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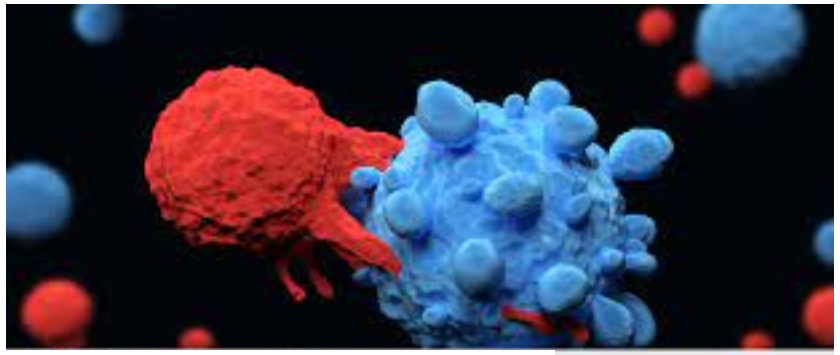
Education



Emerging Applications of CAR T-cell Therapy in Cancer

Veronika Bachanova, MD, PhD

Professor of Medicine

University of Minnesota

March 15, 2022

Outline

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- Review principles of CAR T-cell therapy, including its mechanism of action and cellular targets.
- Describe current data about the recent and emerging applications of CAR T-cell therapy in multiple myeloma, lymphoma, other hematologic cancers, and solid tumors.
- Discuss the limitations and challenges of CAR T-cell therapy, including common side effects and toxicities.
- Report on the guidelines available for determining treatment strategies using CAR T-cell therapy.
- Identify factors that should be considered when determining individuals' eligibility for. and potential benefit from, CAR T-cell therapy.

Principles of cellular therapy

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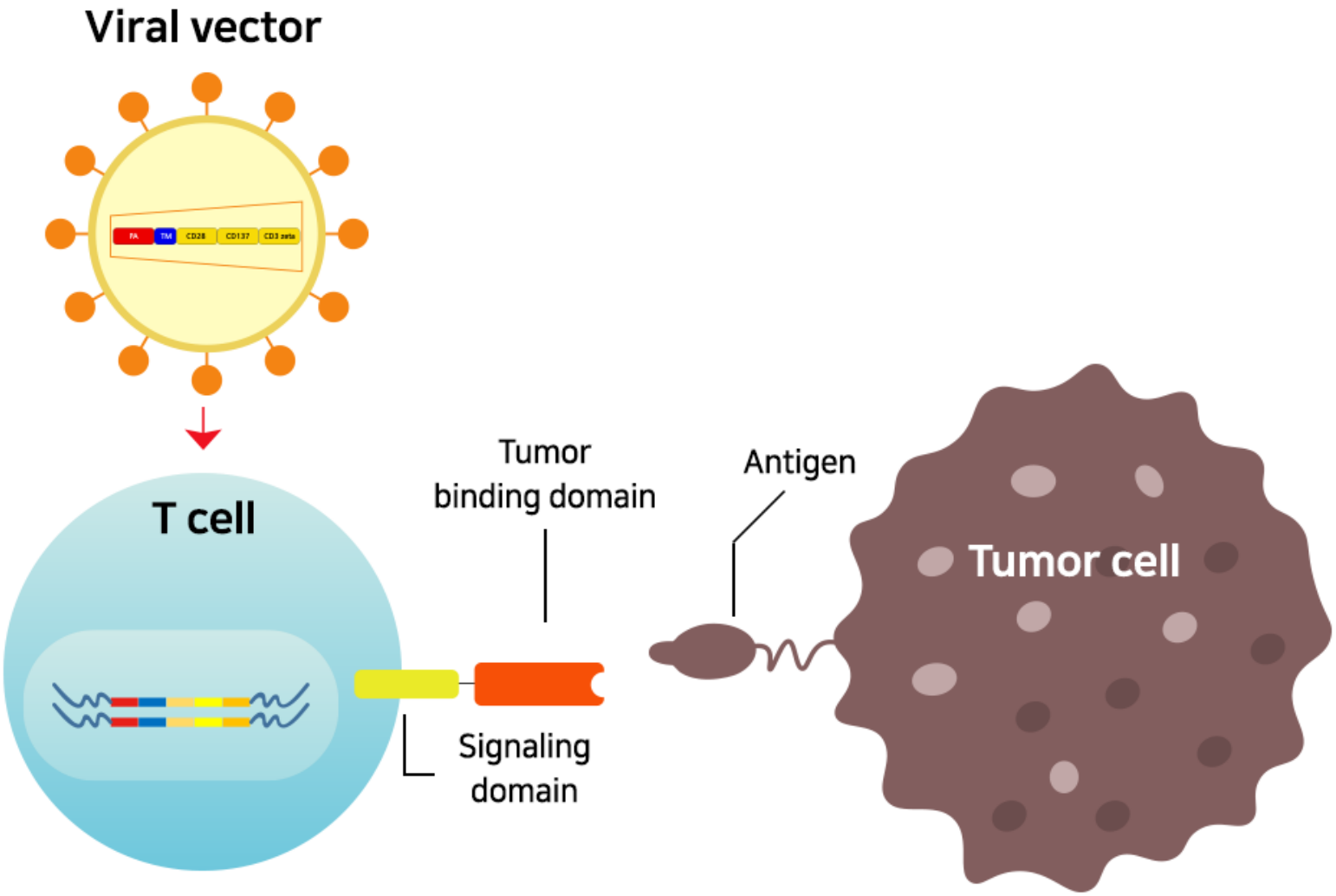
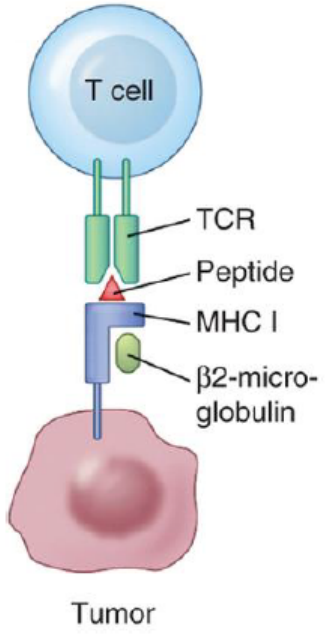


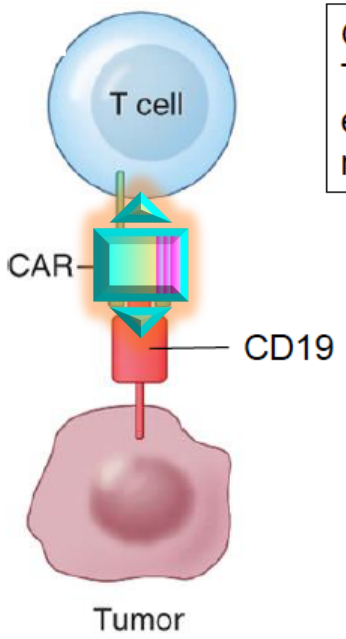
Chimeric Antigen Receptor (CAR) Modified T cells

Physiologic

Normal T cell



CAR T cell



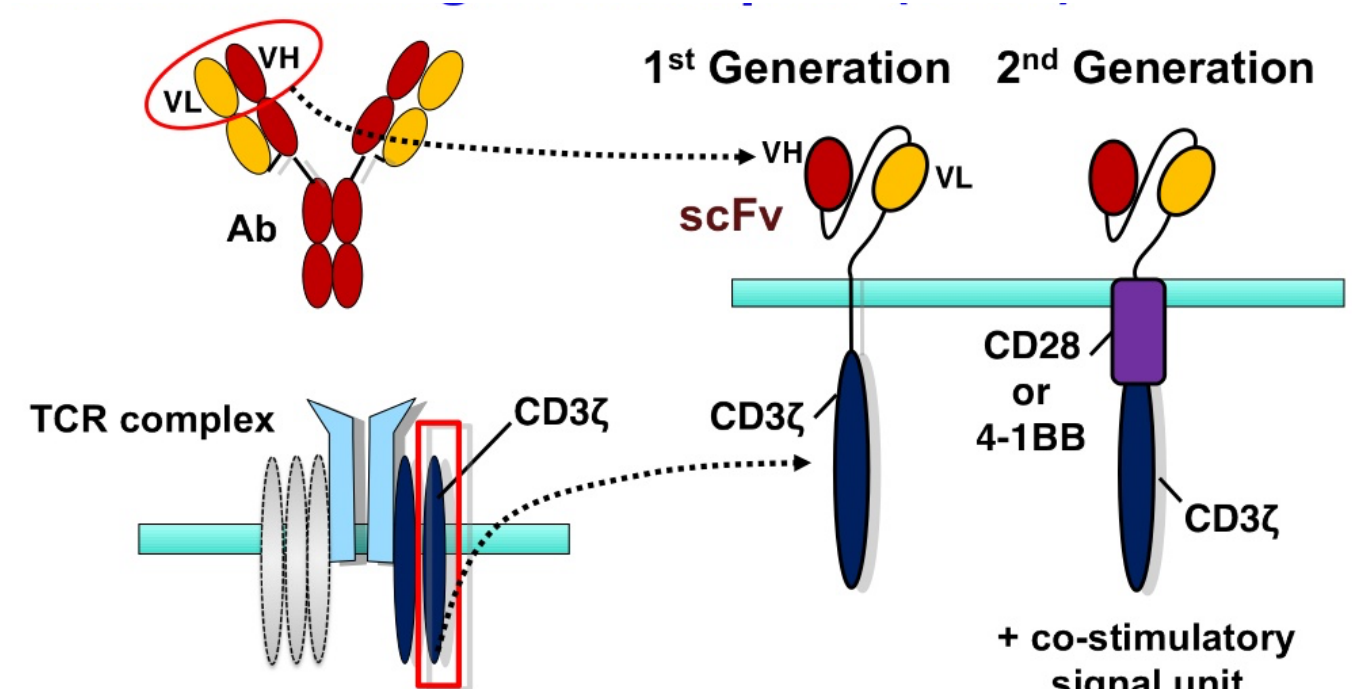
Genetically engineered T cells altered to express an artificial receptor, CAR

Synthetic receptor

CAR redirects patients own T cells to kill tumor cells

Adapted from Hinrichs & Restifo. Nat Biotech 2013

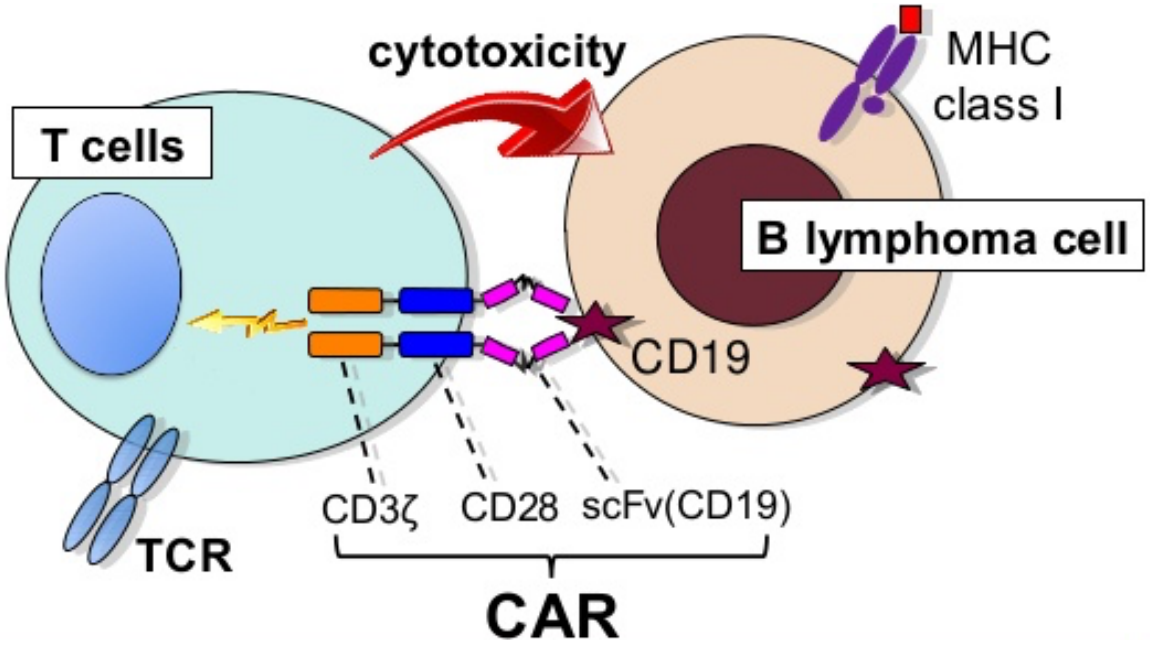
Synthetic CAR Receptor is expressed on T cell surface



1. Antigen Binding Domain. -Recognizes CD19 antigen on B cell
2. Costimulatory Domain. -Increases T-cell activation & enhances cytolytic function
3. CD3-zeta chain signaling domain. -Induces T-cell activation

Adapted from: Maus MV, et al. Blood. 2014;123:2625-35.

