CAR-T Cell Therapy

Current Successes, New Frontiers, and Challenges

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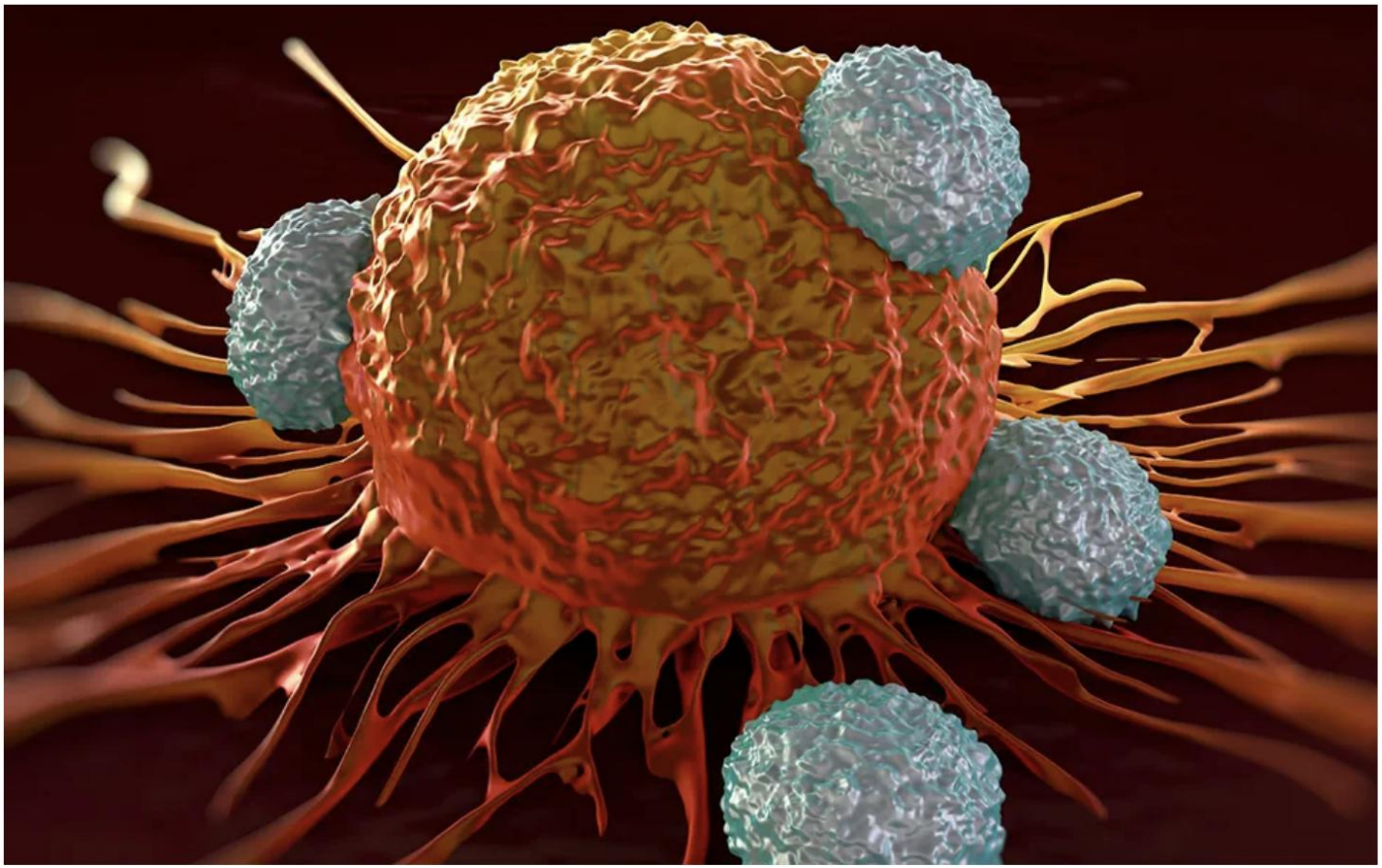
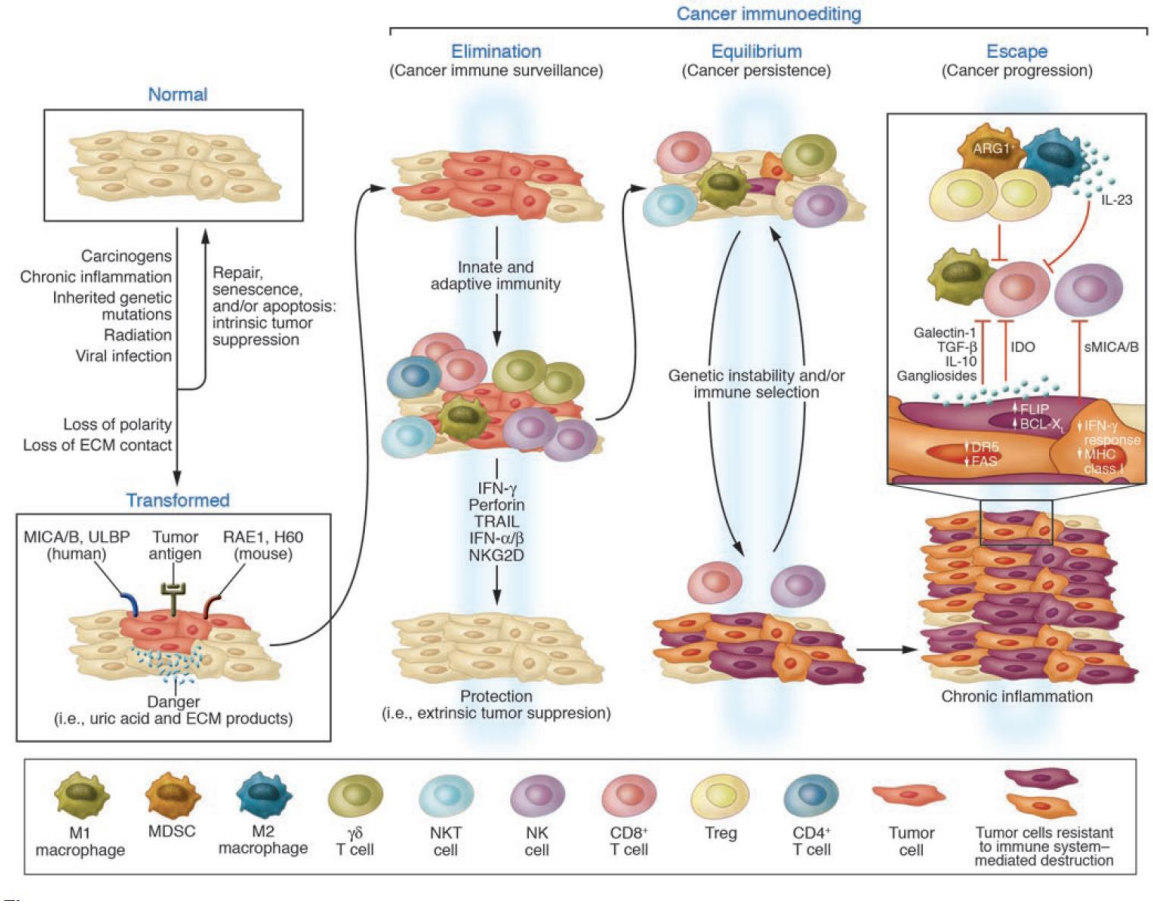
The Immune system's protective role



