



Incidence, Mitigation, and Management of Neurologic Adverse Events in the CARTITUDE-2 Study of Patients with Multiple Myeloma Treated with Ciltacabtagene Autoleucel (cilta-cel)

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INTRODUCTION

- Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) is a chimeric antigen receptor T cell (CAR-T) therapy with 2 B-cell maturation antigen (BCMA)-targeting, single-domain antibodies designed to confer avidity
- CARTITUDE-2 (NCT04133636) is a phase 2, multicohort, open-label study assessing the efficacy and safety of cilta-cel in patients with multiple myeloma (MM) in various clinical settings
- Treatment-emergent neurotoxicities are known side effects of CAR-T therapies and can be mild to life threatening, requiring careful monitoring and management¹⁻⁵
 - Movement and neurocognitive treatment-emergent adverse events (TEAEs) were observed in 5 of 97 patients treated with cilta-cel in the CARTITUDE-1 study⁶
 - Grade 3 Parkinsonism has been reported in a study with another anti-BCMA CAR-T therapy, idecabtagene vicleucel⁷
- Here, we describe the patient management strategies implemented to identify and reduce the incidence of neurologic AEs in patients from CARTITUDE-2 who had progressive MM after 1–3 prior lines of therapy

OBJECTIVE

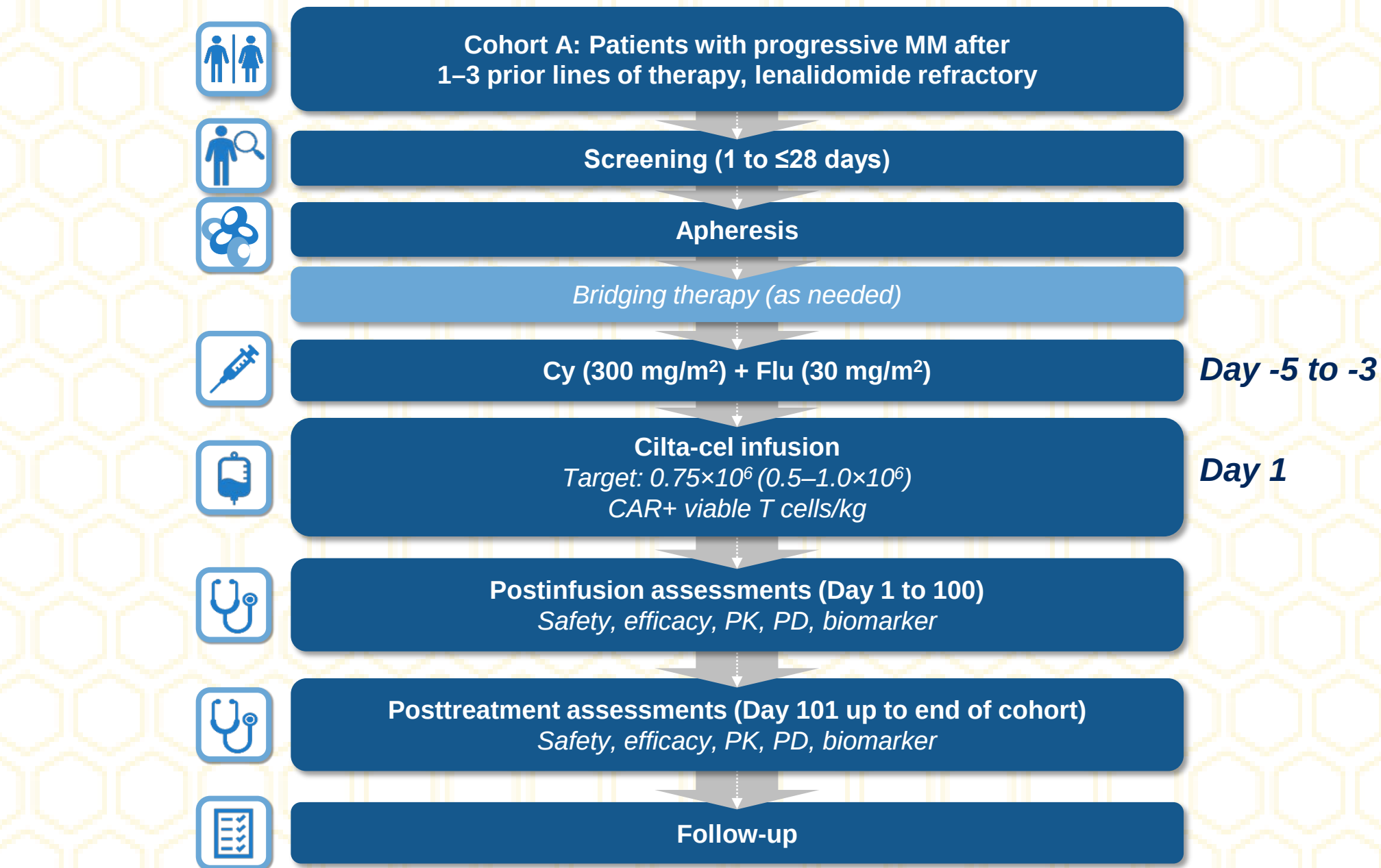
To describe patient management strategies for neurologic AEs in CARTITUDE-2

