

A PCR Test Detecting Clinically Relevant Expansion and Proliferation of CD19 Directed Chimeric Antigen Receptor T-cells

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CASE STUDY

PATIENT • 15 year-old female

DIAGNOSIS • Pre-B acute lymphoblastic leukemia

A 15-year-old Hispanic female that was diagnosed with pre-B acute lymphoblastic leukemia in February 2023. She underwent COG high risk four drug induction as per AALL 1732.

Initial Treatment Plan

Her end of induction disease burden was 5.2% blasts, consistent with induction failure. Her lymphocytes were collected at this time, in anticipation of using CD19 chimeric antigen receptor (CAR) T-cells in the future.

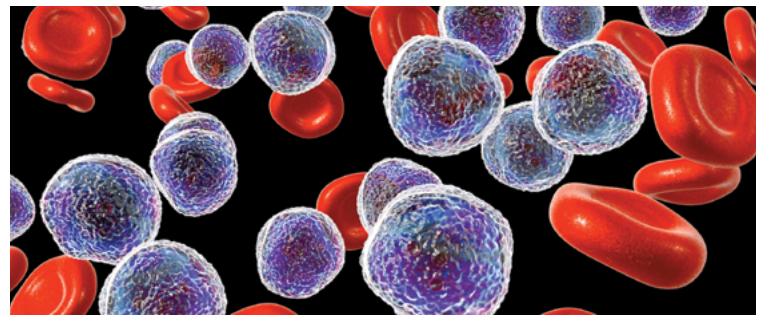
She then proceeded with a course of blinatumomab with no response and persistent leukemia (70% B lymphoblasts in bone marrow)

Approach

She was subsequently planned for Tisagenlecleucel infusion and underwent lymphodepleting chemotherapy. She tolerated her CAR T-cell infusion well without any significant issues.

Results

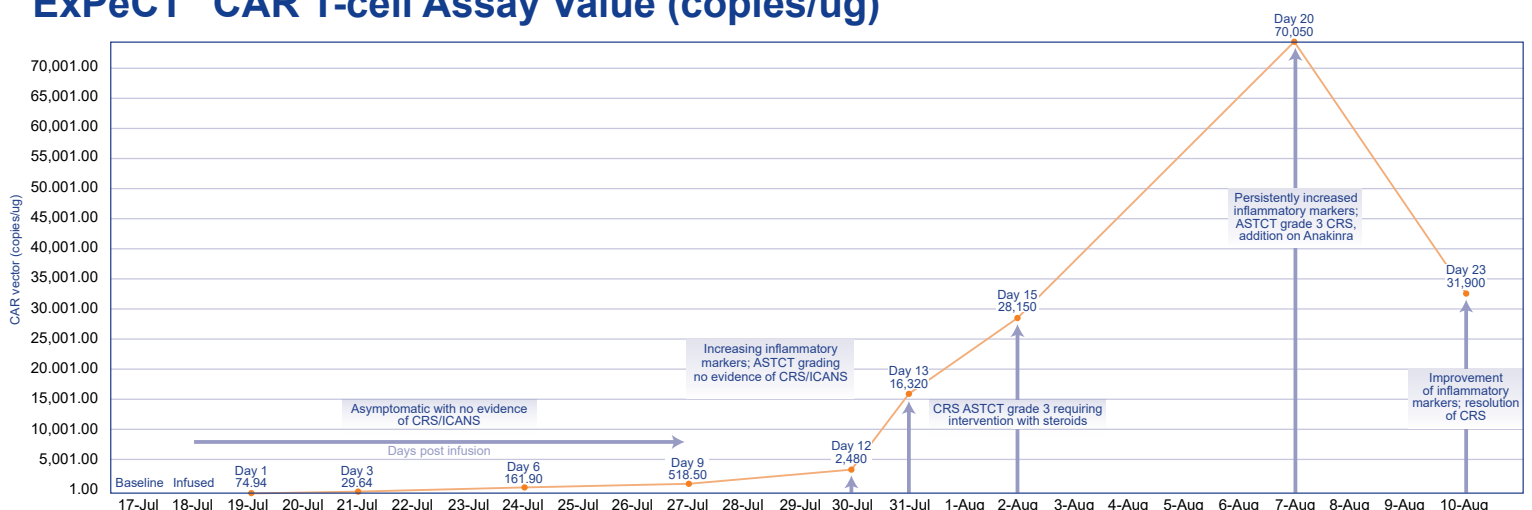
Unfortunately, despite having great expansion as demonstrated by the ExPeCT CAR T-cell assay, she still had 70% blasts at the end of CAR therapy. The patient is currently receiving palliative chemotherapy.



