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CAR T-Cell Therapy: It's Role after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

April 17- 23, 2021

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It's Role After Transplant

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4/22/21

A National Cancer Institute Designated Cancer Center

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Disclosures

Research Support	**BMS/Celgene; Curis;**
Consultancy	**Acrotech; ADC Therapeutics; Astra-Zeneca; BeiGene, BMS/Celgene/Juno; Diiachi Sankyo Janssen/Pharmacyclics; Karyopharm Kite/Gilead; Legend; Morphosys; Myeloid Therapeutics; Novartis; Spectrum; TG Therapeutics, Verastem**
Employment	**NONE**
Major Stockholder	**NONE**
Speakers Bureau	**NONE**

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Updated 3/1/21

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Objectives

- Discuss how the immune system and CAR-T share a common theme
- Discuss where CAR T-cell therapy plays a role in the treatment of patients with blood disorders
- Discuss the evaluation process for candidacy for CAR T-cell therapy
- Discuss the CAR-T journey for patients and their family before, during and after the procedure
- Discuss the potential toxicities and impact on quality of life long-term

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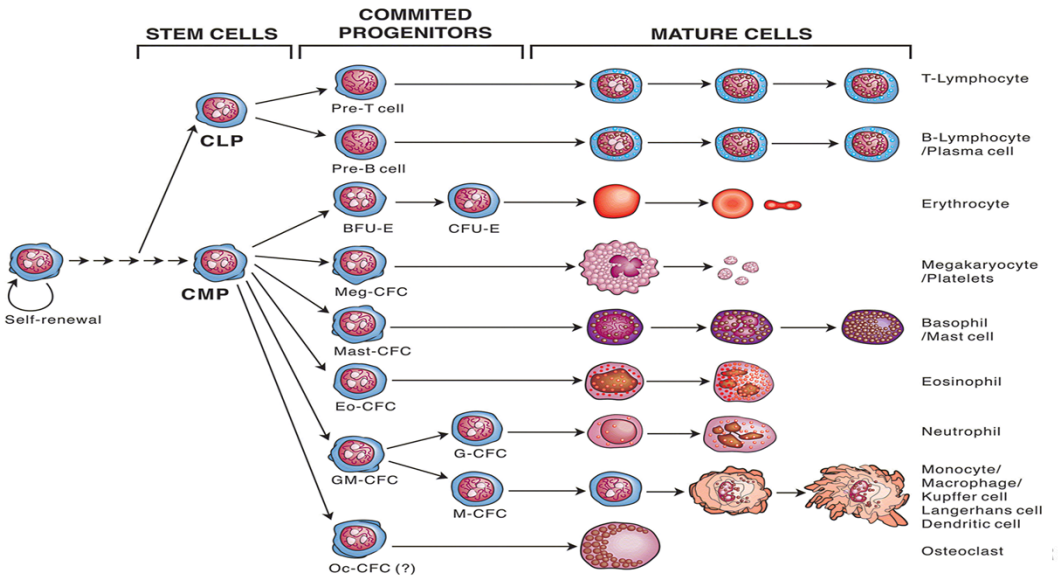
Our Immune System



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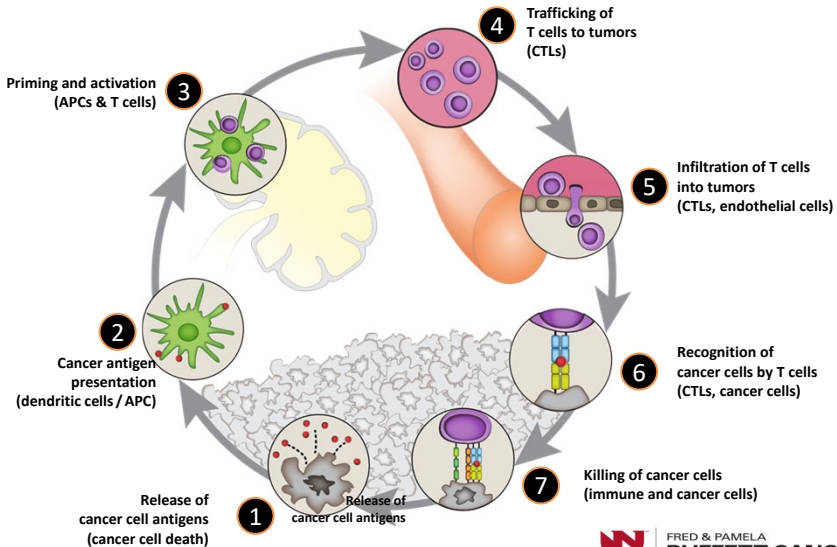
How T-cells Fight Cancer



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Chen DS, Mellman I. *Immunity.* 2013;39:1-10

