CAR T-cell Therapy for Multiple Myeloma: Who's a Good Candidate

Celebrating a Second Chance at Life Survivorship Symposium

May 3-9, 2025

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HealthOne's Sarah Cannon Cancer Institute at Presbyterian St. Luke's Medical Center

Disclosures

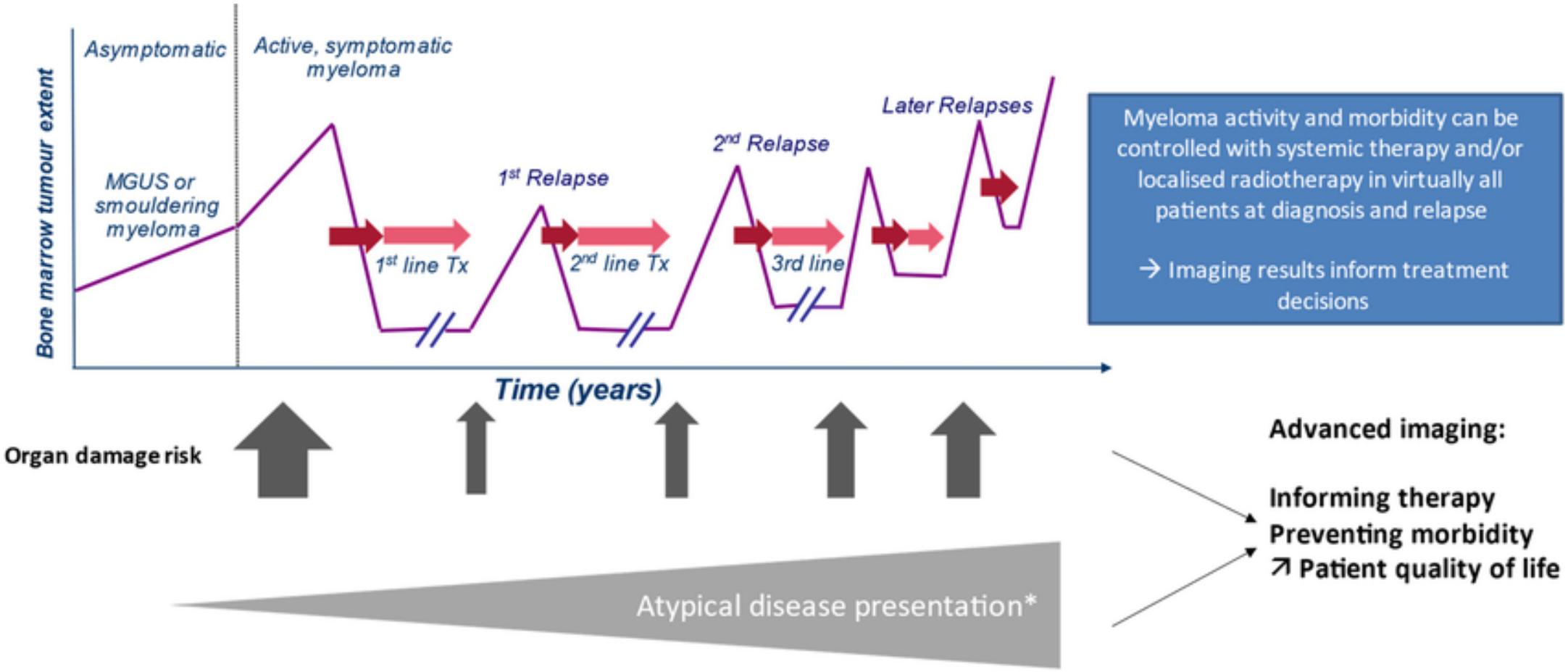
- Johnson and Johnson: Advisory board
- Legend: Advisory board

Learning Objectives

- Why CAR T?
  - A history of myeloma treatment.
- What is a CAR T?
- Steps involved in undergoing CAR T-cell therapy.
- Potential outcomes after CAR T-cell therapy: does it cure cancer?
- Potential short- and long-term risks associated with CAR T-cell therapy.
- Impact of CAR T-cell therapy on quality of life
- Who’s a good candidate for CAR T-cell therapy?