Mechanism of action: Direct cell to cell killing of cancer cells



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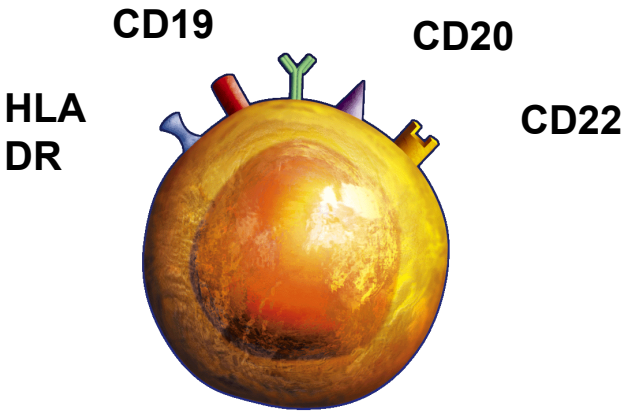
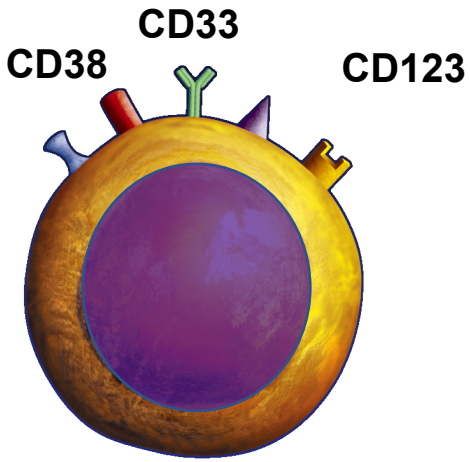
Targets Expression on Cancer Cells

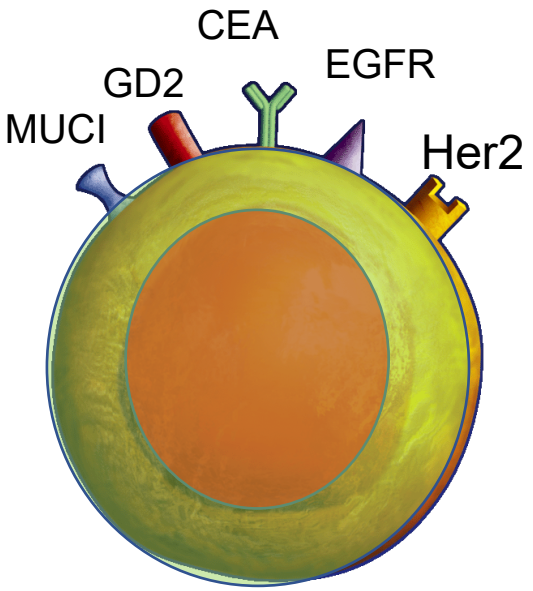
B-cell Targets



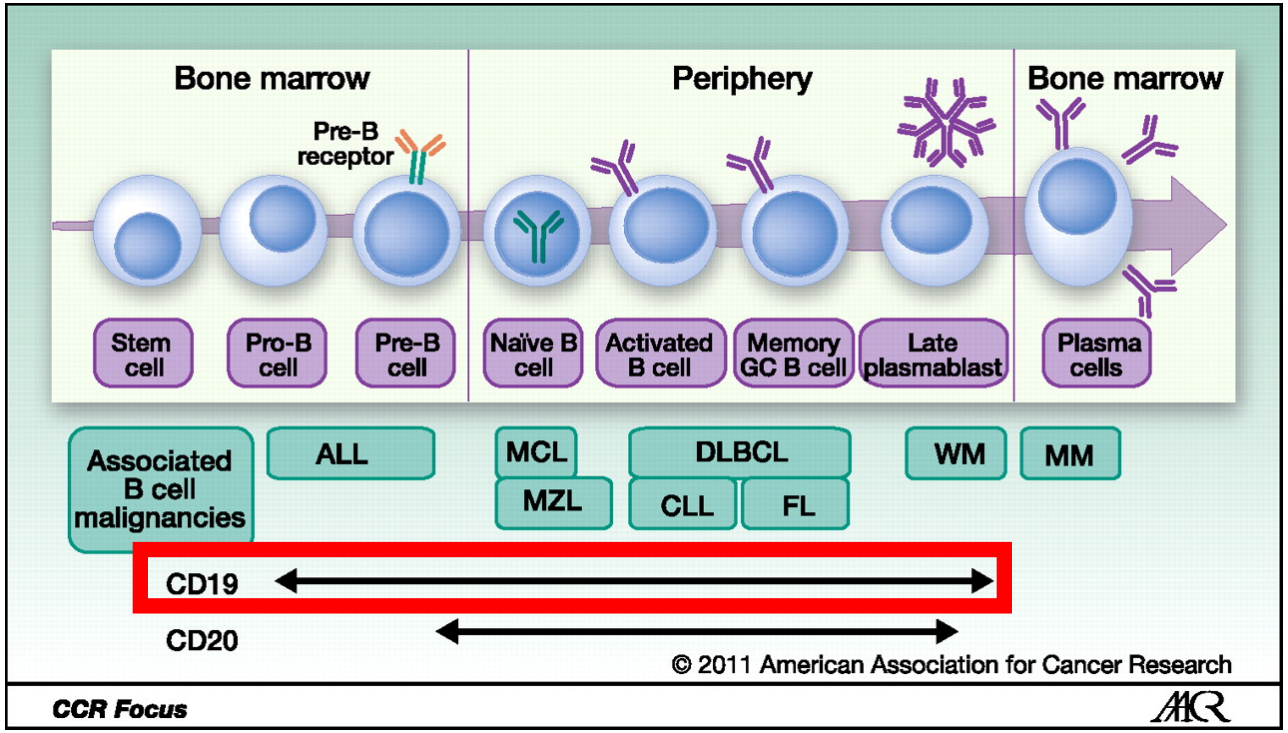
AML Targets



Solid Tumors Cancer Cells



B Cell Malignancies are CD19+

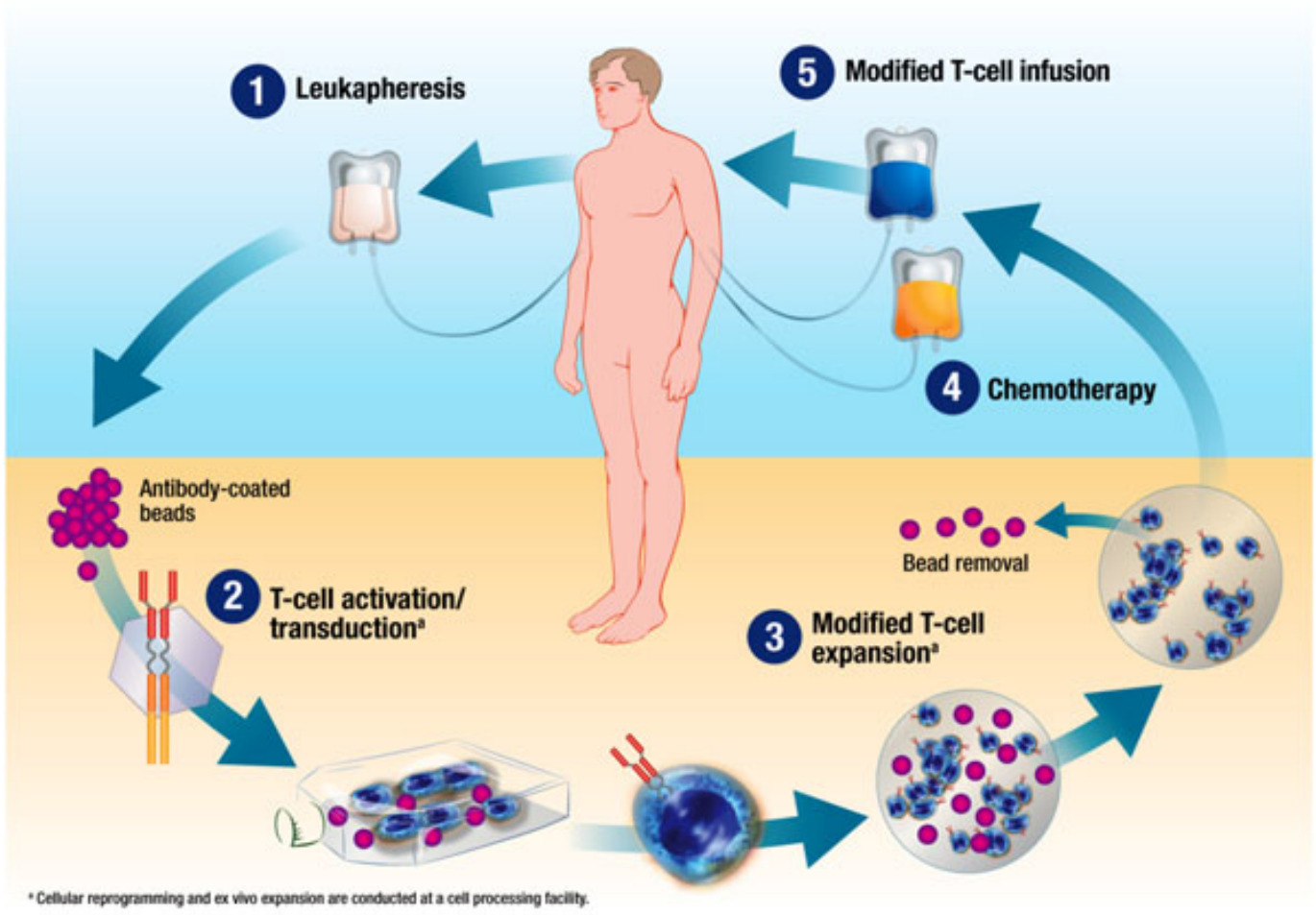


- CD19 is expressed throughout B-cell development; therefor it is expressed in most B cell malignancies
- CD19 expression is not expressed on pluripotent bone marrow stem cells

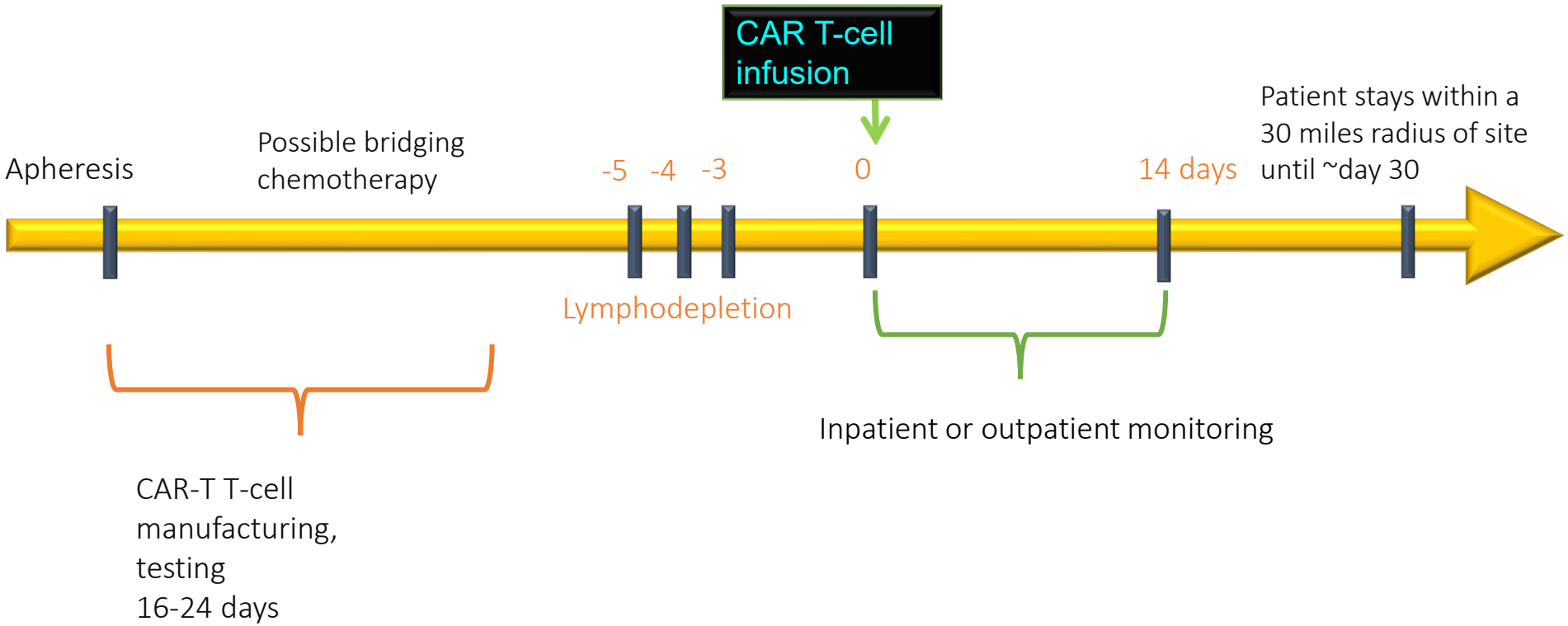
Blanc et al. Clinical Cancer Research 2011

Each CAR-T product is custom made and patient specific
Ex vivo CAR-T cell manufacturing

GENE TRANSFER Using Retrovirus or Adenovirus



The Road to Remission using autologous CAR-T



Source: https://decisionresourcesgroup.com/drg-blog/u-s-medical-communitys-perception-car-t-cell-therapies/

Currently FDA approved autologous CAR-T cell therapies

Lymphoma Relapsed/Refractory antiCD19	**B-cell Acute Leukemia Relapsed/Refractory** antiCD19	**Multiple Myeloma Relapsed/Refractory** anti BCMA

• **Aggressive B-cell lymphoma**
  • Tisa-Cel
  • Axi-Cel
  • Liso-Cel
• **Follicular lymphoma**
  • Axi-Cel
• **Mantle cell lymphoma**
  • Brexucabtagene
	• **B-cell ALL (0-26 yrs)**
	  – Tisa –Cel (8/2017)
	• **B-cell ALL(>18 yrs)**
	  – Brexucabtagene
		• Idecabtegene (BCMA)
		• Ciltacebtagene (BCMA)

High Efficacy of CD19 CAR-T's for patients with relapsed/refractory aggressive B cell lymphoma

	Axi-cel Yescarta (ZUMA-1)	*Tisa-cel* Kymriah (JULIET)	*Liso-cel* Breyanzi (TRANSCEND)
Indications	relapsed or refractory after 2 or more lines of systemic therapy	relapsed or refractory after 2 or more lines of systemic therapy	relapsed or refractory after 2 or more lines of systemic therapy
Number of pts in pivotal studies (enrolled/infused)	111/101	165/111	342/268
Prior ASCT **Refractory disease**	21% 79%	49% 55%	33% 67%
Overall Response	**82%**	**52%**	**73%**
Complete Response	**58%**	**38%**	**53%**

