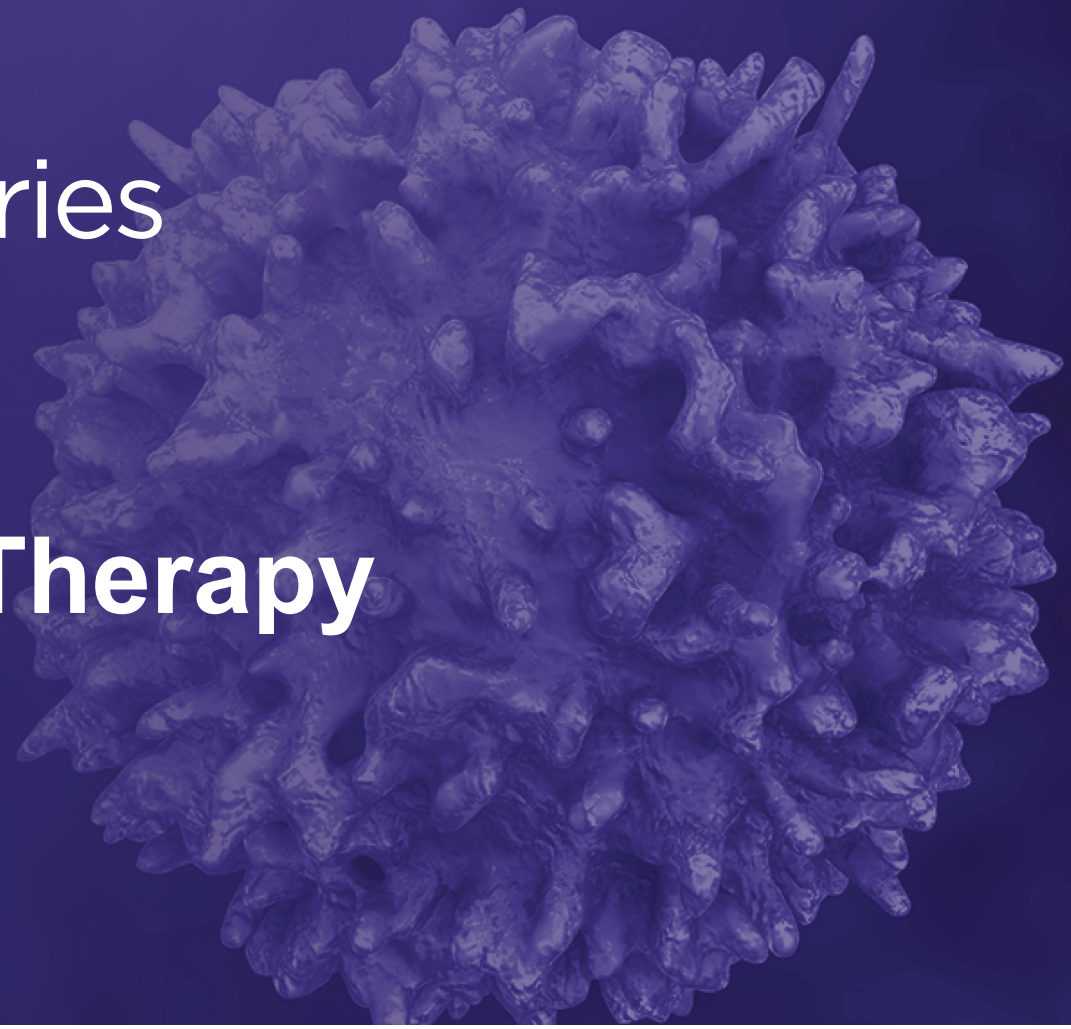
JADPRO Clinical Case Series

Second-Line CAR T-Cell Therapy for Multiple Myeloma



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PRESENTER

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Program Agenda

- Review the most recent FDA approval for ciltacabtagene autoleucel (cilta-cel) and the CARTITUDE-4 study that helped facilitate this newest approval
- Review the selection of appropriate patients for CAR T-cell therapy in the second line
- Review some barriers that make accessing CAR T-cell therapy challenging
- Review the role of the advanced practitioner (AP) in caring for patients undergoing CAR T-cell therapy