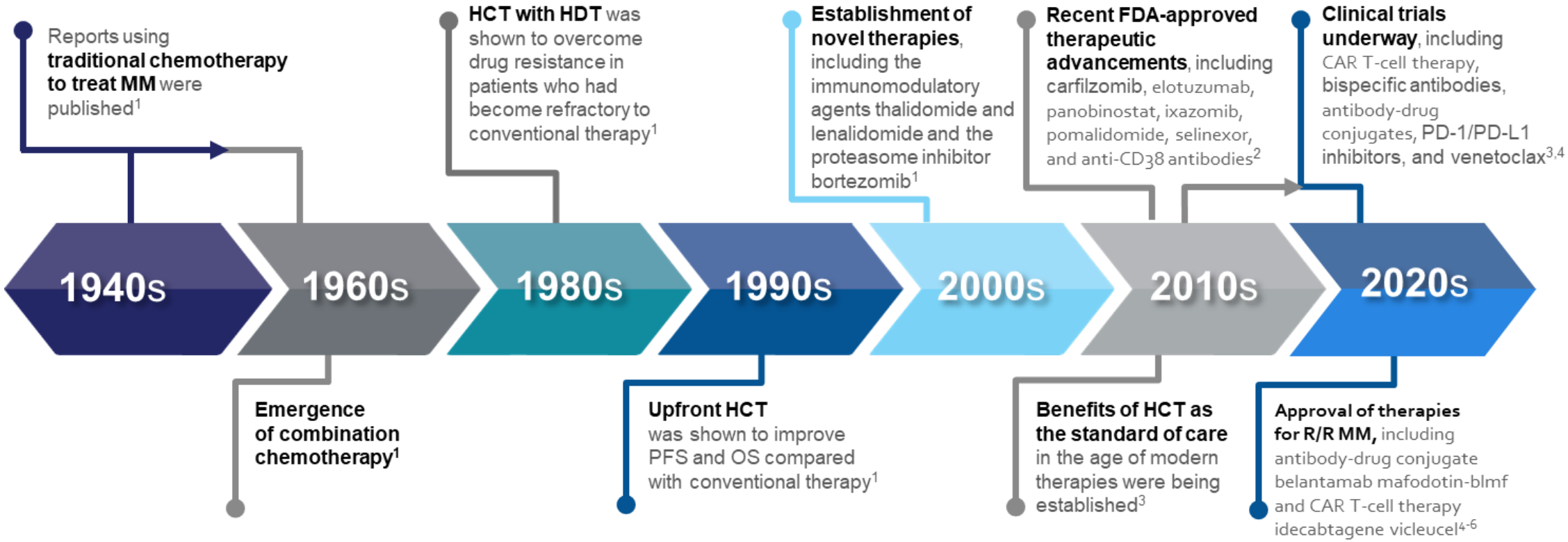
A History of Myeloma Treatment

Relapsed/Refractory disease



*Extramedullary disease, asecretory/oligosecretory disease

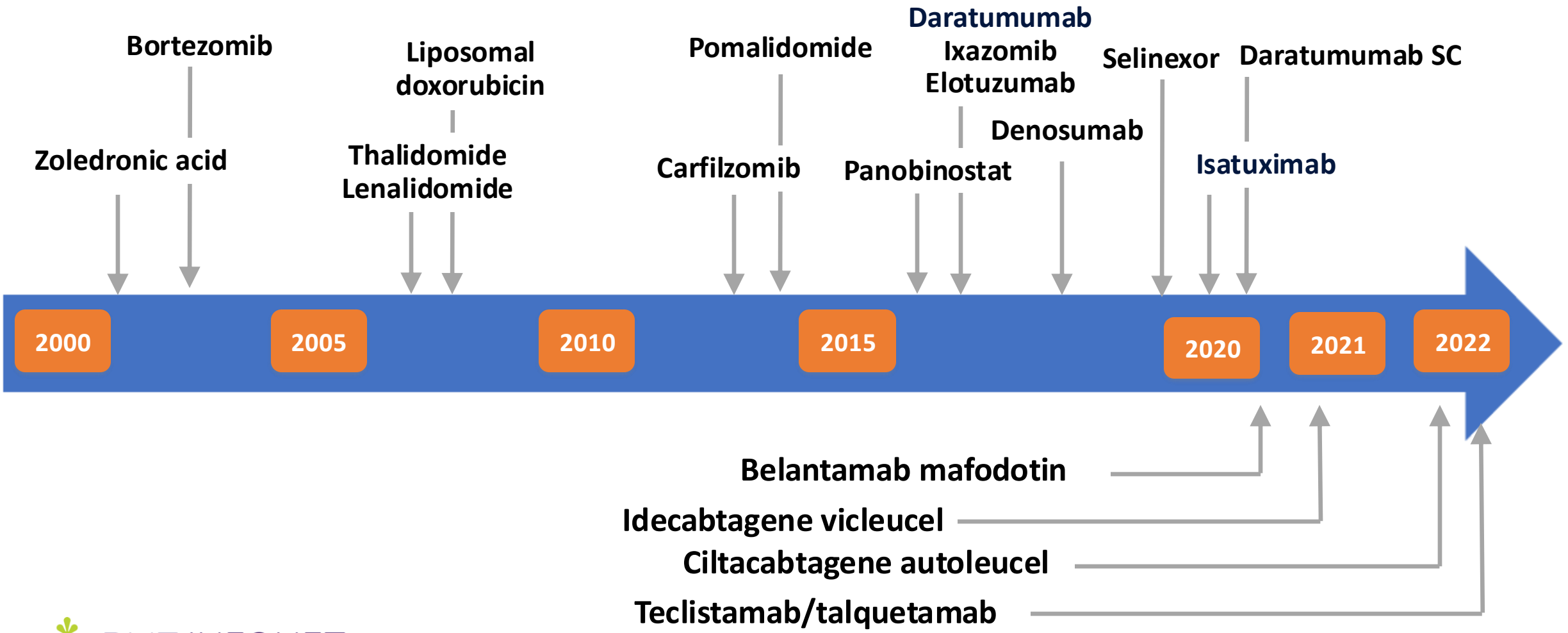
History of MM Treatments



CAR, chimeric antigen receptor; HDT, high-dose therapy; OS, overall survival; PD-1, programmed cell death 1; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; R/R, relapsed/refractory.

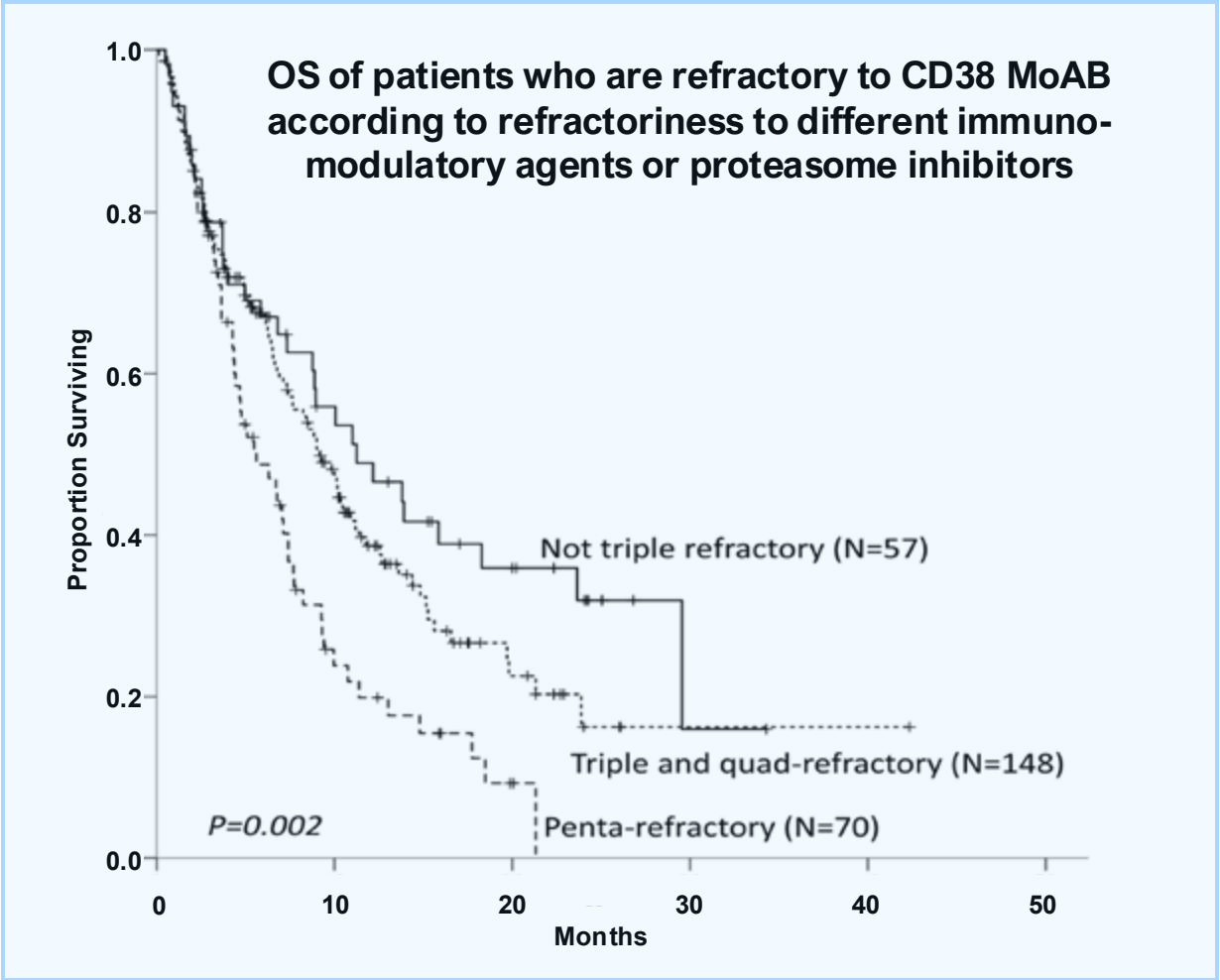
1. Laubach J, et al. *Annu Rev Med.* 2011;62:249-264. **2.** Rajkumar SV. *Am J Hematol.* 2020;95(5):548-567. **3.** Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905. **4.** Zanwar S, et al. *Blood Cancer J.* 2020;10(8):84. doi: 10.1038/s41408-020-00350-x. **5.** US Food and Drug Administration. FDA granted accelerated approval to belantamab mafodotin-blmf for multiple myeloma. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma. Updated August 6, 2020. Accessed May 6, 2021. **6.** US Food and Drug Administration. FDA approves first cell-based gene therapy for adult patients with multiple myeloma. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cell-based-gene-therapy-adult-patients-multiple-myeloma. Updated March 27, 2021. Accessed May 17, 2021.