https://www.uhhospitals.org/

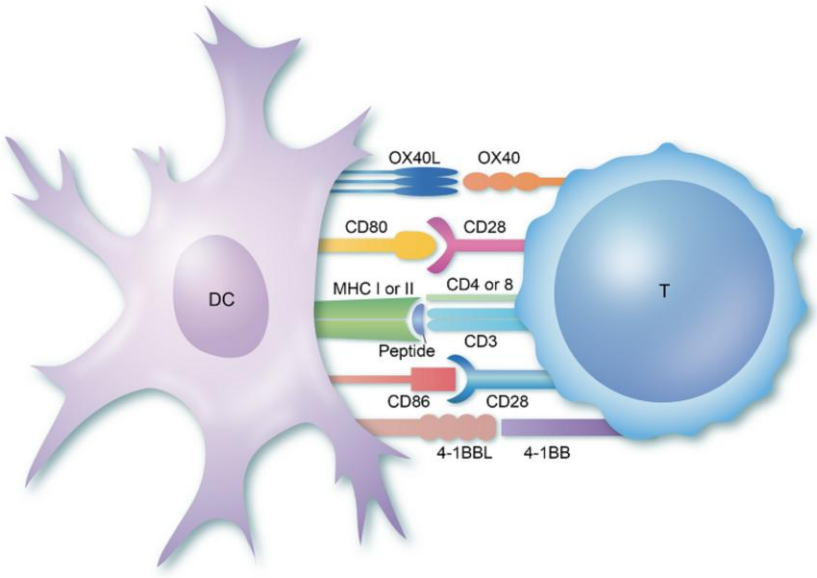
Immune surveillance



Swann and Smyth, Immune surveillance of tumors, The Journal of Clinical Investigation, 2007

The T-cell

- T cells are able to recognize and eliminate cancer cells with the same efficiency as virus-infected cells
- CD8+ CTLs are able to lyse tumor cells directly upon recognition of peptide–MHC class I complexes expressed by the tumor
- CD4+ T cells play a vital role in priming CTLs explaining why activated CTLs, but not naive CTLs, can mediate potent antitumor effects in the absence of CD4+ T cells.