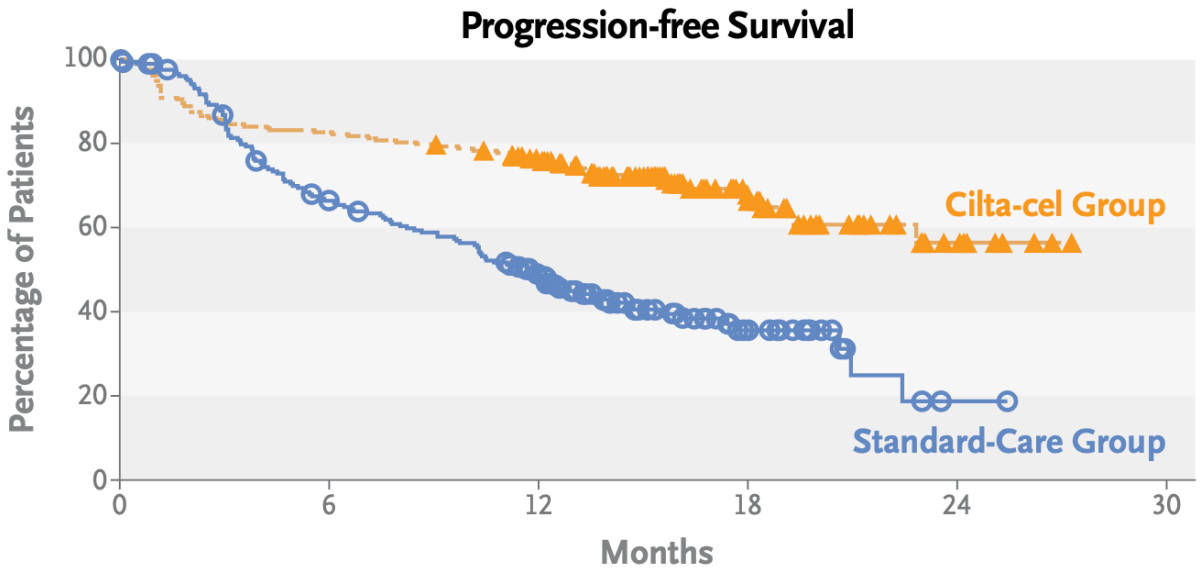
Introduction

- Cilta-cel is a **dual-binding B-cell maturation antigen (BCMA)-directed** CAR T-cell therapy
  - First FDA approval in 2022
    - Adults with relapsed/refractory (R/R) multiple myeloma **after 4 or more lines** of therapy (including a proteasome inhibitor (PI), immunomodulatory drug (IMiD), and anti-CD38 monoclonal antibody)
    - Phase 1b/2 CARTITUDE-1 study: **Median PFS of approximately 3 years**[1] in a heavily pre-treated population (median 6 lines)

- Cilta-cel was tested in **earlier-line** therapy in CARTITUDE-4
  - Global, phase 3 RCT that compared cilta-cel to SOC (either DPd or PVd) in lenalidomide-refractory patients who had received at least 1 prior line of therapy

Munshi N, et al. *HemaSphere.* 2023;*7(S3):*e6102468. San-Miguel J, et al. *N Engl J Med.* 2023;389(4):335-347. Cilta-cel, ciltacabtagene autoleucel; DPd, daratumumab, pomalidomide, dexamethasone; OS, overall survival; PFS, progression-free survival; PVd, pomalidomide, bortezomib, dexamethasone; RCT, randomized controlled trial; SOC, standard of care.

Introduction continued



San-Miguel J, et al. *N Engl J Med.* 2023;389(4):335-347. ISS, International Staging System; ORR, overall response rate.

CARTITUDE-4 Results

- Cilta-cel **significantly reduced the risk of disease progression or death** (HR, 0.26; *P* < .0001)
  - Median PFS was not reached in the cilta-cel arm; 11.8 months in SOC arm
  - At 12 months, PFS was 76% in cilta-cel vs 49% with SOC
  - **Benefit was seen in all subgroups**
    - High-risk cytogenetics, soft-tissue plasmacytomas, ISS Stage III disease, exposure to anti-CD38 antibodies
    - ORR was 85% in cilta-cel vs. 68% in SOC

On April 5, 2024, cilta-cel gained FDA approval for **use in second line in patients with lenalidomide-refractory disease** after at least 1 prior line of therapy (including IMiD, PI)

Case 1: Selecting Patients for CAR T-Cell Therapy in the Second Line for MM

- Mr. Smith is a 74-year-old man with a past medical history of hypertension (HTN) and benign prostatic hyperplasia (BPH) who was first diagnosed with IgA lambda multiple myeloma (MM) in 2022, complicated by a left pubic ramus fracture
- FISH results: 1q21 amplification and t(4;14)
- Bone marrow biopsy: 60% to 70% plasma cell involvement
- Previous treatment
  - 1a. RVd 8 cycles, VGPR
  - 1b. ASCT, VGPR
  - 1c. Lenalidomide maintenance

