DAR-T - Personalized Pre-Infusion Intelligence for CAR-T Toxicity Management

THE CLINICAL UNMET NEED

CAR-T therapy has transformed outcomes for patients with difficult-to-treat hematological malignancies. Yet its clinical benefit is accompanied by potentially serious and highly variable adverse events—including Cytokine Release Syndrome (CRS), Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), and Cardiovascular Toxicity

The central clinical challenge is patient variability.

Two patients receiving the same CAR-T product may experience markedly different biological responses and toxicity profiles

EMERGING OPPORTUNITY

Current CAR-T toxicity management is built around careful surveillance, early recognition, standardized grading and rapid intervention.
The ASTCT consensus framework has provided an essential standardized approach for grading CRS and neurological toxicity.
However, grading begins once clinical manifestations emerge.
The emerging opportunity is to complement this reactive framework with pre-infusion patient-specific biological assessment.

Clinical Question

Can we interrogate how an individual patient's biology responds to the intended CAR-T product before infusion?

DAR-T is designed to investigate that patient-specific response before therapeutic infusion

THREE CRITICAL TOXICITY DOMAINS

01 | CRS Cytokine Release Syndrome Intelligence

CRS represents a systemic inflammatory response initiated by CAR-T activation and amplified through interactions involving immune cells, cytokines and vascular biology

Evaluates

IL-6 • IL-1β • IFN-γ • TNF-α • IL-10 • GM-CSF • Immune-cell activation • Systemic inflammatory response

Clinical objective	Output
Identify patient-specific biological response patterns that may indicate an increased propensity toward an excessive inflammatory response	**CRS** Response Signature

02 ICANS Neurotoxicity Intelligence

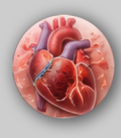
CAR-T-associated neurotoxicity involves more than cytokine elevation alone.Research has implicated endothelial activation, inflammatory signaling and blood–brain-barrier disruption in severe neurological toxicity following CD19 CAR-T therapy

Evaluates

Endothelial activation • Neuroinflammatory signaling • Cytokine dynamics • Blood–brain-barrier-associated biology • Immune activation signatures

Clinical objective	Output
Characterize the patient's biological response for patterns potentially relevant to neurological vulnerability	**ICANS** Response Signature

03 | CARDIOTOXICITY Cardiovascular Response Intelligence



Cardiovascular complications associated with CAR-T therapy may include hypotension, arrhythmias, myocardial injury, ventricular dysfunction and heart failure.Clinical studies have demonstrated associations between severe inflammatory responses, cardiac biomarker elevation and subsequent cardiovascular events

Evaluates

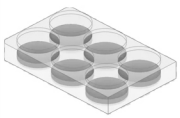
Cardiac stress biology • Inflammatory injury signals • Endothelial activation • Cardiomyocyte response • Cytokine-associated cardiovascular stress

Clinical objective	Output
Identify biological response patterns potentially associated with increased cardiovascular vulnerability following CAR-T exposure	**Cardiotoxicity** Response Signature

THREE CRITICAL TOXICITY DOMAINS : Test the interaction before the therapeutic exposure

1 PATIENT SAMPLE

2 PATIENT-DERIVED MICROPHYSIOLOGICAL PLATFORM



Patient-specific biological environment generated ex vivo.

3 EXPOSURE TO AN ALIQUOT OF THE INTENDED CAR-T PRODUCT

The patient's biological system is challenged with the CAR-T product under controlled laboratory conditions.

4 MULTIMODAL BIOLOGICAL READOUTS

Cytokines + cellular responses + molecular signatures + endothelial/neuroinflammatory signals + cardiac-response indicators

5 DAR-T ANALYTICS

Integration and interpretation of patient-specific biological-response patterns.

