Update on CAR-T Therapy

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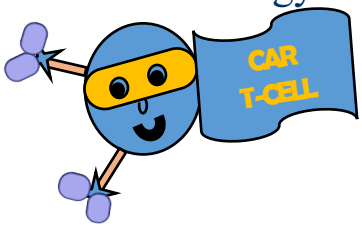

UNC LINEBERGER UNC CANCER CARE

1

Overview

- CAR-T Cell Therapy Overview
- Clinical Trial Results and FDA Approvals
- Toxicities and Management
  - Cytokine Release Syndrome
  - Neurotoxicity
- Future Directions

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2

CAR-T Cell Therapy Overview

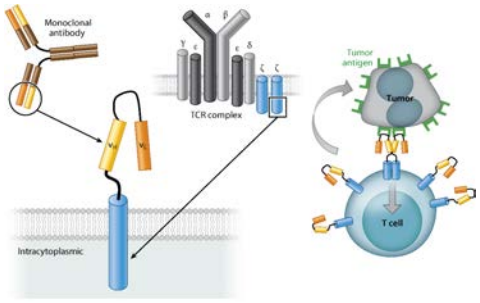
3

Cancer and the Immune System

- Cancer often develops when tumor cells evade immune surveillance or suppress immune response, leading to cell proliferation
- Therapeutic approaches:
  - overcome immune tolerance helping immune system be more targeted and effective at eliminating tumor cells

4

Chimeric antigen receptor T-



Ramos CA, et al. 2016. Annu. Rev. Med. 67:165–83

- Hybrid molecule composed of an extracellular antigen-recognition site from an antibody and intracellular signaling domain of T-cell receptor
- CAR binds antigen on surface of tumor cells -> T cell activation and killing of tumor cells
- Second generation CARs have costimulatory region which can enhance activation

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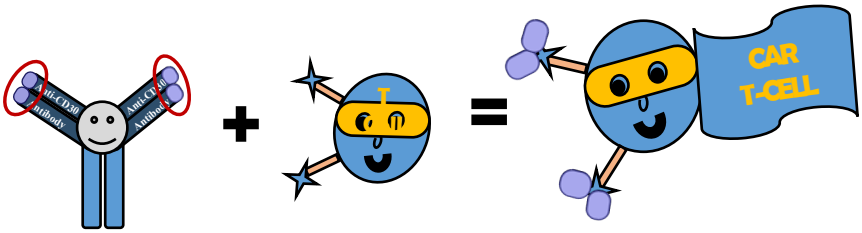

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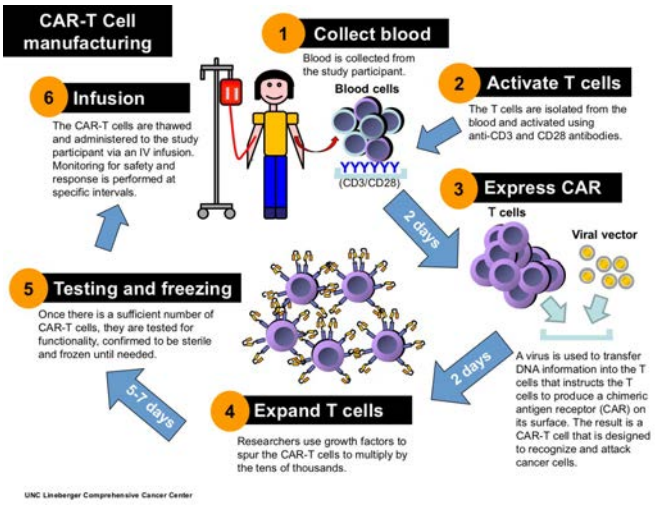


7

Lymphodepletion

- Usually prior to CAR-T cell infusion, patients receive lymphodepletoin
- Reduces endogenous lymphocytes
- Increases availability of homeostatic cytokines that promote survival of transferred T cells
- Cyclophosphamide/fludarabine most common regimen used

8

Clinical Activity of CAR-T Cells

9

Case Example

- 18 yo F initially diagnosed with ALL in 2010 at age 11
- Treated with aggressive pediatric regimen and achieved remission
- However, relapsed 1 year post therapy – underwent transplant
- 5 years later, found to have relapsed on routine blood work

10

Anti-CD19 CAR-T Cells

- CD19 – cell surface marker present on B cells -> potential target in B-cell malignancies such as B-ALL and B-cell lymphoma

11

CD19 Directed CAR-T Cells in ALL

- CAR-T cell trials in ALL show high complete response (CR) rates of 70-90% with durable remissions
- Is this treatment feasible in our patients?

