ADVANCING CANCER CURES

The mission of The Leukemia & Lymphoma Society® (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

We fund **RESEARCH** to advance lifesaving treatments

We drive **ADVOCACY** for policies that protect patient access to lifesaving treatment

We provide patients and families with hope, guidance, education and **SUPPORT**

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WHAT IS NEW IN CAR T-CELL THERAPY?

David Miklos, MD, PhD
Chief, BMT and Cell Therapy Division
Professor of Medicine
Stanford University
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Assistant Professor of Medicine
Director, Myeloma Cellular Immunotherapy
Division of BMT & Cell Therapy,
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WELCOMING REMARKS

BLOOD CANCERS: MANAGING SIDE EFFECTS

Lizette Figueroa-Rivera, MA
Sr. Director, Education & Support
The Leukemia & Lymphoma Society

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Stanford MEDICINE | Center for Cancer Cell Therapy

Advances in Chimeric Antigen Receptor Therapy for Leukemia and Lymphoma

David Miklos MD/PhD

Professor of Medicine
Chief BMT and Cell Therapy Division
Stanford University School of Medicine

Leukemia and Lymphoma Society Presentation
Tuesday, February 15, 2022

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Dr. Miklos' Disclosures:

Stanford MEDICINE | Center for Cancer Cell Therapy

- CAR-T, AlloHCT, cGVHD, and MRD are evolving fields and this presentation reflects the critical opinion of Dr. Miklos alone
- Scientific Advisory Boards:
  - Adaptive Biotechnologies, Novartis, Juno-Celgene-BMS, Kite-Gilead, Pharmacyclics-AbbVie, Janssen, Pharmacyclics, Allogene, Precision Bioscience, Miltenyi Biotech, Sanofi
- Industry Contracted Research:
  - Pharmacyclics - AbbVie, Kite-Gilead, Novartis, Roche, Genentech, Becton Dickinson, Isoplexis
- **Dr. Miklos does not hold equity or stock in any of these companies**

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B Cells Express Surface Proteins CD19 and CD20

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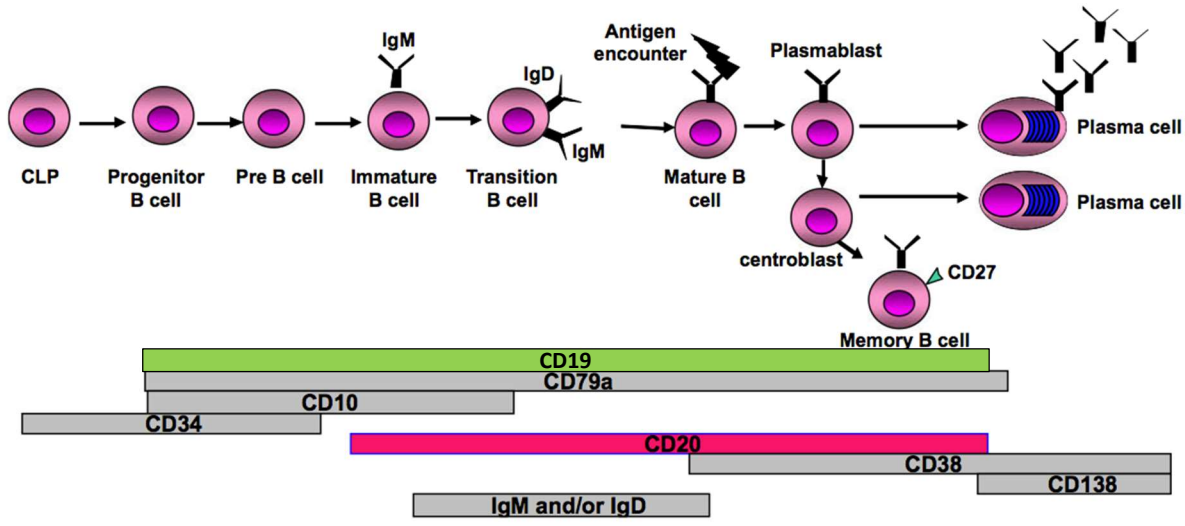

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Leukemia and Lymphoma arise from maturation arrest and most expresses CD19 and CD20

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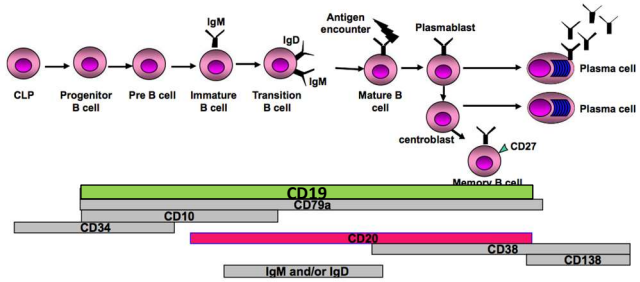

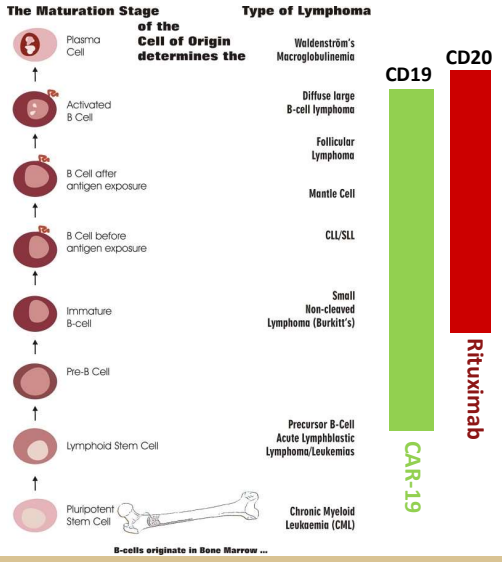

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What is CAR-T?

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CAR T therapy is the name given to

Chimeric Antigen Receptor (CAR) T cells that are genetically modified to recognize specific tumor antigens causing T Cell activation and proliferation causing cytotoxic durable destruction of cancer.

- CAR T cells are considered **"a living drug"** since they proliferate and persist for long periods of time
- CAR T cells are generally created from the patients own blood cells although this technology is evolving to develop "off the shelf" allogeneic CAR T cells.

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CAR-T cells: Mechanism of Action

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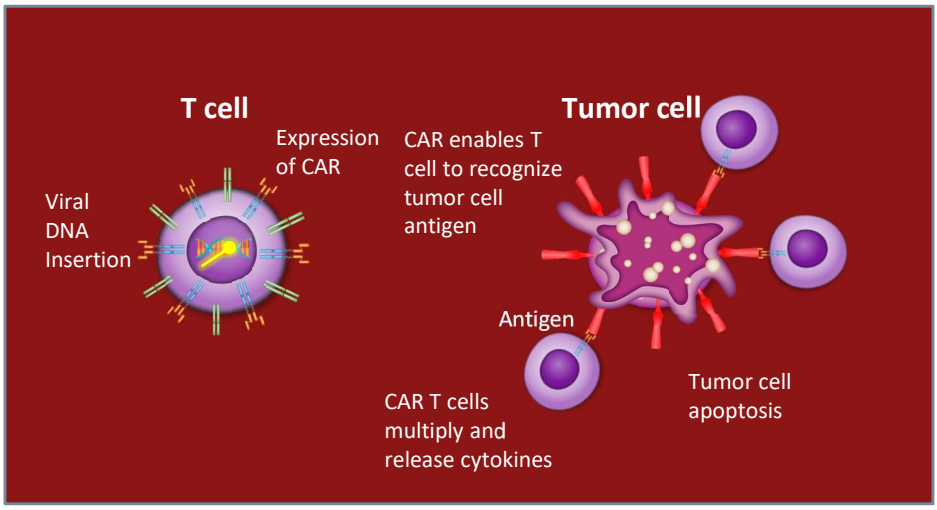

CAR19 is a "living Therapy" that expands 2-4 logs in one week

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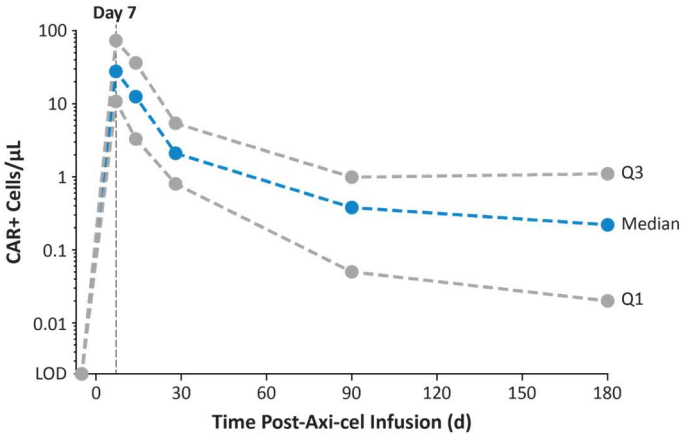

LOD = 0.002/1×10^5 peripheral blood mononuclear cells.

qPCR validated assay as per Locke et al. *Mol Ther*. 2015.