Myeloma Drugs Approved Since 2000



Remains Need for New Treatment

- MAMMOTH STUDY
- MM refractory to anti-CD38 monoclonal antibodies (MoAB)
- Proteosome inhibitor (PI)
  - Bortezomib
  - Carfilzomib
- Immunomodulatory drug (IMiD)
  - Lenalidomide
  - Pomalidomide

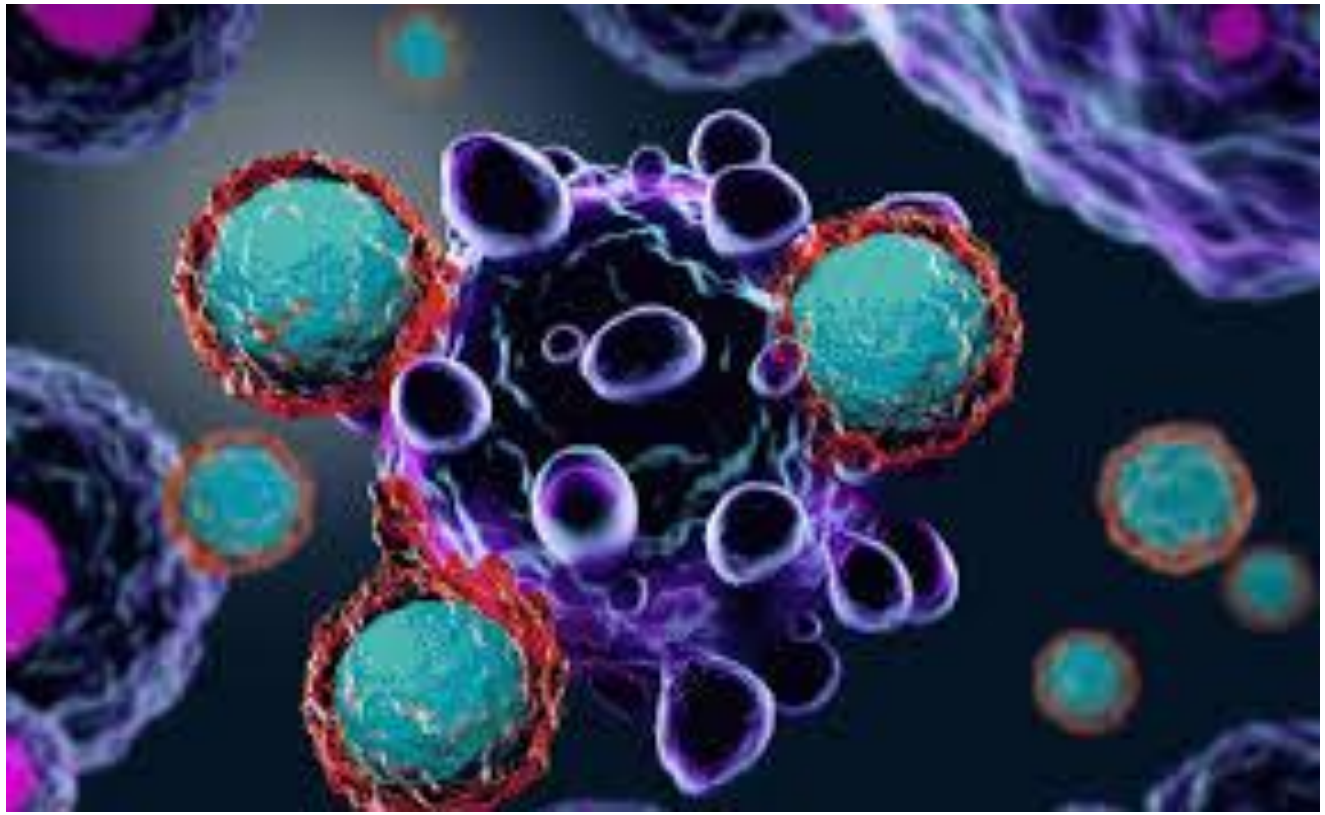


Gandhi UH, et al. *Leukemia*. 2019;33(9):2266–2275.

CAR T: What and How?

