expectations[2]

Expectations for Caregivers During LD Chemo[2]

- ✓ Be at least 18 years old
- ✓ Be able to drive
- ✓ Stay with the patient 24 hours/day in the outpatient setting
- ✓ Live with the patient at a place within close proximity of the treating facility
- ✓ Transport patient to/from appointments
- ✓ Actively engage with the medical team
- ✓ Manage and administer the patient's medications
- ✓ Practice good home precautions
- ✓ Contact the medical team with any questions or regarding any symptoms or adverse events

References: 1. Perica K, et al. *Biol Blood Marrow Transplant.* 2018;24:1135-1141. **2.** Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34. **3.** Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316.

PATIENT CASE

Catherine[a]: CAR T Infusion

Patient identification | Apheresis | Bridging[b] | **LDC and Infusion** | Monitoring and long-term follow-up

Patient Notes:

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- Patient decides to proceed with CAR T

- Completed without incident and cells sent to manufacturer

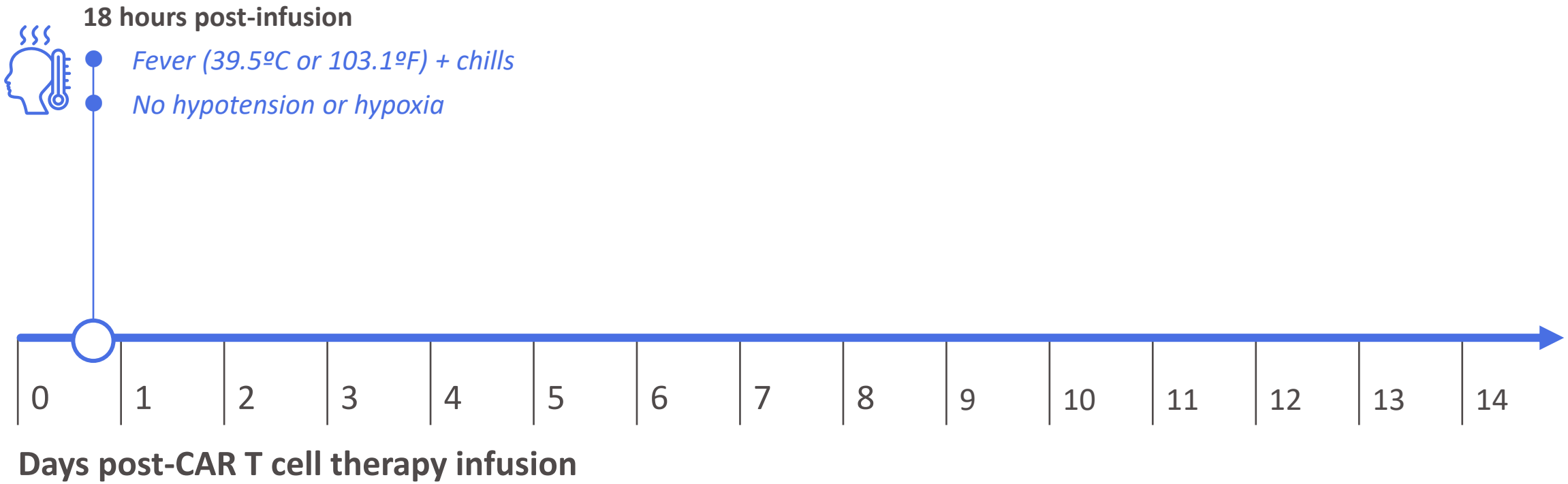
- Completed 16 days prior to lymphodepleting chemotherapy (LDC)

- LDC regimen: fludarabine + cyclophosphamide over 3 days
- Infection cleared
- CAR T cells infused (Day 1)
- Patient is monitored over the next several hours with no signs of acute reactions

[a]Patient depicted is hypothetical. [b]Not all approved CAR T cell therapies require bridging therapy; bridging therapy may be optional per physician's discretion.
LDC, lymphodepletion chemotherapy.

Catherine: Acute Monitoring Period[a]

Short-term monitoring (≥14 days post infusion)



[a]Patient depicted is hypothetical.

Management Question 2

Given Catherine's signs and symptoms, which of the following is the most important next step?

A. Workup for cytokine release syndrome (CRS)

B. Workup for infection

C. Workup for neurotoxicity

D. Both A and B

Management Question 2

Given Catherine's signs and symptoms, which of the following is the most important next step?