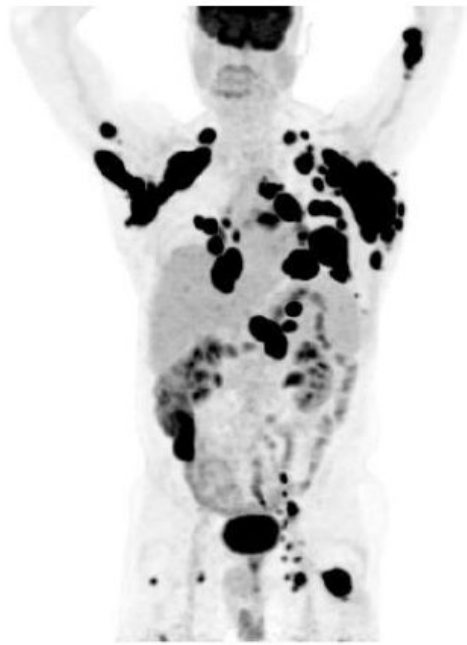
t al. *NEJM* (2017), Schuster et al. *NEJM* (2019), Abramson et al. *Lancet* (2020)

Profound efficacy

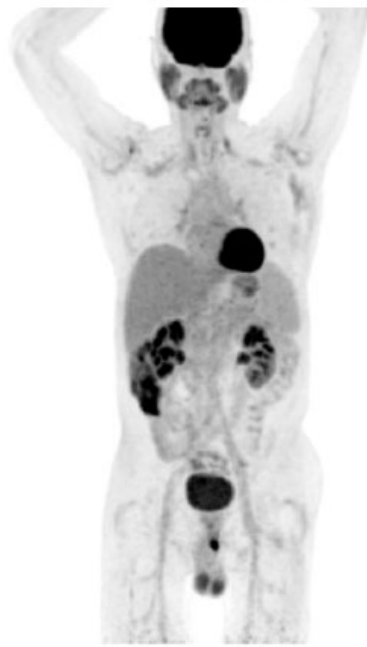
62 yo M with DLBCL
Prior therapies

- R-CHOP
- Radiation
- R-GDP
- Radiation
- R-ICE
- R-Revlimid

Baseline



3 months



Remains in CR at 9 months following infusion of KTE-C19, ZUMA-1 trial.

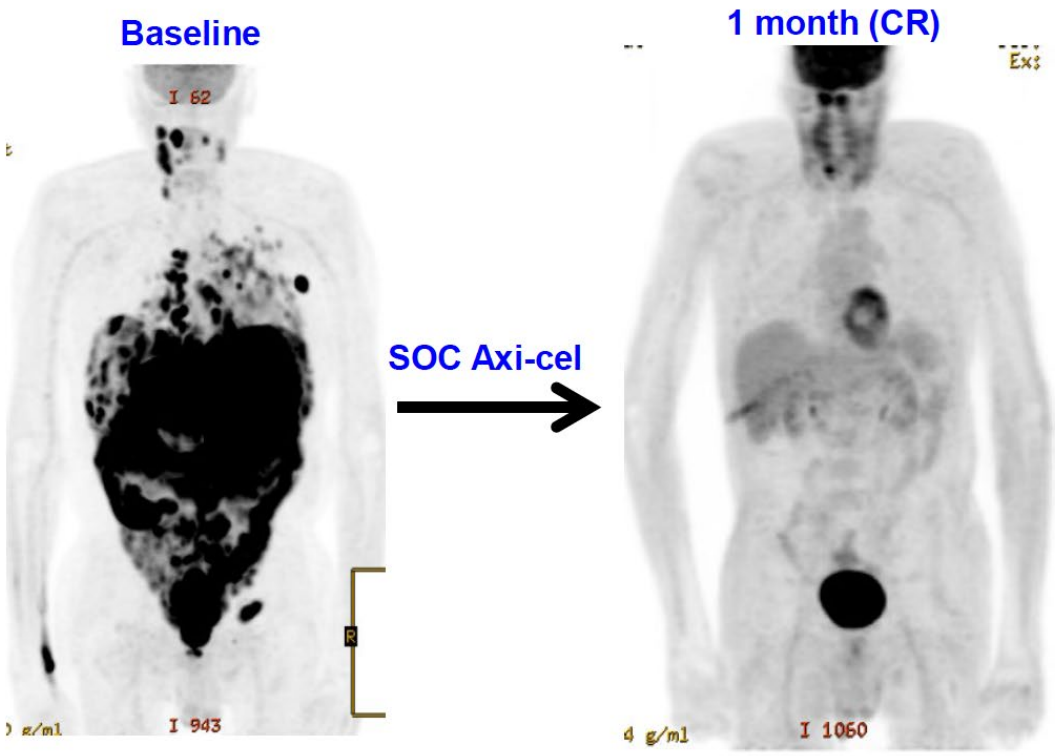
Patients with large tumor bulk can respond to CAR-T19

Subject with Multiple Co-morbidities

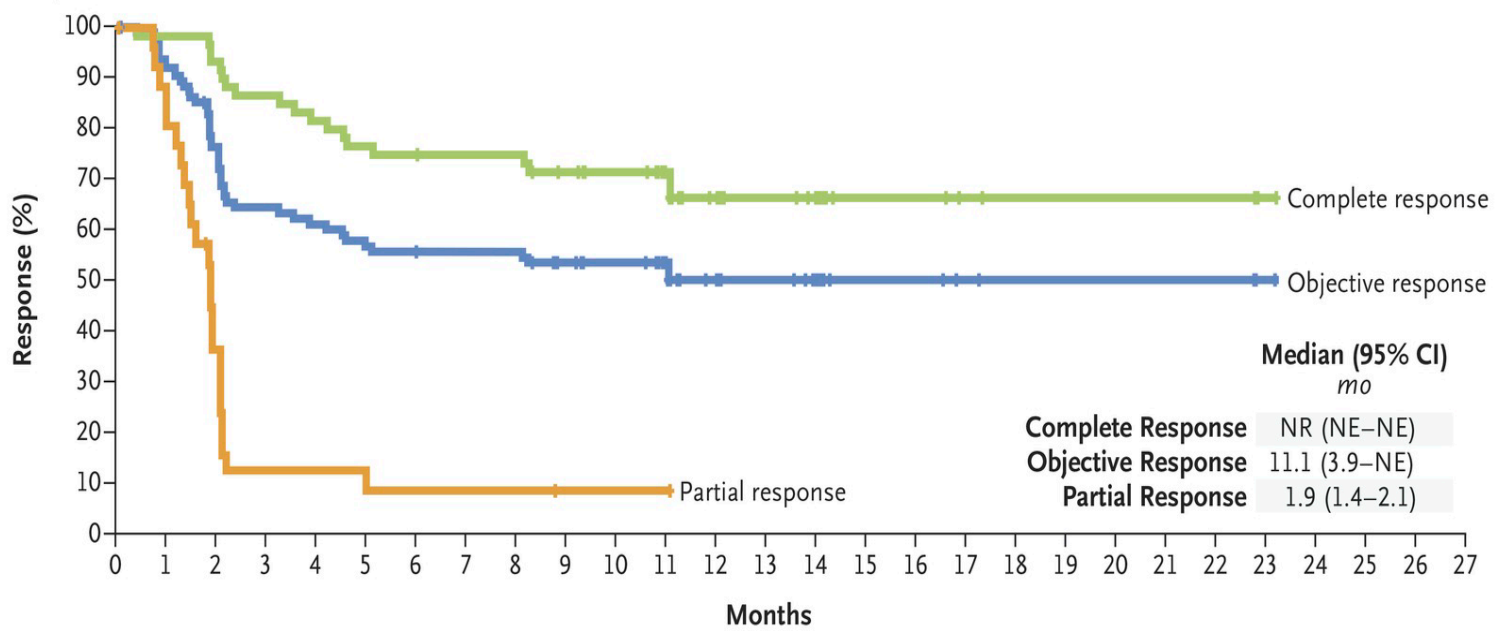
68 yo M with DLBCL-GCB

Prior therapies – 7
- R-CHOP
- ICE → Zevalin
- R-ESHAP
- R-Hypercytoxan
- Gemcitabine
- Bendamustine
- R-Hypercytoxan

Co-morbidities
- ECOG PS 3
- EF – 45%
- Pulmonary embolism
- GI bleed
- Obstructive jaundice → Biliary catheter

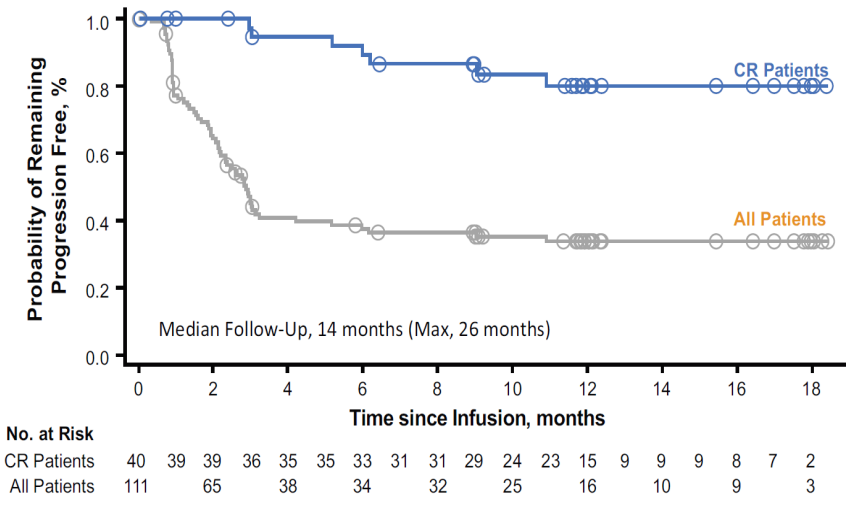


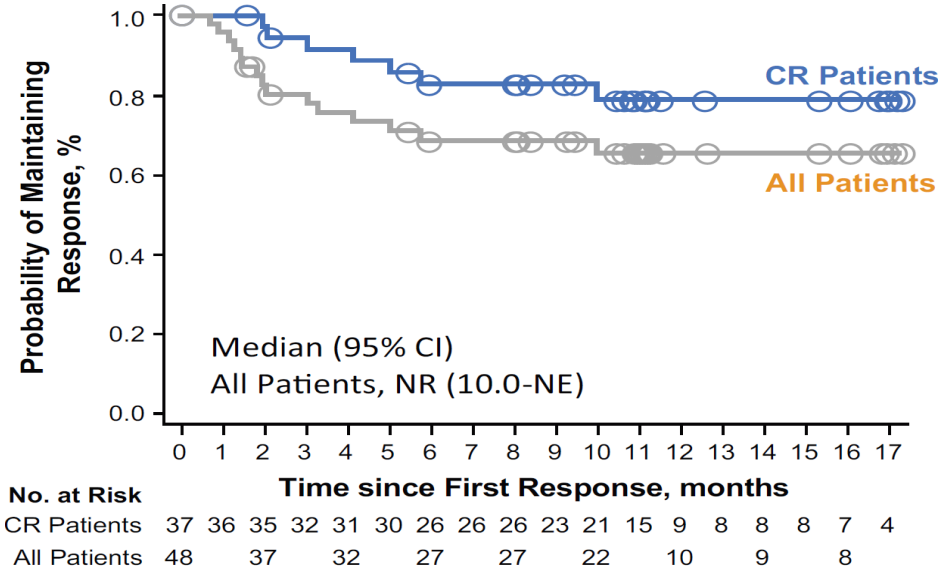
Axicabtagene ciloleucel in B Cell Lymphoma
Duration of Response



Neelapu et al. NEJM 2017

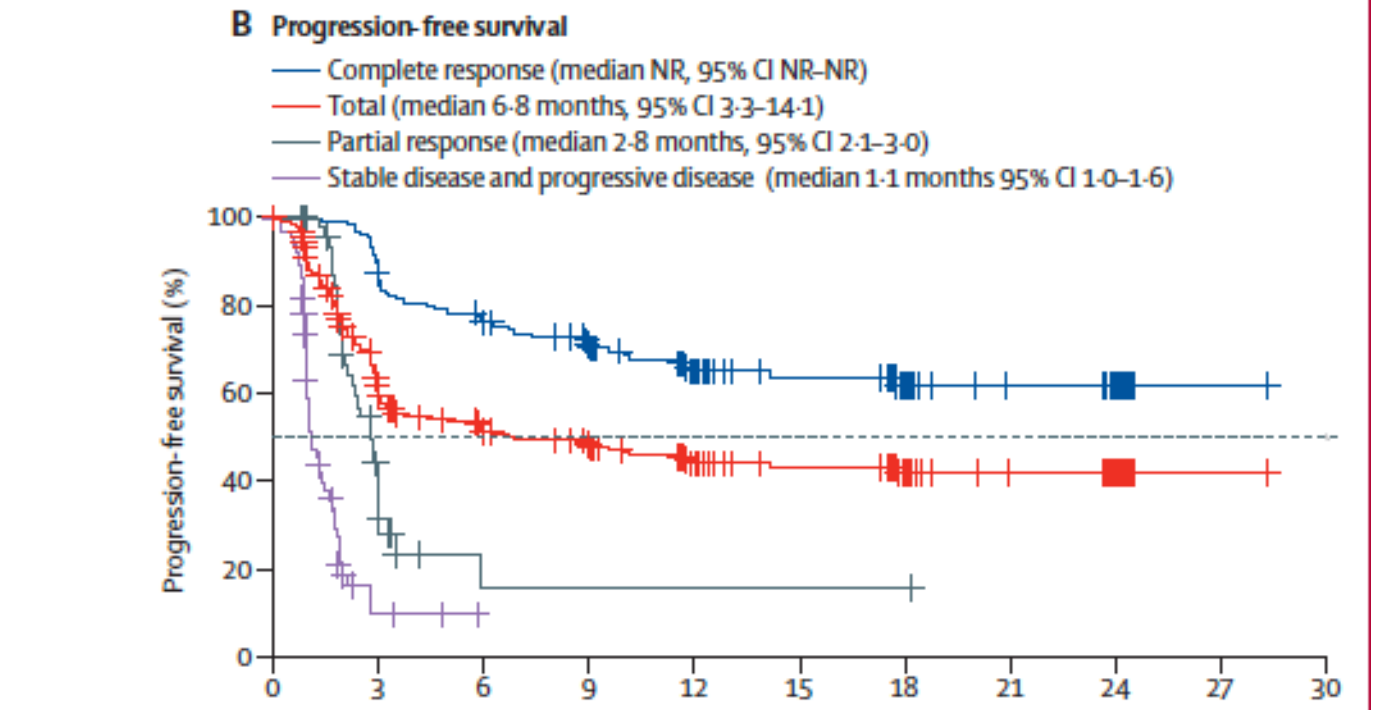
Survival of patients with DLBCL after Tisagenlecleucel (JULIET trial)





SJ Schuster et al. N Engl J Med 2019;380:45-56.