12

Phase II ELIANA trial

- Global CAR-T cell therapy registration trial with study enrollment across 25 centers in US, Canada, European Union, Australia, and Japan
- Product name: Tisagenlecleucel
- Enrolled patients aged 3 to 23 years with relapsed or refractory B-cell ALL
  - Primary refractory, refractory to chemotherapy after first relapse, relapsed after second line therapy, ineligible for allogeneic stem cell transplant
- Patients received median of 3 prior lines of therapy and 61% had prior transplant

Maude et al., NEJM 2018

13

Phase II ELIANA Trial: Patients

- 92 patients enrolled -> 75 underwent infusion of CAR-T cells
- What happened to other 17 patients?
  - 7 had CAR-T product related issues
  - 7 died
  - 3 had adverse events prior to CAR-T infusion
- Median time of 45 days from enrollment to infusion

14

Phase II ELIANA Trial: Patient Characteristics

- Medan age: 11 years
- Median of 3 prior therapies
- 61% had undergone prior allogeneic stem cell transplant

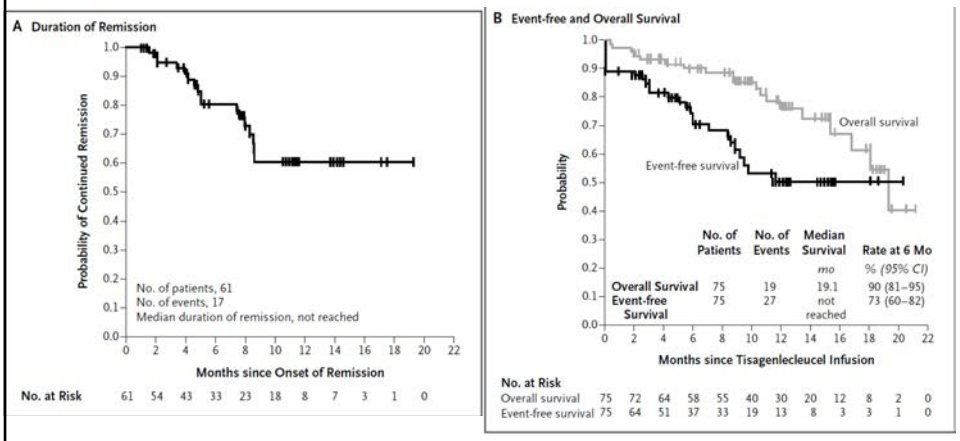
15

Phase II ELIANA Results

- 81% of patients achieved complete remission or complete remission with incomplete blood count recovery
- Event free survival: 73% at 6 months, 50% at 12 months
- Overall survival: 90% at 6 months, 76% at 12 months

16

Phase II ELIANA Results



Maude et al., NEJM 2018

17

FDA Approval

- August 30, 2017 – FDA approved first anti-CD19 CAR-T cell product, tisagenlecleucel (Kymriah), for the treatment of pediatric and young adult patients (under 25) with relapsed/refractory B-cell precursor acute lymphoblastic leukemia

18

CD19-Directed CAR-T Cells in B-cell Lymphoma

- Responses have also been seen in patients with heavily pre-treated Diffuse Large B-cell lymphoma and Follicular Lymphoma

19

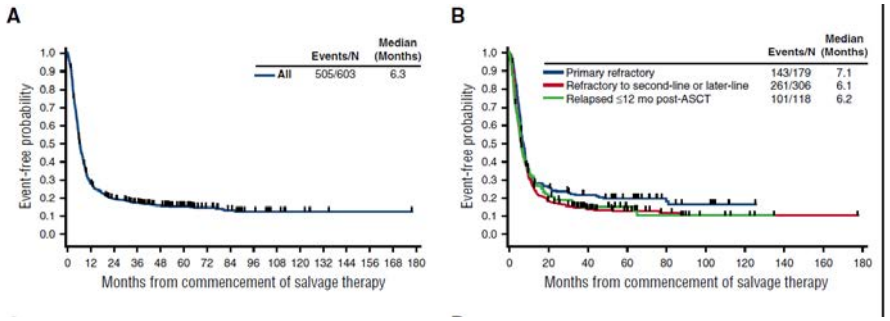
Refractory DLBCL Prognosis

- Prognosis terrible for patients with DLBCL resistant to chemotherapy or who relapse within 12 months of autologous stem cell transplantation
- Objective response rate – 26%
- Complete response rate – 7%
- Median overall survival – 6.3 months

Crump et al., Blood 2017

20

Refractory DLBCL Prognosis



Crump et al., Blood 2017

21

Zuma Trial

- Multicenter phase 2 study in patient with refractory DLBCL
- Product: Axicabtagene ciloleucel (axi-cel)- Yescarta

Neelapu et al., NEJM 2017

22

Phase II Zuma Trial: CAR-T Manufacturing

- 111 patients enrolled, 101 treated
- What happened to other 10 patients?
  - 1 unsuccessful manufacture
  - 4 adverse events
  - 1 died from disease progression
  - 2 did not meet criteria (no longer measurable disease)
- Median time from cell procurement to delivery of axi-cel – 17 days