A. Workup for cytokine release syndrome (CRS)

B. Workup for infection

C. Workup for neurotoxicity

D. Both A and B

The correct answer is D.

CRS Clinical Presentation

Not all patients will develop CRS, but when it occurs the severity can range from mild to life-threatening or fatal[1]

- Severity may but does not always correlate with disease burden[2]

Typical onset is within 1 to 5 days, but varies[1]

- Time-to-onset can be delayed and can present beyond 14 days[3]

The first symptom is typically fever, which can be high grade (>40ºC or >104ºF)[1]

— Additional signs and symptoms may include respiratory distress,[1] hypotension,[1] tachycardia[2] and neurologic symptoms[1]

— Although fever is a key indicator of CRS, other AEs, such as infection, should also be assessed and ruled out when fever arises

References: 1. Oluwole OO, Davila ML. *J Leukoc Biol.* 2016;100:1265-1272. **2.** June CH, et al. *Science*. 2018;359:1361-1365. **3.** Lee DW, et al. Biol Blood Marrow *Transplant*. 2019;25:625-638.

CRS Recognition

The importance of timely recognition of CRS cannot be overstated given the potential for mortality. Note that CRS and neurotoxicity can occur simultaneously[1,2]

Routine Monitoring

Vital signs including temperature, O_2 saturation, etc[1]

Review of systems and physical exam[1]

- Focus on cardiovascular, pulmonary, and neurologic systems
- Survey for occult infection

Laboratory monitoring of inflammatory markers[1,2]

- CRP
- Cytokines*
- Ferritin
- LDH

Focused Assessment Based on Symptoms

Fever[1]

- Blood and urine culture
- Targeted imaging to assess for potential sources of infection

Tachycardia[1]

- Electrocardiogram to assess for arrhythmia

Hypotension/persistent tachycardia[1]

- Echocardiogram to assess for decreased ejection fraction

*May be sent out for testing.
CRP, C-reactive protein; LDH, lactate dehydrogenase.
References: 1. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55. **2.** Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625-638.

Management Question 3

Catherine's lab cultures come back negative for infection, and you determine she has Grade 2 CRS according to ASTCT grading system.
What intervention(s) should you consider according to ASTCT guidelines?

A. Watch and wait

B. Basic supportive care (eg, antipyretics)

C. Supplemental oxygen

D. Tocilizumab

E. Corticosteroids

F. B, C, and D

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome.

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The correct answer is F.

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome.

Management of Grade 1 and 2 CRS According to Different CRS Grading Scales

Grade	Lee[1]	ASTCT[2]	Penn[3]	CARTOX[4]
1	• Vigilant supportive care • Assess for infection • Treat fever and neutropenia if present • Monitor fluid balance • Antipyretics, analgesics as needed	• Antipyretics and IV hydration • Diagnostic work-up to exclude infection • Growth factors and antibiotics if neutropenic (optional)	• Treated with supportive care such as antipyretics, antiemetics	• Acetaminophen and hypothermia blanket for the treatment of fever • Ibuprofen can be used as second treatment option for fever, if not contraindicated • Assess for infection using blood and urine cultures, and chest radiography • Empiric broad-spectrum antibiotics and filgrastim if neutropenic • Maintenance IV fluids for hydration • Symptomatic management of constitutional symptoms and organ toxicities • Consider tocilizumab or siltuximab[a] for persistent (lasting >3 days) and refractory fever
2	• Vigilant supportive care • IV fluids or one low dose pressor for hypotension • Oxygen for hypoxia • For patients without extensive comorbidities or younger pts: monitor cardiac and other organ function closely • For older pts or pts with extensive comorbidities: tocilizumab ± corticosteroids	• Supportive care as for grade 1 • IV fluid boluses and/or supplemental oxygen • Tocilizumab ± dexamethasone (or methylprednisolone equivalent)	• IV therapies • Hospitalization to manage CRS-related symptoms including fevers with associated neutropenia	• Supportive care – Manage fever and constitutional symptoms as in grade 1 – Supplemental oxygen – One or more IV fluid bolus of normal saline • Tocilizumab or siltuximab[a] for the treatment of hypotension that is refractory to fluid boluses – Vasopressors if hypotension persists after 2 fluid boluses and anti-IL-6 therapy, consider transfer to ICU, obtain echocardiogram, and initiate other methods of hemodynamic monitoring • Dexamethasone for high-risk pts or pts with persistent hypotension • Tocilizumab or siltuximab[a] ± corticosteroids and supportive care, as recommended for the management of hypotension, for hypoxia, and/or organ toxicity • Symptomatic management of organ toxicities, as per standard guidelines