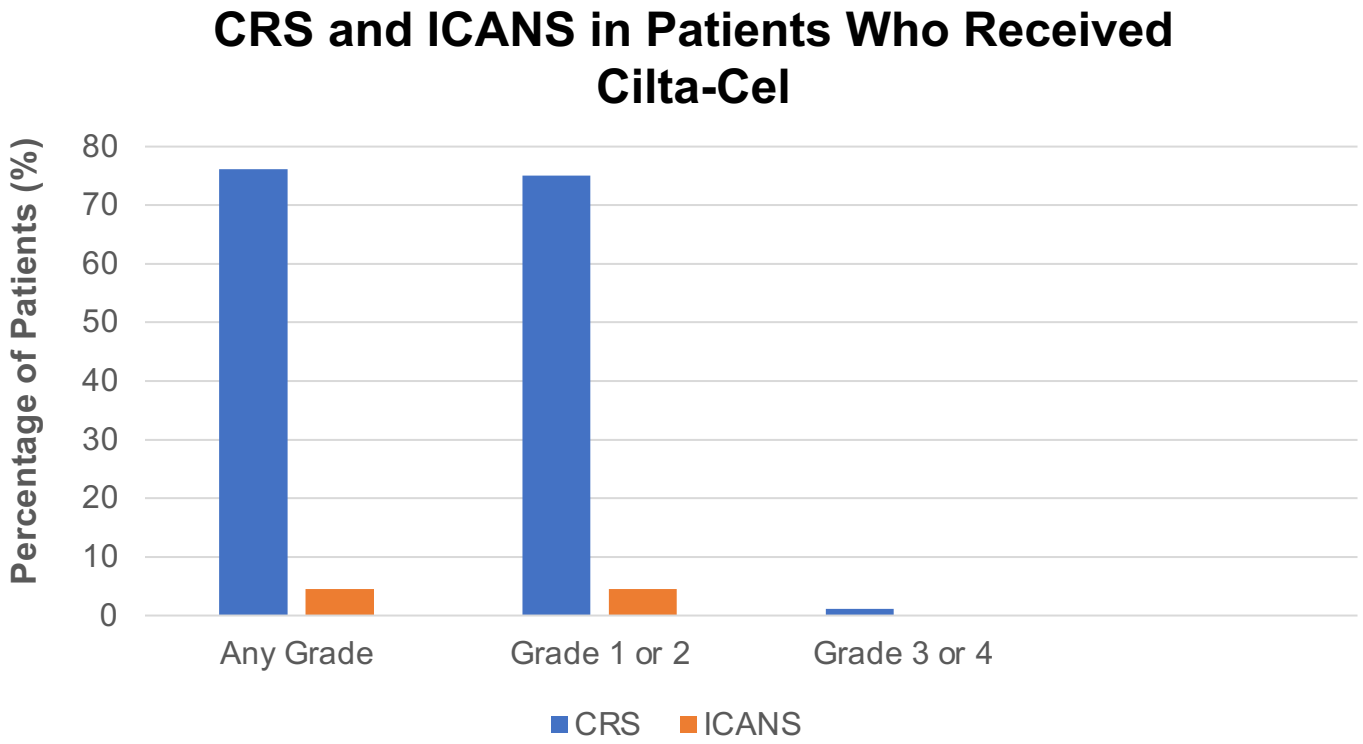
ASCT, autologous stem cell transplant; FISH, fluorescence in situ hybridization; RVd, lenalidomide, bortezomib, dexamethasone; VGPR, very good partial response.

Case 1: Selecting Patients for CAR T-Cell Therapy in the Second Line for MM continued

- 10 months later, Mr. Smith's disease is progressing
  - Treatment options: Daratumumab-based regimen or cilta-cel
- ECOG performance status 1
- Age: 74
- PMH: HTN and BPH
- Has a caregiver
- He and his daughter are very worried about side effects