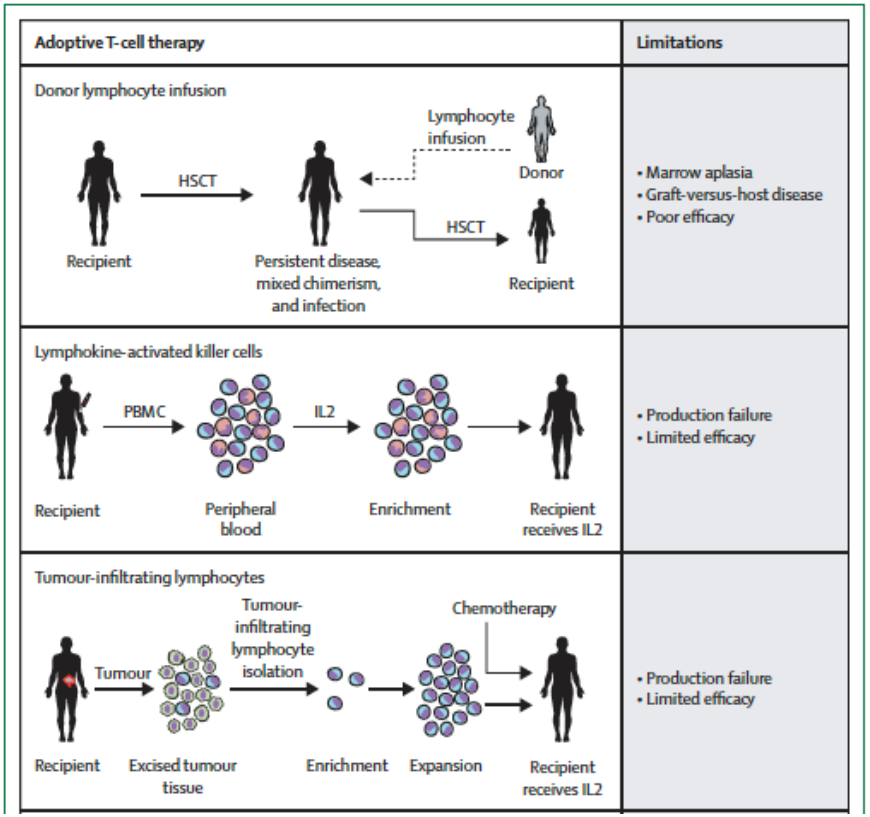


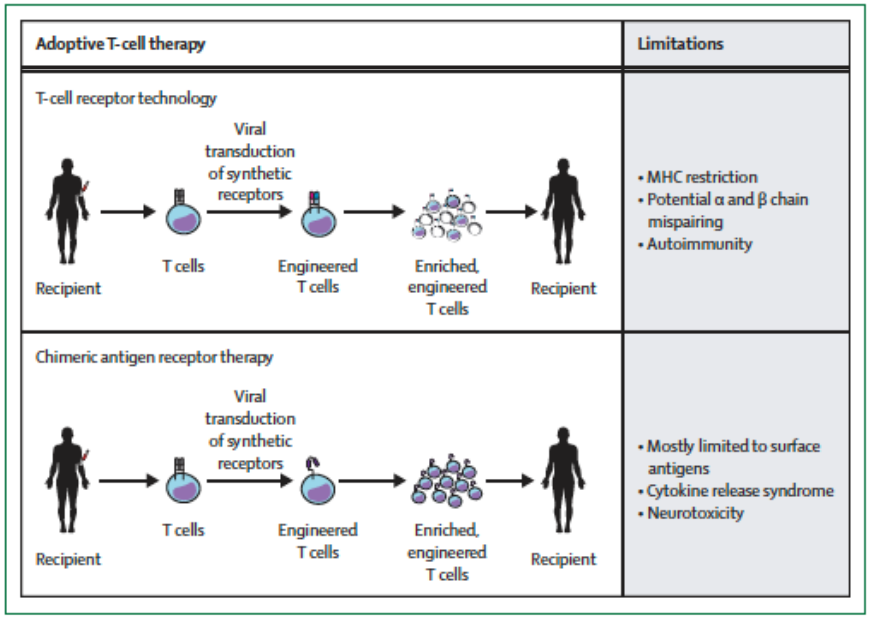
M. Cavanagh, BiteSized Immunology

Toes et al, J Exp Med.1999

Adoptive T-Cell Therapies

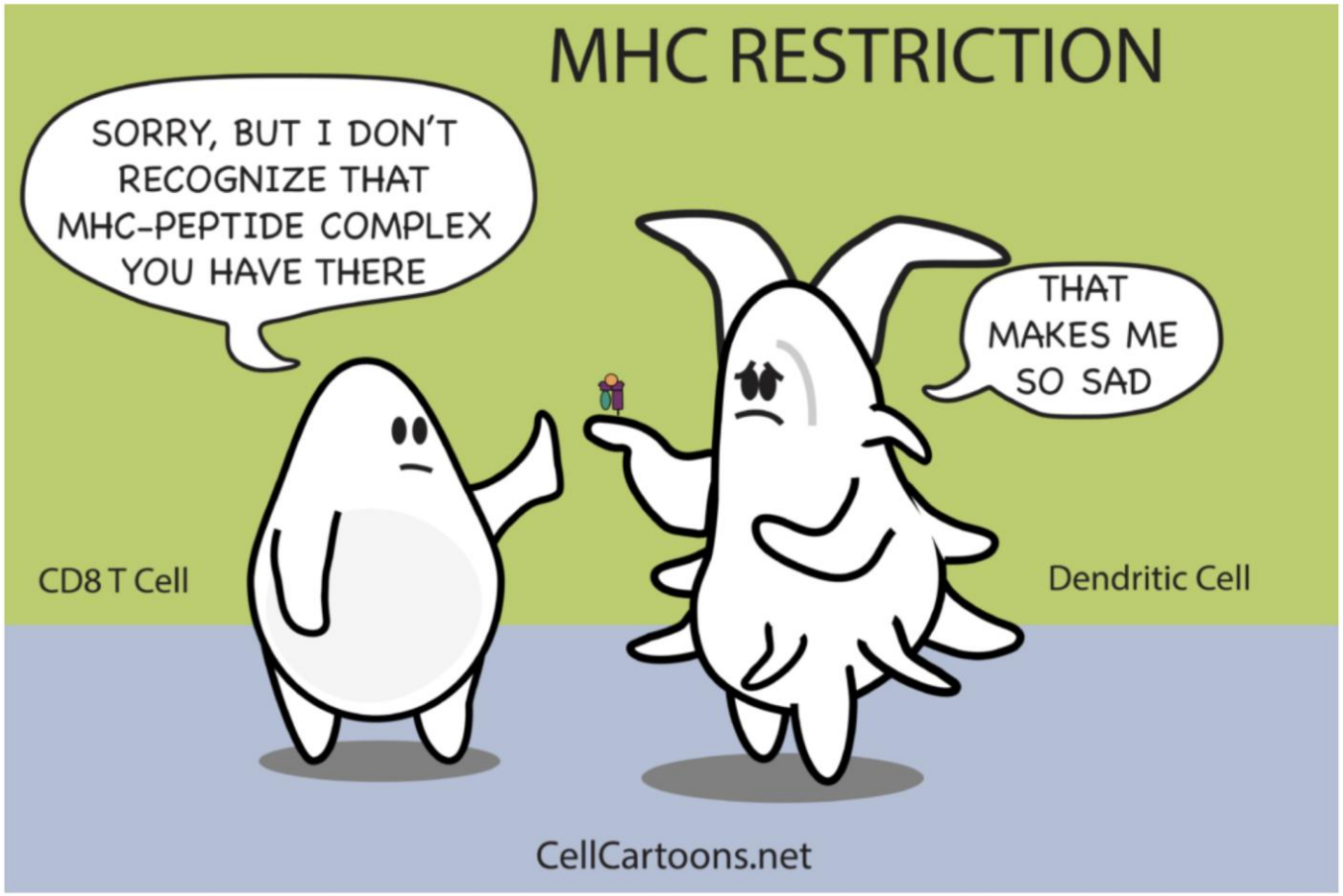
The infusion into a host of autologous or allogeneic immune cells that target their cancer.





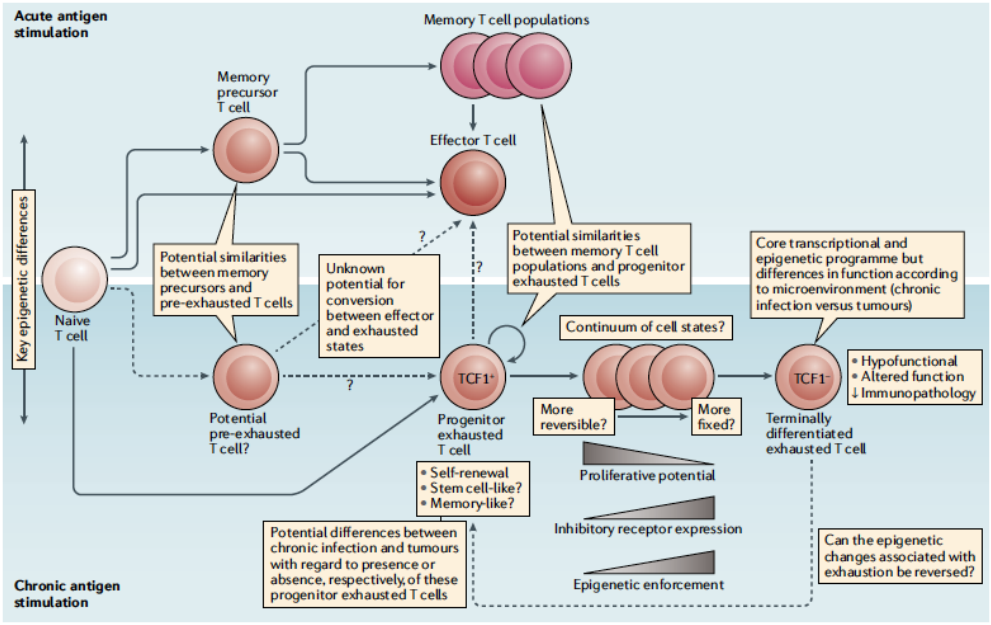
Singh and McGuirk, Lancet Oncology, 2020

T cells: The Shortfalls



T-cells cannot run a marathon

- T cell dysfunction usually occurs due to exposure to persistent antigens.
- T cell dysfunction is related to the level of antigen stimulation
- Cancer and chronic infections lead to T cell exhaustion culminating in loss of effector functions and alteration of their transcriptional program
- Enhanced co-expression of multiple inhibitory receptors



Blank et al., Nature Reviews Immunology, 2019

Blackburn et al.. *Nat Immunol.* 2009; Agnellini et al., *PNAS* 2007; Honda et al., *Immunity.* 2014; Okazaki et al, T., *Nat Immunol.* 2013; Wherry et al, . *J Virol.* 2003; Zajac A.J., *J Exp Med.* 1998; Ahmadzadeh M., *Blood.* 2009; Kamphorst. *Science.* 2017.