23

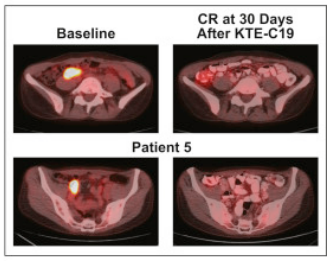
Phase II Zuma Trial: Patients

- Median age: 58 years (range 23-76)
- 24% were 65 years or older
- 69% had 3 or more prior lines of therapy

24

Phase II Zuma Trial: Results

- Objective response rate -82%
- Complete response rate – 54%
- Overall survival at 18 months – 52%



Neelapu et al., NEJM 2017

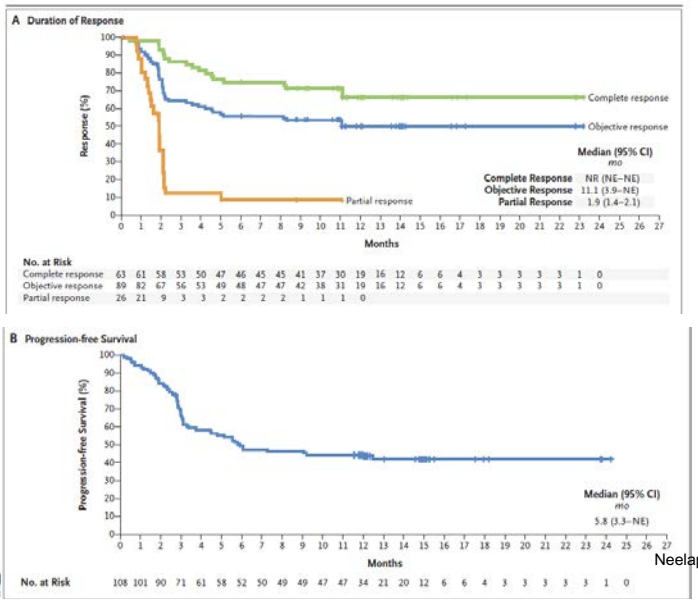
25

Phase II Zuma Trial: Sustained Remissions

- At median follow up of 15.4 months, 42% of patients continued to have response with 40% continuing to have complete response

26

Phase II Zuma Trial: Results



Neelapu et al., NEJM 2017

27

JULIET Trial

- Multicenter phase 2 study in patient with relapsed/refractory DLBCL
- Received >/= 2 lines of therapy (including rituximab and anthracycline) or relapsed following transplant
- Product: CTL019 - Tisegenlecleucel - Kymriah

Schuster et al., NEJM 2017

28

Phase II Juliet Trial: CAR-T Manufacturing

- 160 patients enrolled, 106 treated
- What happened to other patients?
  - 11 unsuccessful manufacture
  - 16 deaths
  - 16 physician discretion
  - 3 adverse events
- Only 68 evaluable for efficacy
- Median time from leukapheresis to infusion: 113 days

29

Phase II Juliet Trial: Patients

- Median age: 56 years (range 22-74)
- Median number of prior therapies: 3 (range: 1-6)

30

Phase II Juliet Trial: Results

- Objective response rate -53% (50%)
- Complete response rate – 40% (32%)
- Median duration of response and S not reached but probability relapse free at 6 months – 74%

31

FDA Approved

- October 18, 2017: FDA approved Axi-cel (Yescarta) for treatement of adults with relapsed or refractory large B-cell lymphoma following 2 prior therapies
- May 1, 2018: FDA expanded Kymriah (tisagenlecleucel) to include treatment of adult patients with relapsed or refractory DLBCL after 2 or more lines of systemic therapy

32

TABLE 1. Composition, efficacy and safety comparisons

	Axicaptagene ciloleucel[1]	Tisagenlecleucel[2]	Lisocaptagene maraleucel[3]
Study populations	DLBCL, TFL, PMBCL	R/R DLBCL	†CORE DL 2
Target Antigen	CD19	CD19	CD19
Lymphodepletion	Flu/Cy	Flu/Cy	Flu/Cy
Costimulatory Domain	CD28	4-1BB	4-1BB
T-cell Composition	Unspecified	Unspecified	1:1 CD4:CD8
Cell Dose	2 x 10^6 cells/kg	5 x 10^8	1 x 10^8
OR (Best)	82% (N=108)	53% (N=81)	81% (N=27)
OR (6 Month)	41% (N=101)	37% (N=46)	50% (N=14)
CR (Best)	58% (N=108)	40% (N=81)	63% (N=27)
CR (6 Month)	36% (N=101)	30% (N=46)	50% (N=14)
Any Grade†† CRS / NT	94% / 87% (N=108)	58% / 21% (N=99)	24% / 17% (N=29)
≥ Grade 3 CRS††	12% (N=108)	23% (N=99)	0% (N=29)
≥ Grade 3 NT††	31% (N=108)	12% (N=99)	7% (N=29)
Grade 5 AEs	4% (N=108)^A	none	-