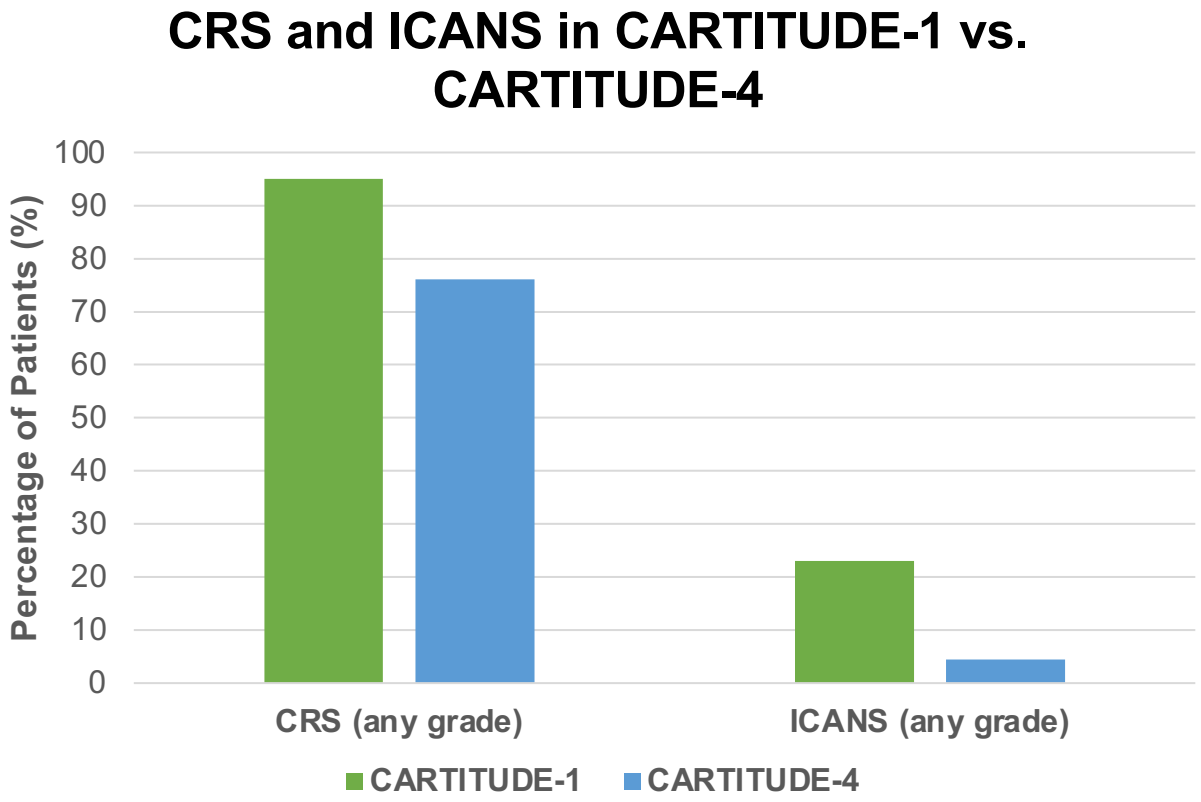
ECOG, Eastern Cooperative Oncology Group.

CARTITUDE-4: CRS and ICANS



- Approximately 75% of patients had cytokine release syndrome (CRS), mostly grade 1 or 2
- Approximately 5% had immune effector cell-associated neurotoxicity (ICANS); all were grade 1 or 2

San-Miguel J, et al. *N Engl J Med.* 2023;389(4):335-347.



- Compared to CARTITUDE-1, CARTITUDE-4 showed **decreased rate and severity** of CRS and ICANS

Cilta-cel may be less toxic and better tolerated in earlier-line treatment

Berdeja J, et al. *Lancet.* 2021;398(10297), 314-324. San-Miguel J, et al. *N Engl J Med.* 2023;389(4):335-347.

Case 1 Polling Question Results

Question: Do you think this patient would be a good candidate for CAR T-cell therapy in the second line, and should he be referred for therapy?

a. Yes, he would be a good candidate, but his age precludes him from safely receiving CAR T-cell therapy so I would not refer him **7%**

b. Yes, he would be a good candidate and he has aggressive disease features, so he should receive a referral **86%**

c. No, he would not be a good candidate because he is too hesitant about side effects, so I would not refer him for treatment. **7%**

Case 1: Selecting Patients for CAR T-Cell Therapy in the Second Line for MM continued

- CAR T-cell side effects can be serious but are largely managed with established protocols
- Mr. Smith moves forward with the referral to speak with the CAR T-cell physician
- The CAR T-cell physician finds him to be an appropriate candidate
  - Decides to pursue cilta-cel
  - Started on bridging with DPd until he can start apheresis

Case 2: Navigating Barriers to CAR T-Cell Therapy for MM

- Mr. Fitzgerald is a 62-year-old man with R-ISS stage II lambda light chain multiple myeloma, with gain 1q and complex cytogenetics, who initially presented with renal failure
- Treatment history
  - 1a. Bortezomib and dexamethasone then switched to RVd upon renal recovery
    - PR/VGPR
  - 1b. Autologous stem cell transplant
    - VGPR
  - 1c. Lenalidomide maintenance
- His free light chains are increasing, and he now has new evidence of measurable disease
- As such, CAR T-cell therapy is a consideration