Overcoming the shortfalls

CAR-T cells

Chimeric **A**ntigen **R**eceptor (CAR) T-cells

- A new class of medicinal product
- A form of adoptive T-Cell therapy
- Manufactured from autologous human living cells
- They are genetically eingineered human T-cells
- Manufactured on demand
- Regarded as a Gene Therapy Medicinal Product (GTMP)
- Among the most expensive medicinal products ever marketed

CAR-T Cells

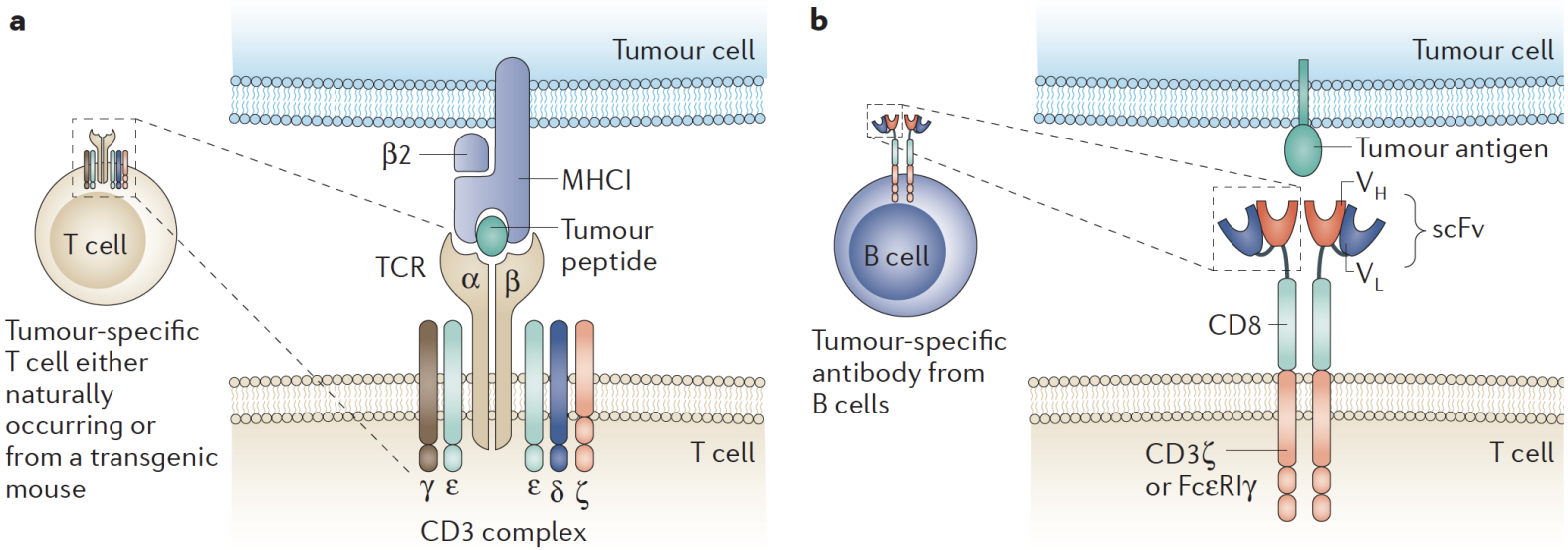
- CARs are composed of a single-chain variable-fragment (scFv) antibody specific to tumor associated antigen **(TAA)**
- fused to a transmembrane (TM) domain, which is further fused to a
- T-cell signaling moiety, most commonly either the CD3ζ or Fc receptor γ cytoplasmic signaling domains

Tumour-associated antigens

- Molecules that are expressed by cancer cells and, to a limited degree, by normal tissues.
- TAAs can serve as targets for T cells and/or antibodies.
- These antigens can be proteins, carbohydrates or lipids, and are classified into several categories on the basis of their expression characteristics:

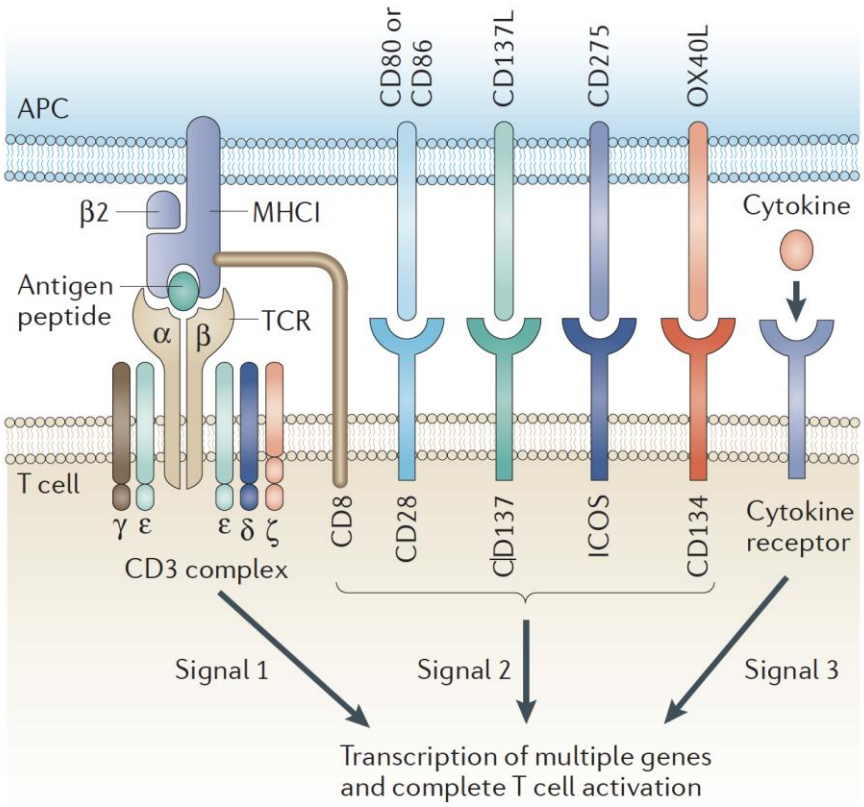
- Mutated — these are proteins with unique mutations in their amino acid sequence that are present only in cancer cells.
- Cancer-testis — expressed only by tumours and testis.
- Differentiation — expressed by a limited range of normal tissues.
- Overexpressed — these antigens can be expressed on a wide range of normal tissues, but are expressed much more highly in tumours.
- Idiotypic — unique protein sequences in the T cell receptor (TCR) or B cell receptor of leukaemias and lymphomas.
- Oncoviral — proteins encoded by tumorigenic viruses.

