JADPRO Clinical Case Series

Management of Patients With Multiple Myeloma Receiving CAR T-Cell Therapy: Timing, Adverse Events, and Coordination of Care

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Program Agenda

- Evaluate treatment options for relapsed/refractory disease and when CAR T-cell therapy might be considered
- Review management of common adverse events associated with CAR T-cell therapy, including cytokine release syndrome
- Discuss coordination of care and care continuity during CAR T-cell therapy

Introduction

- Multiple myeloma is the second most common hematologic malignancy
  - Cancer of the bone marrow characterized by shorter remission times with each relapse
- CAR T-cell therapy is an innovative treatment approach that involves genetic engineering of a patient's T cells to specifically target receptors on myeloma cells, leading to direct destruction of the targeted cells.
  - Idecabtagene-vicleucel FDA approved in 2021
  - Ciltacabtagene-autoleucel FDA approved in 2022

Case 1: CAR-T as a Treatment Option

- Ms. Green: 61-year-old female diagnosed with MM in 2015
- FISH positive for gain of 1q21 and monosomy 13
- Prior lines of therapy
  1. VRd x 6 cycles with MR
  2. KPd > ASCT > daratumumab x 3 cycles with progression
  3. EPd with SD

ASCT = autologous stem cell transplantation; EPd = elotuzumab, pomalidomide, dexamethasone; FISH = fluorescence in situ hybridization; KPd = carfilzomib, pomalidomide, dexamethasone; MM = multiple myeloma; MR = minimal response; SD = stable disease; VRd = bortezomib, lenalidomide, dexamethasone.

Case 1

Potential options

- Clinical trial with CAR T-cell therapy
- Clinical trial bispecific antibody treatment
- Standard of care daratumumab, carfilzomib, pomalidomide, and dexamethasone

Response Rates

Treatment	Reference	Overall Response
KarMMa phase II idecabtagene-vicleucel	Munshi et al., 2021	73%
CARTITUDE-1 phase II ciltacabtagene autoleucel	Berdeja et al., 2021	97%
MajesTEC-1 phase 1/2 teclistamab	Moreau et al., 2022	63%
Daratumumab + KPd	Jasielec et al., 2020	86%

Munshi NC, et al. *N Engl J Med.* 2021;384:705-716; Berdeja JG, et al. *Lancet.* 2021;398:314-324; Moreau P, et al. *N Engl J Med.* 2022;387:495-505; Jasielec J, et al. *Blood*. 2020;136:50.

Case 1: Polling Question

Of the following, which would be the most compelling reason to choose CAR T-cell therapy over a bispecific antibody for Ms. Green?

A. Aggressiveness of disease **25%**

B. Ms. Green states that she does not have a caregiver that could accompany her for treatments **0%**

C. The patient does not prefer continuous therapy **0%**

D. Depth and durability of response **75%**

Case 1: Patient Chooses CAR T-Cell Therapy

- Hope of obtaining a deeper, more durable response
- Treatment sequencing strategy
- No routine serial treatments

- Ms. Green consents to trial and starts screening prior to apheresis and bridging of daratumumab, bortezomib, and dexamethasone.

Case 2: Identifying and Managing CRS and Other Common AEs During CAR T-Cell Therapy

- Mrs. Small: 74-year-old female initially diagnosed with MM in June 2015
- Prior treatment history includes 4 lines with PI, IMiD, and MoAb
  - FISH: -17p, -13q, t(11,14)
  - PET/CT: progressive L3 vertebral body lesion r/t myeloma
  - SPEP: M protein 0.7 g/dL (nadir with last line 0.1 g/dL)
- Current regimen elotuzumab, pomalidomide, and dexamethasone

AEs = adverse events; CRS = cytokine release syndrome; IMiD = immunomodulatory drug; MoAb = monoclonal antibody; PET/CT = positron emission tomography/computed tomography; PI = proteasome inhibitor; SPEP = serum protein electrophoresis.

Case 2

- Granted a slot on ide-cel
- Apheresis > LD (cyclophosphamide and fludarabine) > CAR T-cell infusion
- Day 1: Temperature 39°C (102.2°F)
  - Treatment
    - Acetaminophen 650 mg PO every 4 hours PRN
    - Vancomycin 1250 mg IV BID
    - Cefepime 2000 mg IV every 8 hours
  - ID workup: CXR, urine culture, blood cultures

BID = twice daily; CXR = chest X-ray; ID = infectious disease; ide-cel = idecabtagene-vicleucel; IV = intravenously; LD = lymphodepletion; PO = by mouth; PRN = as needed.