[1]Neelapu, *NEJM* 2017, ZUMA-1
[2]Schuster, ASH 2017, JULIET
[3]Abramson, ASH 2017, TRANSCEND
^2 patients Grade 5 CRS
†CORE Group (proposed pivotal pop'n) including DLBCL, NOS tFL, FL3B, ECOG 0-1, and R/R patients
††CAR T toxicity grading scales differ across studies

Courtesy of and adapted from C. Turtle MBBS, PhD

Chow et al., Blood 2018

33

Questions for DLBCL

- When to use CAR-T?
- Current clinical trial comparing autoSCT to CAR-T

34

Poll 1

Which of the following is NOT currently approved for indications for CAR-T cells?

- Tisagenlecleucel
- Axicabtagene ciloleucel (axi-cel)- Yescarta
- Cabazitaxel
- Rituximab
- Anthracycline

35

Toxicities and Management

36


10 Breakthrough Technologies The List + Years +
Immune Engineering
Genetically engineered immune cells are saving the lives of cancer patients. That may be just the start.
Biomedicine
Biotech's Coming Cancer Cure
Supercharge your immune cells to defeat cancer? Juno Therapeutics believes its treatments can do exactly that.
by Antonio Regalado June 18, 2015
Sections
The Washington Post
Health & Science
This 8-year-old is free of cancer — for now — after a 'breakthrough' treatment
By Laurie McGinley
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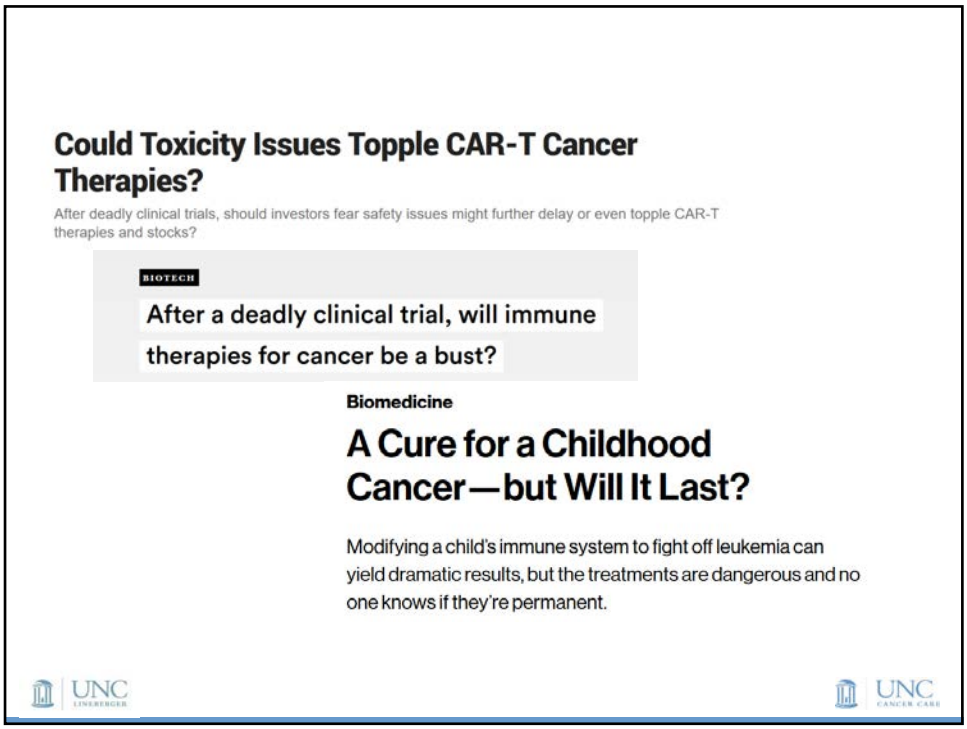
37


Could Toxicity Issues Topple CAR-T Cancer Therapies?
After deadly clinical trials, should investors fear safety issues might further delay or even topple CAR-T therapies and stocks?
BIOTECH
After a deadly clinical trial, will immune therapies for cancer be a bust?
Biomedicine
A Cure for a Childhood Cancer—but Will It Last?
Modifying a child's immune system to fight off leukemia can yield dramatic results, but the treatments are dangerous and no one knows if they're permanent.
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38