Lisa-cell for relapsed/refractory DLBCL, PML, Grade 3b FL - TRANSCEND trial

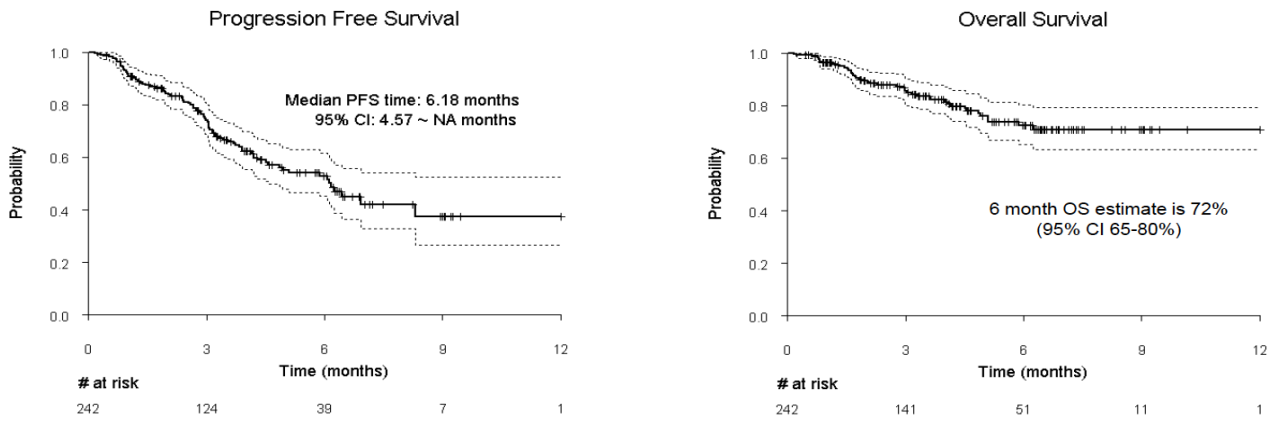


Number at risk											
Complete response	136	116	98	85	63	45	31	23	14	1	0
Partial response	50	14	2	2	2	2	2	0	..	..	..
Stable disease and progressive disease	70	3	0	..	..	..	..	..	..	..	..
Total	256	133	100	87	65	47	33	23	14	1	0

Abramson, Lancet, 2020

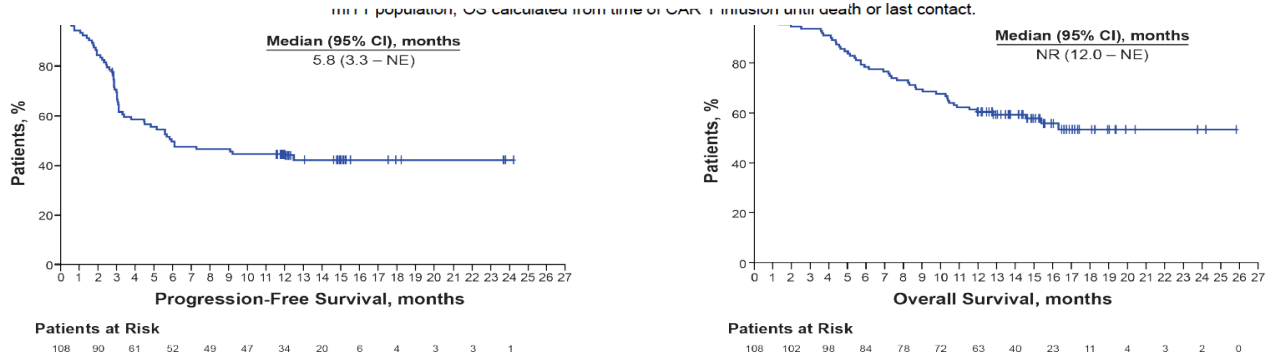
Survival after Axi-Cell for DLBCL in Real-World analysis 13 US Centers CAR-T Consortium (over 45-61% would NOT fit the eligibility for trials)

Real-world



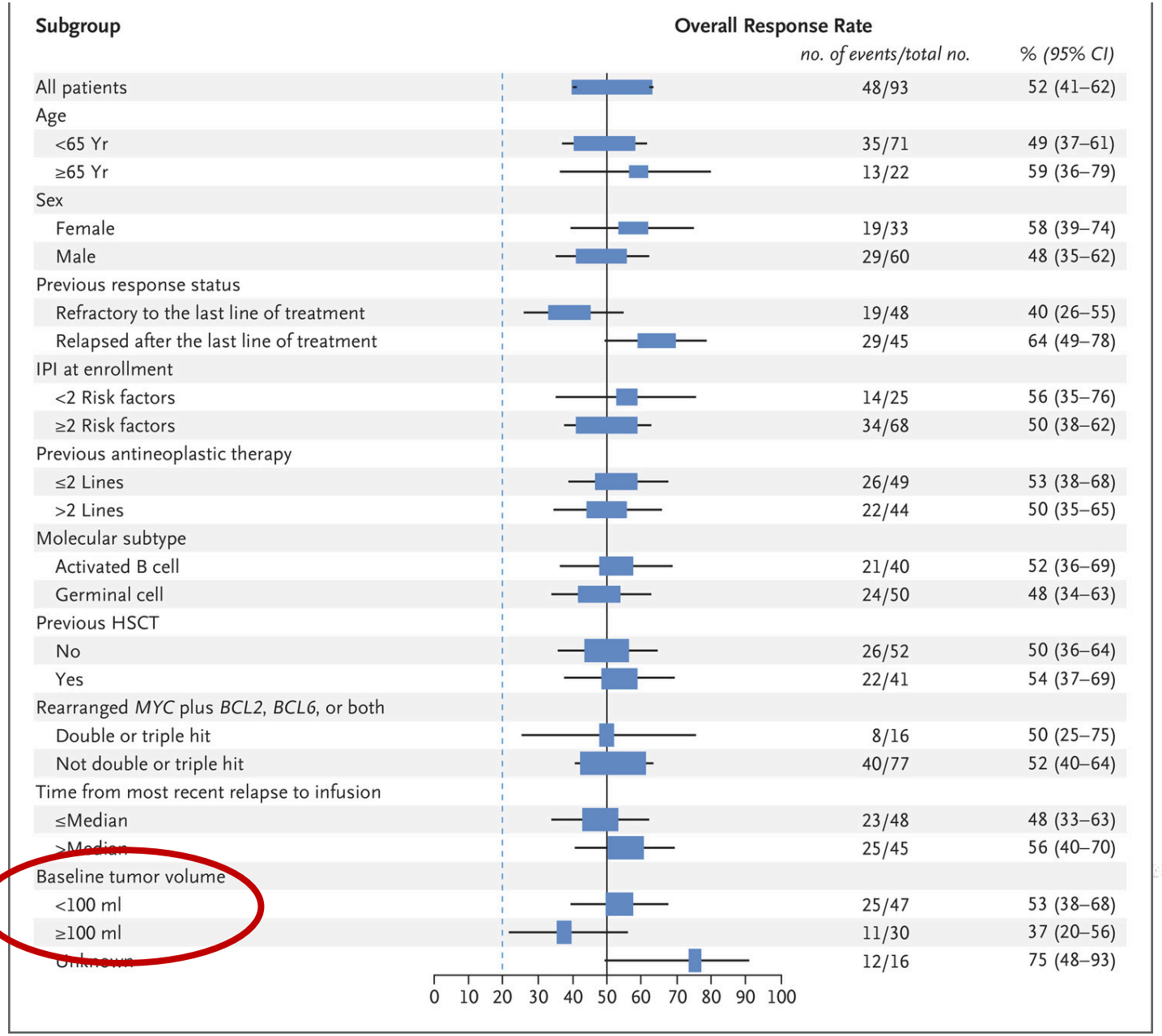
Riedel P, ASH 2021

ZUMA 1



Neelapu, Locke et al. *NEJM*. 2017 Dec 28;377(26):2531-2544

Which Clinical Factors Are Associated with Response to CAR-T19 (Tisa-cell) ?

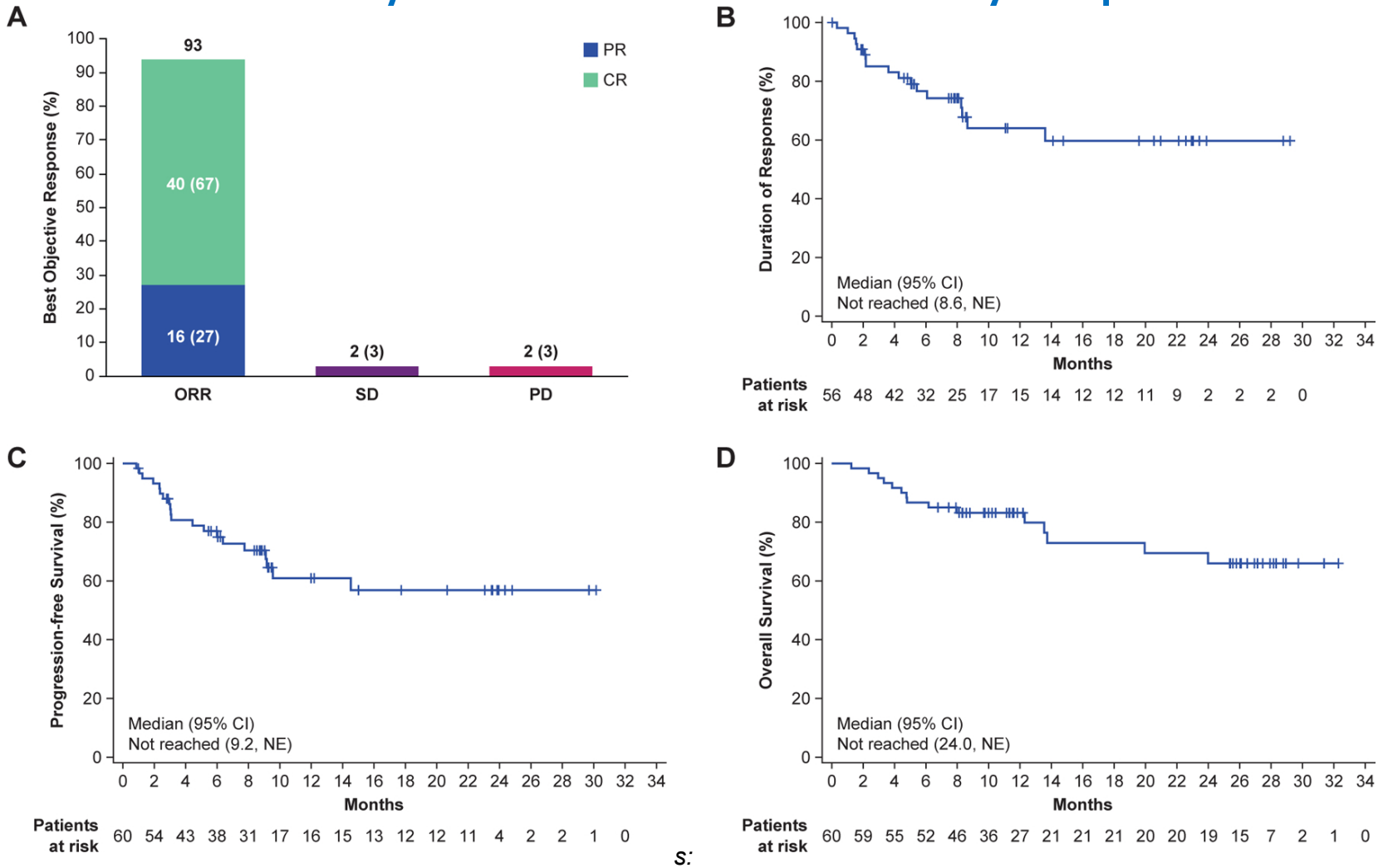


Subgroup	Overall Response Rate	
	no. of events/total no.	*% (95% CI)*
All patients	48/93	52 (41–62)
Age		
<65 Yr	35/71	49 (37–61)
≥65 Yr	13/22	59 (36–79)
Sex		
Female	19/33	58 (39–74)
Male	29/60	48 (35–62)
Previous response status		
Refractory to the last line of treatment	19/48	40 (26–55)
Relapsed after the last line of treatment	29/45	64 (49–78)
IPI at enrollment		
<2 Risk factors	14/25	56 (35–76)
≥2 Risk factors	34/68	50 (38–62)
Previous antineoplastic therapy		
≤2 Lines	26/49	53 (38–68)
>2 Lines	22/44	50 (35–65)
Molecular subtype		
Activated B cell	21/40	52 (36–69)
Germinal cell	24/50	48 (34–63)
Previous HSCT		
No	26/52	50 (36–64)
Yes	22/41	54 (37–69)
Rearranged *MYC* plus *BCL2*, *BCL6*, or both		
Double or triple hit	8/16	50 (25–75)
Not double or triple hit	40/77	52 (40–64)
Time from most recent relapse to infusion		
≤Median	23/48	48 (33–63)
>Median	25/45	56 (40–70)
Baseline tumor volume		
<100 ml	25/47	53 (38–68)
≥100 ml	11/30	37 (20–56)
Unknown	12/16	75 (48–93)

0 10 20 30 40 50 60 70 80 90 100

SJ Schuster et al. N Engl J Med 2019;380:45-56.