Locke and Neelapu ET al. AACR 2017 #9986

Two main CAR-T Toxicities: Cytokine Release Syndrome and Neurologic

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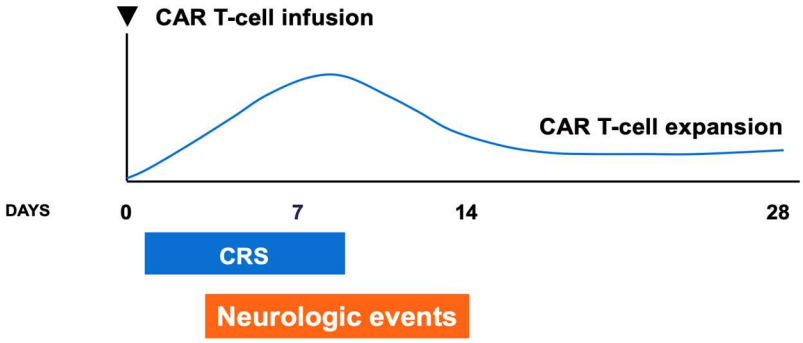

- May occur within minutes or hours but generally appears within days or weeks
- Coincides with maximal T-cell expansion

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Cytokine Release Syndrome – The 7th CAR-T patient was a 5 year-old Hero

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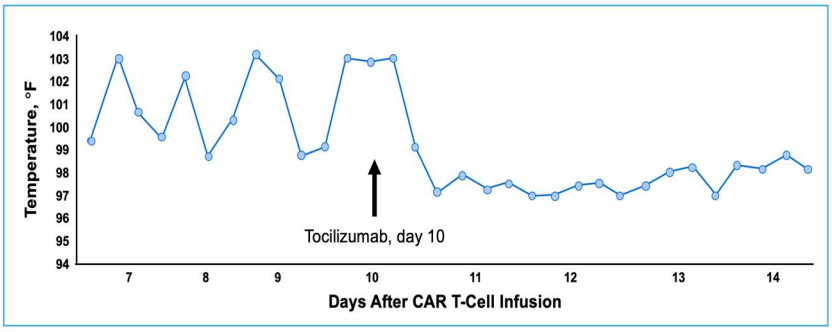

Emily was 5 yo with refractory acute lymphoblastic leukemia when she was the 7th patient treated at Children's Hospital of Philadelphia - CHOP.
Her unrelenting fevers and hypotension reminded Carl June of his own daughter's juvenile arthritis.
Tocilizumab had been recently FDA approved for JA. Drs. Grupp and June tried it.

The Promise and Price of Cellular Therapies
By Siddhartha Mukherjee, New Yorker.com

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Cytokine Release Syndrome Treatment
Tocilizumab blocks IL-6 Receptor

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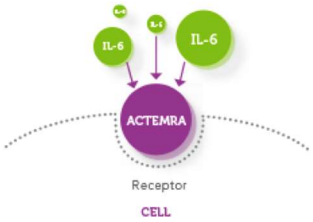
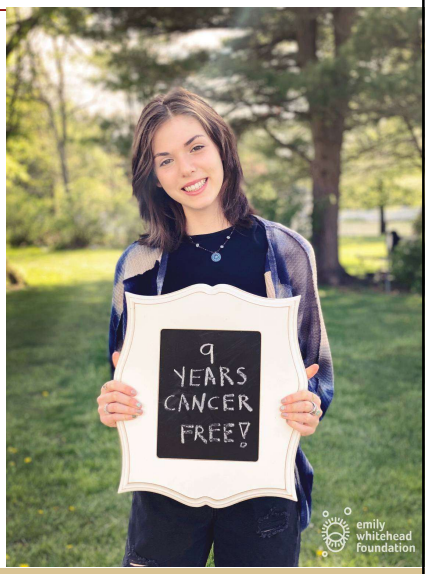
- IL-6 receptor inhibitor
- Blocks IL-6-mediated effects
- Monoclonal antibody with $t_{1/2}$ ~21 days
- Indicated for the treatment of rheumatologic disorders





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Chimeric Antigen Receptor (CAR) Modified T cells

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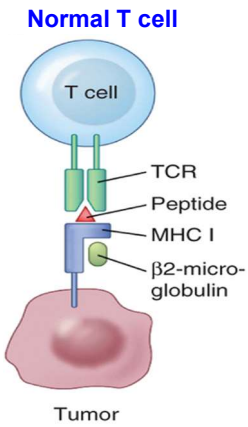

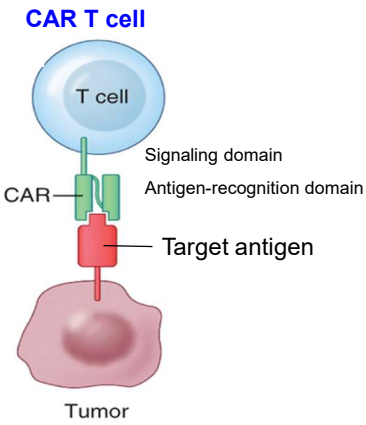

CAR-T benefits:

- **Expansion and proliferation**
- **Localization**
- **Cytotoxic Killing**
- **Persistence**

Adapted from Hinrichs & Restifo. Nat Biotech 2013

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Three Anti-CD19 CAR T-cell Products are FDA Approved as 3rd Line Therapy for Rel/Ref DLBCL

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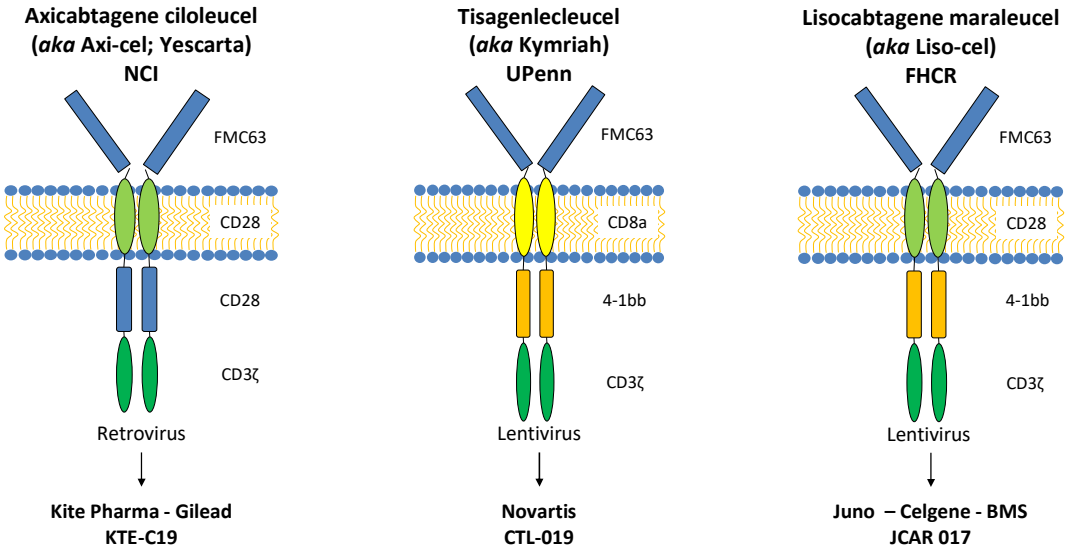

[1] Adapted from: van der Stegen SJ et al. Nat Rev Drug Discov. 2015 Jul;14(7):499-509.

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Different CAR-T Expansion Rates and Persistence are based upon Costimulatory Domain

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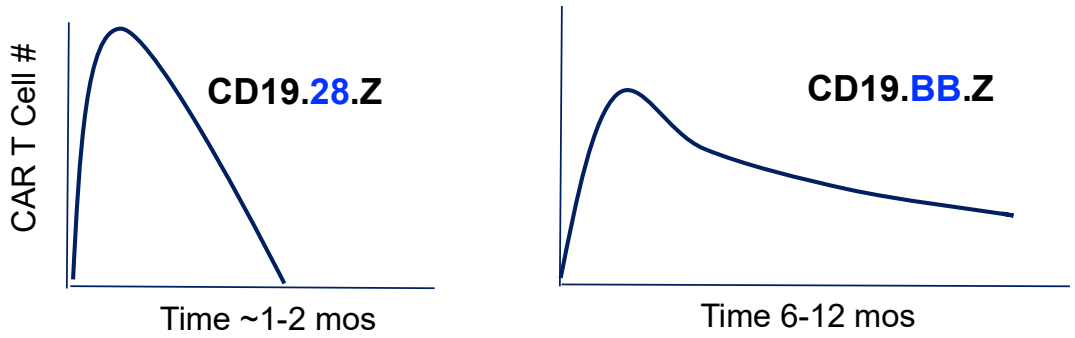

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Treatment Schema for CAR T-cell Therapy

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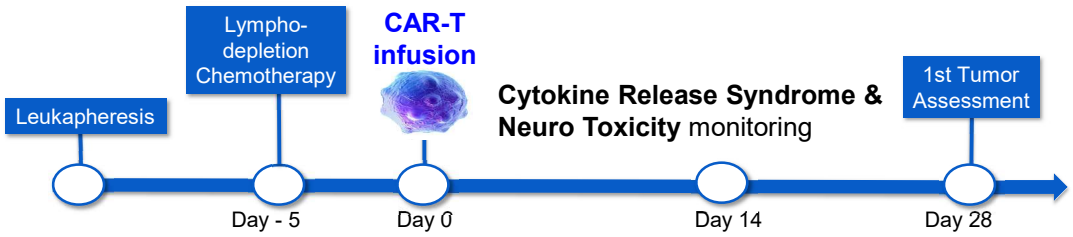
Fludarabine 30mg/m2
Cyclophosphamide 250-500mg/m2