METHODS

Study Design

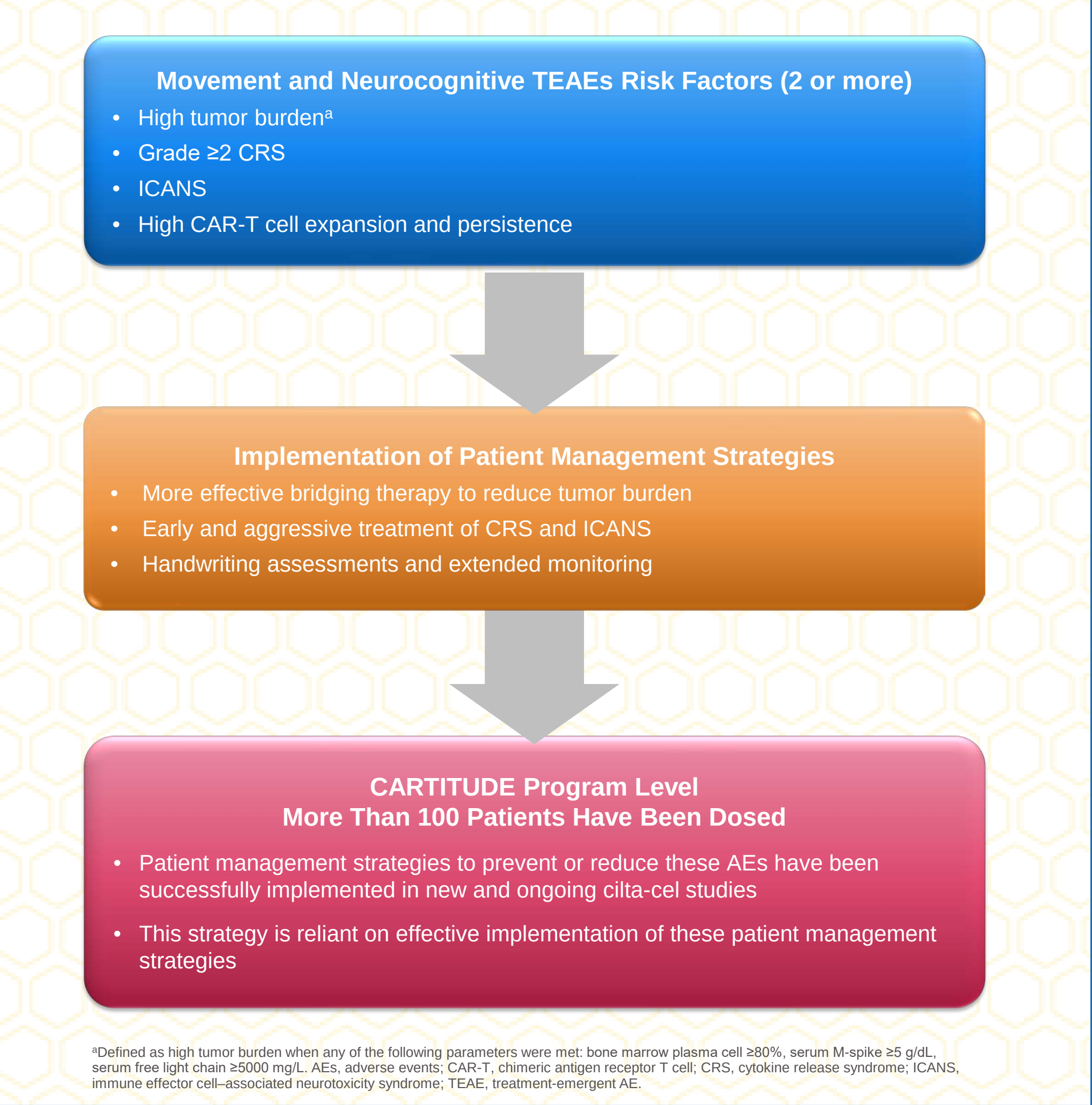
- The CARTITUDE-2 study design is shown in **Figure 1**
- Patients from Cohort A had progressive MM after 1–3 prior lines of therapy including a proteasome inhibitor and an immunomodulatory drug, were lenalidomide refractory, and had no prior exposure to BCMA-targeting agents