CAR-T for R/R Mantle cell lymphoma



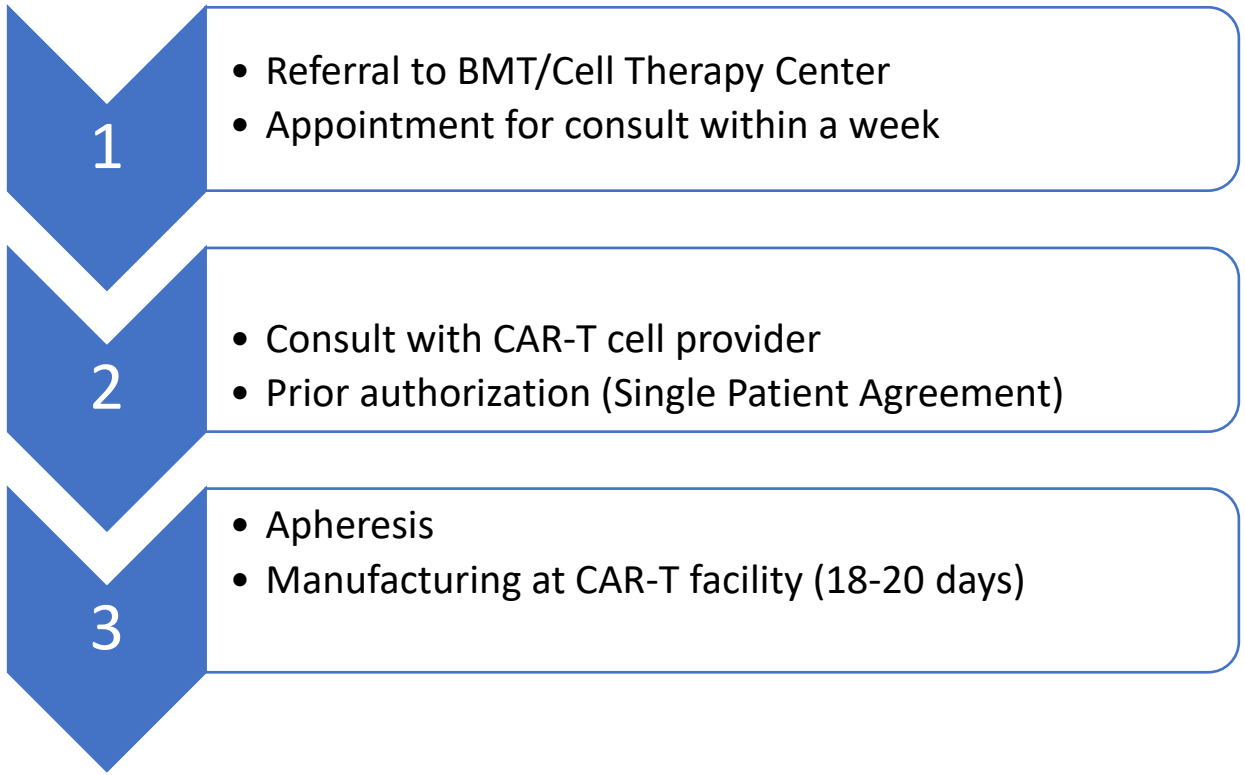
s:

N Engl J Med. 2020 Apr 2; 382(14): 1331–1342.

CAR-T SOC and disease indications summary

Product	Axi-cel Yescarta	Brexu-Cel Tecartus	Liso-Cel Breyanzi	Tisa-Cel Kymriah	Ide-Cel Abecma	Cilta-cel Carvykti
CAR-T Antigen target; co-signaling; T cell composition	CD19 (FMC63) CD28	CD19 (FMC63) CD28	CD19 (FMC63) 41BB 1:1 CD4, CD8	CD19 (FMC63) 41BB	BCMA 41BB	BCMA 41BB
Aggressive B-NHL Diffuse large B-cell lymphoma	X		X	X		
High grade B-NHL	X		X	X		
Large B-NHL transformed from follicular lymphoma	X		X	X		
Large B-NHL transformed from indolent lymphoma			X			
Primary mediastinal B-cell NHL (PMBCL)	X		X			
Mantle cell lymphoma		X				
Follicular lymphoma-Grade 3B			X			
Follicular lymphoma-Grade 1/2/3A	X					
B-Acute Lymphocytic Leukemia (B-ALL) Pediatric, young adult(<=25yo)				X		
Adult (>= 18 yo)		X				
Multiple Myeloma					X	X

University of Minnesota
CAR-T Therapy Process Overview



Management of patient awaiting CAR-T therapies

Bridging therapy to control tumor but minimize toxicity
Use preventive antimicrobials to minimize infections
Often managed by referring oncologist

- Gem-Ox (or alternative)
- Steroids
- Radiation
- Ibrutinib or Revlamid in non-GCB subtype

Preparation for CAR-T Administration

4

- Patient work-up (organ function, Echo, CT)
- Review results visit and plan treatment

5

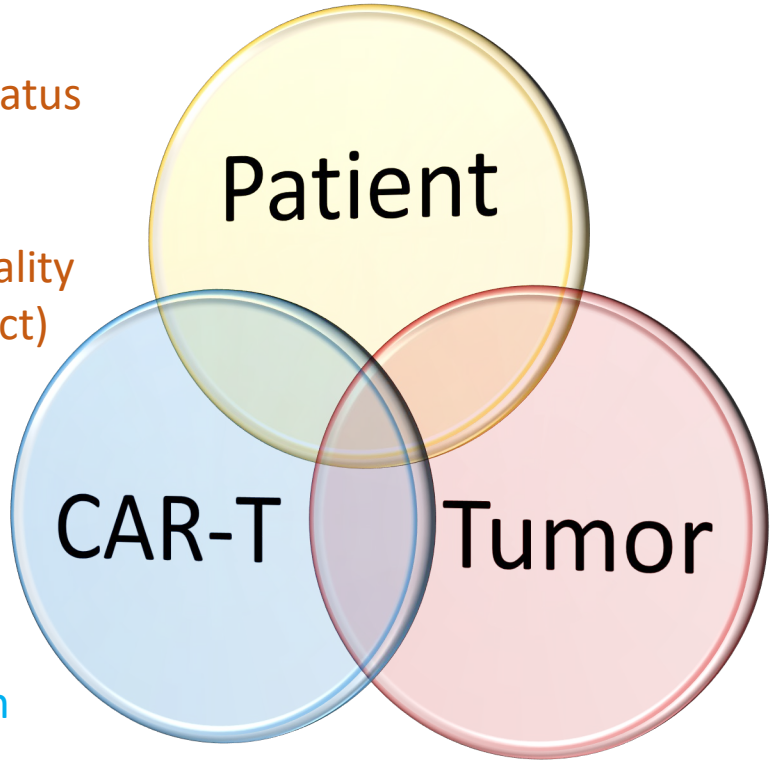
- Lymphodepleting chemotherapy (Flu/Cy x 3 days outpatient)

6

- CAR-T infusion – inpatient versus outpatient
- Inpatient and outpatient daily monitoring x 14 days
- 28 days stay within 30 min drive
- Long term monitoring in LTFU protocol for survival and secondary cancers

Relevant factors for achieving remission with CAR-T therapy

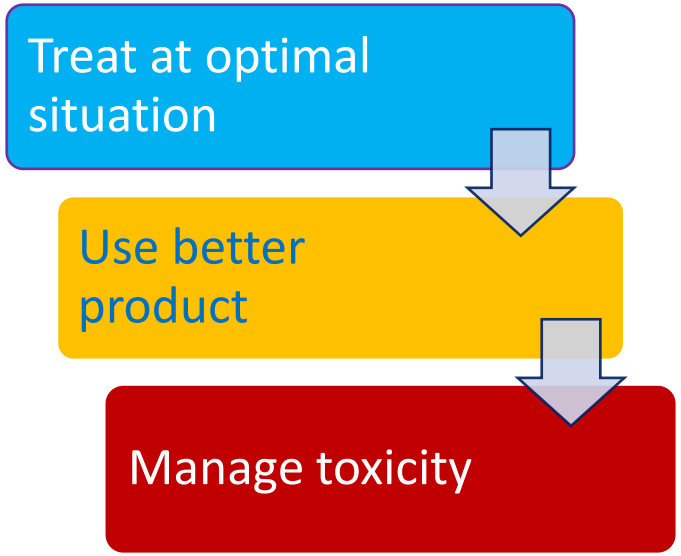
Age/Performance Status
Clinical factors
Comorbidities
Immune system (quality
Of apheresed product)
Prior therapies



Tumor heterogeneity
Tumor burden
Antigen densitiy
Accessibility
Microenviroment

Dose
Intrinsic T cell health
CAR-T construct ec
Signaling domain
CM T cell composition

Key practical determinants of outcomes after CAR-T



1) Patient selection – early referral, smaller tumor bulk, KPS, manage comorbidities
2) Quality of T cells (central memory phenotype, novel constructs, CAR-T exhaustion)
3) Bridging therapy (“art” of oncology)
4) Assess and manage of toxicity (treatment mortality is about 5%)

CD19 CAR-T in Practice

- Early referral is critical for APPROVED DISEASES
  - Aggressive B cell lymphoma: Failure of 2 lines of therapy or autologous HCT
  - Mantle cell lymphoma: relapsed and refractory disease
    - Relapse after autologous HCT, ineligible for AHCT, ibrutinib failure
  - Follicular lymphoma: relapsed and refractory disease
    - Failure of chemo-immunotherapy (refractory or duration of response <2 years)
    - Failure to autologous HCT or >=3 lines of therapy
    - Short duration of remission with 2nd or subsequent line of therapy

- Presence of co-morbidities
  - Organ function is relevant but well controlled comorbidities and age should not be a barrier to CAR-T therapy
  - Age should not be a barrier to successful CAR-T therapy

Clinical scenarios of aggressive B-cell lymphoma without effective therapy

- 61yo pt with DLBCL Resistant to primary therapy (R-CHOP, R-EPOCH) and not a candidate for transplant

- 71 yo pt with relapsed triple hit DLBCL with failure to achieve remission with R-ICE salvage chemotherapy

- 52 yo pt gous HCT (< 12 mont

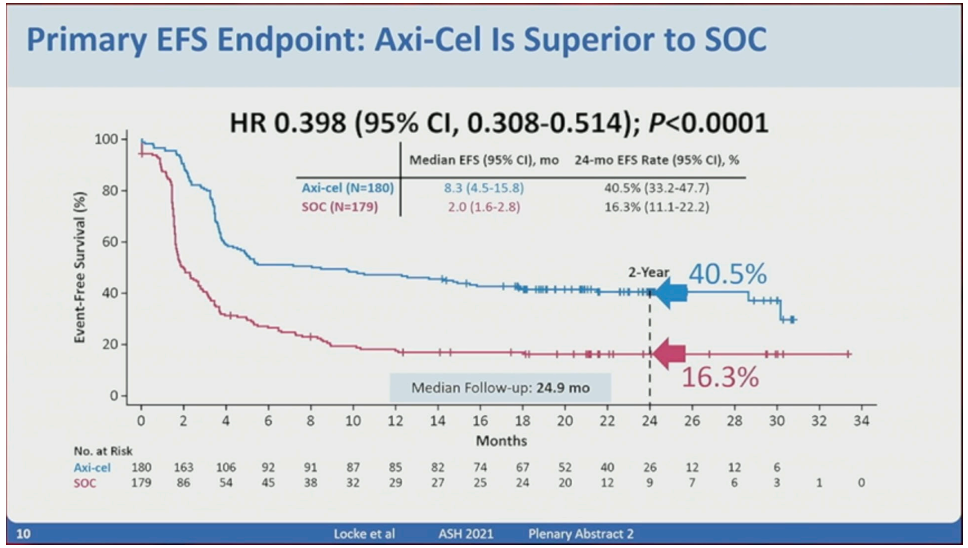
Pre-CAR-T era: Median survival ~ 10 months