[a]Siltuximab is not currently indicated for treatment of CRS for CAR T cell therapy.
ICU, intensive care unit.
References: 1. Lee DW, et al. Blood. 2014;124(2):188-195. **2.** Neelapu SS. *Hematol Oncol*. 2019;37(S1):48-52. **3.** Porter DL, et al. *Sci Transl Med*. 2015;7(303):303ra139. **4.** Neelapu SS, et al. *Nat Rev Clin Oncol.* 2018;15(1):47-62.

CRS Management

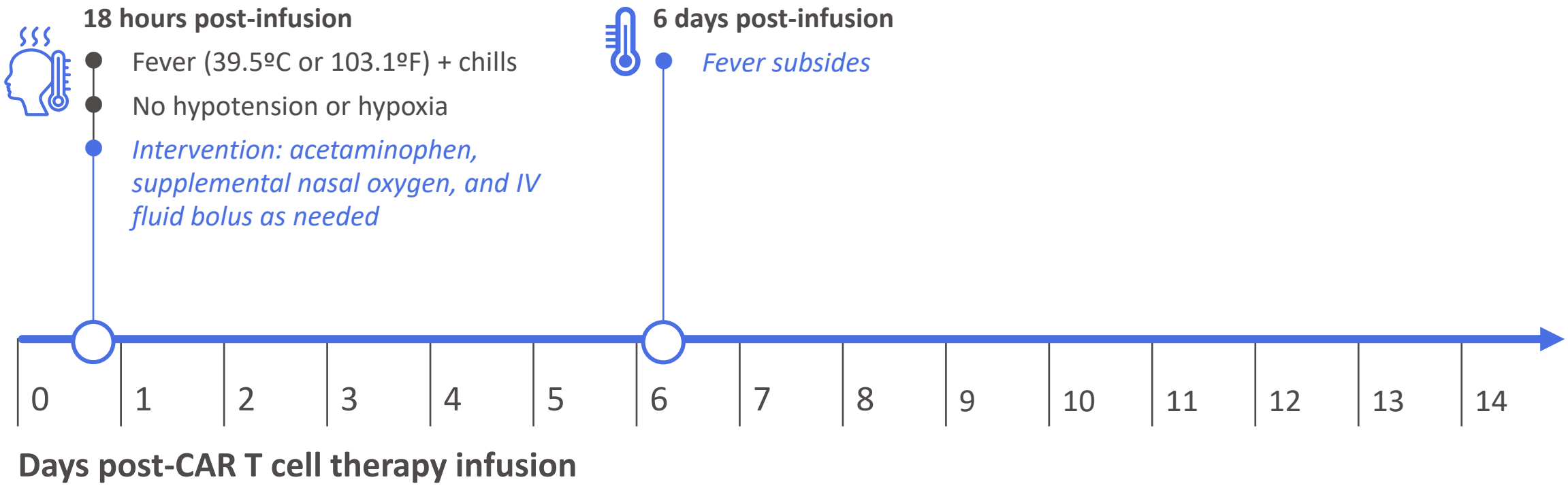
Several supportive care interventions may be utilized, depending on the severity of symptoms[1]

Intervention	When used for CRS management
Antipyretics (eg, acetaminophen)	To control fever
Supplemental oxygen	For hypoxia
Anti-infective agents	For patients with infections, febrile neutropenia, and/or who are hemodynamically unstable
IV fluids and vasopressors	As needed for hypotension

Reference: Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55.

Catherine: Acute Monitoring Period[a]

Short-term monitoring (≥14 days post infusion)



[a]Patient depicted is hypothetical.

Management Question 4

Catherine’s adverse events have resolved, and she is being discharged. How long must she stay within close proximity of the treatment center?

A. At least 1 week following CAR T cell infusion

B. At least 2 weeks following CAR T cell infusion

C. At least 4 weeks following CAR T cell infusion

Management Question 4

Catherine’s adverse events have resolved, and she is being discharged. How long must she stay within close proximity of the treatment center?

A. At least 1 week following CAR T cell infusion

B. At least 2 weeks following CAR T cell infusion

C. At least 4 weeks following CAR T cell infusion

The correct answer is B.