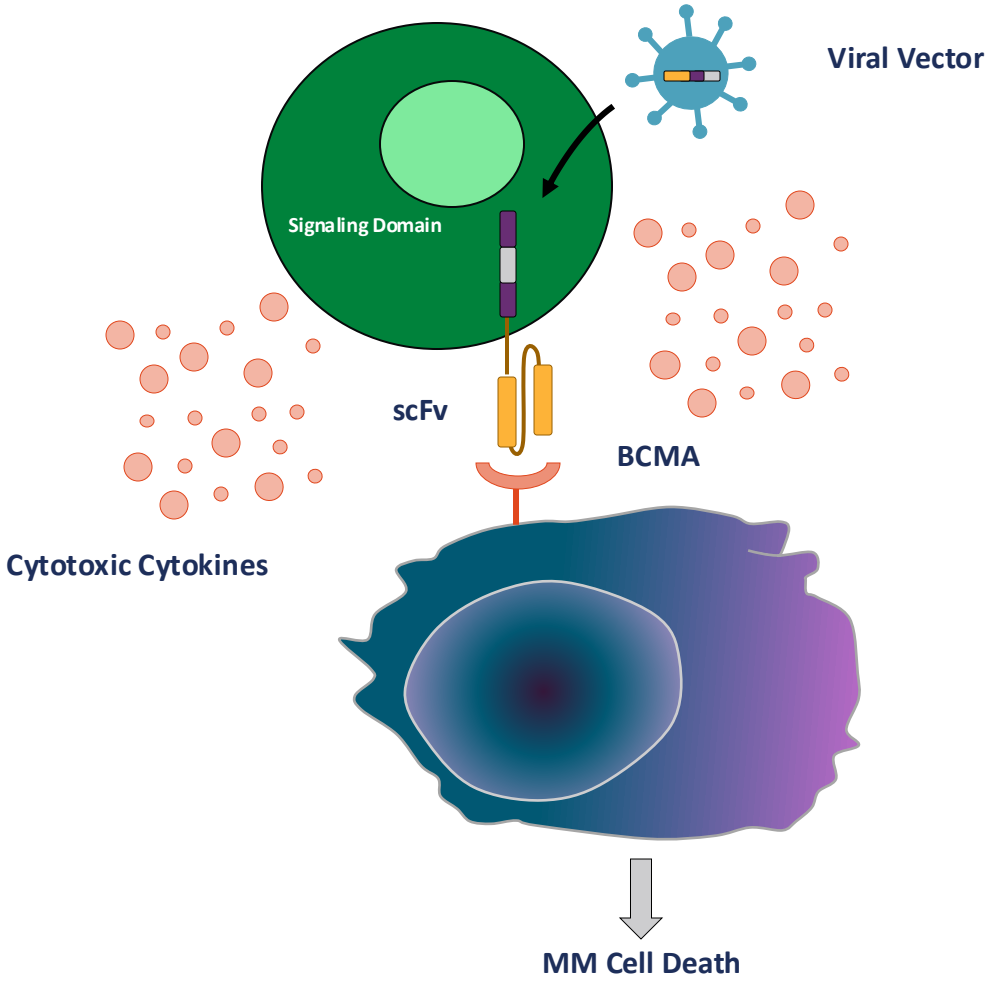
Immune Effector Cell Therapy

- Treatments that harness the body's own immune system to fight cancer
- White blood cells such as T cells used to target cancer
- Bispecific antibodies link cancer cell and T cell
- CAR T cells



CAR T Cell

- Chimeric Antigen Receptor T cell
- Patient's own T cells are modified to grow a new receptor
- New receptor allows T cell to target a protein on a cancer cell
- Protein or antigen needs to be unique to the type of cancer
- Myeloma: B cell maturation antigen (BCMA)

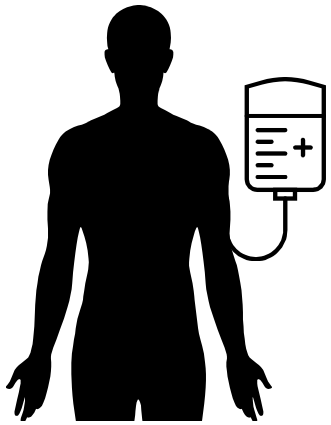


Yu. J Hematol Oncol. 2020;13:1.

CAR T Cell Treatment Timeline

Leukapheresis

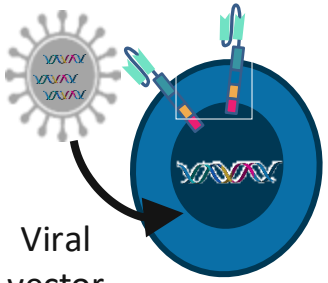
Collect patient's white blood cells

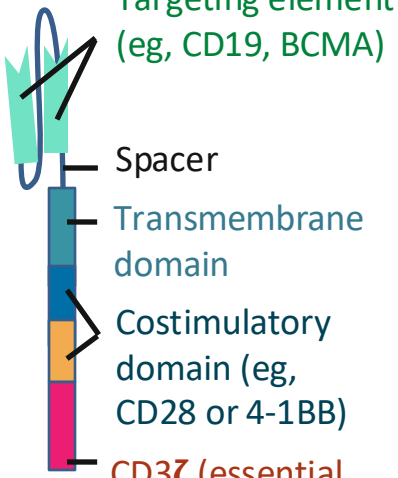


Manufacturing

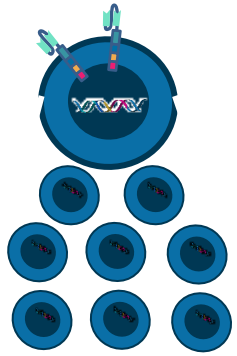
Isolate and activate T-cells

Engineer T-cells with CAR gene





Expand CAR T-cells

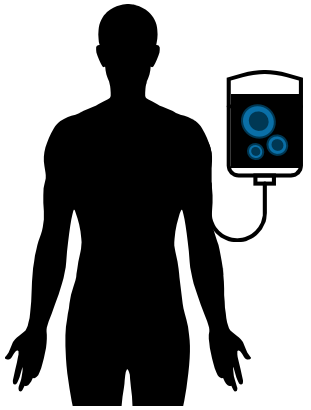


Median manufacturing time: 17-28 days

Patients undergo lymphodepleting (and possibly salvage/bridging) therapy

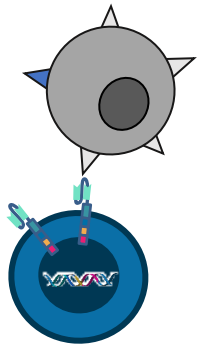
Infusion

Infuse same patient with CAR T-cells



Activity

eg, CD19, BCMA



Majors. EHA 2018. Abstr PS1156. Lim. Cell. 2017;168:724. Sadelain. Nat Rev Cancer. 2003;3:35. Brentjens. Nat Med. 2003;9:279. Park. ASH 2015. Abstr 682. Axicabtagene ciloleucel PI. Tisagenlecleucel PI.