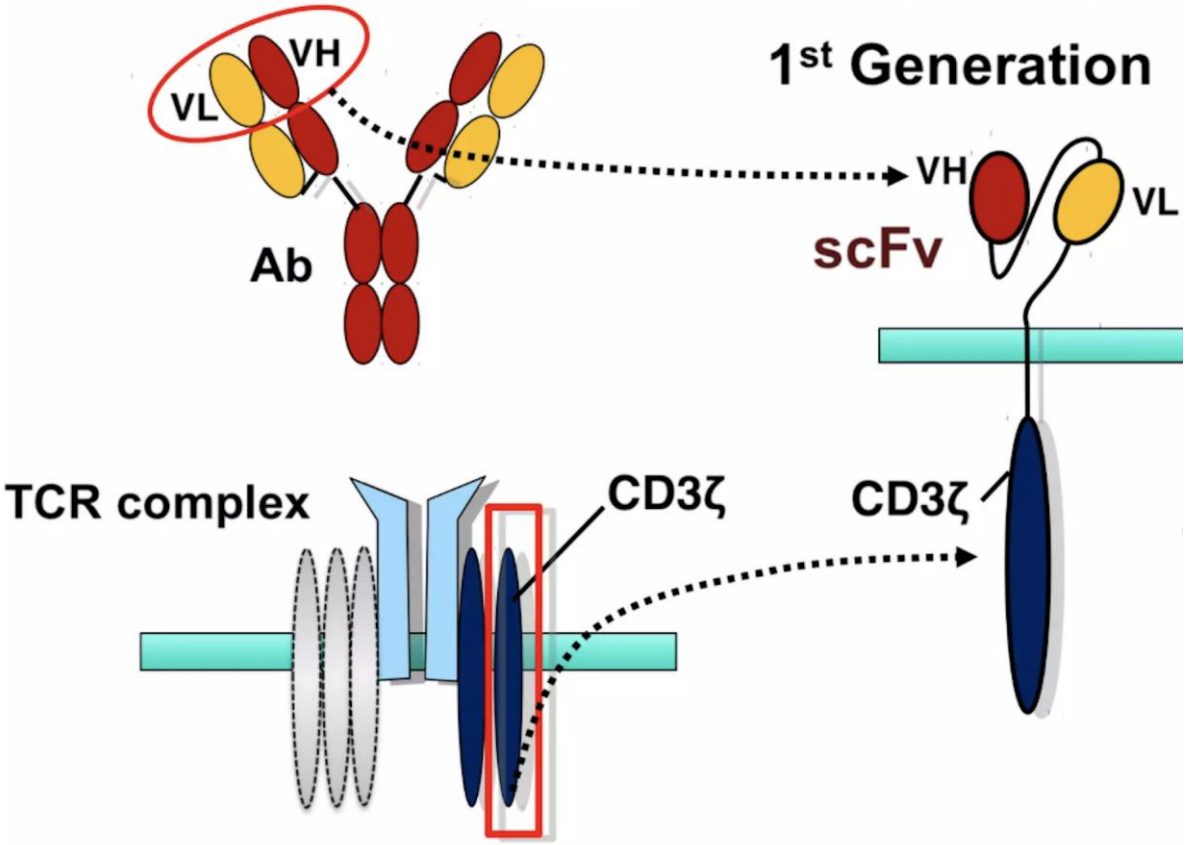
Derivation of TCRs and CARs for the genetic modification of T cells

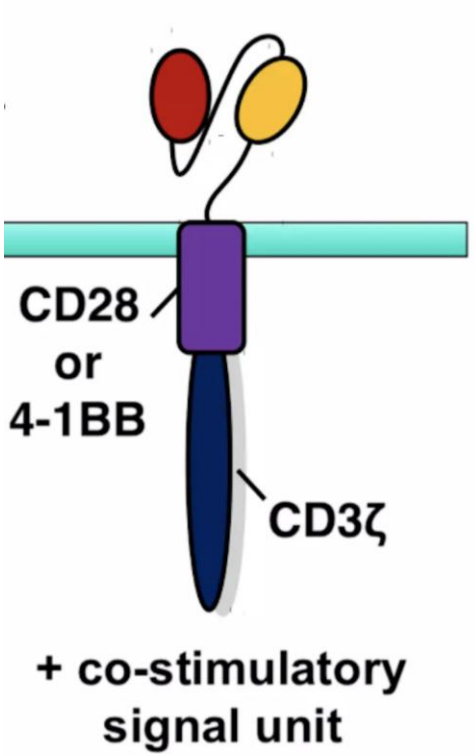


Kershaw et al, Nature Reviews Cancer, 13, 525–541 (2013)