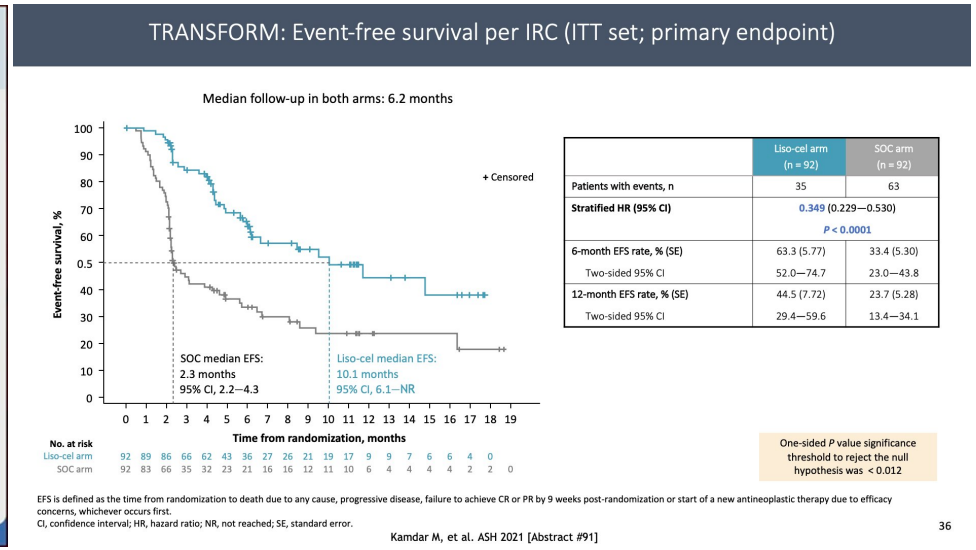
SCHOLAR -1 Crump, JCO, 2016

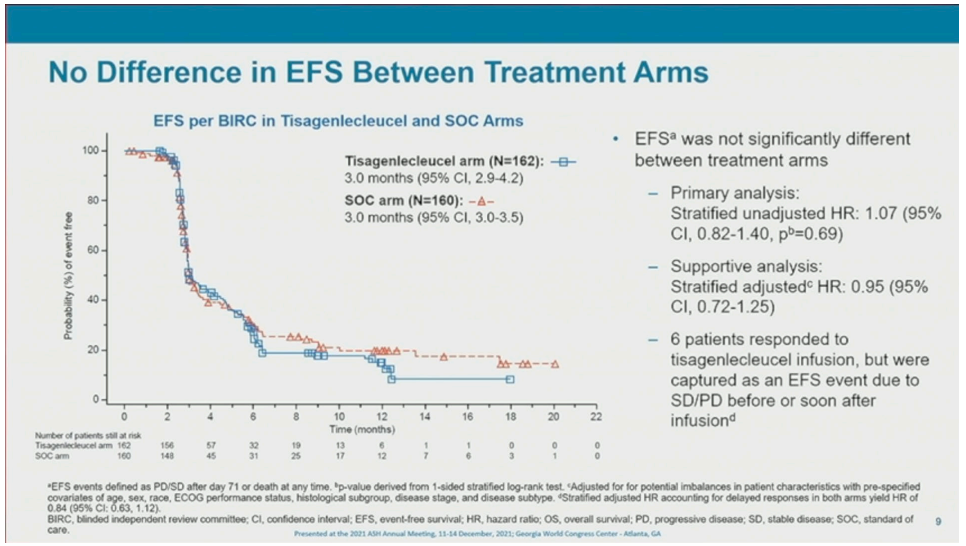
Emerging indication in DLBCL: 2nd line randomized trials CAR-T19 vs Autologous SCT for R/R DLBCL

	ZUMA-7 Axi-cel (Kite)	BELINDA Tisa-cel (Novartis)	TRANSFORM Liso-cel (Celgene/BMS)
EFS (1º endpoint)	**Met** HR 0.398 (p<0.0001)	**Not met** HR 1.01 (p=0.69)	**Met** HR, 0.349 (p<0.0001)
Overall Response Compete Response (CAR-T vs SOC)	83%/65% vs 50%/32%	46%/28% vs 43%/28%	86%/66% vs 48%/39%
Median PFS	14.7 mo vs 3.7 mo (HR 0.49, 95% CI 0.37-0.65)	N/A	14.8 mo vs 5.7 mo (HR, 0.406; p=0.0001)

Emerging indication in DLBCL: 2nd line randomized trials CAR-T19 vs Autologous SCT for R/R DLBCL





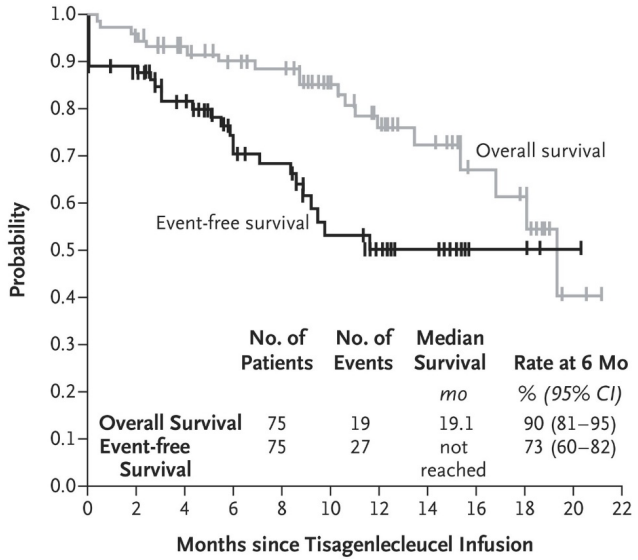


ASH 2021 oral abstracts

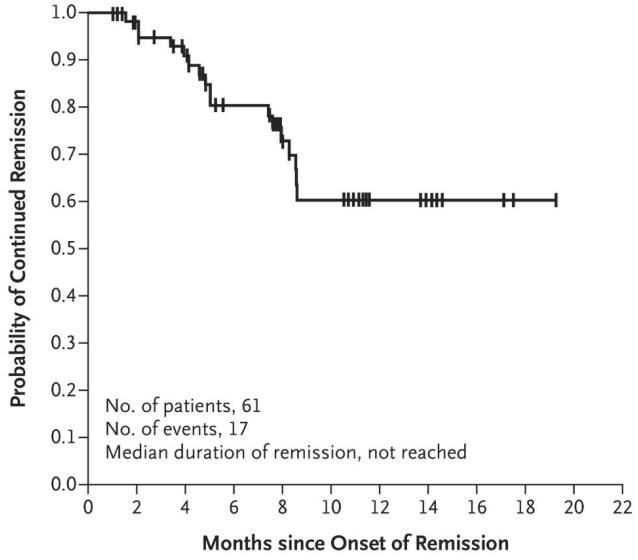
FDA-approved CAR T Cell Therapies for B-Acute Lymphoblastic Leukemia

Tisagenlecleucel

- ELIANA: patients up to age 25 years with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse



Maude et al. NEJM 2018

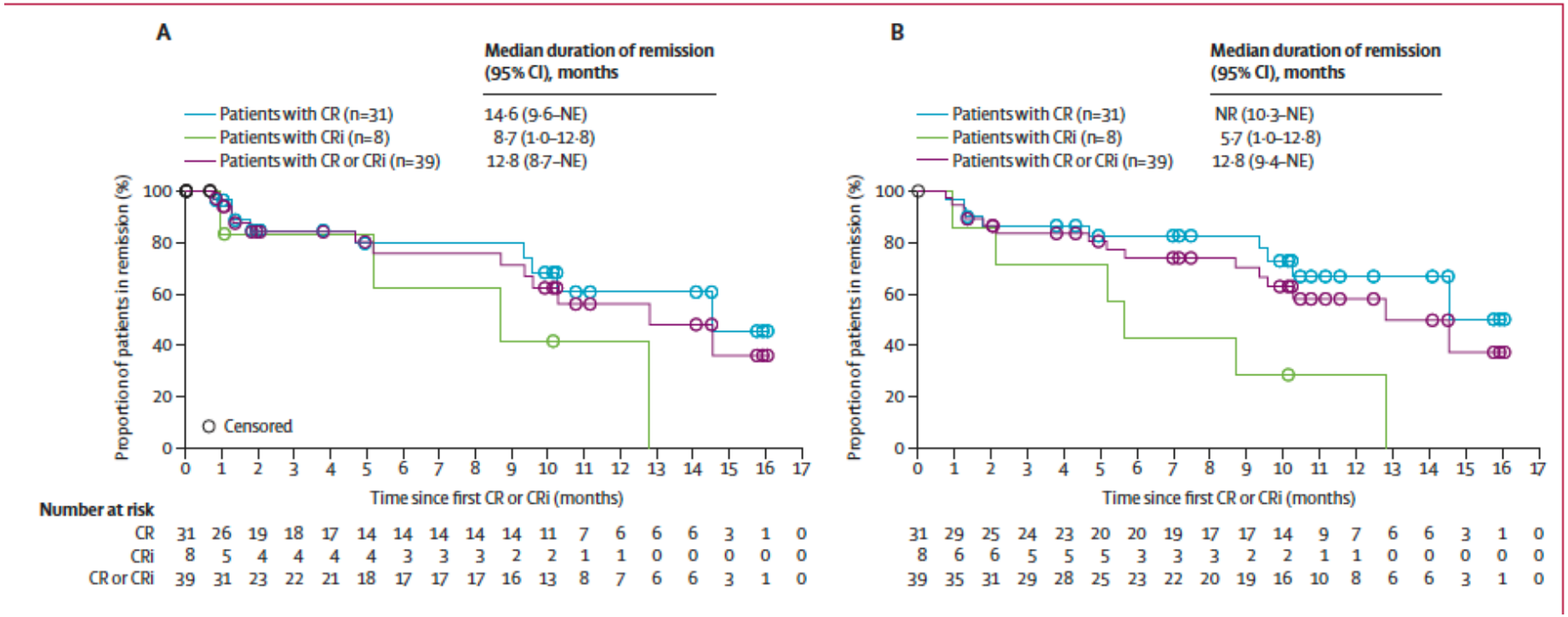


Brexucabtagene for adult R/R ALL

	Treated patients (n=55)	Enrolled patients (n=71)
Age, years	40 (28–52)	44 (30–59)
≥65 years	8 (15%)	11 (15%)
Sex		
Female	22 (40%)	30 (42%)
Male	33 (60%)	41 (58%)
Relapsed or refractory subgroup		
Primary refractory	18 (33%)	21 (30%)
Relapsed or refractory to two or more previous systemic therapy lines	43 (78%)	54 (76%)
First relapse with remission ≤12 months	16 (29%)	20 (28%)
Relapsed or refractory post allogeneic SCT¶	24 (44%)	29 (41%)
Bone marrow blasts at baseline‡		
n	55	70
Median (IQR)	60% (17–90)	67% (34–90)
≤5%‖	5 (9%)	6 (8%)
>5% to 25%‖	10 (18%)	10 (14%)
M3 bone marrow involvement (>25% blasts)‖	40 (73%)	54 (76%)

Response	
Overall Response	**71%**
Complete response	**56%**

Proportion of patients with R/R B-ALL in remission over time

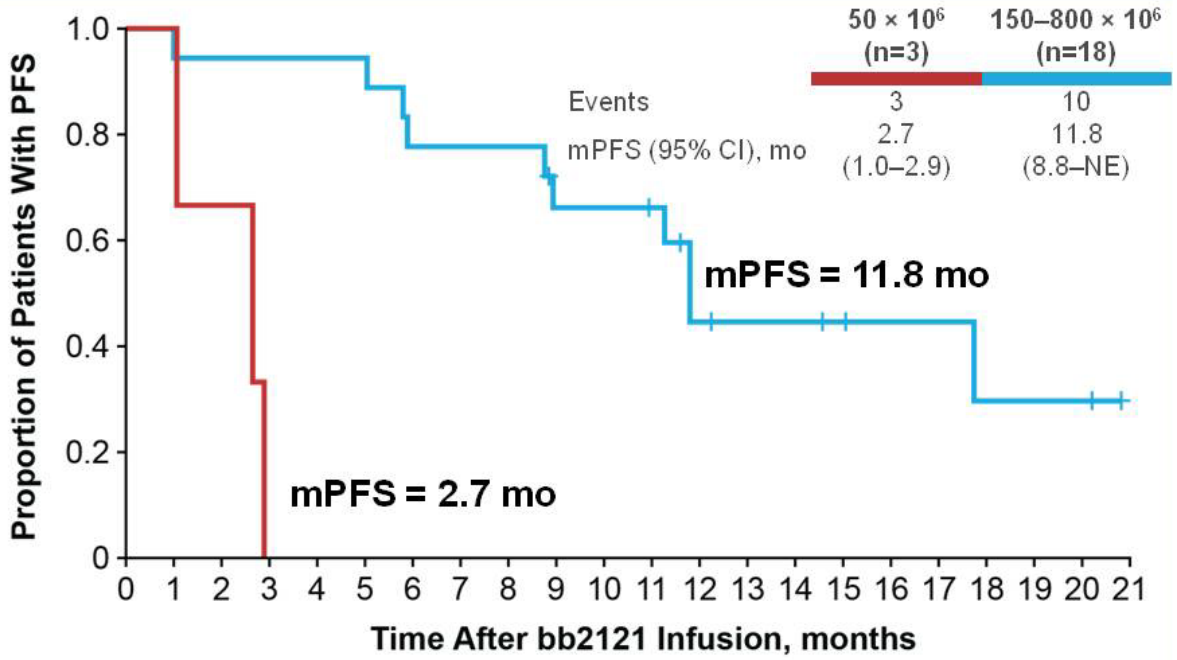


With and without censoring for patients who underwent subsequent allogeneic stem cell transplantation

Shah B, Lancet, 2021

BCMA+ CAR T Therapy for Myeloma

- B cell maturation antigen (BCMA)
- Phase I CRB-401 study
- Previously treated patients with relapsed/refractory multiple myeloma



Raje et al. ASCO 2018

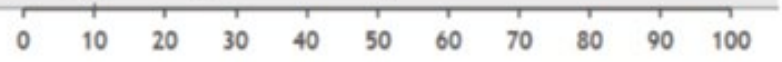
FDA approved CAR-T therapy for Multiple Myeloma

	Ide-Cel – Phase 2 (KarMMA-1)[1,2] N = 128	Cilta-Cel – Phase 1b/II CARTITUDE-1[3,4] N = 97
ORR/CR, %	**73% / 33%**	**98% / 83%**
Median PFS, mo	8.6 mo	NR, 2-Yr PFS 60.5%
CRS, Any Gr / ≥ Gr 3	84% / 5%	95% / 5%
ICANS, Any Gr / ≥ Gr 3	18% / 3%	21% / 10%*
Drug use	Toci: 52% Steroid: 15%	Toci: 69% Steroid: 22% Anakinra: 19%

1. Munshi N et al NEJM 2021. 2. Anderson L et al. ASCO 2021. Abstr. 8016. 3. Berdeja J et al. Lancet 2021. 4. Martin T et al. ASH 2021. Abstr. 549.