Slide credit: clinicaloptions.com

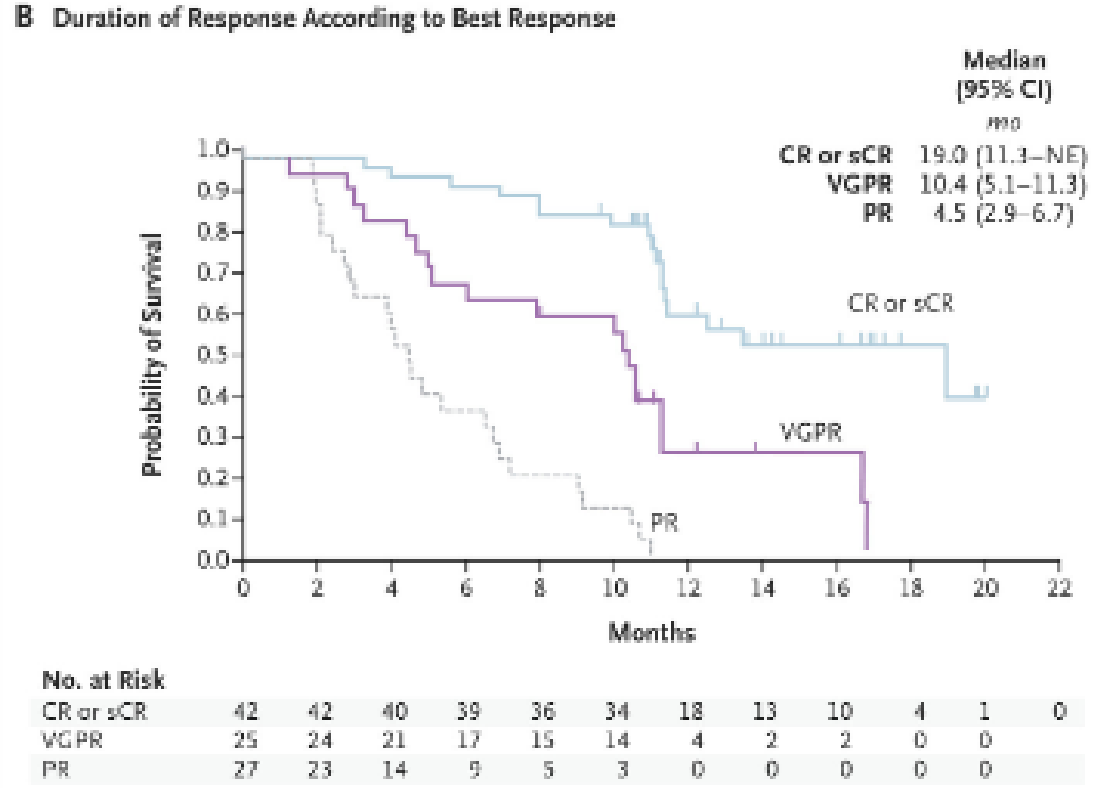
CAR T-Cell Therapy Patient Journey

Apheresis	1	1 day	Immune cells from the patient are collected
(Manufacturing) Patients return home	2	4–6 weeks	Standard of care therapy is permitted until CAR T cells are ready for infusion
Lymphodepletion (chemotherapy)	3	3 days	Fludarabine and Cytoxan are used to create “immunologic space” to CAR T cells to expand
Infusion (Hospitalization or daily outpatient monitoring)	4	2 weeks	Required period close to CAR-T center Caretaker support needed
Close Follow up	5	Within 2 weeks	

Outcomes:
Does CAR T cure cancer?

Late Line Abecma: KarMMa-2 Trial

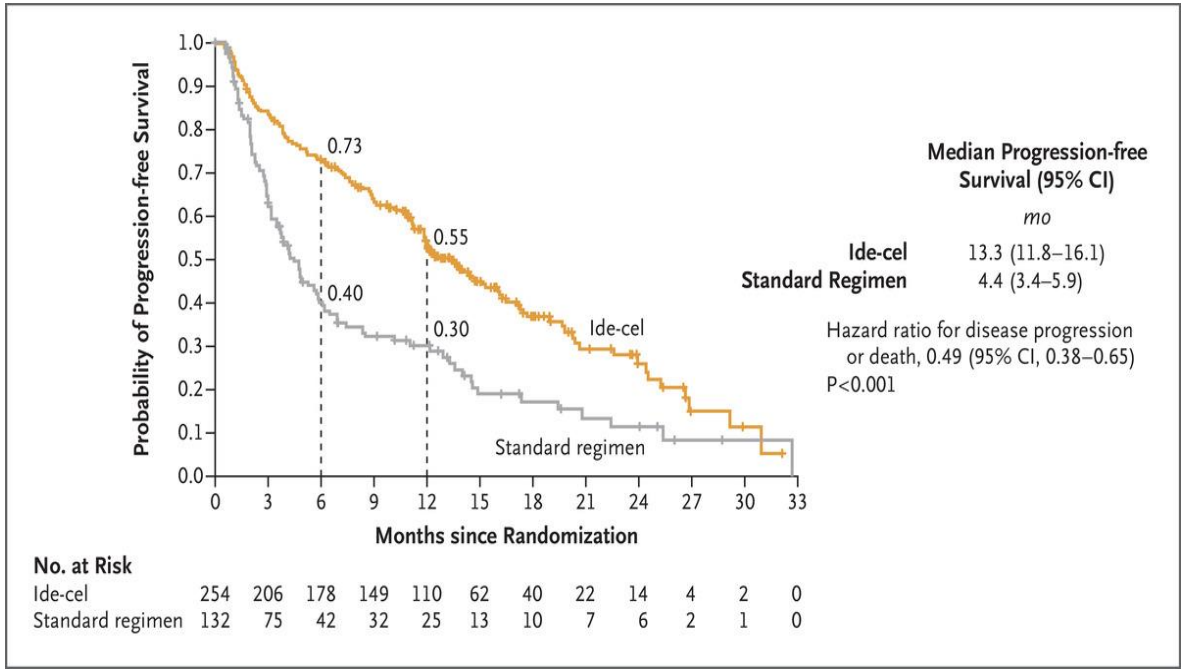
- Average 6 prior lines of treatment
  - CD38 mab (dara, isa)
  - PI (bortezomib, carfilzomib)
  - IMiD (lenalidomide, pomalidomide)
- Overall response: 81%
- Complete remission rate: 28%
- Remission lasts longer the better the response to treatment
  - Complete remission: 19 months
  - Partial remission (50%) better: 4.5 months



Munshi NC et al. N Engl J Med 2021;384:705-716

Earlier Line Abecma: KarMMa-3 Trial

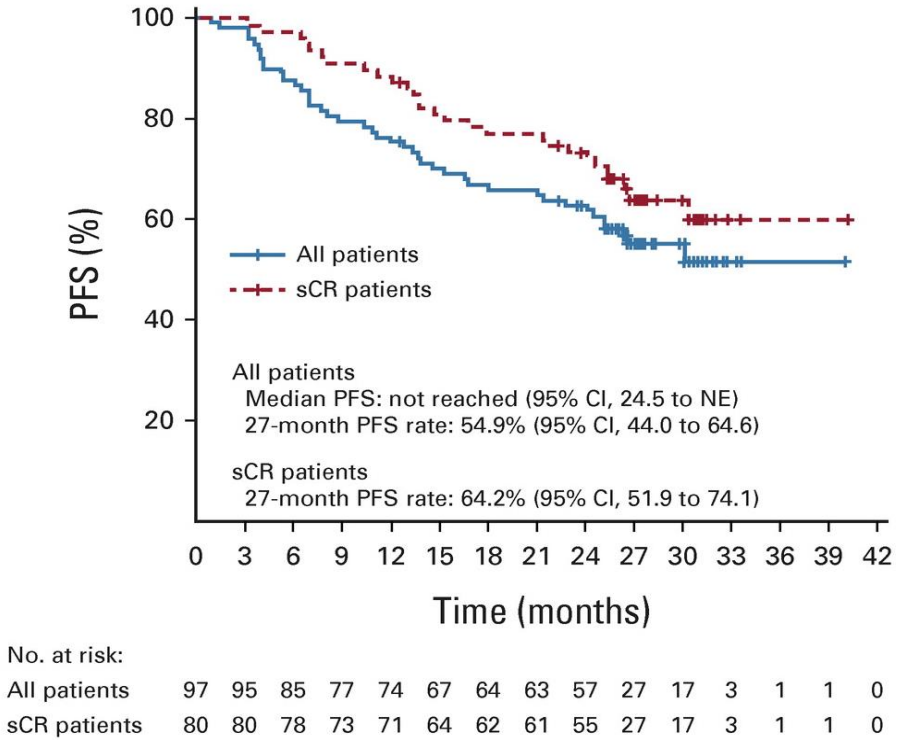
- Abecma vs selected standard of care regimen in patients with 2-4 prior lines of therapy including:
  - CD38 mab (dara, isa)
  - PI (bortezomib, carfilzomib)
  - IMiD (lenalidomide, pomalidomide)
- 65% triple refractory
  - All types of drugs had stopped working
- Standard of care: 4.4 months for MM to come back
- Ide cel: 13.3 months for MM to come back



P Rodriguez-Otero et al. N Engl J Med 2023;388:1002-1014.