CRS, ICANS, CARDIOTOXICITY RESPONSE SIGNATURE

PERSONALIZED CLINICAL INTELLIGENCE

POSITIONING

DAR-T evaluates the biological interaction between an individual patient's ex vivo MicroPhysiology and the intended CAR-T product to generate patient-specific response signatures that support clinical management post-infusion

FROM REACTIVE MANAGEMENT TO PERSONALIZED PREPAREDNESS

Current Clinical Paradigm

CAR-T Infusion | Patient Monitoring | Clinical Signs/ Symptoms | CRS / ICANS Recognition | ASTCT Grading | Clinical Intervention

This remains essential and should continue according to established institutional protocols and clinical guidelines

VS

DAR-T ADDS A PRE-INFUSION LAYER

Intended CAR-T Product | PATIENT-SPECIFIC EX VIVO INTERACTION | DAR-T BIOLOGICAL INTELLIGENCE | CRS | ICANS | CARDIOTOXICITY | PERSONALIZED CLINICAL PREPAREDNESS | Standard Monitoring + ASTCT Grading + Physician-Directed Management

DAR-T is therefore intended to complement rather than replace established CAR-T toxicity-management pathways

WHY PERSONALIZATION MATTERS

PATIENT × DISEASE × CAR-T PRODUCT = PATIENT × CAR-T INTERACTION

PATIENT
- Genetic background
- Baseline immune state
- Comorbidities
- Cardiovascular reserve
- Endothelial susceptibility

DISEASE
- Tumor burden
- Antigen load
- Disease-associated inflammation

CAR-T PRODUCT
- Cellular phenotype
- Activation
- Expansion
- Persistence
- Cytokine-producing potential

PATIENT × CAR-T INTERACTION

The biological response that emerges when the patient's system encounters the therapeutic cells.

DAR-T focuses on this fourth dimension

WHAT COULD DAR-T ADD TO THE CAR-T TEAM?

DAR-T is intended to provide treating physicians with an additional patient-specific biological dataset before infusion

Such information could potentially support:

Risk-informed surveillance

Identification of patients whose ex vivo responses suggest the need for particularly close post-infusion observation

Multidisciplinary preparedness

Earlier consideration of neurological or cardiovascular involvement when biological response patterns indicate potential vulnerability

Patient-specific biological baselines

A structured pre-infusion reference against which subsequent biological changes could potentially be interpreted

Clinical decision Support:

An additional biological intelligence layer to complement clinical history, disease characteristics, laboratory findings and physician judgment.

Selected Clinical Evidence

- **Brudno JN, Kochenderfer JN.** *Current understanding and management of CAR T cell-associated toxicities. Nature Reviews Clinical Oncology. 2024*
- **Yang C, Nguyen J, Yen Y.** *Complete spectrum of adverse events associated with chimeric antigen receptor (CAR)-T cell therapies. Journal of Biomedical Science. 2023*
- **Xiao X, Huang S, Chen S, et al.** *Mechanisms of cytokine release syndrome and neurotoxicity of CAR T-cell therapy and associated prevention and management strategies. Journal of Experimental & Clinical Cancer Research. 2021.*
- **Lee DW, et al. ASTCT** *consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. Biology of Blood and Marrow Transplantation. 2019*
- **Alvi RM, et al.** *Cardiovascular events among adults treated with chimeric antigen receptor T-cells. JACC: CardioOncology. 2019*
- **Neelapu SS, et al.** *Chimeric antigen receptor T-cell therapy—assessment and management of toxicities. Nature Reviews Clinical Oncology. 2018*
- **Gust J, et al.** *Endothelial activation and blood–brain barrier disruption in neurotoxicity after adoptive immunotherapy with CD19 CAR-T cells. Cancer Discovery. 2017*
- **Incorvaia D.** *Study of Yescarta patients reveals genetic red flags for CAR-T therapy side effects. Fierce Biotech. July 2026. The report discusses emerging genetic associations from Yescarta-treated populations; these findings require further validation before clinical use*

DAR-T TRANSCELL BIOLOGICS

From population-level toxicity management to patient-specific biological intelligence.