Case Example

- 18 yo F with ALL treated with CD19 directed CAR-T cells
- Developed high grade fever to 40C within 24 hours of CAR-T cell infusion with tachycardia, fatigue, decreased appetite
- Managed with Tylenol, cooling blanket
- Received empiric broad spectrum antibiotics
- Work up negative for infection

39

Case Example

- On day 1 after CAR-T cell infusion, developed hypotension with systolic blood pressure of 80 mmHg with hypoxia
- Treated with IV fluid bolus and supplemental O2
- Hypotension not responsive to fluid boluses and required vasopressor support
- Received dose of tocilizumab with response to hypotension and hypoxia

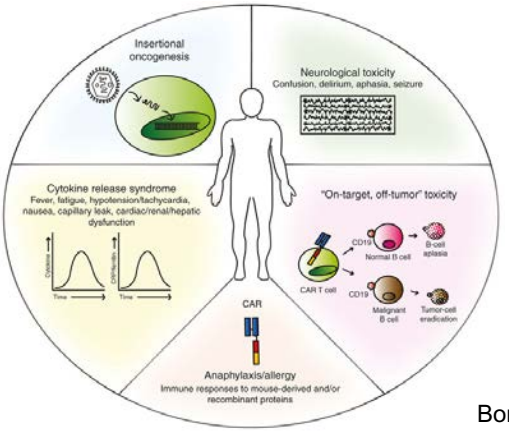
40

Case Example

- On day 6, she developed handwriting impairment and the following day she became confused and disoriented
- She subsequently developed expressive aphasia and slurred speech
- These symptoms lasted for 3 days and then resolved and she was discharged

41

Toxicities of CAR-T Therapy



Bonifant et al.,
Mol Ther Oncolytics, 2016

42

Cytokine Release Syndrome

- Systemic inflammatory event triggered resulting from release of cytokines (including IL-6 and interferon-gamma) associated with proliferation and activation of T cells
- Typically presents with constitutional symptoms, such as fever, malaise anorexia, and myalgias, but can affect any organ system
- Usually occurs within first week after CAR-T cell therapy and peaks within 1-2 weeks of cell administration (differs according to product)
  - Median time of onset – Kite product – 2 days; Novartis product – 3 das

43

CRS Symptoms

TABLE 1. Signs and Symptoms of CRS

Organ system	Signs/Symptoms
Constitutional	Fever, rigors, malaise, fatigue, anorexia, myalgias/arthralgias, nausea/vomiting
Dermatologic	Rash
Gastrointestinal	Nausea/vomiting/diarrhea
Respiratory	Tachypnea, hypoxemia (potentially requiring supplemental oxygen/ventilation)
Cardiovascular	Tachycardia, hypotension
Coagulation	Disseminated intravascular coagulation (DIC) characterized by elevated D-dimer, hypofibrinogenemia, bleeding
Renal	Azotemia
Hepatic	Transaminitis, hyperbilirubinemia
Neurologic	Altered mental status, confusion, delirium, aphasia, hallucinations, tremor, seizures, ataxia

44

Risk Factors for Severe CRS

- Bulky disease
- Comorbidities
- Early onset CRS (within 3 days of cell infusion)

45

CRS Management - Symptoms

- Fever- usually first presenting symptom and occur in most patients with CRS
  - Use acetaminophen for comfort but often doesn't relieve fever
  - Often experience fever-associated tachycardia and chills
  - Work up and treat for infection
- May develop anorexia, nausea, vomiting -> require anti-emetics
  - Nausea and anorexia can last for weeks after other symptoms have resolved
- Myalgias and headaches – require pain meds

46

CRS Management - Labs

- Check IL6 (takes longer to return), CRP, and ferritin
- IL6 induces CRP production by hepatocytes so CRP good marker for CRS
  - Fast and easily available
  - Declining CRP levels, although potentially lagging behind declines in cytokine levels by 1-2 days, may be useful to identify peak of syndrome in individual patient

47

CRS Grading

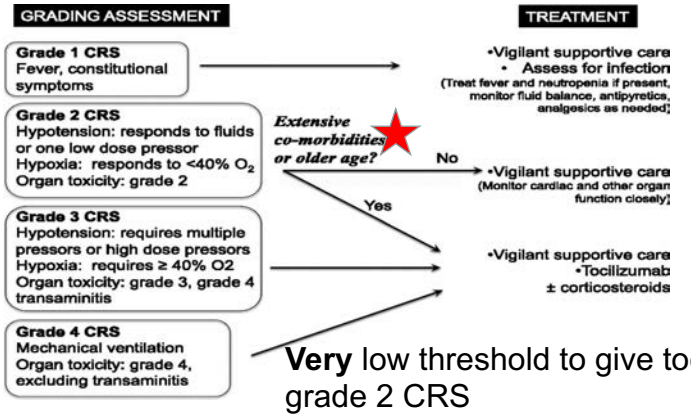
Table 2 | **Grading of cytokine-release syndrome (CRS)**