Late Line Carvykti: CARTITUDE-1 Trial

- Average 6 prior lines of treatment
  - CD38 mab (dara, isa)
  - PI (bortezomib, carfilzomib)
  - IMiD (lenalidomide, pomalidomide
- Overall response rate: 98%
- Complete remission: 83%
- On average, myeloma under control for 35 months
- Minimal residual disease negative: no average relapse rate at 3 years

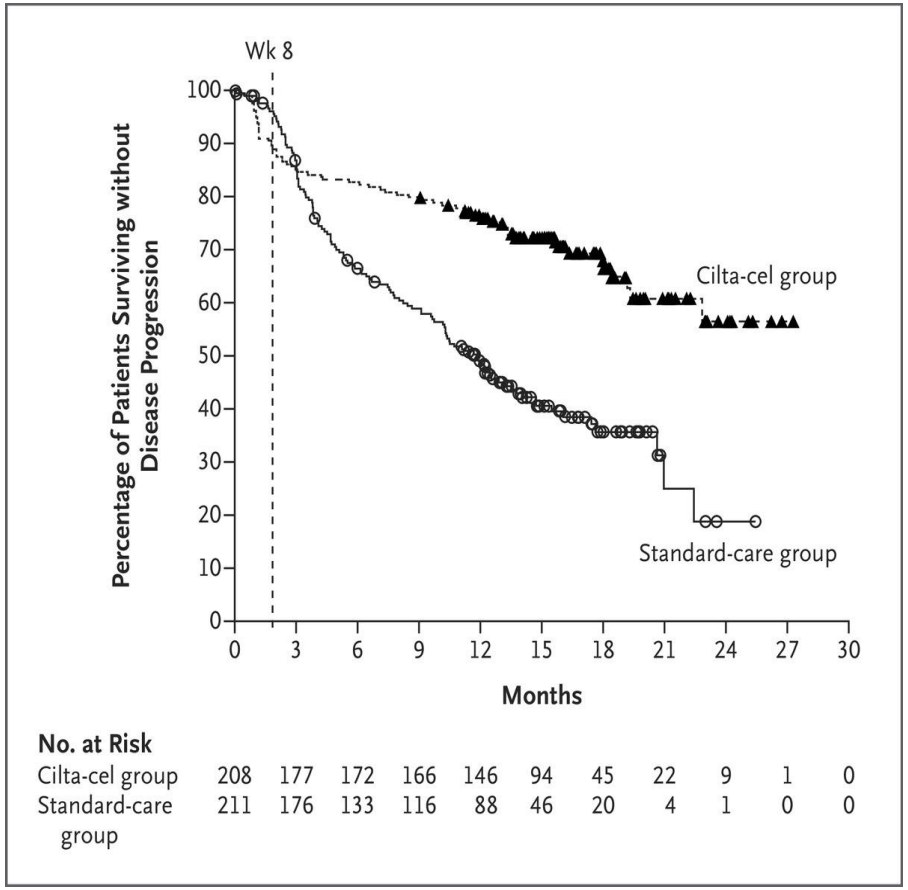


J Berdeja et al. Lancet 2021;398:314-324.

Martin et al. Journal Clin Oncol 2022; 41 (6): 1265-1274

Earlier Line Carvykti: CARTITUDE-4 Trial

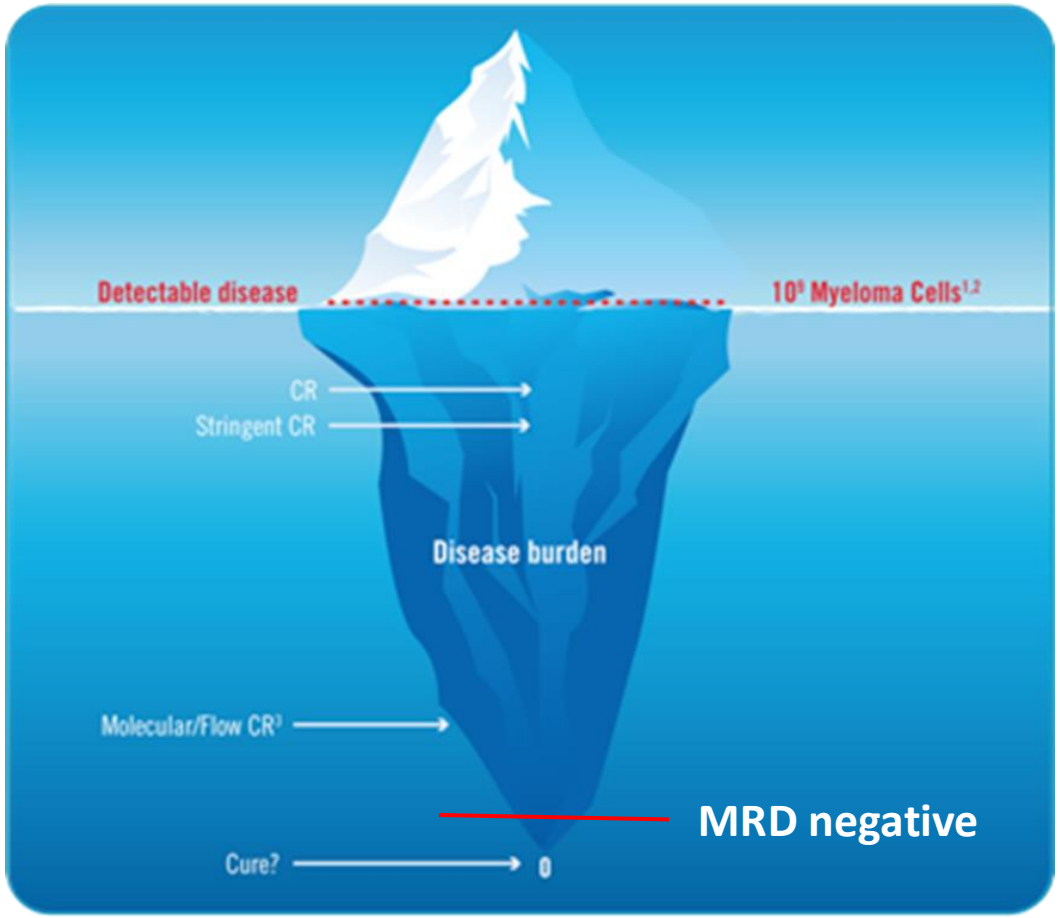
- Carvykti vs standard of care in MM with 1-3 prior lines of therapy
- Lenalidomide refractory
- 15% triple refractory
- CAR T has better outcomes than standard of care (SOC)
  - CAR T: no average relapse rate at 30 month
  - SOC: 80% at 30 months



J San-Miguel et al. N Engl J Med 2023;389:335-347.

Does CAR T cure cancer?