Disease Response Assessment
PetCT 1, 3, 6 months after CAR-T



Bridging Therapies are given after apheresis while waiting for CAR-T production & delivery

- Manufacturing time varies by product

Low blood counts
3 weeks ---------- 6 weeks

Neutropenia support may require G-CSF shots in 25-50%
Goal: ANC>1000

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Zuma-1 patients were chemo-refractory or relapsed after autologous Transplants

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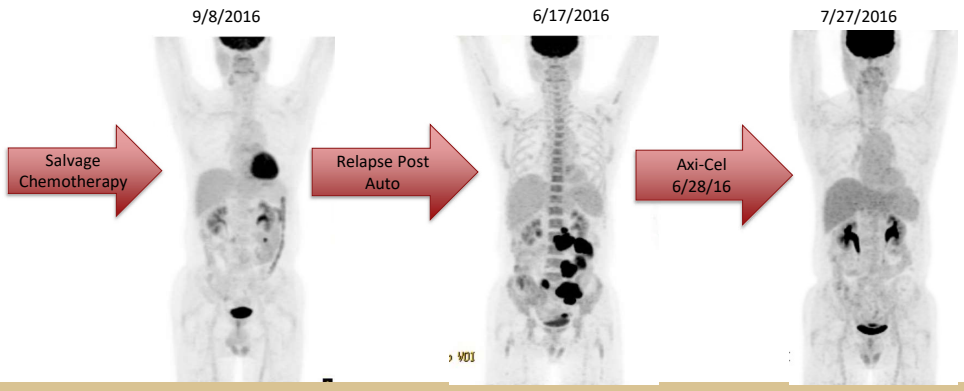
65 y/o male with follicular lymphoma that transformed to diffuse large cell lymphoma
R-CHOP x8 cycles provided partial response.
Salvage chemo: 4 cycles of R-DHAP provided complete response
Relapsed within 6 months of autologous transplant
Axi-Cel therapy devoid of fever, CRS, or neurotoxicity and provided complete response



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ZUMA-1: Axi-cel in r/r large B-cell lymphoma

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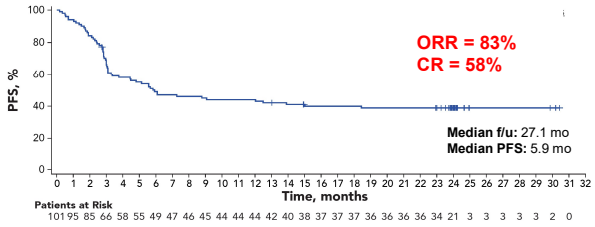
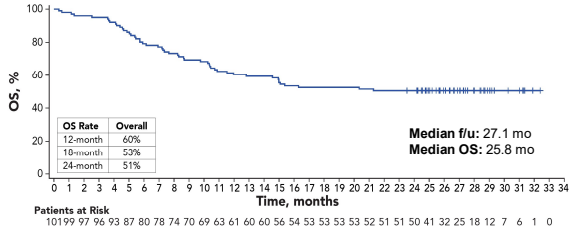
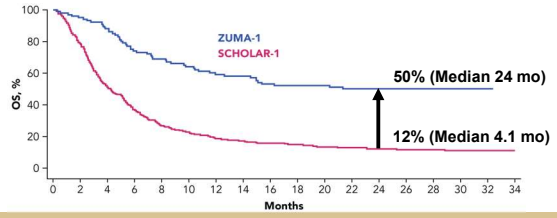
PFS: 39% progression-free at 27.1 mo



OS: 51% alive at 27.1 mo



Standardized OS Comparison: ZUMA-1 vs. SCHOLAR-1 (historical)



Neelapu et al. *N Eng J Med* 2017
Locke et al. *Lancet Oncol* 2019
Neelapu et al. ASH 2019

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Rel/Ref DLBCL Multicenter Trials in NHL

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	ZUMA-1 Axicabtagene ciloleucel (n=101)	**JULIET** Tisagenlecleucel (n=93)	**Transcend** Lisocabtagene Maraleucel (n=344; 269 infused)
Overall Response	82%	52%	73%
Complete Response	58%	40%	53%
Median DOR	11.1 months	Not reached (est. 12 mo DOR 65%)	Not reached (est.12 mo DOR 55%)

Locke F et al. Cancer Discovery 2018 Schuster SJ et al., N Engl J Med; 2018 Abramson JS et al., Lancet Sept. 2020 20

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Overall Response	82%	52%	73%
Complete Response	58%	40%	53%
Median DOR	11.1 months	Not reached (est. 12 mo DOR 65%)	Not reached (est.12 mo DOR 55%)
CRS (all - ≥3 grade)	92% - 11%	58% - 22%	42 - 2%
NT (all - ≥3 grade)	67% - **32%**	21% - **12%**	30% - **10%**

* UPENN grading used

Locke F et al. Cancer Discovery 2018 Schuster SJ et al., N Engl J Med; 2018 Abramson JS et al., Lancet Sept. 2020 21

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Nearly 5000 LBCL Patients Are Now Eligible For FDA Approved CAR19 as 3rd Line Therapy

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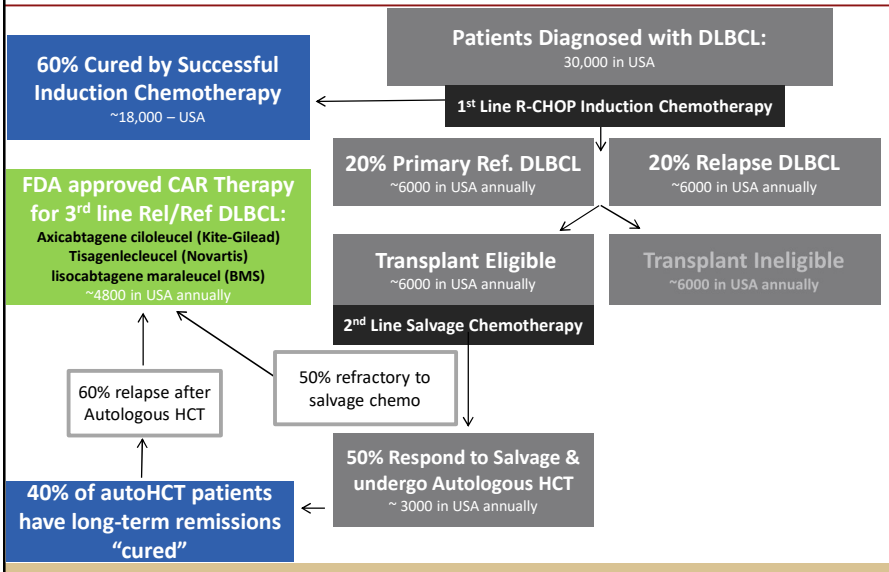

Jonathan W. Friedberg. *Hematology*. 2011:498-505. Howlader N, et al. *SEER Cancer Statistics Review*, 1975-2013. Gisselbrecht C, et al. *J Clin Oncol*. 2010;28:4184-4190. Neelapu SS et al. N Engl J Med; 2017 Dec 28, Schuster SJ et al., N Engl J Med; 2018 Dec 1 22