Figure 1. Study Design



- Patients received a single cilta-cel infusion (target dose: 0.75×10⁶ CAR+ viable T cells/kg) 5–7 days after start of lymphodepletion (daily cyclophosphamide [300 mg/m²] and fludarabine [30 mg/m²] for 3 days)
- The primary objective was minimal residual disease (MRD) 10⁻⁵ negativity assessed using next-generation sequencing (Adaptive Biotechnologies, Seattle, WA; version 2.0)
- The secondary outcomes were overall response rate (International Myeloma Working Group response criteria), duration of response, time and duration of MRD negativity, and incidence and severity of AEs
- Immune effector cell–associated neurotoxicity syndrome (ICANS) and cytokine release syndrome (CRS) were graded by American Society for Transplantation and Cellular Therapy criteria; neurotoxicities not classified as ICANS were graded per Common Terminology Criteria for AEs version 5.0
- Patient management strategies were implemented to prevent or reduce neurologic AEs in CARTITUDE-2 (**Figure 2**)
 - Of the 20 patients in Cohort A who received cilta-cel treatment, 18 were dosed after implementation of patient management strategies

Figure 2. Patient Management Strategies for Neurologic AEs in CARTITUDE-2



RESULTS

Patients

- As of Jan 4, 2021, 20 patients in Cohort A received cilta-cel; median follow-up was 5.8 months (range, 2.5–9.8)
 - Median age was 60 years (range, 38–75); 65% were male
- Patients received a median of 2 prior lines of therapy (range, 1–3)

Neurologic AEs in Cilta-cel–Treated Patients

- Neurotoxicities occurred in 20% of patients (**Table 1**)
- Median time to onset of symptoms of ICANS was 8 days (range, 7–11)
- Median duration was 2 days (range, 1–2)
- 3 patients had Grade 1/2 ICANS; all 3 had concurrent CRS (Grade 1/2)
- Supportive measures (steroids) were administered to 2 of the 3 patients; ICANS resolved in all 3 patients
- Only 1 patient exhibited other neurotoxicity: developed Grade 2 isolated facial paralysis on Day 29 after cilta-cel infusion
 - The patient was treated with dexamethasone for 29 days and recovered after 51 days
- None of the patients from Cohort A in CARTITUDE-2 experienced other neurotoxicities characterized by a cluster of movement and neurocognitive TEAEs as seen in CARTITUDE-1⁶

Table 1. Neurologic AEs

Neurotoxicities	Grade 1/2	Grade ≥3
ICANS, n (%)	3 (15)	0
Other neurotoxicities ^a , n (%)	1 (5)	0

^aEvents not reported as ICANS (ie, onset after a period of recovery from CRS and/or ICANS). AEs, adverse events; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome.

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KEY FINDINGS STATEMENT

- Successful new patient management strategies have been implemented in the CARTITUDE program to prevent and reduce the incidence of neurotoxicity

CONCLUSIONS

- Neurologic AEs were generally manageable in patients with MM following treatment with cilta-cel in CARTITUDE-2
- The incidence of movement and neurocognitive TEAEs seen in CARTITUDE-1 appeared to be reduced in Cohort A of CARTITUDE-2 due to implementation of patient management strategies, including the use of effective bridging therapy to decrease baseline tumor burden
 - There was no incidence of Grade ≥3 neurotoxicity or any-grade movement and neurocognitive TEAEs in patients from Cohort A
- These results suggest early detection and management of neurologic AEs can help optimize patient care
- Data from subsequent patients dosed (>100 patients across the CARTITUDE study program) suggest these new patient management strategies have been successfully implemented in new and ongoing cilta-cel studies

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