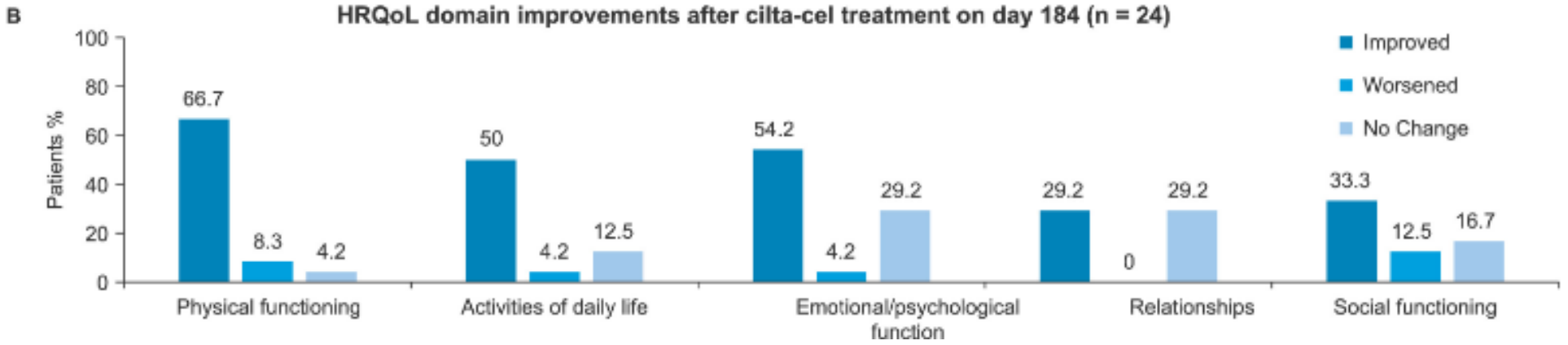
- Probably not
- Long periods of disease control without treatment.
- Deeper the response the better!
- Responses are deeper and last longer the earlier we use CAR T in treatment of myeloma.
- Studies looking at newly diagnosed myeloma patients.



Quality of Life and Side Effects

Quality of Life

- 6-month post-treatment follow-up
  - About 60% reduction in pain, fatigue, gastrointestinal issues, and neuropathy
  - Expectations of treatment met: 71%
  - Expectations of treatment better than expected: 21%
  - CAR T better than previous treatments: 71%

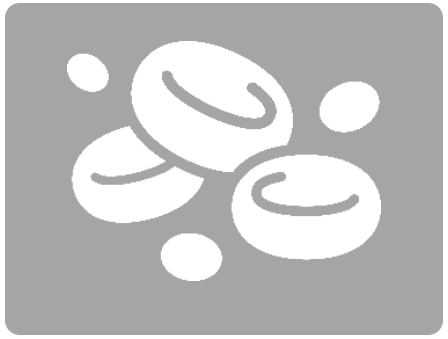


Cohen, A., et al. Clin Lymphoma Myeloma Leuk. 2023;(1):68-77.

CAR T: Expected Toxicities

Cytokine release syndrome (CRS)

Neurotoxicity (ICANS)



Cytopenias

Infections

	CRS	ICANS
Onset	1–9 days after CAR T-cell infusion	2–9 days after CAR T-cell infusion
Duration	5–11 days	3–17 days
Symptoms	• Fever • Difficulty breathing • Dizziness • Nausea • Headache • Rapid heartbeat • Low blood pressure	• Headache • Confusion • Language disturbance • Seizures • Delirium • Cerebral edema
Management	• Actemra (tocilizumab) • Corticosteroids • Supportive care	• Antiseizure medications • Corticosteroids

*Based on the ASTCT consensus; †Based on vasopressor; ‡For adults and children >12 years; §For children ≤12 years; ‖Only when concurrent with CRS

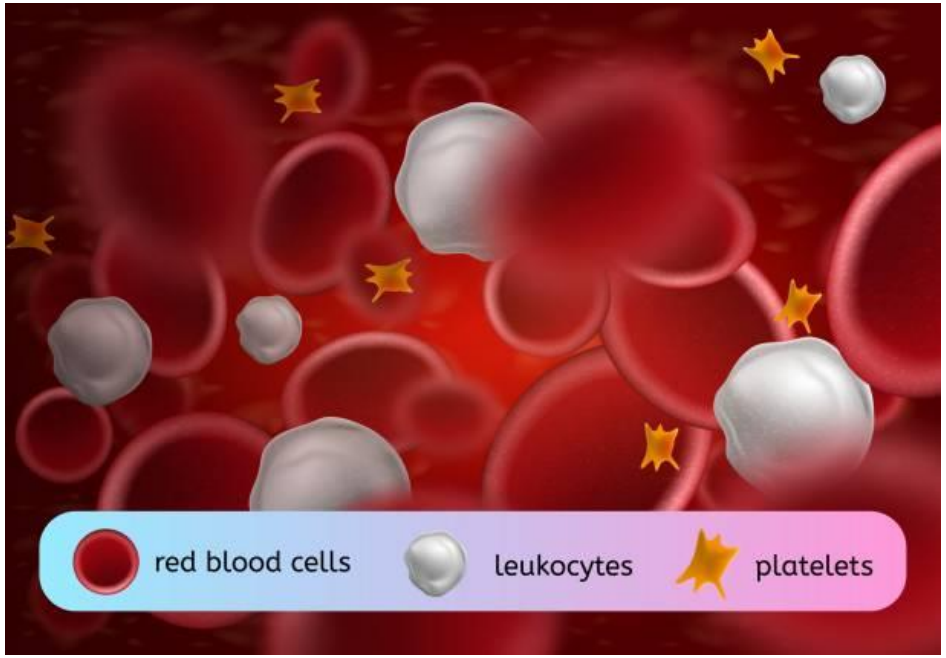
Xiao X et al. *J Exp Clin Cancer Res.* 2021;40(1):367. Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25:625; Shah N et al. *J Immunother Cancer*. 2020;8:e000734.

Late Side Effects

- Low blood counts (60%)
- Infections (60%)
- Hemophagocytic Lymphohistiocytosis (2%)
- Hypogammaglobulinemia (100%)
  (low antibody levels)
- Late neurotoxicity (10%)
- Another type of cancer (4%)

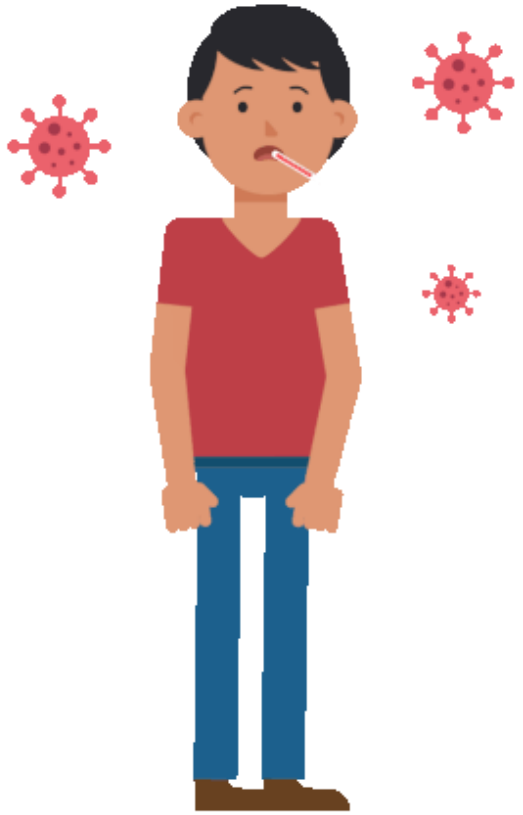
Low Blood Counts

- 3 to 6 months post CAR T
- Monitor blood counts weekly
- Ok to receive transfusions
- Ok to receive shots to boost white blood cell count
- Bone marrow biopsy may be needed
- Stem cell boost may be needed