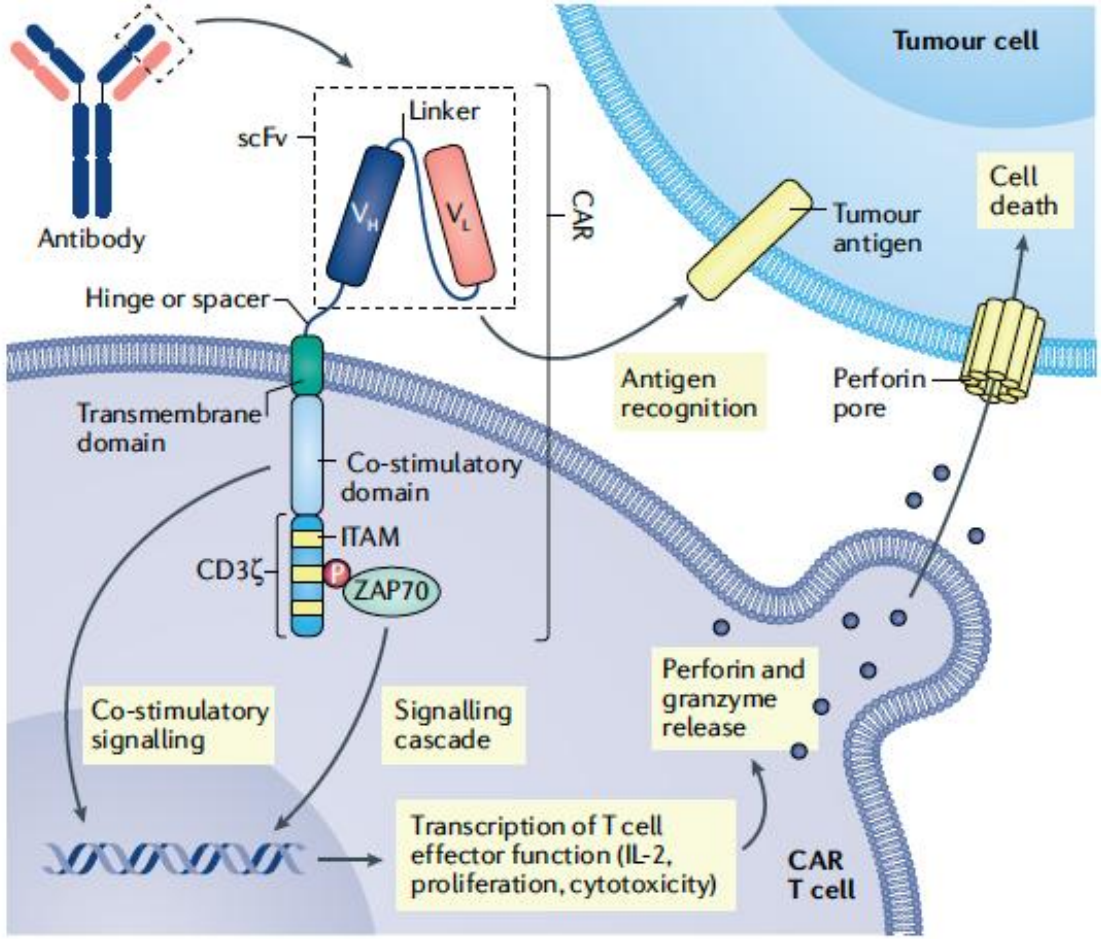
T-Cell Activation




VH
VL
Ab
1st Generation
VH
VL
scFv
CD3ζ
TCR complex
CD3ζ


2nd Generation
CD28
or
4-1BB
CD3ζ
+ co-stimulatory
signal unit

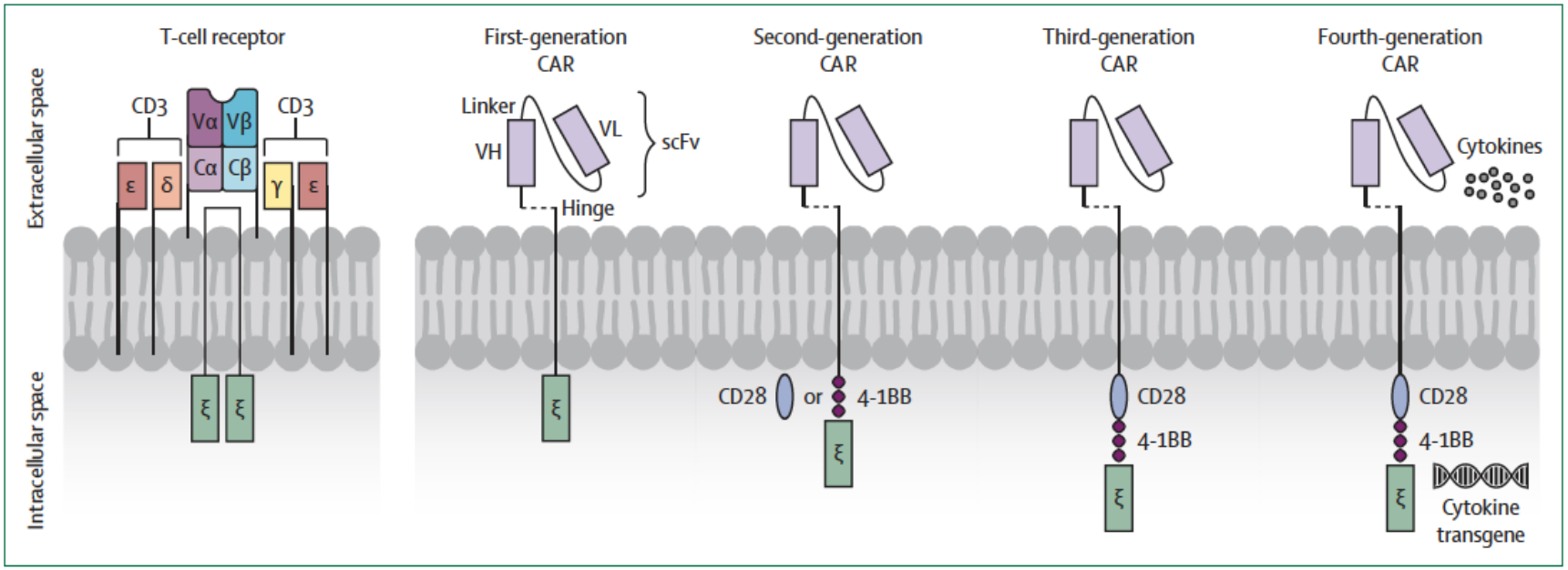
Second generation CAR-T cell

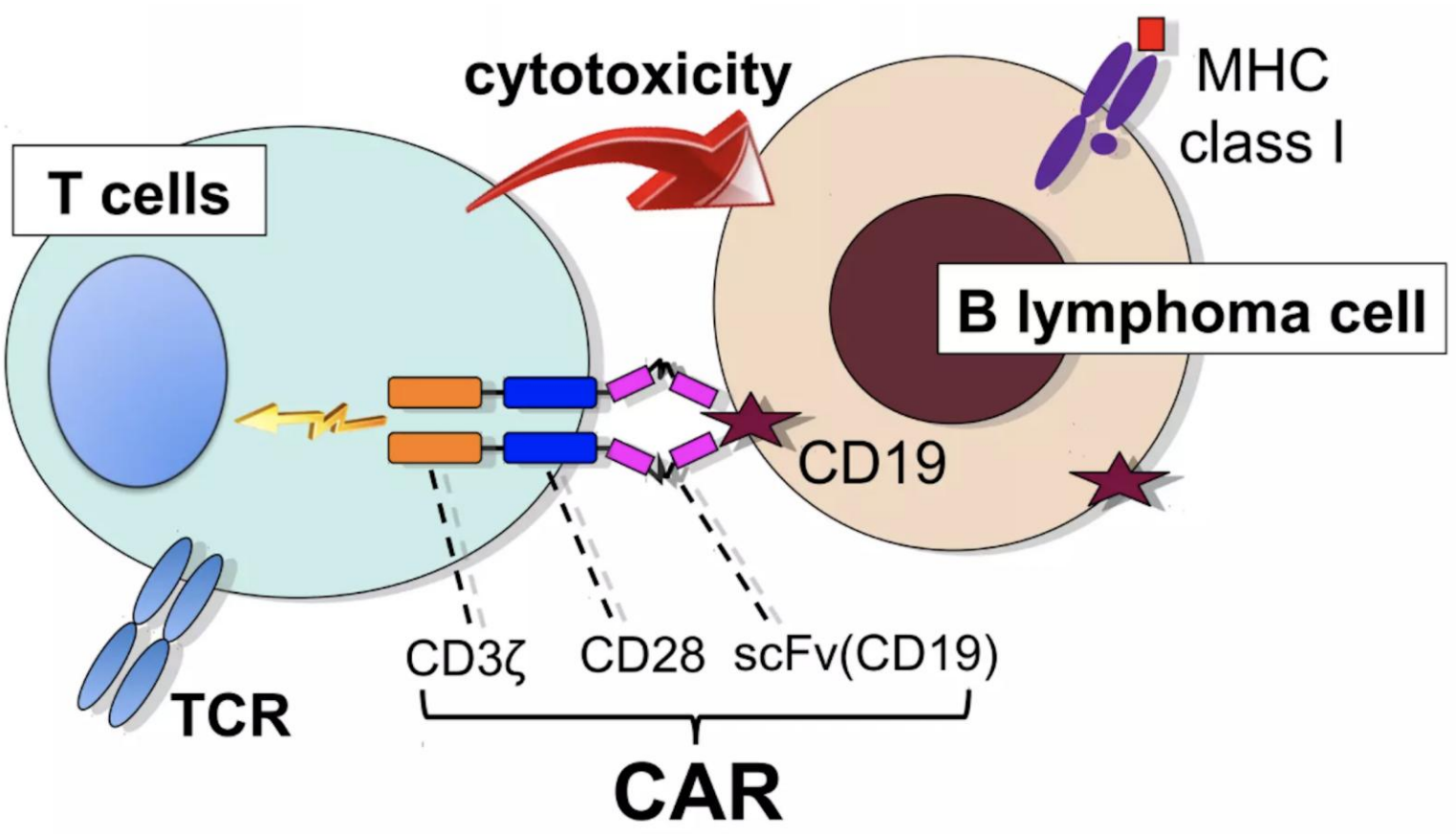