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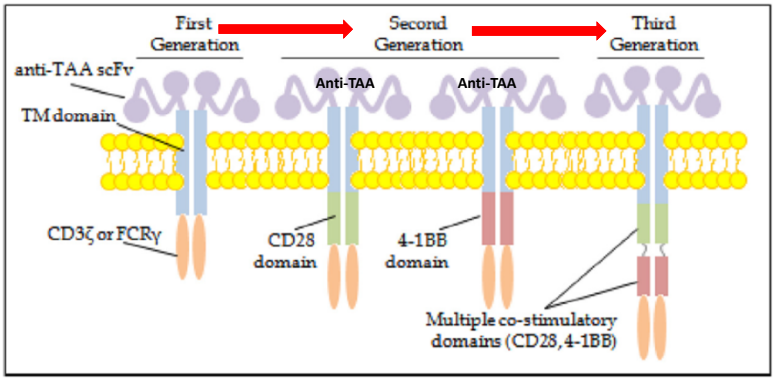
T-cells To CAR-T cells



TAA= Tumor associated antigen

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Geyer et al. Cytotherapy 2016

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T-cells To CAR-T cells

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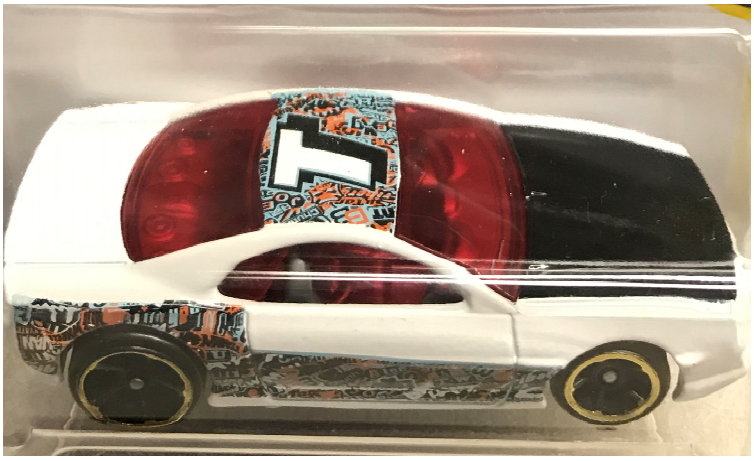
Where does CAR T-cell Currently Fit?



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Courtesy of Susan Blumel

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FDA Approved

CAR-T cell	Disease approved	Target
Axi-cel (Yescarta)	LBCL; MCL; FL	CD19
Tisa-cel (Kymriah	LBCL; ALL	CD19
Liso-cel (Breyanzi)	LBCL	CD19
Ide-cel (Abecma)	MM	BCMA

Indications:

- LBCL; MCL; FL→ After at least two prior lines of therapy
- ALL→ Up to age 25 that is refractory or in 2nd relapse or later
- MM→ After 4 prior lines of therapy (specific drugs must have exposure)

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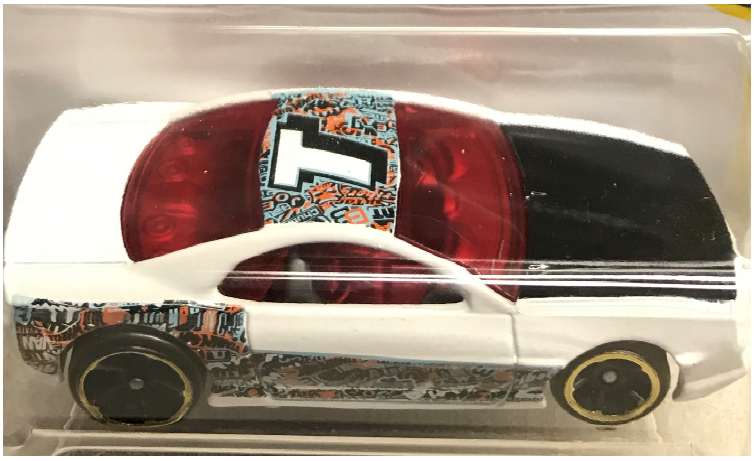
The Journey To



Courtesy of Susan Blumel

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Consultation

- Disease type
  - LBCL; MCL, FL, MM
- Prior Treatments
  - Appropriate exposure pre-CAR-T
- Tolerance to prior treatments
  - Intensity of past therapies
  - Transplant
- Disease status
  - Relapse
    - Duration of remission
  - Refractory
  - Never in remission

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Workup

- Disease Burden
  - Physical exam
  - Imaging
- Cardiac function
  - Echocardiogram
- Infectious disease
  - HIV; Hep B; Hep C
- Laboratory
  - Bone marrow reserve
    - CBC
  - Hepatic reserve
    - LFTs/Bilirubin
  - Renal reserve
    - CrCl
  - Pulmonary reserve
    - Pulse Ox

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Brain to Vein Time

- Insurance
  - Private vs Public
- Prior Authorization
  - On label
- Single case agreement
  - Payment for the product
  - Payment for the care post infusion
- Pre-apheresis treatment
  - Disease burden
  - Disease velocity
  - Anticipated time to T-cell removal (apheresis)