Post-infusion Monitoring

The practice of inpatient versus outpatient monitoring varies, depending on physician discretion, institutional guidelines, and CAR T cell products[1]

- Patients must remain within close proximity to the CAR T cell therapy treatment center for at least 2 weeks following infusion to ensure quick access to care, regardless of whether the patient received the CAR T cell therapy as an inpatient or outpatient[2,3]
- Depending on the patient, product, and center, inpatient monitoring may be required for a period of time[1,4]

- Under certain circumstances, outpatient administration and monitoring may be appropriate per the treating physician's discretion[1]
  - When this occurs, patients are usually observed in the treating center for a few hours after the CAR T cell therapy infusion to monitor for acute reactions; if none occur, they are permitted to leave the treatment center[4]
  - Hospitalization may be necessary if toxicities develop[4]

References: 1. Brudno JN, Kochenderfer JN. *Blood Rev.* 2019:34:45-55. **2.** US Food and Drug Administration. Accessed June 27, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor **3.** Neelapu SS, et al. *Nat Rev Clin Oncol*. 2018;15(1):47-62. **4.** Maus MV, Levine BL. *Oncologist*. 2016;21:608-617.

Catherine: Acute Monitoring Period[a]

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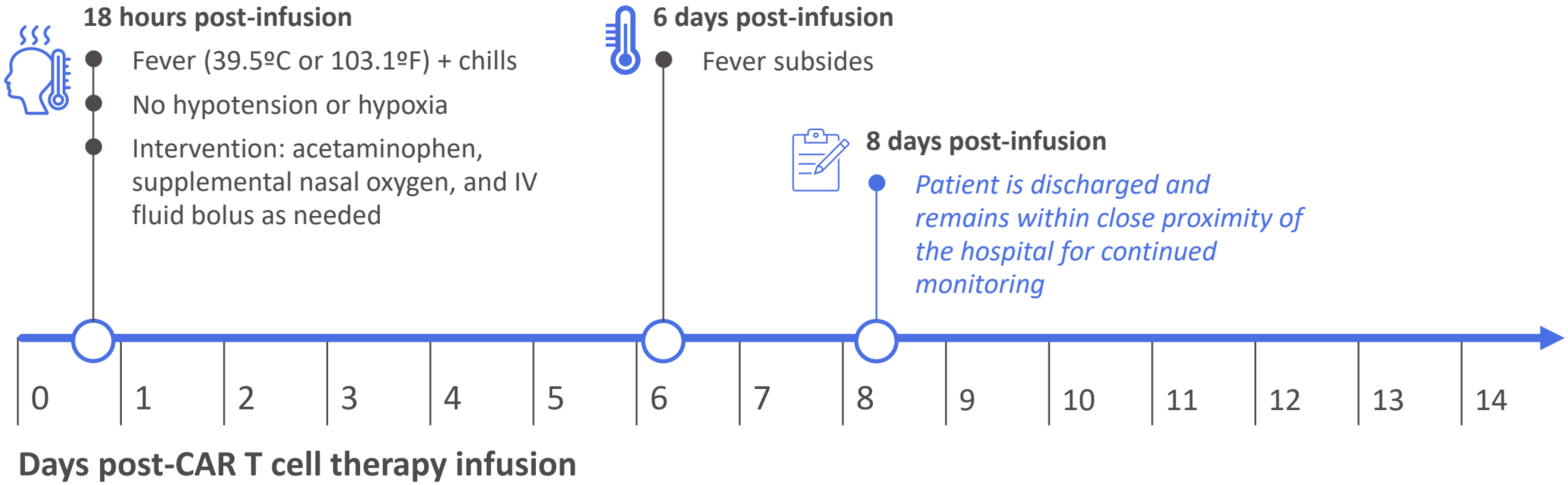


[a]Patient depicted is hypothetical.