Ide-cel (Abecma) Outcome in Patient Subgroups (KarMMa-1)

Subgroup		N	CR Rate, % (95% CI)
Age group, years	<65	83	
	≥65	45	
Sex	Male	76	
	Female	52	
Ide-cel target dose level, CAR+ T cells	150×10^6	4	
	300×10^6	70	
	450×10^6	54	
R-ISS stage at enrollment	I or II	104	
	III	21	
High-risk cytogenetics del(17p), t(4;14), t(14;16)	Yes	45	
	No	66	
Tumor burden at baseline, % BMPCs	≥50%	65	
	<50%	57	
Tumor BCMA expression	≥50%	109	
	<50%	3	
Extramedullary disease	Yes	50	
	No	78	
Penta-refractory*	Yes	33	
	No	95	
Bridging therapy	Yes	112	
	No	16	



Munshi N et al NEJM 2021.

BCMA CAR-T in Practice

- FDA approval
  - Exposure to proteasome inhibitor, IMiDs, CD38 antibody
  - After 4 prior lines of therapy
- BCMA CART in standard of care practice, close to 50% of the patients do not meet registration trial criteria
- Emerging experience to be seen for myeloma
  - Renal insufficiency
  - Plasma cell leukemia
  - Concurrent amyloidosis
- Manufacturing access is limited. **Early referral is key!**

Challenges and limitations of autologous CAR-T cell therapy

OPTUMHealth™ Education

- Each autologous CAR-T product is unique “custom made” with variable and waiting time “from order to infusion”
- Delay in effective therapy for patients with aggressive cancers can be detrimental
- Access issues (not all patients who can benefit are currently referred)
  - Concerns are distance of center from home
  - Resources for 24 hours care
- Failures to collect, manufacture and meet specification (Impaired T cells)
- Less then half of patients with commercial CAR-T achieve achieve durable remissions
  - Loss of target (CD19 negative relapse)
  - Poor CAR-T expansion and CAR-T exhaustion
- Toxicity - neurotoxicity (ICANS) and cytokine release syndrome (CRS)

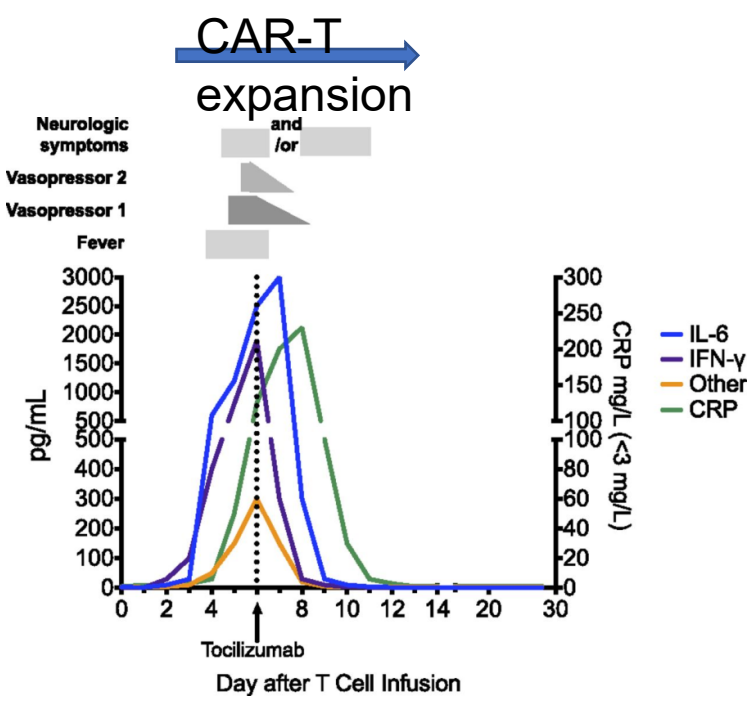
Important Black Box Warning on All CAR-T Products

- **Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving CAR-T.** Do not administer CAR-T to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab with or without corticosteroids.

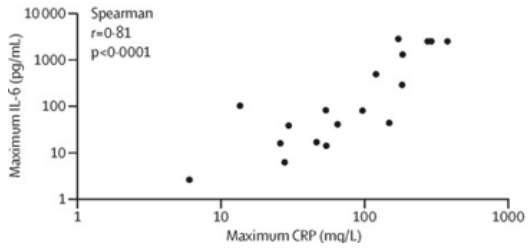
- **Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving CAR-T**, including concurrently with CRS, after CRS resolution or in the absence of CRS. Monitor for neurologic events after treatment with CAR-T. Provide supportive care and/or corticosteroids as needed.

- **CAR-T is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS**)

Unique toxicity: Cytokine Release Syndrome (CRS)



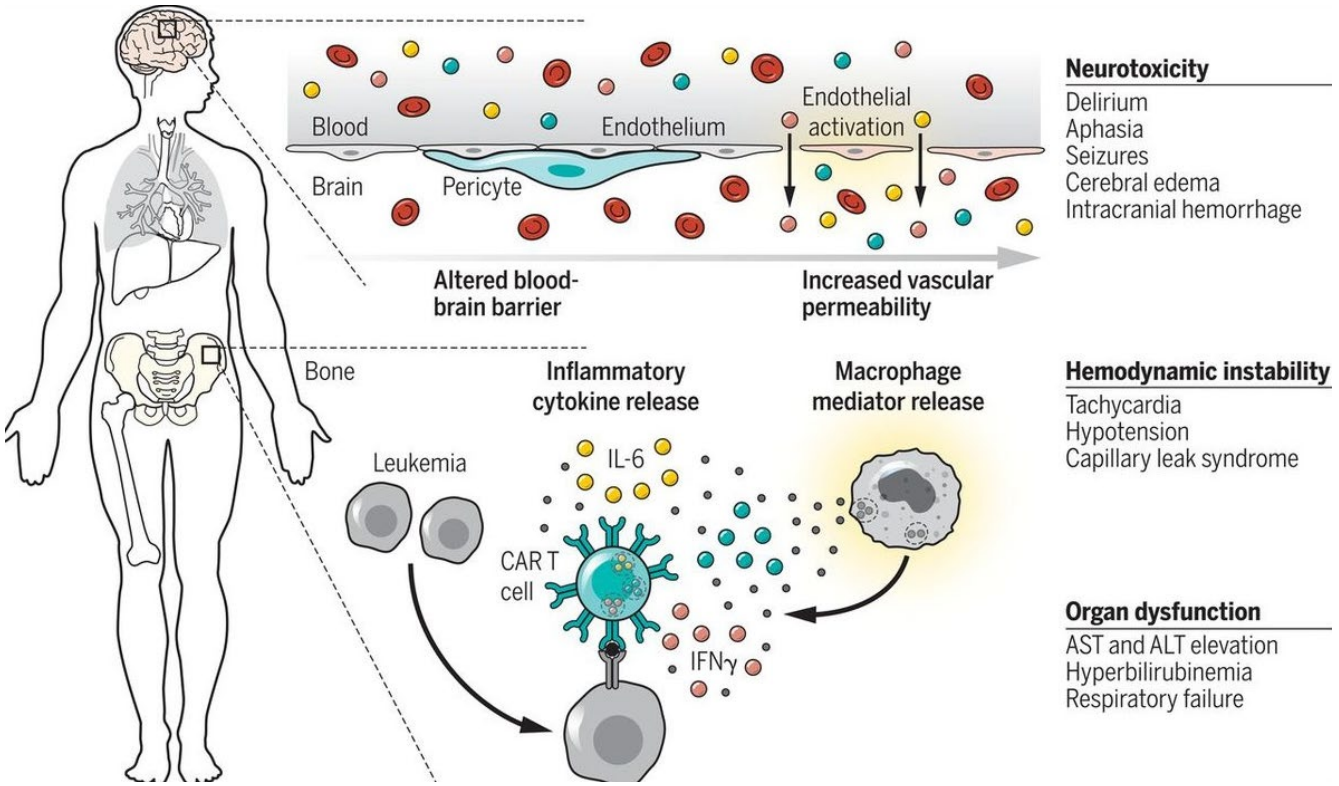
IL-6 vs. CRP



Tocilizumab is IL6R MoAb effective in treatment of CRS

Grupp SA, et al. N Engl J Med. 2013;368:1509-18.

Cytokine Release Syndrome (CRS) and ICANS pathophysiology



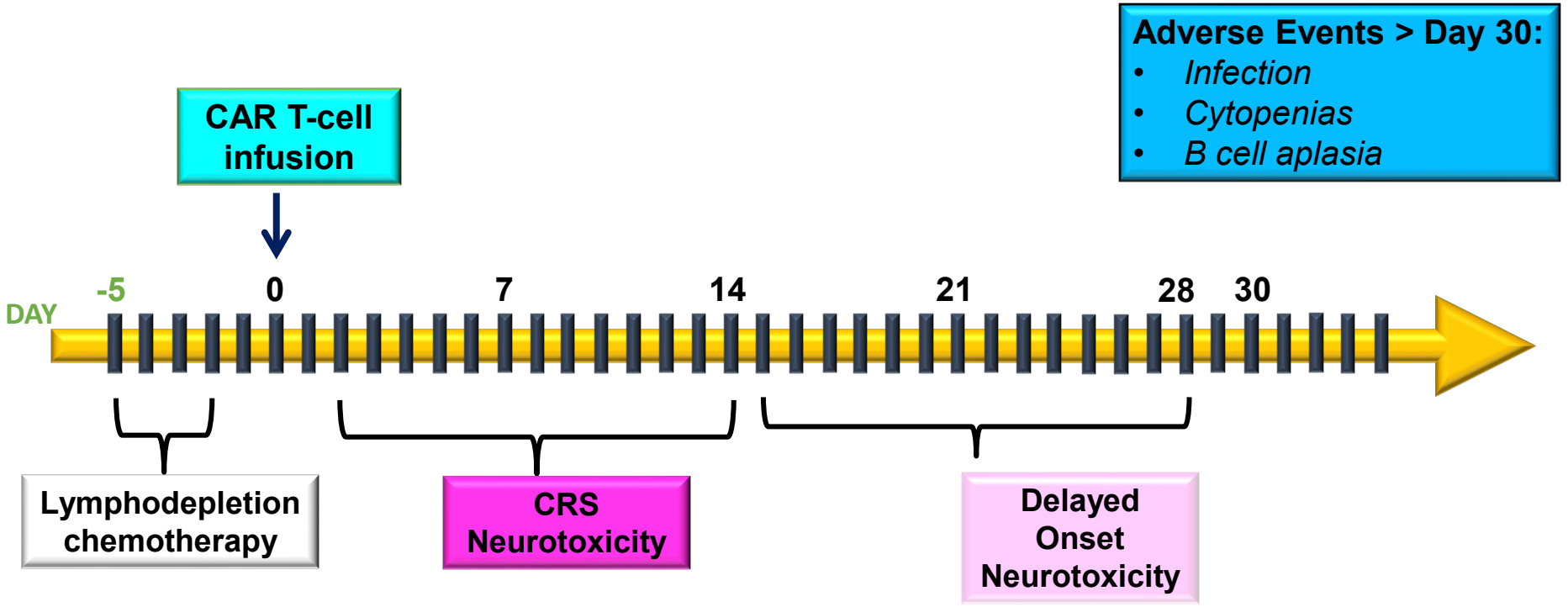
June et al. Science 2018

CRS: Clinical Signs & Symptoms

Organ System	Symptoms
Constitutional	Fever, rigors, malaise, fatigue, anorexia, myalgias, arthralgias
Skin	Rash
Respiratory	Tachypnea, hypoxemia
Cardiovascular	Tachycardia, hypotension, changes in cardiac output
Coagulation	Elevated D-dimer, hypofibrinogenemia, bleeding
Renal	Azotemia
Hepatic	Transaminitis, hyperbilirubinemia

Lee DW, et al. Blood. 2014;124:188-195.

CAR T Toxicities Timeline



Brudno JN, et al. Blood. 2016;127:3321-30. Neelapu SS, et al. Nat Rev Clin Oncol. 2018; 15:47-62.

ASBMT Consensus Grading for CRS Associated with Immune Effector Cells (IEC)

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever*	$T_m \geq 100.4^oF$	$T_m \geq 100.4^oF$	$T_m \geq 100.4^oF$	$T_m \geq 100.4^oF$
With either:				
Hypotension	None	Responsive to fluids	Requiring 1 vasopressor (w/ or w/o vasopressin)	Requiring multiple vasopressors (excluding vasopressin)
And/or				
Hypoxia	None	Low-flow nasal cannula or blow-by	High-flow nasal cannula, face mask, non-rebreather mask, or Venturi mask	Requiring positive pressure (CPAP, BiPAP Intubation and mechanical ventilation)

- Organ toxicities associated with CRS may be graded according to CTCAE v5.0, but they do not influence CRS grading
- Low-flow nasal cannula: O2 delivered at <6 L/minute.

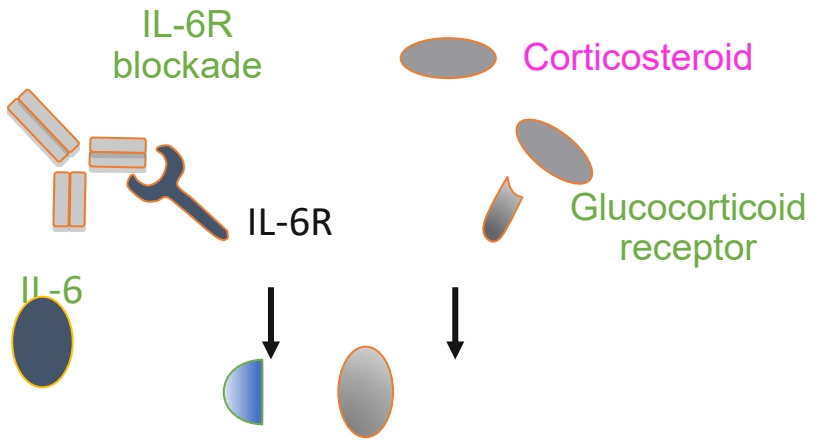
Lee DW, et al. Biol Blood Marrow Transplant. 2018 Dec 25. pii: S1083-8791(18)31691-4.