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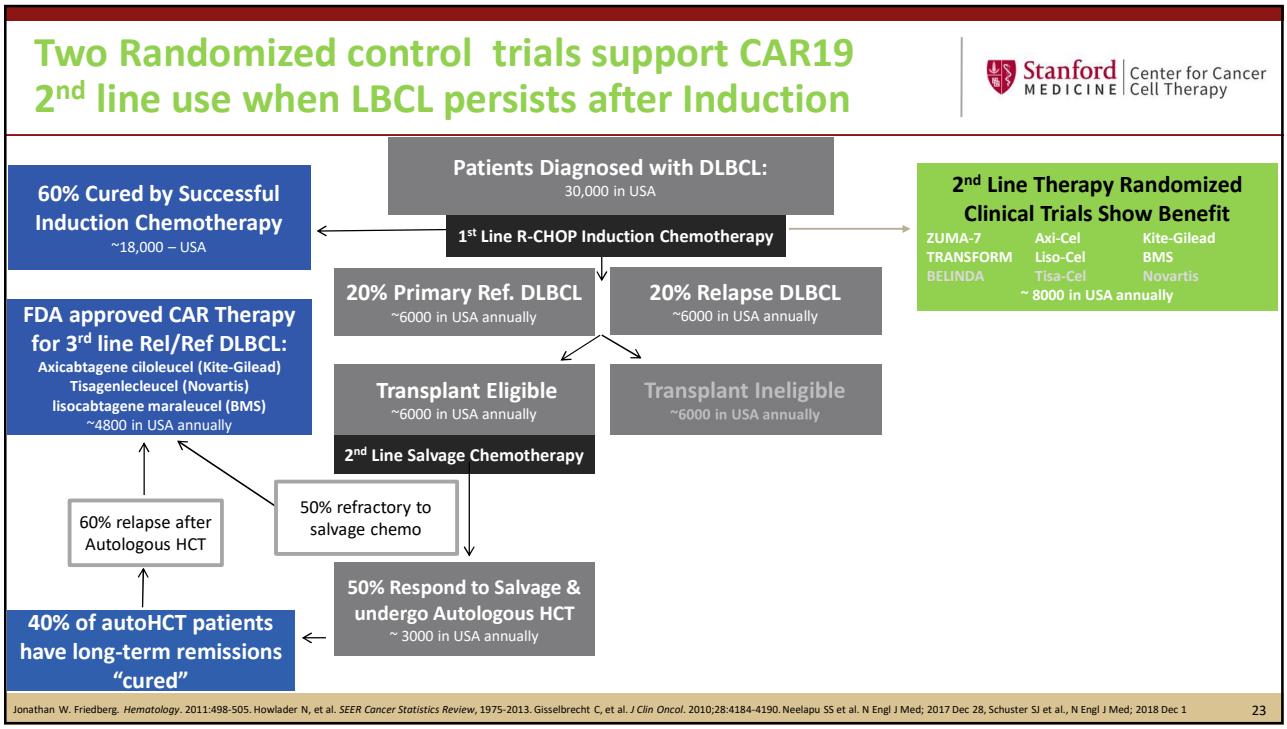
Two Randomized control trials support CAR19 2nd line use when LBCL persists after Induction
Stanford MEDICINE | Center for Cancer Cell Therapy
Patients Diagnosed with DLBCL:
30,000 in USA
60% Cured by Successful Induction Chemotherapy
~18,000 – USA
1st Line R-CHOP Induction Chemotherapy
2nd Line Therapy Randomized Clinical Trials Show Benefit
ZUMA-7 Axi-Cel Kite-Gilead
TRANSFORM Liso-Cel BMS
BELINDA Tisa-Cel Novartis
~ 8000 in USA annually
20% Primary Ref. DLBCL
~6000 in USA annually
20% Relapse DLBCL
~6000 in USA annually
FDA approved CAR Therapy for 3rd line Rel/Ref DLBCL:
Axicabtagene ciloleucel (Kite-Gilead)
Tisagenlecleucel (Novartis)
lisocabtagene maraleucel (BMS)
~4800 in USA annually
Transplant Eligible
~6000 in USA annually
Transplant Ineligible
~6000 in USA annually
2nd Line Salvage Chemotherapy
50% refractory to salvage chemo
60% relapse after Autologous HCT
50% Respond to Salvage & undergo Autologous HCT
~ 3000 in USA annually
40% of autoHCT patients have long-term remissions "cured"
Jonathan W. Friedberg. Hematology. 2011:498-505. Howlader N, et al. SEER Cancer Statistics Review, 1975-2013. Gisselbrecht C, et al. J Clin Oncol. 2010;28:4184-4190. Neelapu SS et al. N Engl J Med; 2017 Dec 28, Schuster SJ et al., N Engl J Med; 2018 Dec 1
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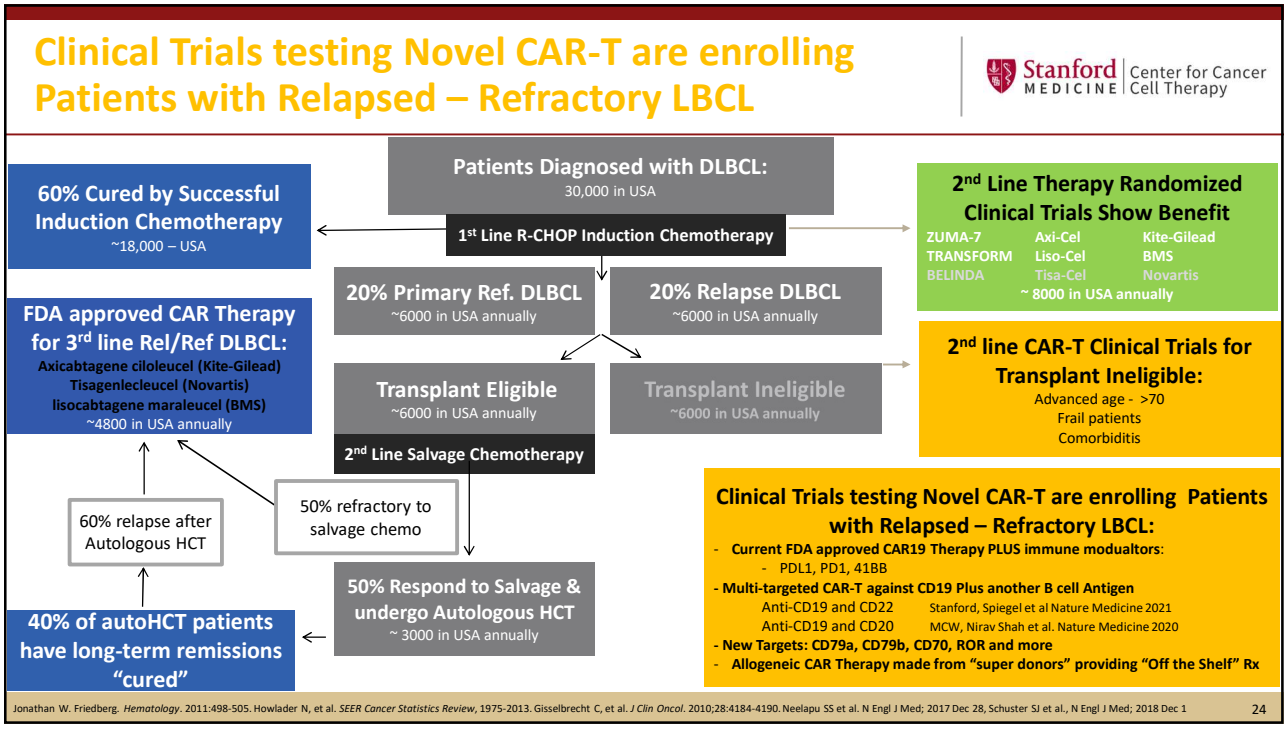
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Transplant Eligible
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Transplant Ineligible
~6000 in USA annually
2nd line CAR-T Clinical Trials for Transplant Ineligible:
Advanced age - >70
Frail patients
Comorbiditis
2nd Line Salvage Chemotherapy
50% refractory to salvage chemo
60% relapse after Autologous HCT
50% Respond to Salvage & undergo Autologous HCT
~ 3000 in USA annually
40% of autoHCT patients have long-term remissions "cured"
Clinical Trials testing Novel CAR-T are enrolling Patients with Relapsed – Refractory LBCL:
- Current FDA approved CAR19 Therapy PLUS immune modualtors:
- PDL1, PD1, 41BB
- Multi-targeted CAR-T against CD19 Plus another B cell Antigen
Anti-CD19 and CD22 Stanford, Spiegel et al Nature Medicine 2021
Anti-CD19 and CD20 MCW, Nirav Shah et al. Nature Medicine 2020
- New Targets: CD79a, CD79b, CD70, ROR and more
- Allogeneic CAR Therapy made from "super donors" providing "Off the Shelf" Rx
Jonathan W. Friedberg. Hematology. 2011:498-505. Howlader N, et al. SEER Cancer Statistics Review, 1975-2013. Gisselbrecht C, et al. J Clin Oncol. 2010;28:4184-4190. Neelapu SS et al. N Engl J Med; 2017 Dec 28, Schuster SJ et al., N Engl J Med; 2018 Dec 1
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Zuma-7 (axi-cel) and Transform (liso-cel) RCT for DLBCL Patients with Induction Failure or Relapse within 1 year

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- First-Line Therapy Chemotherapy-Resistant DLBCL and relapsed DLBCL within one year have poor Prognosis

2nd line RCT Eligibility

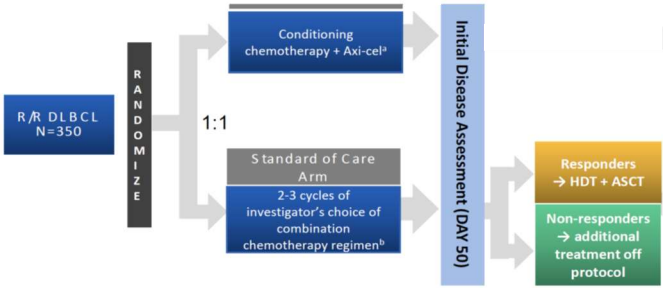
DLBCL or TFL with:

- Stable disease after 4 cycles of R-CHOP
- Progressive disease after 6 cycles of R-CHOP
- Relapse within 1 year of induction

Table 3. Response Rate and Survival According to Prognostic Factors

Factor	Total No. of Patients	Response CR/CRu/PR			3-Year Event-Free Survival		3-Year Overall Survival	
		No. of Patients	%	P	%	P	%	P
All patients	398	246	63		31		50	
CR/CRu		148	38		51		70	
Prior rituximab								
No	147	122	83	< .001	47	< .001	66	< .01
Yes	244	124	51		21		40	
Relapse, > 12 months	160	140	88	< .001	45	< .001	64	
Refractory, < 12 months	228	106	46		20		39	< .001
saaIPI								
< 2	224	160	71	< .001	40		62	
> 1	146	76	52		18	< .001	32	< .001

Abbreviations: CR, complete response; CRu, unconfirmed complete response; PR, partial response; saaIPI, secondary age-adjusted International Prognostic Index.