PATIENT CASE

Catherine[a]: Monitoring and Long-term Follow-up

Patient identification | Apheresis | Bridging[b] | LDC and Infusion | **Monitoring and long-term follow-up**

Patient Notes:

- Eligible for CAR T cell therapy based on evaluation by her oncology team
- Patient decides to proceed with CAR T

- Completed without incident and cells sent to manufacturer

- Completed 16 days prior to lymphodepleting chemotherapy (LDC)

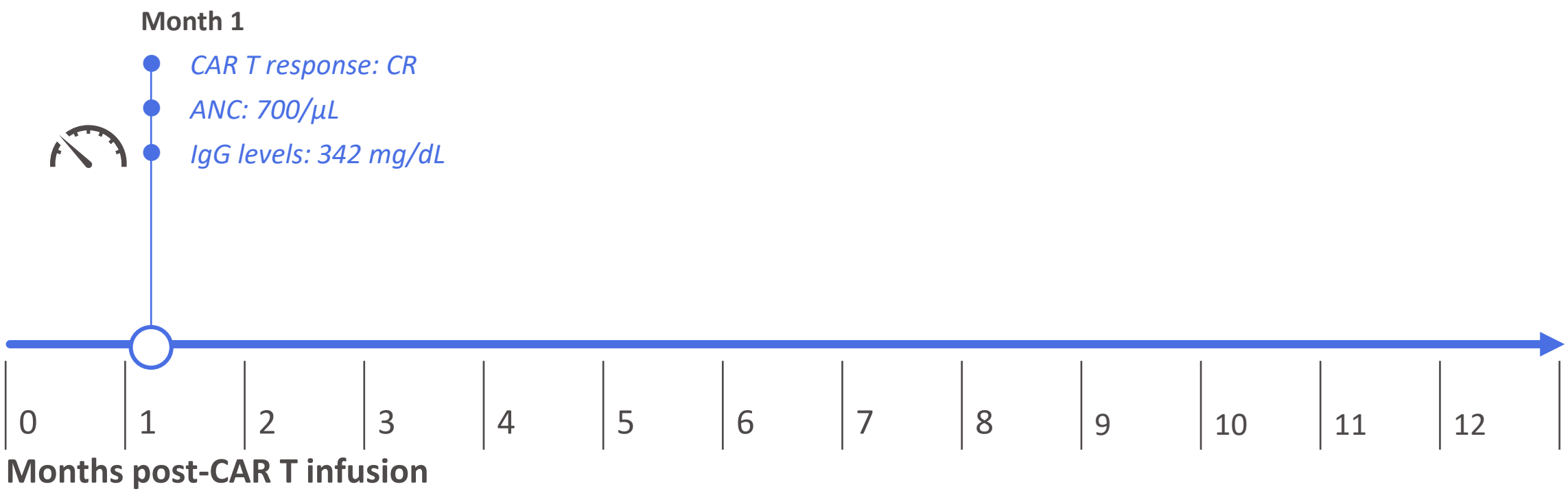
- LDC regimen: fludarabine + cyclophosphamide over 3 days
- Infection cleared
- CAR T cells infused (Day 1)
- Patient is monitored over the next several hours with no signs of acute reactions

- After adverse events resolve and **≥2-week monitoring period**, patient returns to primary oncologist
- CAR T cell therapy treatment team primary oncologist and maintain ongoing communication on the **long-term recovery**

[a]Patient depicted is hypothetical. [b]Not all approved CAR T cell therapies require bridging therapy; bridging therapy may be optional per physician's discretion.
LDC, lymphodepletion chemotherapy.

Catherine: Long-term Monitoring Period[a]

Long-term monitoring



Note: This patient case serves as an example, and results with CAR T cell therapy will vary.

[a]Patient depicted is hypothetical.
CR, complete response.

Management Question 5

At Catherine’s first monthly evaluation, her IgG level was 342 mg/dL. What type of care should be considered?

A. Intravenous IgG infusions

B. Growth factors

C. No treatment needed

Management Question 5

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A. Intravenous IgG infusions

B. Growth factors

C. No treatment needed

The correct answer is A.

Hypogammaglobulinemia

Understanding the Risk

- B cells produce antibodies that recognize foreign antigens and protect against infection[1]
- CAR T cells can kill healthy B cells in addition to malignant B cells (on-target, off-tumor effect)[1]
- This activity can lead to B-cell aplasia, chronic immunodeficiency, and hypogammaglobulinemia (IgG <400 mg/dL)[1]
- B-cell aplasia may persist in ongoing responders; it was observed for up to 1 and 2 years[2]:
  - In **50%** and **25%** of patients with **LBCL**, respectively
  - In **71%** and **59%** of patients with **B-ALL**, respectively

Monitoring and Follow-up Care

- Check immunoglobulin G (IgG) levels monthly[3]
- Consider monthly immunoglobulin infusions for patients who develop frequent infections, especially those with IgG <400 mg/dL[1]
- Given how long this complication can last, IgG replacement may be necessary[1]

Note: Institutional and product guidelines may vary[1]

B-ALL, B-cell acute lymphoblastic leukemia.