Symptom or sign of CRS	CRS grade 1*	CRS grade 2‡	CRS grade 3‡	CRS grade 4‡
Vital signs				
Temperature ≥38 °C (fever)	Yes	Any	Any	Any
Systolic blood pressure <90 mmHg (hypotension)	No	Responds to IV fluids or low-dose vasopressors	Needs high-dose or multiple vasopressors§	Life-threatening
Needing oxygen for SaO_2 >90% (hypoxia)	No	FiO_2 <40%	FiO_2 ≥40%	Needing ventilator support
Organ toxicities‖				
• Cardiac: tachycardia, arrhythmias, heart block, low ejection fraction • Respiratory: tachypnoea, pleural effusion, pulmonary oedema • GI: nausea, vomiting, diarrhoea • Hepatic: increased serum ALT, AST, or bilirubin levels • Renal: acute kidney injury (increased serum creatinine levels), decreased urine output • Dermatological: rash (less common) • Coagulopathy: disseminated intravascular coagulation (less common)	Grade 1	Grade 2	Grade 3 or grade 4 transaminitis	Grade 4 except grade 4 transaminitis

Neelapu et al., Nature Reviews Clinical Oncology 2017

48

CRS Management Algorithm



Very low threshold to give tocilizumab for grade 2 CRS

Lee, D.W., et al., *Current concepts in the diagnosis and management of cytokine release syndrome.* Blood, 2014. **124**(2): p. 188-95.

49

Tocilizumab

- Anti-IL-6 receptor antibody
- FDA approved for the treatment of CRS occurring after CAR-T cell therapy
- Use does not seem to affect efficacy of CAR-T cell therapy
- Fever often resolves within a few hours and pressors and other supportive care measures can be weaned quickly
- Give second dose after 6 hours if condition does not improve or stabilize
- If hypotentsion persists after 1-2 doses of toclizumab, can give steroids

50

FDA Approval

- August 30, 2017: At the same time FDA approved Kymriah, FDA also approved tocilizumab for treatment of cytokine release syndrome

51

Corticosteroids

- Suppress inflammatory response
- Since suppress T cell function and can induce T cell apoptosis, concern that could interfere with efficacy
- Use in CRS refractory to tocilizumab or neurotoxicity

52

CRS in Clinical Trials

- ALL trial
  - CRS occurred in 77% of patients
  - Median time to onset: 3 days
  - Median duration: 8 days
  - 37% received tocilizumab
  - 47% admitted to ICU with median stay of 7 days
  - 25% treated with high dose pressors
  - 13% intubated
  - 9% received dialysis

53

CRS in Lymphoma Clinical Trials

- Kite
  - CRS occurred in 93% of patients
  - 37% grade 1, 44% grade 2, 9% grade 3, 3% grade 4, 1% grade 5
  - 17% patients received vasopressors
  - Median time after infusion to onset: 2 days, median time to resolution – 8 days
- Novartis
  - CRS occurred in 74% of patients (23% grade 3 or higher)
  - 21% received tocilizumab

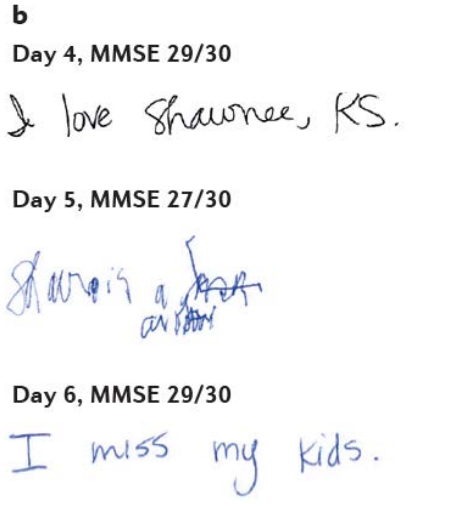
54

Neurotoxicity/CAR-T cell related encephalopathy syndrome (CRES)

- Typically present with toxic encephalopathy -> diminished attention, language disturbance, impaired handwriting
- Confusion, disorientation, agitation, aphasia, somnolence, tremors
- Severe symptoms: seizures, motor weakness, incontinence, mental obtundation, increased intracranial pressure, papilledema, cerebral edema

55

Example of Dysgraphia



Neelapu et al., Nature Reviews Clinical Oncology 2017

56

Neurotoxicity

- Risk factors: high tumor burden, cell dose, CRS, pre-existing neurological abnormalities
- Can have neurologic symptoms during CRS associated with high fevers
- Can occur later after CRS has subsided, often after day 5
- Delayed neurotoxicity with seizures and confusion has occurred during 3rd to 4th week after CAR-T cell therapy in 10% of patients
- Mechanism of action unknown -> IL-6 directed neurotoxicity? Infiltration of CAR-T cells into CSF?