Gisselbrecht et. al, JCO 2010 2010 Sep 20;28(27):4184-90

Event Free Survival in 2nd line Randomized trials

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PRIMARY OUTCOME	ZUMA-7 (axi-cel)	TRANSFORM (liso-cel)	BELINDA (tisa-cel)
EFS RATE, %			
CAR T Arm	40.5%	44%	-
Control Arm (SOC)	16.3%	23.7%	-
DURATION EFS, MO			
CAR T Arm	8.3	10.1	3
Control Arm (SOC)	2	2.3	3
CR, %			
CAR T Arm	65%	66%	28%
Control Arm (SOC)	32%	39%	28%

Fred Locke, David Miklos … NEJM 2021. Manali Kamdar … ASH 2021 Abstract #91. Michael Bishop… NEJM 2021.

Event Free Survival in 2nd line Randomized trials

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PRIMARY OUTCOME	ZUMA-7 (axi-cel)	TRANSFORM (liso-cel)	BELINDA (tisa-cel)
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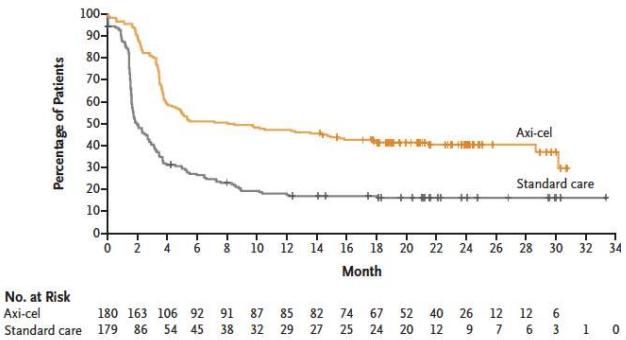
Fred Locke, David Miklos … NEJM 2021. Manali Kamdar … ASH 2021 Abstract #91. Michael Bishop… NEJM 2021. 27

Event Free Survival in 2nd line Randomized trials

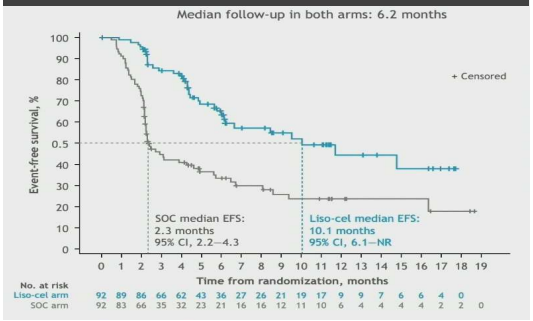
Stanford MEDICINE | Center for Cancer Cell Therapy

ZUMA-7 Axi-Cel



Median EFS= 8.3 months
2-year EFS= 41%
Grade 3/4 CRS= 6%
Grade 3/4 ICANS= 22%

TRANSFORM Liso-Cel



Median EFS= 10.1 months
1-year EFS= 44%
Grade 3/4 CRS= 1%
Grade 3/4 ICANS= 4%

Fred Locke, David Miklos … NEJM 2021. Manali Kamdar … ASH 2021 Abstract #91. 28

CAR19 is FDA approved for Rel/ref Mantle Cell Lymphoma and Follicular Lymphoma

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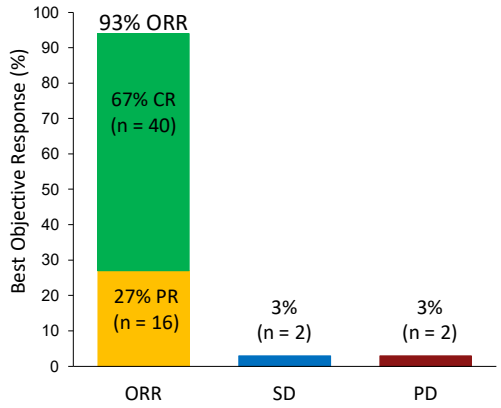
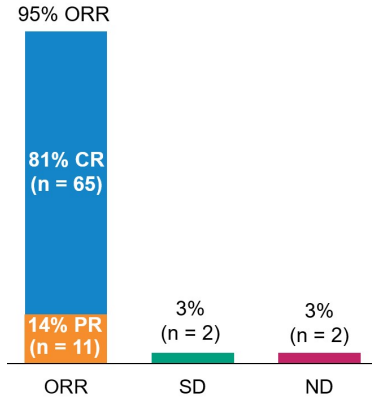
Mantle Cell Lymphoma
Zuma-2 study n=60



Brexucabtagene Autoleucel is FDA approved for Relapsed **MCL**

Follicular Lymphoma
Zuma-5 study n=80



Axicabtagene ciloleucel is FDA approved for **Rel/ref FL**

CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression free survival; PR, partial response; SD, stable disease.

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CAR-T Cell Therapy in Adult B cell Acute Lymphoblastic Leukemia: What's New?

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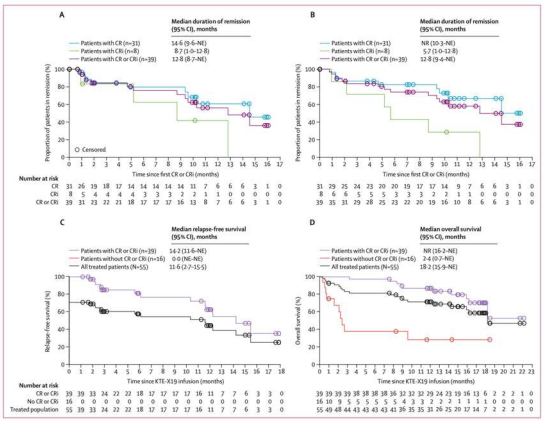
- **Brexucabtagene Autoleucel (Tecartus) is first FDA approved CAR-T for adults with r/r B-ALL**

- **Phase II Zuma 3 (N=55):**
  - 71% CR/Cri; 97% of whom were MRD-neg
  - Median DOR: 12.8 months
  - Median LFS: 11.6 months
  - 13% Grade 3-4 CRS
  - 25% Grade 3-4 ICANs

KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study



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CAR-T in Adult B-ALL: Relapse is Common

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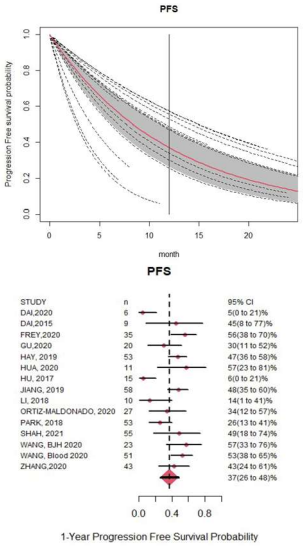
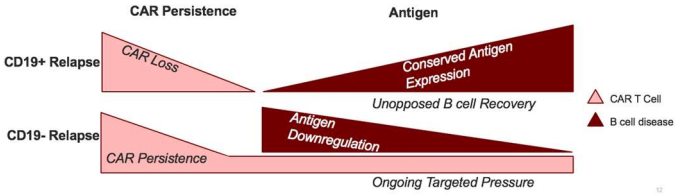


Two common patterns of relapse post-CAR:

- Relapse with Conserved Antigen expression in context of CAR Loss
- Relapse with Antigen Downregulation/Loss in context of CAR Persistence



Grover et al. *Blood Adv.* 2021 Oct 5:bloodadvances.2020003482.

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CD19 Antigen Loss is a Common Cause of treatment failure after CAR19 Therapy

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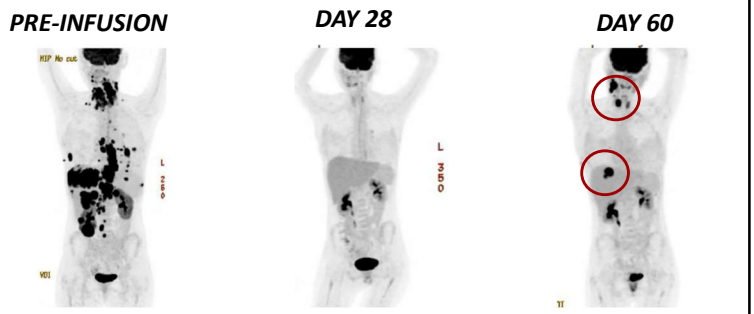
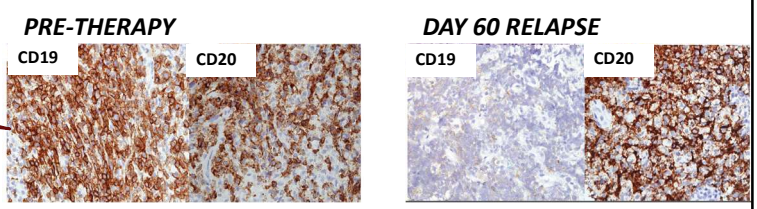
- 5/15 (28%) ZUMA-1 patients w/ disease progression after therapy were CD19 negative#
- 34 patients treated with commercial Axi-Cel at Stanford*
  - 16 developed disease progression
  - 12 were biopsied at time of progression
  - Six (50%) showed CD19 loss