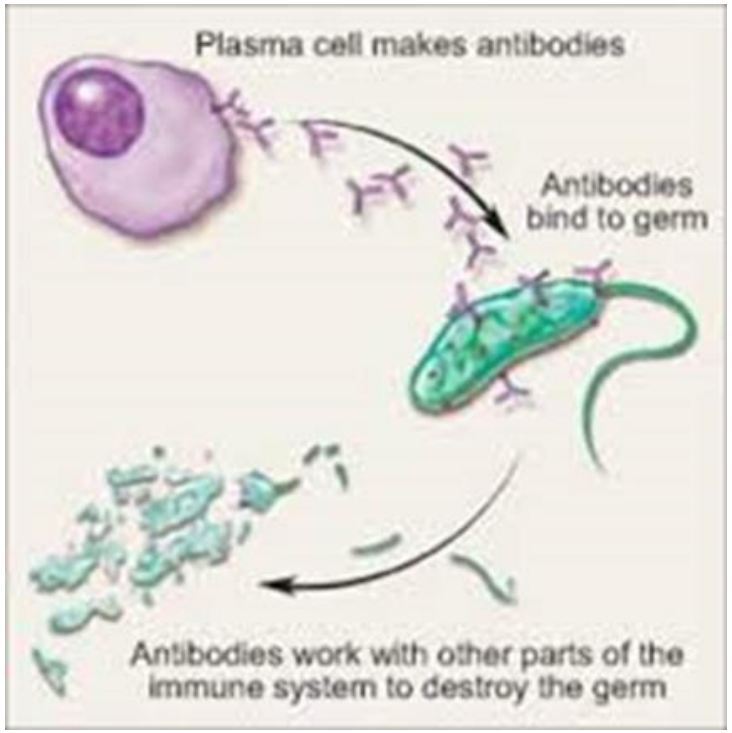
Infections

- Increased risk of infection for up to 18 months
- Caused by low normal B lymphocytes (type of white blood cell)
- Antivirus medication for one year
- PJP prevention medication for one year
- May need anti mold medication
- Look for an infection when you have a fever



Hypogammaglobulinemia

- Low antibody levels
- Lasts for at least 6 to 12 months or longer
- IGG levels checked monthly
- Administer IVIG for IGG level less than 400
- If the patient has frequent infections, administer IVIG for IGG level less than 600



Hemophagocytic Lymphohistiocytosis (HLH)

- White blood cells become SUPER activated
- Severe inflammation
- Elevated liver tests, low blood counts, big liver or spleen, rash, confusion, fever.
- SEE YOUR CAR T DOCTOR IMMEDIATELY!
- Specialized tests and treatment
- Very rare: happens early and less than 2% of the time

Late Neurologic Toxicities

- Guillian-Barre syndrome
- Symptoms that look like Parkinson's Disease
- Slow thinking
- Confusion
- Cranial nerve palsies
- Visional changes
- Weakness

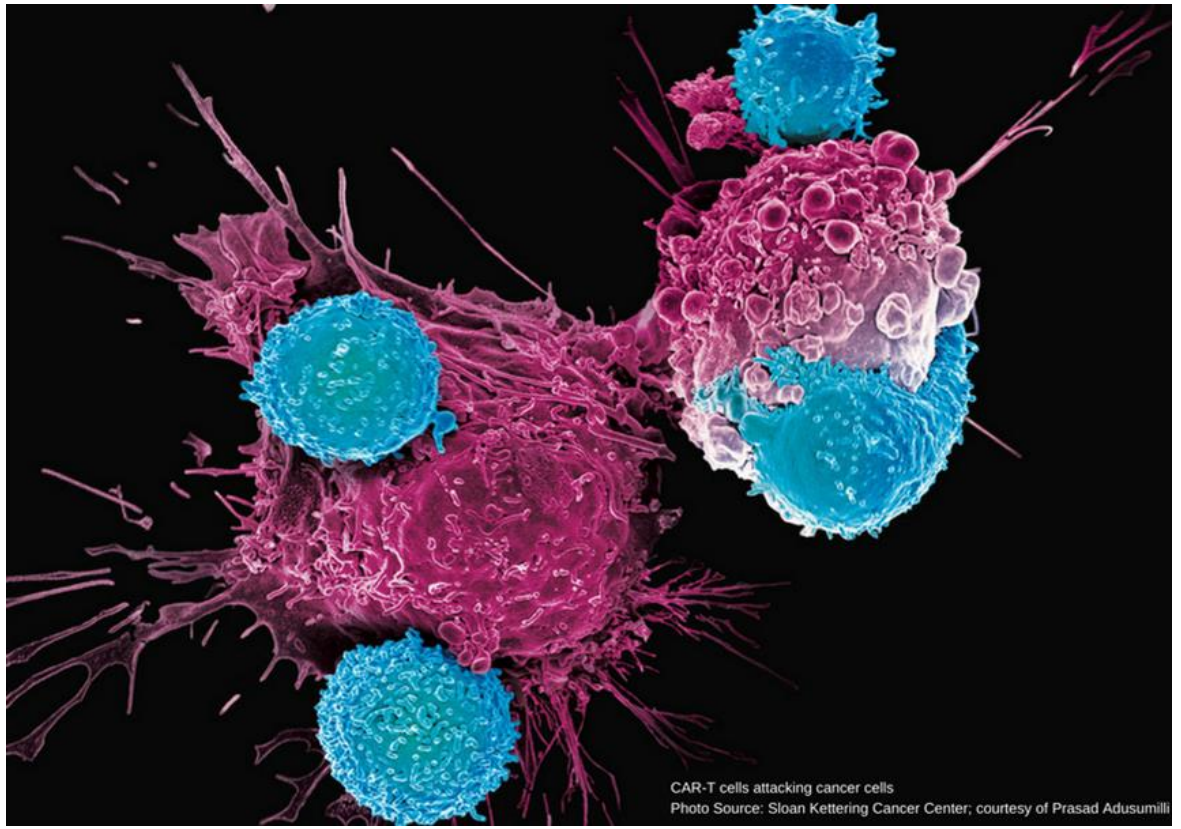
Who is a candidate for CAR T?

CAR T Candidate

- RELAPSED myeloma
- One previous treatment and REFRACTORY to IMiD
- Two previous treatments including CD38 ab, IMiD, PI
- Healthy organs (good kidneys, lungs and heart)
- Able to care for yourself independently
- Have a caregiver available for 30 days
- Next best treatment is always available on a clinical trial!

Final Thoughts

- CAR T earlier in treatment for deeper and longer responses
- Better understanding of which patients are going to have problems
- Better management and PREVENTION of problems!
- Off the shelf products
- Combination therapies


CAR-T cells attacking cancer cells
Photo Source: Sloan Kettering Cancer Center; courtesy of Prasad Adusumilli

Questions?

Tara Gregory, MD
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HealthOne's Sarah Cannon Cancer Institute at Presbyterian St. Luke's Medical Center

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