57

Grading of Neurotoxicity/CRES (CAR-T Related Encephalopathy Syndrome)

Table 4 | **Grading of CAR-T-cell-related encephalopathy syndrome (CRES)**

Symptom or sign	Grade 1	Grade 2	Grade 3	Grade 4
Neurological assessment score (by CARTOX-10*)	7–9 (mild impairment)	3–6 (moderate impairment)	0–2 (severe impairment)	Patient in critical condition, and/or obtunded and cannot perform assessment of tasks
Raised intracranial pressure	NA	NA	Stage 1–2 papilloedema‡, or CSF opening pressure <20 mmHg	Stage 3–5 papilloedema‡, or CSF opening pressure ≥20 mmHg, or cerebral oedema
Seizures or motor weakness	NA	NA	Partial seizure, or non-convulsive seizures on EEG with response to benzodiazepine	Generalized seizures, or convulsive or non-convulsive status epilepticus, or new motor weakness

CAR, chimeric antigen receptor; CARTOX-10, CAR-T-cell-therapy-associated toxicity 10-point neurological assessment CSF, cerebrospinal fluid; EEG, electroencephalogram; NA, not applicable.
*In the CARTOX-10, one point is assigned for each of the following tasks that is performed correctly (normal cognitive function is defined by an overall score of 10): orientation to year, month, city, hospital, and President/Prime Minister of country of residence (total of 5 points); name three objects — for example, point to clock, pen, button (maximum of 3 points); write a standard sentence, for example, 'our national bird is the bald eagle' (1 point); count backwards from 100 in tens (1 point).
‡Papilloedema grading is performed according to the modified Frisén scale[80].

Neelapu et al., Nature Reviews Clinical Oncology 2017

58

Management of Neurologic Toxicity of CAR-T cells

- Work up depends on presentation: MRI, lumbar puncture, EEG
- Tocilizumab does not cross BBB and therefore hasn't been shown to be effective - > use only if concurrent CRS
  - Could saturate IL-6 receptors and increase serum IL-6 levels which would increase CSF IL-6 levels which could worsen neurotoxicity
- First line agent: systemic corticosteroids
  - Dexamethasone – preferred first line treatment for patients with neurological toxicity given excellent CNS penetration
- Treat seizures with standard anti-epileptic therapy
- Consider keppra prophylaxis

59

Neurotoxicity in Clinical Trials

- ALL trial
  - 40% experienced neurotoxicity
  - 13% grade 3 neurologic events
  - 50% grade 3 neurologic events resolved within 10 days

60

Neurotoxicity in Clinical Trials

- Kite Trial
  - 64% experienced neurotoxicity (28% grade 3 or higher)
  - Median time of onset on day 5 post infusion with median time of resolution of day 17 post infusion
- Novartis Trial
  - 58% experienced neurotoxicity (18% grade 3 or higher)
  - Median time of onset on day 6 from infusion and median duration of 14 days

61

B Cell Aplasia (CAR-19)

- CAR-19 targets any cells expressing CD19, including normal B cells, leading to B cell aplasia
- B cell aplasia leads to hypogammaglobulinemia since B cells produce immunoglobulins
- Patients receive monthly IVIG as long as B cell aplasia occurs

62

Poll 2

Which of the following can be given to a patients when they present Grade 3 CRS (hypotension and/or hypoxia) or Grade 4 CRS (mechanical ventilation)?

- Tocilizumab
- Corticosteroids
- Dexamethasone
- Keppra prophylaxis

63

Future Directions and UNC Trials

64

Future CAR Approvals

- BCMA CAR – myeloma – will likely be approved soon

65

Current and Upcoming UNC Trials

- CD30 CAR – Lymphoma (Hodgkin, ALCL, etc.)
- CD19 CAR with suicide gene (ALL, CD19+ lymphoma)
- CD138 CAR – Multiple myeloma

66

Future Directions – Solid Tumors?