Lymph node analysis pre-CAR and at Day 60 highlighted loss of CD19 but preservation of CD20 expression



#Placks V, … Miklos D, Bot A, Neelapu S; **Blood 2021**

*Jean Oak et. al, ASH2018 Abstract #4656

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CD19 loss or down-regulation occurs after axi-cel

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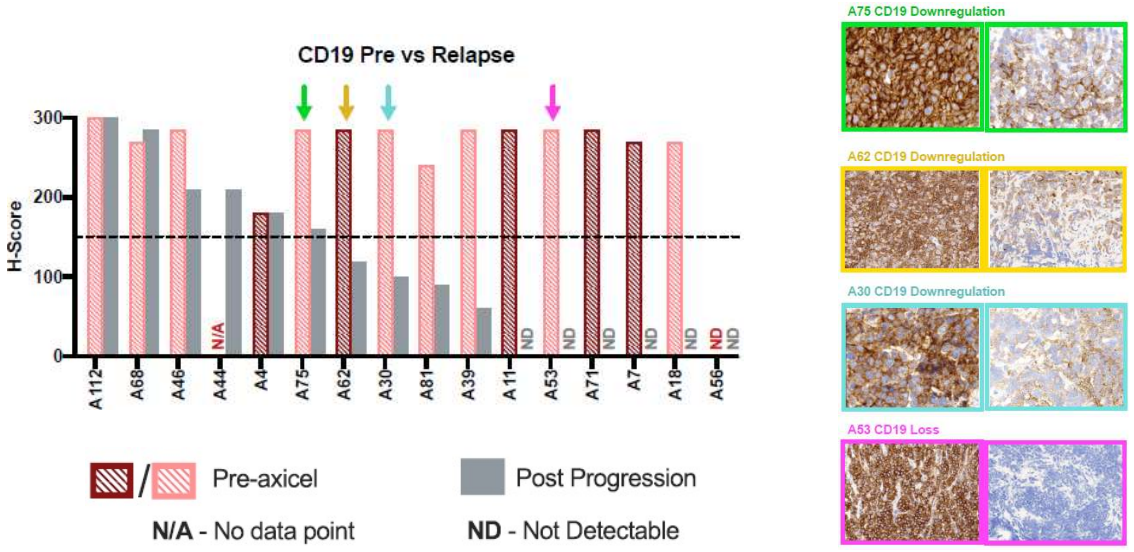

Spiegel, Patel, Muffly…Feldman, Mackall, Miklos. Nature Medicine 2021

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Simultaneous targeting of two tumor antigens may overcome antigen loss and improve efficacy

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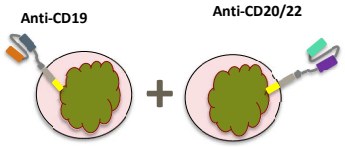
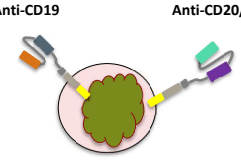
Co-administration



Pros:
- Defined dose for each CAR

Cons:
- Multiple production runs
- Potential competition
- When to infuse 2nd dose

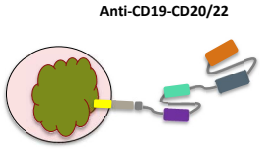
Co-expression
(co-transfection or bicistronic)



Pros:
- Each CAR molecule signals independently
- Reduces steric concerns

Cons:
- Can generate multiple CAR populations

Bivalent-bispecific receptor



Pros:
- Each cell expresses both scFVs

Cons:
- Distal scFV may have signalling deficiencies

Cronk RJ, *et al. Cancers* 2020; 12:2523.

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Clinical Trials testing Novel CAR-T are enrolling Patients with Relapsed – Refractory LBCL

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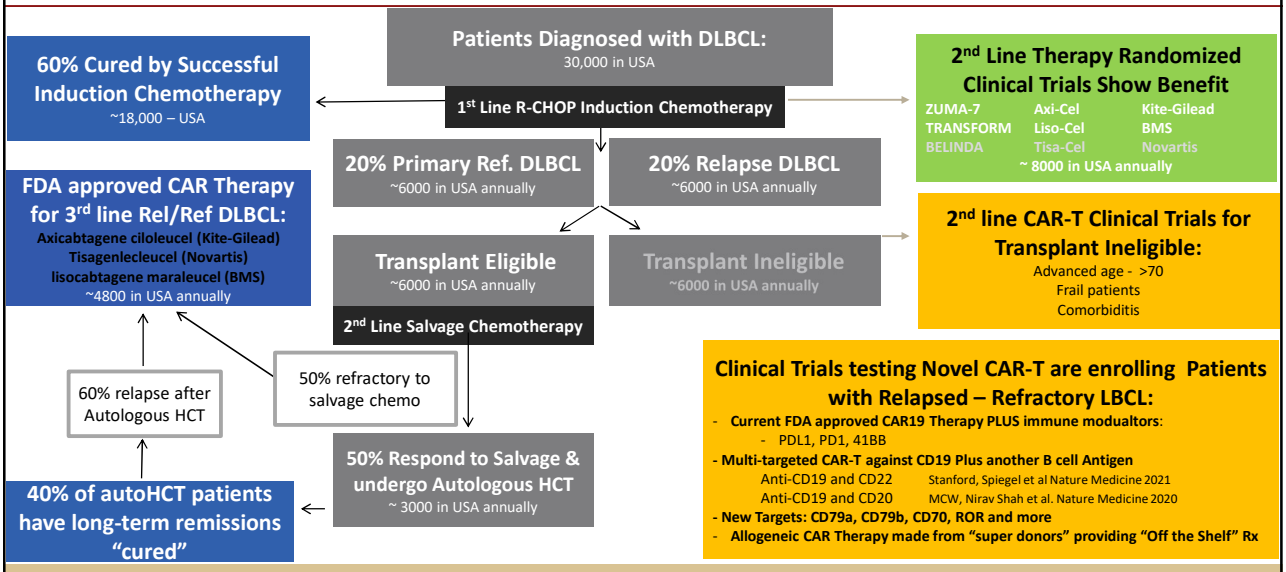

Jonathan W. Friedberg. *Hematology*. 2011:498-505. Howlader N, et al. *SEER Cancer Statistics Review*, 1975-2013. Gisselbrecht C, et al. *J Clin Oncol*. 2010;28:4184-4190. Neelapu SS et al. N Engl J Med; 2017 Dec 28, Schuster SJ et al., N Engl J Med; 2018 Dec 1

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2022 Lymphoma CAR-T Summary:

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- **Patients with rel/ref DLBCL are now eligible for three FDA approved CAR-T products:**
  - Axicabtagene ciloleucel **Axi-Cel** Kite-Gilead
  - Tisagenlecleucel **Tisa-Cel** Novartis
  - Lisocabtagene maraleucel **Liso-cel** BMS
- **Extending CAR-19 therapy to patients with additional CD19 malignancies:**
  - **Mantle Cell Lymphoma** Brexucabtagene Autoleucel
  - **Follicular Lymphoma** Axicabtagene ciloleucel
- **Brexucabtagene Autoleucel is first FDA approved CAR-T for adults with r/r B-ALL**
- **Anticipate FDA approval of Axi-Cel and Liso-cel for 2nd line LBCL therapy**

- **<u>CAR19 Weakness or Mechanism of Failure:</u>**
  - Leukemia and Lymphoma may down regulate CD19 expression (CD19 antigen loss)
  - **Multi-Targeted CAR-T Therapy may overcome CD19 antigen loss**

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CAR-T Cell Therapy in Multiple Myeloma

Surbhi Sidana, MD
Stanford University

Feb 15, 2022

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Disclosures

Consulting : Magenta Therapeutics, BMS, Janssen, Sanofi, Oncopeptides

Contracted Research: Magenta Therapeutics, BMS, Allogene, Janssen

I will be discussing non-FDA approved indications during my presentation

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Objectives

1. Review BCMA CAR-T: FDA approved and advanced clinical development (ide-cel, cilta-cel)
2. Other BCMA targeted CAR-T therapies in US
3. Non-BCMA targets in development

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CAR-T Therapy in MM

- Abecma (Ide-cel) approved for late line therapy (after 4 treatment lines)
- Other CAR-T therapies under investigation for late line and earlier treatment

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Targets for CAR-T in MM

BCMA (several constructs)

- Ide-cel
- Cilta-cel
- Others

In early development

- CS1 (SLAMF7)
- CD138
- CD38
- GPRC5D
- Others

Sidana and Shah. *Blood Adv*. 2019;3(21):3473-348

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BCMA (B cell maturation antigen)

- On normal and cancerous plasma cells
- Also on normal memory B-cells (immune system cells)
- Intensity of expression can vary with time
- Soluble BCMA shed in blood after removal by an enzyme called γ-secretase