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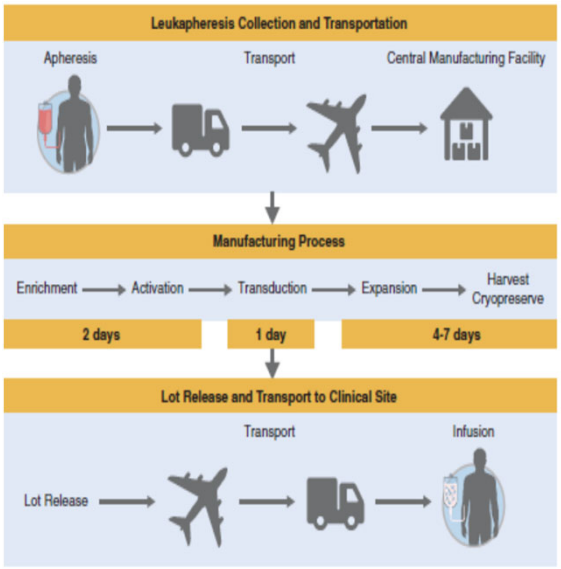
Vein to Vein Time

What you're doing post-apheresis

- Monitor fitness
- Monitor for infections
- Bridging treatment:
  - Steroids
    - Distance from infusion
  - Radiation
    - Problem locations
    - Low risk locations
  - Low dose chemotherapy
    - Distance from lymphodepleting chemotherapy



Roberts et al. Leukemia & Lymphoma 2017

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Lymphodepleting (LD) Chemo

- Fludarabine/Cyclophosphamide
  - Most common LD chemotherapy
  - Doses differ depending on the CAR-T construct
  - 3 days of treatment
  - At least 2 days of rest prior to infusion
- Bendamustine
  - Only available with Tisa-cel (Kymriah)
  - Two days of treatment
- No LD chemo
  - Only available with Tisa-cel (Kymriah)

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The Infusion

1. Where is it done?
   - Often in the patients room or in the infusion center if being administered in out-patient.
2. How long does is last
   - Minutes but depending on product
   - Some products are a single bag or multiple
   - Some products are in vials (Liso-cel)
3. What does it feel like?
   - Painless
   - Odor (DMSO) that the family may smell but not the patient
     - Same smell as transplant infusion

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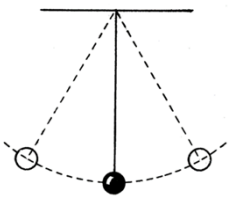
Management of Toxicity: Experience Matters

Grade



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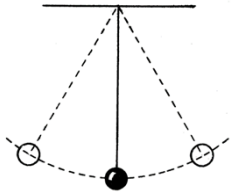
Management of Cytokine Release Syndrome (CRS)

Fever
Fatigue
Nausea/Vomit

Grade

Low blood pressure
Low oxygenation
Organ dysfunction

Tocilizumab—IL-6 receptor mAB



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Management of ICANS

Shake of the Hand

Tremor
Agitation
Word finding
Weakness

Grade

Coma
Seizure
Brain swelling

ICANS = Immune effector cell-associated neurotoxicity syndrome

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Post Infusion Monitoring Days 1-14

- Cytokine release syndrome (CRS) and immune cytokine associated neurotoxicity syndrome (ICANS)
  - Availability of at least 2 doses of tocilizumab per CAR-T patient
  - Steroid
    - Dose based on severity of ICANS
- Infections
  - Prophylactic medications
    - Short term: Antibiotics & antifungals
    - Long term: Antiviral & Anti-PJP (PCP)
- Blood transfusions
  - Red blood cell and platelets
- Replacement of electrolytes
- Intravenous fluid

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Post Discharge Monitoring Days 15-28

- Count recovery post flu/cy
  - Red blood cell and platelets transfusion less frequent
- Double dip
  - Growth factor use for sporadic neutropenia
  - Possibly more common after CRS/ICANS
- Remain in close proximity to CAR-T center
  - 24/7 caregiver
  - Monitor for recurrence of CRS/ICANS
  - Multiple visits per week

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Days 29 and Beyond

- Returning home
  - Discussion with local Oncologist (if necessary)
  - Cytopenias (low blood counts) may persist but transfusion less frequent
  - Sporadic neutropenia (low white blood cells) may return
  - Slow return to work
- Monitor for recurrent infections
  - B-cell aplasia = low immunoglobulins→ IVIG use
- Response evaluation around D=100
  - Potentially before if concern for progression
- No driving for 8 weeks
  - Includes heavy machinery
  - Return to side streets or rural road first

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Summary

- Use of CAR-T has been an effective therapy in difficult-to-treat situations with prospect of prolonged disease free survival
- No head to head trials in LBCL to determine safest or most effective CAR-T
  - Individual discussion with CAR-T team
- CAR-T access may be limited by Brain to Vein time
- Half the battle is getting to CAR-T
- Toxicity management has improved with time

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Questions?

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