Summary

- 15-year-old patient with refractory ALL received Tisagenlecleucel infusion and developed delayed CRS and ICANS (onset at day 13).
- Use of CAR T-cells ExPeCT assay showed proliferation and expansion of CAR T-cells, solidifying the diagnosis of CRS, given the atypical onset.
- Detection of CAR T-cell expansion had a direct correlation of worsening CRS for the patient.
- Detection of CAR T-cell decrease in expansion correlated with clinical improvement of symptoms.

ExPeCT™ CAR T-cell Assay Value (copies/ug)



Impact to the Patient

She tolerated her CAR T-cell infusion well without any significant issues. 13 days post infusion, she presented with a fever and increasing inflammatory markers. She was given 2 doses of tocilizumab, but fever persisted. Subsequently, she ended up being hypotensive and transferred to the ICU for pressor support. Due to persistent pressor requirement, she received 2 doses of dexamethasone, with some improvement. But as she continued to require pressors, she was given four doses of methylprednisolone, which ended up having a significant improvement in her symptoms.

This patient had a slightly delayed onset of cytokine release syndrome (CRS), compared to her disease burden. The ExPeCT assay showed a direct correlation between the expansion of CAR and worsening clinical symptoms for the patient, which provided important information to confirm the diagnosis of CRS. Improvement of the patient's symptoms also correlated with a decrease in the CAR T-cell copies detected by the assay.

CRS typically occurs within the first 14 days of CAR infusion [1,2], though it can occur as late as 28 days post infusion [3,4]. CRS is typically a diagnosis of exclusion. However, this ExPeCT assay aids in the diagnosis, given the correlation of CAR T-cell expansion and onset of CRS symptoms. Larger studies will be used to further validate the use of this test.

Date of Result	ExPeCT Result	Clinical Data
7/17/2023	Not Detected (pre-infusion)	Baseline; Pt infused 7/18/2023
7/19/2023 - Day 1	74.94 copies/ug	Asymptomatic w/ no evidence of CRS/ICANS
7/21/2023 - Day 3	29.64 copies/ug	Asymptomatic w/ no evidence of CRS/ICANS
7/24/2023 - Day 6	161.9 copies/ug	Asymptomatic w/ no evidence of CRS/ICANS
7/27/2023 - Day 9	518.5 copies/ug	Asymptomatic w/ no evidence of CRS/ICANS
7/30/2023 - Day 12	2,480 copies/ug	Asymptomatic w/ no evidence of CRS/ICANS
7/31/2023 - Day 13	16,320 copies/ug	Increasing inflammatory markers; ASTCT grading no evidence of CRS/ICANS
8/2/2023 - Day 15	28,150 copies/ug	CRS ASTCT grade 3 requiring intervention with steroids
8/7/2023 - Day 20	70,050 copies/ug	Persistently increased inflammatory markers; ASTCT grade 3 CRS, addition of Anakinra
8/10/2023 - Day 23	31,900 copies/ug	Improvement of Inflammatory markers; resolution of CRS

CRS = Cytokine Release Syndrome, ICANS = Immune Effector Cell-Associated Neurotoxicity Syndrome.

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