Carpenter et al. *Clin Cancer Res*. 2013;19(8):2048-2060

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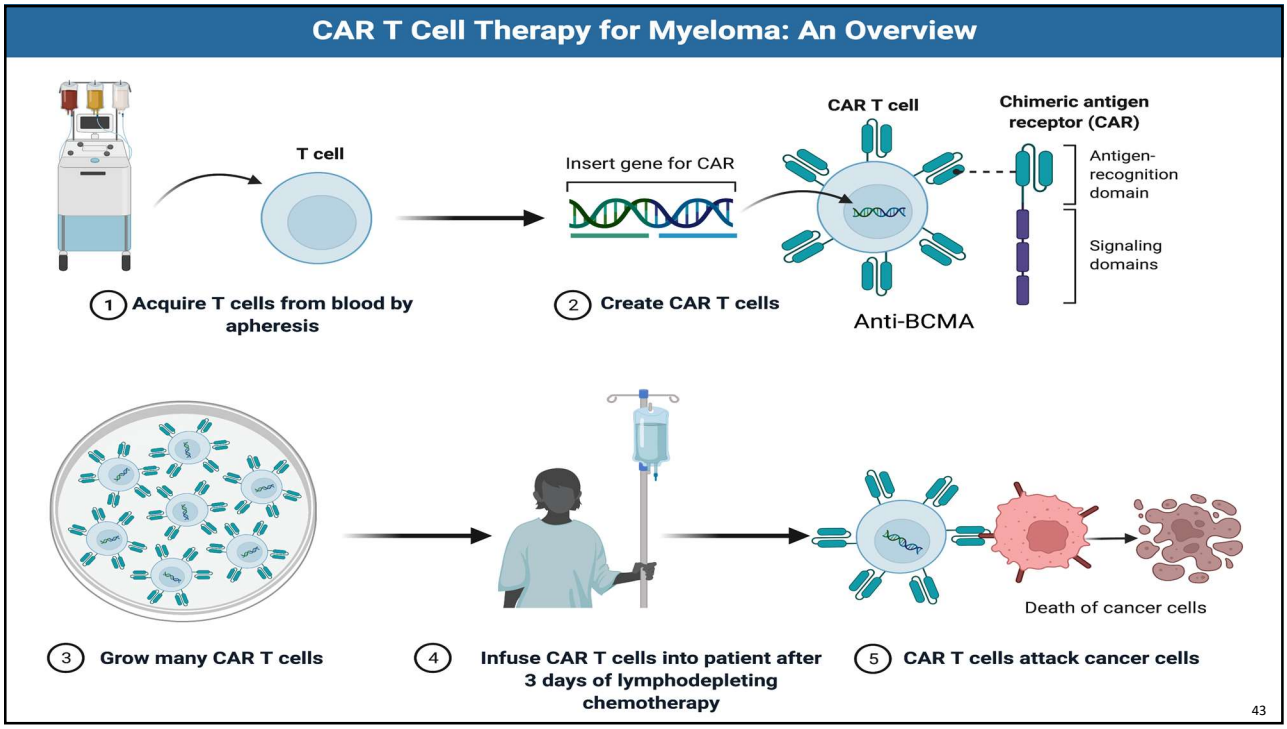

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Outcomes and recent FDA approved drugs in triple class refractory MM

Triple class refractory = Heavily pre-treated myeloma, including progression on

- Proteasome inhibitor (bortezomib, carfilzomib)
- Immunomodulatory drug (lenalidomide, pomalidomide)
- Anti-CD38 antibody (daratumumab)

	Response rate
Selinexor[1]	26%
Belantamab mafodotin[2,3]	31%
Triple Class Refractory [4]	31%

1. Chari et al. NEJM 2019;381(8):727-738; 2. Lonial et al. *Lancet Oncol*. 2020;21(2):207-221; 3. Lonial et al. ASCO 2020 abstract 436, JCO 2020;38(15_suppl):8536. 4. Gandhi et al. *Leukemia*. 2019;33(9):2266-2275

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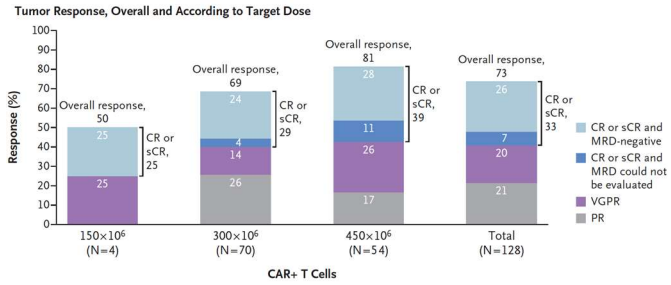
Idecabtagene Vicleucel (Ide-cel): FDA Approved March 2021

Baseline Characteristics	N=128
Median Prior Treatments	6
Triple Class Refractory	84%

Overall response rate: 73%
CR rate: 33%
MRD negativity: 26%



Munshi et al. NEJM 2021;384(8):705-716

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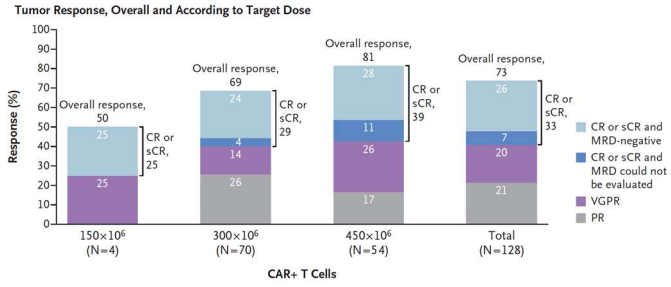

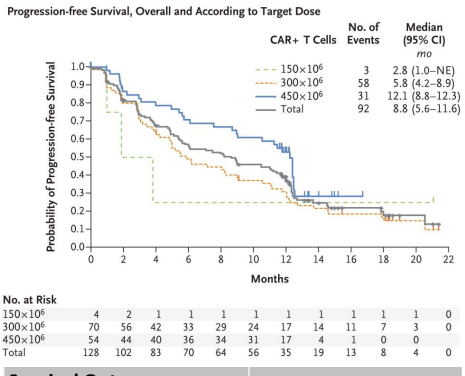

Survival Outcomes	
Median progression free survival	8.8 months
Median PFS in CR	20.2 months
Median OS	19.4 months

Munshi et al. NEJM 2021;384(8):705-716

Ide-cel: Safety

Adverse Events	
Cytokine release synrome (all; severe)	84% (5%)
Neurotoxicity/ICANS (all; severe)	18% (3%)
Infections (all; severe)	69% (22%)
Severe low neutrophil count > 1 month	41%
Severe low platelet count> 1 month	48%

Munshi et al. NEJM 2021;384(8):705-716

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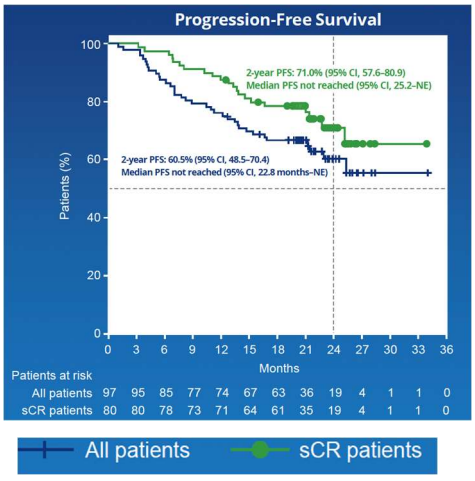
Ciltacabtagene Autoleucel (Cilta-cel)

Baseline Features	
Patients	97
Median prior treatments	6
Triple Class Refractory	88%

Efficacy	
Overall response rate	**98%**
sCR rate	83%
MRD negative rate (10^{-5})	58%[2]
PFS	2 year: 61%, median NR
OS	2 year: 74%, median NR



1. Martin et al. ASH 2021 *Blood* (2021) 138 (Supplement 1): 549.
2. Usmani et al ASCO 2021. JCO 2021;39(15_suppl):8005.

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Cilta-Cel: Safety

Adverse Events	
Cytokine release syndrome (all; severe)	95% (5%)
Neurotoxicity/ICANS (all; severe)	17% (2%)
Infections (all; severe)	58% (20%)
Severe low neutrophil counts> 1 month*	10%
Severe low platelet count > 1 month*	25%
Delayed neurotoxicity (all; severe)	**12% (9%)**