References: 1. Buitrago J, et al. *Clin J Onc Nurs*. 2019;23(2):42-48. **2.** Puckrin R, Jamani K, Jimenez-Zepeda VH. *Eur J Haematol*. 2024;112(1):41-50. **3**. Callahan C, et al. *Clin J Onc Nurs*. 2019;23(2):35-41.

Catherine: Long-term Monitoring Period[a]

Long-term monitoring

Note: This patient case serves as an example, and results with CAR T cell therapy will vary.

[a]Patient depicted is hypothetical.
CR, complete response.

Management Question 6

Catherine is at risk of infection. When can you consider offering vaccines?

A. Consider inactivated vaccines ≥6 months after CAR T cell therapy

B. Consider inactivated vaccines ≥2 months after CAR T cell therapy

C. Consider live vaccines ≥12 months after CAR T cell therapy and immune reconstitution

D. Both A and C

E. Both B and C

Management Question 6

Catherine is at risk of infection. When can you consider offering vaccines?

A. Consider inactivated vaccines ≥6 months after CAR T cell therapy

B. Consider inactivated vaccines ≥2 months after CAR T cell therapy

C. Consider live vaccines ≥12 months after CAR T cell therapy and immune reconstitution

D. Both A and C

E. Both B and C

The correct answer is D.

Infections

Vaccination

- Although responses to vaccines may be lower in patients that have received CAR T cell therapy compared to immunocompetent individuals, vaccination may reduce infection frequency and severity[1,2]

Example Guidance from ASTCT Committee

To prevent infections in patients that received CAR T cell therapy, consider whether the following are appropriate[2]:

- **3 months** after CAR T cell therapy: consider seasonal influenza vaccine and SARS-CoV-2 vaccines
- **6 months** after CAR T cell therapy: consider inactivated vaccines
- **1 year** after CAR T cell therapy: consider live and non-live adjuvant vaccines

Example Vaccination Recommendations per ASTCT Committee[2]

	Months after CAR T cell therapy					
	>3 mo	>6 mo	>8 mo	>10 mo	>12 mo	>18 mo
Influenza	✓					
RSV	✓					
SARS-CoV	✓					
Pneumococcus		✓	✓	✓		
Diphtheria, tetanus, and acellular pertussis		DTap	Td	Td		
Hepatitis A		✓			✓	
Hepatitis B		✓	✓		✓	
Shingrix					✓	✓

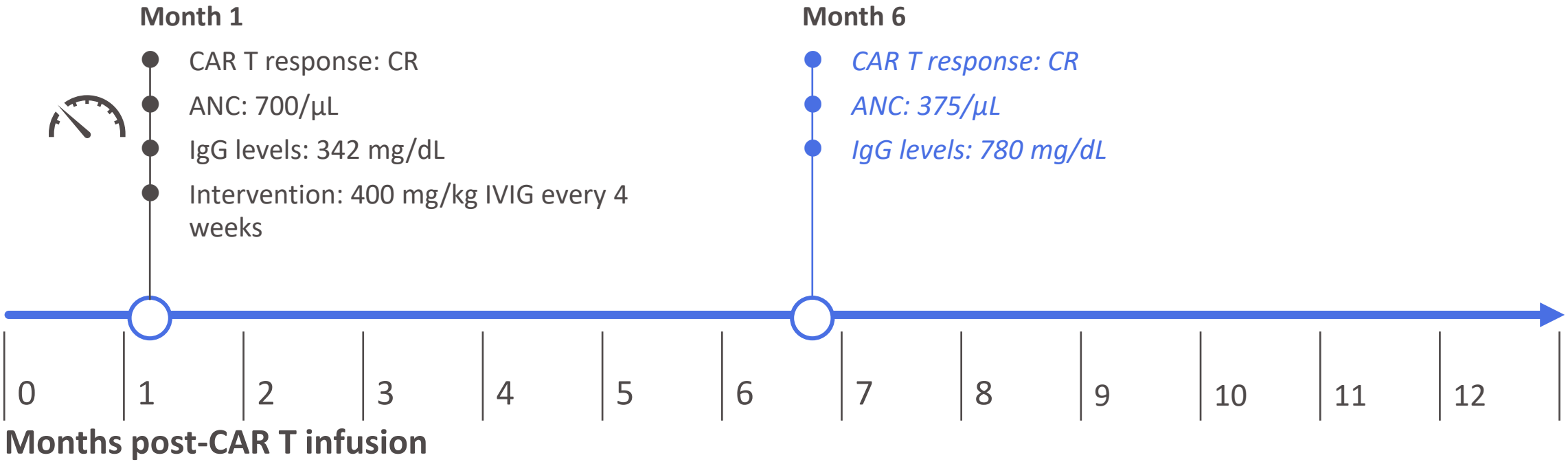
Follow institutional guidance and recommendations from the CAR T cell treatment center for AE management in patients after CAR T cell therapy.