Larson and Maus, Nature Reviews Cancer, 2021

Generations of CARs

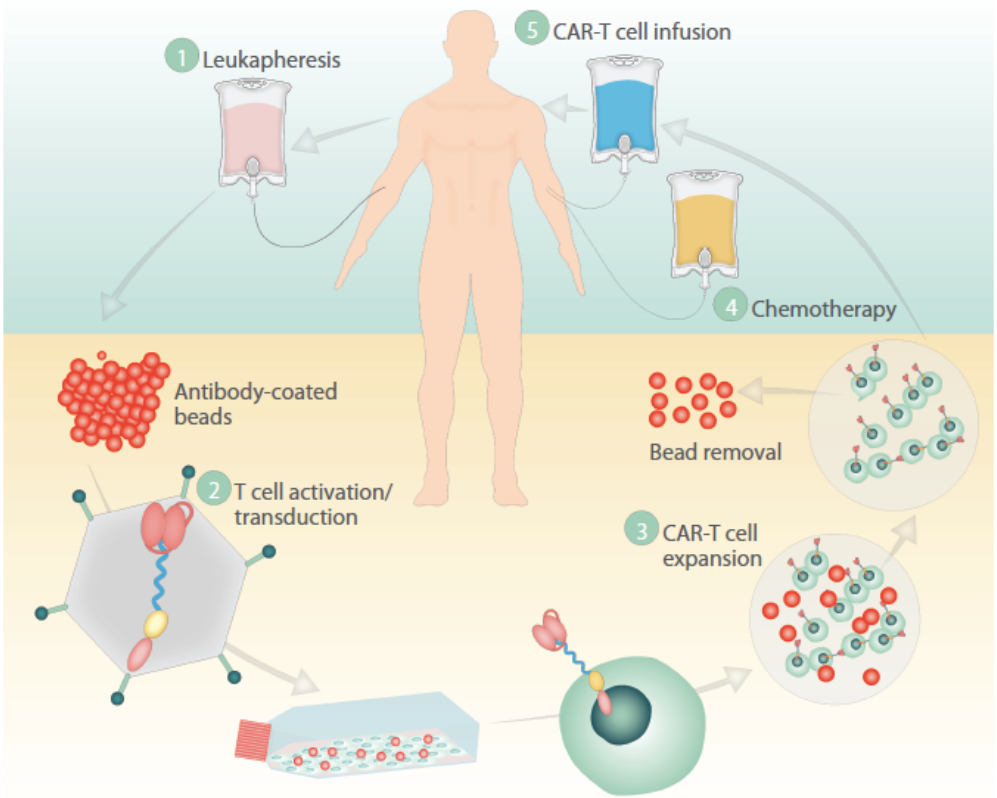
3 main domains




cytotoxicity
MHC
class I
T cells
B lymphoma cell
CD19
CD3ζ
CD28
scFv(CD19)
TCR
CAR

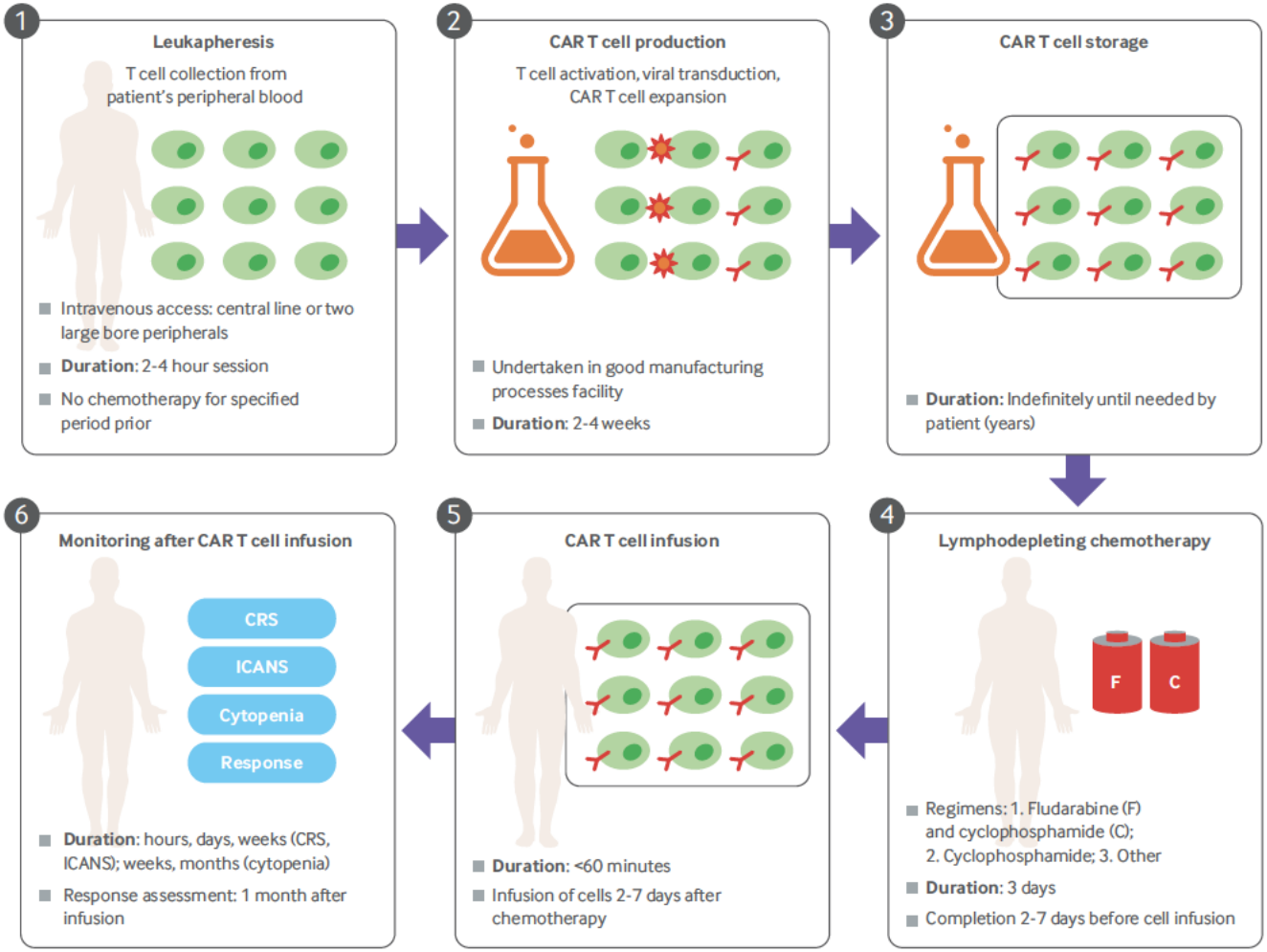
Chimeric antigen receptor (CAR)-T cell therapy