* Long term low counts: > 1 month from onset of cytopenias

1. Martin et al. ASH 2021; 2. Usmani et al ASCO 2021 abstract 8005; 3. Madduri et al ASH 2020 abstract 177

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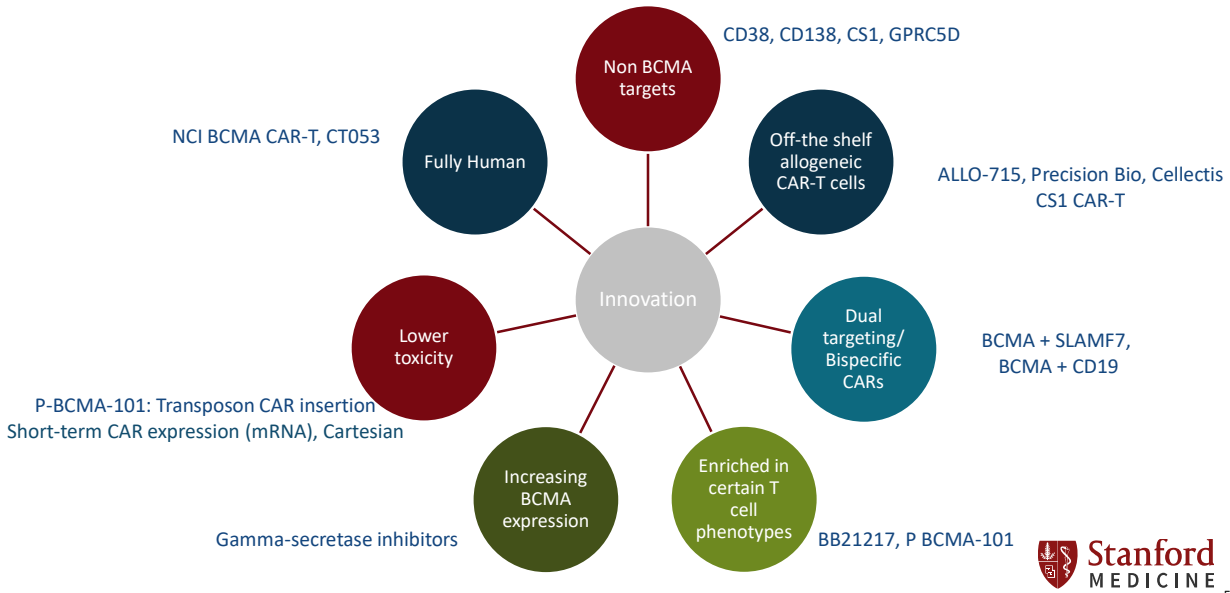
Innovation: Investigational Constructs



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Select BCMA Constructs in Early Clinical Development in US: Preliminary Data

69%	Uniqueness	Phase	N	Overall response rate
CT053/ CARSGen[1]	Fully Human	1b	20	94%
CART-ddBCMA/ Arcellx[2]	Computational designed synthetic binding domain, non-scFv	1	12	100%
BB21217/ Celgene[3]	PI3Ki co-culture, enrich memory phenotype	1a/b	72	69%
P-BCMA/ Posseida[4]	Transposon based, less AE, enriched for stem cell memory phenotype	1	53	44-75%
ALLO-715/ Allogene [5]	Off the shelf, additional LD with antiCD52	1	43	71% @ 320m with FCA
BCMA+GSI/ Fred Hutch & Juno[6]	FCARH143 BCMA CAR+ Gamma secretase inhibition JSMD-194	1	18	89%

1. Kumar et al. ASH 2020; 2: Friggault et al. ASCO 2021; 3: Raje et al. ASH 2021; 4. Costello et al. ASH 2020; 5. Mailankody ASH 2021; 6. Cowan et al. ASH 2021.

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Use of BCMA CAR-T in Earlier Lines

Being investigated in clinical trials

- Early Relapse, randomized trials: CARTITUDE-4, KarMMa-3
- Earlier lines, including front line (BMT-CTN 1902, KarMMa-4, CARTITUDE-2, CARTITUDE-5)

Benefits:

- Better T cell health → potential for higher efficacy and duration of response
- Earlier treatment free interval

Concerns:

- Toxicity (low blood countss and infections; longer term neurotoxicity)

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Non BCMA CAR-T in Clinical Development in US

Target
CD38
CD138
BCMA+CD19
GPRC5D (MCARH109)
CS1/SLAMF7
CS1 Allogeneic (MELANI-01)

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GPRC5D targeted CAR-T cells: First Phase 1 Human Trial

- GPRC5D target is present on plasma cells and some normal cells (hair follicles)
- 17 patients treated on phase 1 trial
- Median 6 prior treatment lines
- Prior BCMA treatment: 59%
- Prior CAR-T: 47%

Efficacy	N=16
Overall response rate	**69%**
ORR, Prior BCMA	80%
ORR, Prior CAR-T	75%

Adverse Events	N=17
CRS (all; severe)	93% (7%)
ICANS (all; severe)	7% (7%)
Infections	19%
Mild nail changes	56%
Mild rash	19%
Mild taste changes	6%

Mailankody et al. ASH 2021. *Blood* (2021) 138 (Supplement 1): 827

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Survivorship and QoL after CAR-T Therapy

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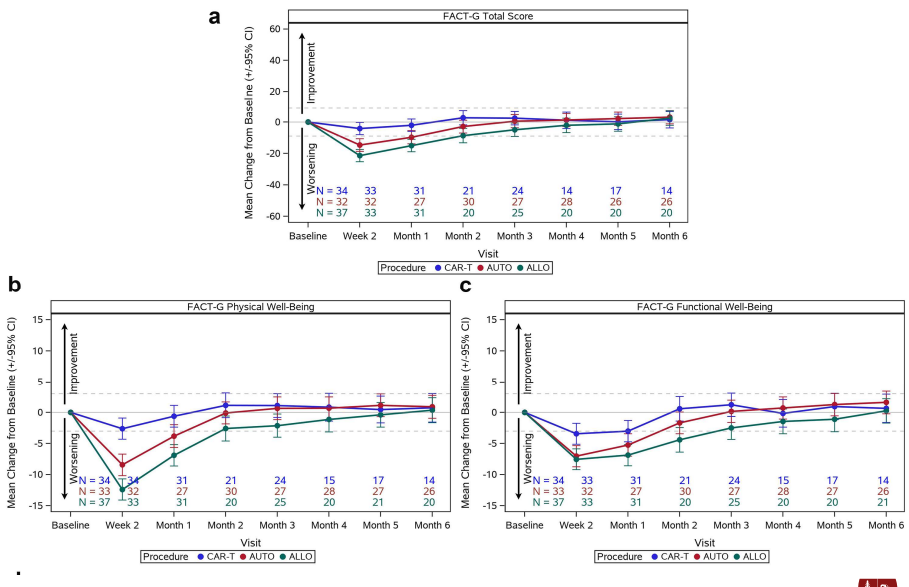
Patient Reported Outcomes: Quality of Life After CAR-T Cell Therapy



Sidana et al. ASH 2019. Manuscript in review

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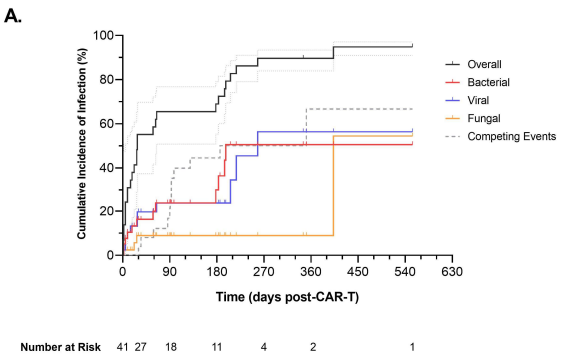
Post CAR-T Cytopenias after Month 1

Severe low blood counts: Very common (50-70%), improve with time

- ANC < 1000
- Platelets < 50,000
- Hemoglobin < 8 g/dL

Treatment: Growth factor medications, transfusions, rarely stem cell boost

Infections: Also common, long-term antimicrobial prophylaxis is necessary



1. Baird J et al, Blood Advances 2021. 2. Jain T et al, Blood Advances 2020

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Summary

- CAR-T therapy: Unprecedented response rates in heavily treated MM.
- Cytokine release syndrome and neurotoxicity are manageable.
- Low blood counts and infections are common, can be long term in some
- Delayed neurotoxicity can occur. Further study is need.
- Non-BCMA targets have shown promising early activity.
- Access to CAR-T remains an issue
- Understand & address quality of life and other late side effects with these newer treatments.

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ASK A QUESTION

BLOOD CANCERS: MANAGING SIDE EFFECTS

Ask a question by phone:

Press star (*) then the number 1 on your keypad.

Ask a question by web:

Click “Ask a question”
Type your question
Click “Submit”

Due to time constraints, we can only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

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LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:

To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET
Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET
Email: www.LLS.org/ContactUs
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation

NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult.

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LLS EDUCATION & SUPPORT RESOURCES

Online Chats

Online Chats are free, live sessions, moderated by oncology social workers. To register for one of the chats below, or for more information, please visit **www.LLS.org/Chat**.

Education Videos

View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**.

Patient Podcast

The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**.

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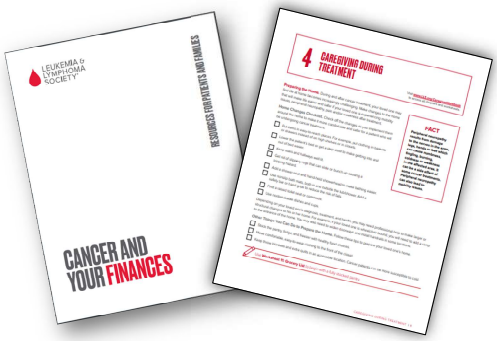
LLS EDUCATION & SUPPORT RESOURCES

The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancers: www.LLS.org/Finances



To order free materials: **www.LLS.org/Booklets**

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We have one goal: A world without blood cancers
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