Table 3 | **CAR targets for the treatment of solid malignancies**

Target	CAR structure	Malignancy	Institution	Reference
PSMA	CD3ζ and CD28	Prostate cancer	MSKCC	NCT01140373 (REF. 76)
			Roger Williams	NCT00664196 (REF. 78)
Mesothelin	CD3 and 4-1BB	Malignant pleural mesothelioma	UPenn	NCT01355965 (REF. 81)
		Pancreatic cancer	UPenn	NCT02465983 (REF. 156)
		Metastatic pancreatic (ductal) adenocarcinoma, epithelial ovarian cancer and malignant epithelial pleural mesothelioma	UPenn	NCT02159716 (REF. 84)
	CD3ζ and CD28	Mesothelioma and malignant pleural disease	MSKCC	NCT02414269 (REF. 85)
	CD3ζ, CD28 and 4-1BB	Mesothelioma, pancreatic and ovarian cancer	NCI	NCT01583686 (REF. 86)
FAP	CD3ζ and CD28	Mesothelioma	University of Zurich (Switzerland)	NCT01722149 (REF. 90)
EGFRvIII	CD3ζ and 4-1BB	Glioma	UPenn	NCT02209376 (REF. 95)
	CD3ζ, CD28 and 4-1BB	Glioma	NCI	NCT01454596 (REF. 97)
EGFR	Unknown	Malignant glioma	Renji Hospital (China)	NCT02331693 (REF. 98)
CEA	CD3ζ and CD28	Liver metastases	Roger Williams	NCT02146466 (REF. 100)
	Unknown	Lung, colorectal, gastric, breast and pancreatic cancer	Southwest Hospital (China)	NCT02349724 (REF. 103)
CD171	CD3ζ and 4-1BB or CD3ζ, CD28 and 4-1BB	Neuroblastoma	Seattle Children's	NCT02311621 (REF. 106)
GD2	CD3ζ, OX40, CD28	Neuroblastoma, osteosarcoma and melanoma	NCI	NCT02107963 (REF. 112)
		Neuroblastoma	Baylor	NCT01822652 (REF. 114)
	CD3ζ, Ox40, CD28, virus specific	Sarcoma	Baylor	NCT01953900 (REF. 115)
Glypican-3	CD3ζ, CD28 and 4-1BB	Advanced-stage hepatocellular carcinoma	Renji Hospital (China)	NCT02395250 (REF. 117)
HER2	CD3ζ and CD28 virus specific	Sarcoma	Baylor	NCT00902044 (REF. 122)
	CD3ζ and CD28	Glioblastoma	Baylor	NCT02442297 (REF. 126)
		Glioblastoma multiforme	Baylor	NCT01109095 (REF. 127)
IL-13	RaCD3ζ and 4-1BB	Glioma	City of Hope	NCT02208362 (REF. 131)

Baylor, Baylor College of Medicine (USA); CEA, carcinoembrionic antigen; City of Hope, City of Hope National Medical Center (USA); EGFRvIII, epidermal growth factor receptor variant III; FAP, prolyl endopeptidase FAP/fibroblast activation protein alpha; MSKCC, Memorial Sloan Kettering Cancer Center (USA); NCI, National Cancer Institute (USA); PSMA, prostate-specific membrane antigen; Roger Williams, Roger Williams Medical Center (USA); Seattle Children's, Seattle Children's Hospital (USA); UPenn, University of Pennsylvania (USA).

67

Challenges to CAR-T in Solid Tumors

- **Problem:** Solid tumors generally more heterogeneous so they are harder to target
  - More difficult to find universal target antigen
- **Possible solution:** CARs that can target multiple antigens

68

Challenges to CAR-T in Solid Tumors

- **Problem:** Suppressive tumor microenvironment
- **Possible solution:** "armored" T cells that express molecules that reduce suppression by Tregs; e.g., preclinical studies of CAR-T cells that secrete checkpoint blocking antibodies

69

Challenges to CAR-T in Solid Tumors

- **Problem:** Often less accessible to CAR-T cells (surrounded by other tissues, organized into different compartments)
- **Possible solution:** Improve CAR-T cells' ability "breech tumor defenses"

70

Challenges to CAR-T in Solid Tumors

- **Problem:** Difficult to target because many target antigens also expressed by normal cells
- **Possible solution:** Identify more specific antigens; tune CARs to "react only to cells that express target antigens at high levels;" "safety valve" measures such as suicide genes

71

Off the Shelf CARs?

- Gene editing being used to delete T cell receptor and other endogenous genes for preparation of allogeneic "off-the-shelf" CAR-T cells

72

Poll 3

In your opinion, which is the most interesting challenge of developing CAR-T cells for solid tumors?

73

Questions about Applications of CAR-T Cells

- How best to deliver to patients?
- Cost?
- Insurance coverage?
- Management of toxicities?
- What line of care to use?

74

Summary

- CD19 directed CAR-T cells have shown promising efficacy in the treatment of ALL and B-cell lymphomas
- Toxicities of therapy include cytokine release syndrome and neurotoxicity
- Cytokine Release Syndrome (CRS)
  - CRS can be seen within 24 hours after CAR-T treatment until 3 weeks after treatment
  - Treatment for CRS will include standard supportive care/infectious workup
  - Additional treatment can include tocilizumab
  - Steroids should be avoided when possible
- Neurotoxicity
  - Can present with a range of neurological symptoms including stroke like symptoms
  - Standard altered mental status workup is appropriate
  - Seizures should be treated with standard anti-epileptic medications
  - Treatment of severe symptoms with dexamethasone

75

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76