Dtap, diphtheria, tetanus, and acellular pertussis; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Td, tetanus-diphtheria.

References: 1. Hayden PJ et al. *Ann Oncol*. 2022;33(3):259-275. **2.** Shahid Z et al. *Transplant Cell Ther*. 2024;30(10):955-969.

Catherine: Long-term Monitoring Period[a]

Long-term monitoring



Note: This patient case serves as an example, and results with CAR T cell therapy will vary.

[a]Patient depicted is hypothetical.

Management Question 7

Catherine’s neutropenia worsens through her Month 6 visit. What treatment should you consider?

A. Filgrastim

B. Antibacterial and antifungal prophylaxis

C. Thrombopoietin receptor agonist

D. Both A and B

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A. Filgrastim

B. Antibacterial and antifungal prophylaxis

C. Thrombopoietin receptor agonist

D. Both A and B

The correct answer is D.

Cytopenias

Monitoring and Follow-up Care

- Monitor blood counts weekly through 60 days post-infusion or as indicated until recovery[1]
- Provide transfusion and/or growth factor support to patients with severe cytopenias, when appropriate.[1] Support may include:
  - Red blood cell transfusions[2]
  - Platelet transfusions[2]
  - Filgrastim[2]

Note: Institutional and product guidelines may vary.[3]

References: 1. Buitrago J, et al. *Clin J Onc Nurs*. 2019;23(2):42-48. **2.** Brudno JN, Kochenderfer JN. *Blood*. 2016;127(26):3321-3330. **3.** Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55.

Infections

Monitoring and Follow-up Care

- Closely monitor patients who become febrile after infusion for signs of infection. Keep in mind that fever may also be a sign of CRS[1]
- Treatment of neutropenia and/or bacterial prophylaxis at onset of severe neutropenia may mitigate or prevent infections[2]

Both expert consensus and evidence-based guidelines have been developed to support revaccination after CAR T cell therapy[3,4]

Example Guidance from ASTCT Committee

To support patients at risk for infection (eg, immunosuppression, presence of cytopenias) consider whether the following are appropriate[5,6]:

- **Antiviral prophylaxis** for ≥6 months after CAR T cell therapy
- **Antibacterial and antifungal prophylaxis** as needed (eg, in high-risk patients, patients with prolonged neutropenia)

Common practice is for centers to extrapolate prophylaxis recommendations from HSCT experiences and expert opinion, although there may be variability in agent, timing, and duration.[5]

Follow institutional guidance and recommendations from the CAR T cell treatment center for AE management in patients after CAR T cell therapy.

ASTCT, American Society for Transplantation and Cellular Therapy.

References: 1. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019:34:45-55. **2.** Dahunsi D. *Clin Hematol Int*. 2025 Mar 26;7(1):47-54. **3.** Kamboj M, et al. *J Clin Oncol*. 2024 May 10;42(14):1699-1721. **4.** Reynolds G, et al. *Transpl Infect Dis.* 2023 Nov;25 Suppl 1(Suppl 1):e14109. **5.** Shahid Z et al. *Transplant Cell Ther*. 2024;30(10):955-969. **6.** Hayden PJ et al. *Ann Oncol*. 2022;33(3):259-275.

Key Points

- Patients may be considered for CAR T cell therapy if they have a disease as defined in commercial indication or in clinical trial, adequate T cell count, no active/uncontrolled infections, sufficient performance status and organ function*

  *Exact criteria may also vary based on the malignancy, treatment, and CAR T cell product

- CRS and neurotoxicity are serious, potentially life-threatening toxicities that require careful monitoring

- Several long-term toxicities may be associated with CAR T cell therapy, including cytopenias, infections, hypogammaglobulinemia, and others, which require periodic long-term monitoring and appropriate management

Thank you for completing this module of CAR T Academy

We hope you found it informative and educational

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