Case 2: Navigating Barriers to CAR T-Cell Therapy for MM continued

- His other medical conditions include HTN and hypothyroidism
- His performance status is good, and he has a family member that can serve as caregiver
- However, Mr. Fitzgerald is hesitant to pursue treatment, as he does not feel financially secure enough
- Additionally, he lives more than 2.5 hours away from the nearest center that offers CAR T-cell therapy

Case 2 Polling Question Results

Question: What barriers, if any, have you encountered regarding the reality of getting patients to CAR T-cell therapy? (Select all that apply.)

a. Medical ineligibility **12%**

b. Insurance barriers **19%**

c. Financial cost **16%**

d. Time from selection to administration **9%**

e. Access to CAR T-cell infusion center **19%**

f. CAR T-cell product availability **9%**

g. Patient concerns about CAR T-cell therapy-related toxicities (e.g. CRS, ICANS) **16%**

Case 2: Navigating Barriers to CAR T-Cell Therapy for MM continued

- More patients are eligible for CAR T-cell therapy
  - There are some barriers that patients may face
    - Product availability, manufacturing issues, socioeconomic barriers, caregiver requirement
  - Case example: Financial concerns
    - Social workers and case managers are helpful
    - Various resources exist for financial assistance (LLS, IMF websites)
    - Example: The Leukemia & Lymphoma Society's (LLS) Susan Lang Pre CAR T-cell Therapy Travel Assistance program
      - Financial assistance for those with significant need who are being evaluated for CAR T-cell treatment

Johnson & Johnson press release. April 6, 2024.

Case 3: Caring for CAR T-Cell Patients as an Advanced Practitioner

- Mrs. Greenberg is a 57-year-old woman with IgA kappa multiple myeloma who received CAR T-cell therapy in the fourth line
- Hospital course
  - She developed grade 1 CRS on Day 5 → 1 dose of IV tocilizumab (8 mg/kg)
  - On Day 7 she had progression to grade 2 CRS → 1 dose of IV tocilizumab (8 mg/kg) and 1 dose of IV dexamethasone (10 mg)
  - CRS resolved and on Day 8 she developed grade 1 ICANS → 1 dose of IV dexamethasone (10 mg)
  - Her ICANS progressed to Grade 2 the day after → Increased dose of antiepileptic drug, stat EEG, stat head CT, neurology consultation, dexamethasone (10 mg IV every 6 hours) until improvement and then tapered off

EEG, electroencephalogram.

Case 3: Caring for CAR T-cell Patients as an Advanced Practitioner continued

- Mrs. Greenberg's CRS and ICANS eventually resolves → discharged to the outpatient setting for at least twice-weekly follow-up
- She is seen on Day 24, and her vital signs are as follows: Temperature, 101°F; heart rate, 109 bpm; oxygen saturation, 90% on room air; respiration rate, 18
  - She is weak and has a nonproductive cough
  - Basic infectious work-up (blood cultures, urinalysis, urine culture, CXR)
- CXR: New consolidation in the left lower lung base

Hemoglobin (Hgb)	8.9 g/dL
White blood cell count (WBC)	1.1 x 10^9/L
Neutrophil count	0.48 neutrophils/mL
Platelet count	60 x 10^9/L
Creatinine	1.2 mg/dL
C-reactive protein	1.2 mg/L
Ferritin	780 ng/mL

Case 3 Polling Question Results

Question: Which of the following would you also do? (Select all that apply.)

a. Start IV cefepime and admit to the hospital **19%**

b. Administer IV tocilizumab (8 mg/kg) **19%**

c. Order additional testing including respiratory viral panel, IgG level, and non-contrast chest CT **42%**

d. Start oral levofloxacin for community acquired pneumonia **12%**

e. Give a dose of growth factor and schedule the patient to come back to the office tomorrow **8%**

Case 3: Caring for CAR T-cell Patients as an Advanced Practitioner continued

- Because she is febrile and neutropenic → starts IV cefepime and is admitted to the hospital
- Because of the duration of steroids during hospital course → provider also orders CMV, HHV6, EBV, adenovirus, and serum fungal markers
- The advanced practitioner speaks to the inpatient provider to give an appropriate handoff
- Mrs. Greenberg is closely monitored for the development of possible CAR T-cell therapy-related toxicities

Clinical Pearls

- Cilta-cel is a therapeutic option for patients with multiple myeloma as early as second line
- Getting all eligible patients to CAR T-cell therapy involves understanding potential barriers patients may face
- Patients who receive CAR T-cell therapy require complex care
    - Advanced practitioners must remain up to date on side-effect guidelines and prophylactic strategies

Q & A

Please type your questions for Michelle Lauer
into the **question box**.

Thank You

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