Case 2: Lab Results

Lab	Value
WBC	0.4K/µL
Hgb	9.3 g/dL
Plt	103K/µL
ANC	0.35K/µL
ALT	8 µ/L
AST	15 µ/L
Creatinine	0.52 mg/dL
CRP	0.43 mg/L
Ferritin	80 ng/mL

Day	CRP	Ferritin
2	53.94 mg/L	138 ng/mL
3	53.94 mg/L	138 ng/mL
4	89.54 mg/L	268 ng/mL

- Negative CXR
- D2: CRS grade 1, ICANS none
  - Treated with tocilizumab
- D4: Hgb 7.2 g/dL, ANC 0.5 K/µL
- D5: Diarrhea
  - Stool cultures negative
  - Treated with loperamide
- D8: Discharge

ALT = alanine transaminase; ANC = absolute neutrophil count; AST = aspartate transaminase; CRP = C-reactive protein; Hgb = hemoglobin; ICANS = immune effector cell-associated neurotoxicity syndrome; Plt = platelets; WBC = white blood cell.

Case 2: Polling Question

When would you consider administering tocilizumab?

A. CRS grade 1, fever for 1 day **57%**
B. CRS grade 1, fever for 3 days **0%**
C. CRS grade 2 **43%**
D. CRS grade 3, previously treated with tocilizumab **0%**

Case 3: Coordination of Care and Care Continuity in CAR T-Cell Therapy

- Mr. Norton: 61-year-old male, status post ciltacabtagene autoleucel, discharged from hospital on day 10
- Day 11 to Day 30: Twice-weekly APP visits for count checks
- By Day 30, APP drafted letter to local oncologist
  - Mr. Norton's clinical course
  - Five key points for continuity of care

Case 3

1. Date of CAR T-cell therapy and response assessment at day 30
2. Mr. Norton's blood counts
   - Check labs every 14 days
   - Transfuse for Hgb < 8 g/dL and Plt <10 K/μL
   - Administer G-CSF as needed for neutropenia
3. Administer IVIG as needed for hypogammaglobulinemia (IgG < 400 mg/dL)

GCSF = granulocyte colony-stimulating factor; IgG = immunoglobulin G; IVIG = intravenous immunoglobulin.

Case 3

4. Continue prophylaxis
   - PJP prophylaxis (pentamadine or Bactrim) for 1 year post–CAR T-cell therapy until CD4 counts > 200 cells/μL
   - Antiviral prophylaxis for 1 year post–CAR T-cell therapy
   - Bacterial prophylaxis for persistent neutropenia: levofloxacin
   - Antifungal prophylaxis for persistent neutropenia: fluconazole
5. No live vaccines; stay abreast with seasonal flu and COVID vaccine 3 months post–CAR T-cell therapy

PJP = pneumocystis jiroveci pneumonia.

Case 3

- On Day 35, Mr. Norton developed neutropenia
- He was started on:
  - G-CSF
  - Levofloxacin
  - Fluconazole

Case 3: Polling Question

What do you think is the best strategy for collaborative practice between community and CAR T-cell therapy sites?

A. The patient should be sent back to the community at day 30 with clear instructions for the community oncologist. **0%**

B. The patient should be sent back to the community at day 30, but with scheduled every-3-month visits at the CAR T-cell therapy site for the first year. **62%**

C. The patient should be managed by the CAR T-cell therapy administering site for the first 3 months, and then sent back to the community for monitoring, with continued follow-up at the CAR T-cell therapy site for the first year. **38%**

D. The patient should be managed by the CAR T-cell therapy administering site for up to 1 year and should be seen by the community as needed for interim monitoring at the direction of CAR T-cell therapy site. **0%**

Clinical Pearls

- Consideration of patient goals and psychosocial factors along with shared decision-making can help patients make the best treatment selection for quality of life and survival benefit.
- Timely resolution of CRS may prevent more severe serious manifestations without compromising efficacy of CAR T-cell expansion and can improve patient outcomes while maintaining durable responses.
- Clear communication and thorough understanding of post–CAR T-cell therapy recovery is essential for seamless continuation of care between care teams.

Q & A

Please type your questions for Rebecca Lu
into the **question box** in the control panel.

Thank You