Toxicities vary by CAR-T product

	Grade ≥3 CRS	Grade ≥3 ICANS
Axi-cell	13%	31%
Tisa-cell	22%	12%
Liso-cel	1%	13%
Brexucabtagene (B-ALL)	24%	25%
Idecabtegene (BCMA)	84% (all) 5%	18%(all) 3%
Ciltacebtagene (BCMA)	95% (all) 5%	21% (all) 10%*

Management of CRS and ICANS

- Tocilizumab - IL-6R Inhibition
  - Tocilizumab: FDA approval for CAR T-cell induced severe or life threatening CRS in August 2017
  - For for any >=Grade 2 or prolonged Grade 1
  - IL-6 blockade demonstrates rapid reversal of CRS symptoms in most patients
- Corticosteroids
  - Suppress inflammatory responses
  - Dexamethasone 10 mg q6h or methylprednisolone 1mg/kg q12h followed by rapid taper

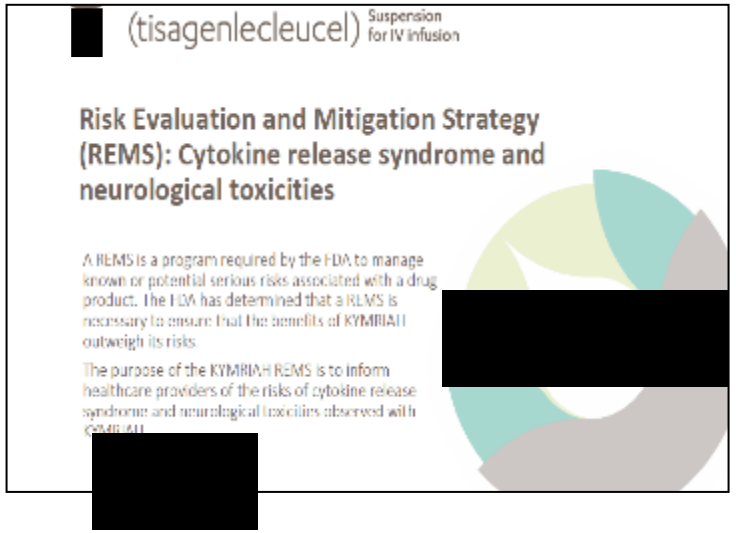


ASCTC Guidelines and sponsors summarize/update recommendations re CRS and ICANS management

Adapted from: Bonifant CL, et al. Oncolytics. 2016;3:16011. SL Maude, et al. Cancer J. 2014;20: 119-122

CAR T is Restricted to Certified Healthcare Facilities

- All CAR-T products are available under a Risk Evaluation and Mitigation Strategy (REMS)
- Healthcare providers who prescribe, dispense or administer must be trained in management of CRS and neurological toxicities and complete the knowledge assessment
- Requires immediate access to 2 doses of tocilizumab for each patient within 2 hours of the infusion if needed

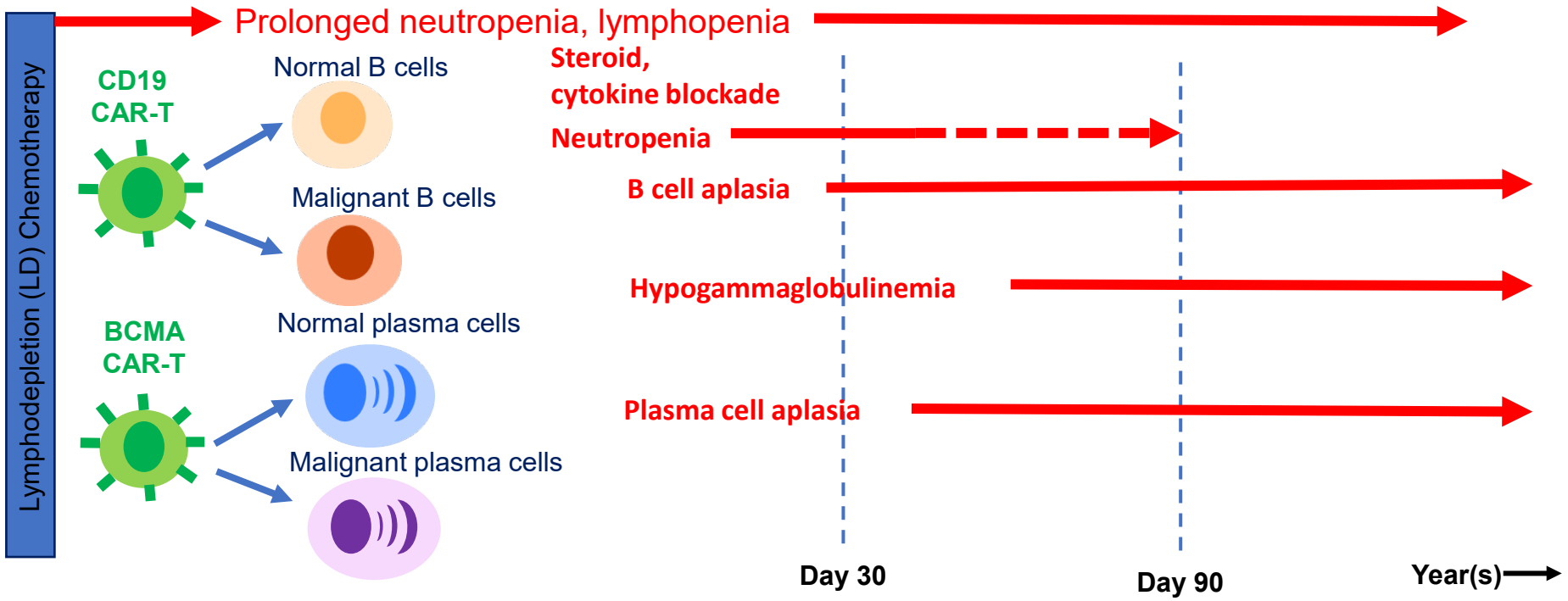


Additional Toxicities Associated with CAR T-cells

- B cell aplasia and hypogammaglobulinemia
  - "On target, off tumor" toxicity of successful CD19 CAR T-cell therapy
  - IVIG replacement may be used to mitigate risk of infection
- Infections (neutropenic and opportunistic)
- Prolonged cytopenias
  - Neutropenia (15% gr3 after day 30; thrombocytopenia 20% gr3)

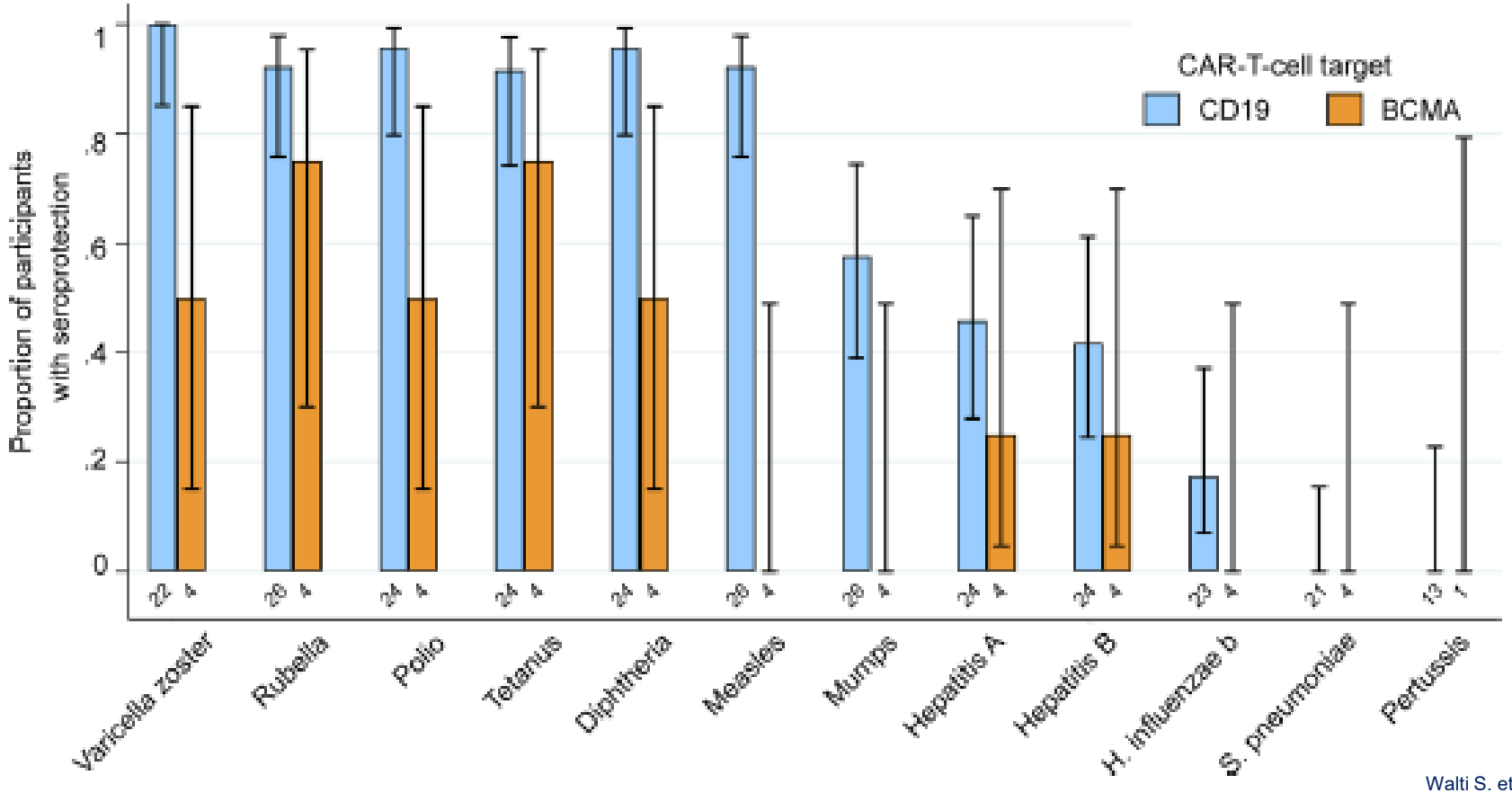
Bonifant CL, et al. Oncolytics. 2016;3:16011.
Brudno JN, et al. Blood. 2016;127:3321-30. Neelapu SS, et al. Nat Rev Clin Oncol. 2018; 124:188-195.

Cellular and Humoral Toxicities of CAR-T Therapy



Immune titer status post CAR-T

Sero-titer status post BCMA CAR-T appears lower than CD19 CAR-T



Walti S. et al. JCI Insights. 2021

Some CAR-T cell clinical trials for solid tumors

Malignancy	Phase	N	Name of Trial	Therapeutic Compounds	Clinical Trial Identifier	Status
GPC3 Positive Hepatocellular Carcinoma	1/2	60	CAR-T Cell Immunotherapy for HCC Targeting GPC3	GPC3	NCT02723942	Completed
Carcinoma, Hepatocellular	1/2	30*	A Study of GPC3 Redirected Autologous T Cells for Advanced HCC (GPC3-CART)	GPC3	NCT02715362	Recruiting
Advanced Lung Cancer	1	22*	CAR-T Cell Immunotherapy for Advanced Lung Cancer	PD-L1	NCT03330834	Not Yet Open
Advanced Solid Tumor	1/2	40*	CTLA-4 and PD-1 Antibodies Expressing MUC1-CAR-T Cells for MUC1 Positive Advanced Solid Tumor	MUC1	NCT03179007	Recruiting
Colon Cancer, Esophageal Carcinoma, Pancreatic Cancer, Prostate Cancer, Gastric Cancer, Hepatic Carcinoma	1/2	60*	A Clinical Research of CAR T Cells Targeting EpCAM Positive Cancer (CARTEPC)	EpCAM	NCT03013712	Recruiting
Pancreatic Cancer	1	30*	A Study of Mesothelin Redirected Autologous T Cells for Advanced Pancreatic Carcinoma (meso-CART)	Mesothelin	NCT02706782	Recruiting

Novel CAR-T Approaches for Cancer Therapy

New tumor targets:

- CD22 targeting CAR-T
- Bispecific CAR19/CAR20 CAR- T
- AML targets – CD33 CAR-T
- T-ALL – CD7 and CD5 CAR-T
- Many others in development

Allogeneic CAR-T products:

- Off the shelf availability
- Non-viral vectors with controlled CAR insertion (CRSISP-Cas9)
- NK CAR cell products (iPS derived, large volume manufacturing)
- NK cell therapeutics
- CAR-T allogeneic off-the-shelf products with multiple modifications to disrupt HLA, B2M and TCR

Many questions remain

OPTUMHealth™ Education

- Toxicity – there is a need to reduce the risks and to better identify risk factors
- Relapse prevention (need to better understand it, for example loss of CD19 and poor CAR T cell function)
- Clinical Care - preventive use of steroids and/or Tociluzumab ?
- Standardization of CRS and ICANS management
- Strategy to prioritize investigational therapies (allo CAR T, NK CAR, New autologous T cells CAR-T constructs) vs SOC CAR-T products
- Need to avoid delay in referrals (advanced patients)
- Need to avoid delays in apheresis& CAR-T approval - work closely with payors to ensure pre-authorization
- Timing of CAR-T therapies and other effective treatment such of autologous HCT, allogeneic HCT (B-ALL, Mantle cell lymphoma, 2nd line therapy for DLBCL)

University of Minnesota
Blood and Marrow Transplant and Cellular Therapy Program
Minneapolis, MN

Center of Experimental Therapeutics
Masonic Cancer Center

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Education

Thank You.