- T cells are removed from the patient's blood
- Engineered to express a chimeric antigen receptor
- Cells are infused back into the patient after expansion

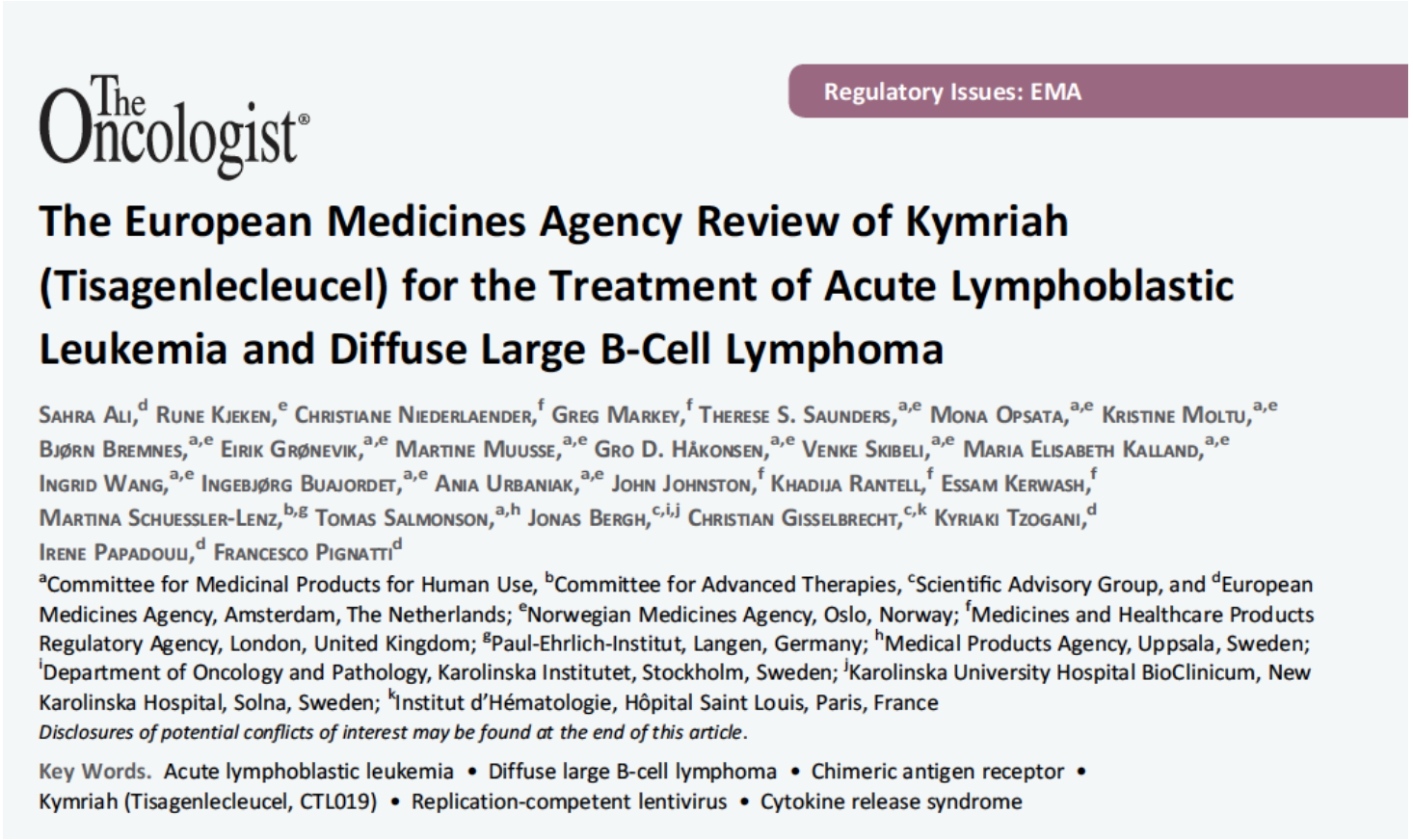


Buechner et al., HemaSphere, 2018

Flow chart


1
Leukapheresis
T cell collection from patient's peripheral blood
Intravenous access: central line or two large bore peripherals
Duration: 2-4 hour session
No chemotherapy for specified period prior
2
CAR T cell production
T cell activation, viral transduction, CAR T cell expansion
Undertaken in good manufacturing processes facility
Duration: 2-4 weeks
3
CAR T cell storage
Duration: Indefinitely until needed by patient (years)
4
Lymphodepleting chemotherapy
F
C
Regimens: 1. Fludarabine (F) and cyclophosphamide (C); 2. Cyclophosphamide; 3. Other
Duration: 3 days
Completion 2-7 days before cell infusion
5
CAR T cell infusion
Duration: <60 minutes
Infusion of cells 2-7 days after chemotherapy
6
Monitoring after CAR T cell infusion
CRS
ICANS
Cytopenia
Response
Duration: hours, days, weeks (CRS, ICANS); weeks, months (cytopenia)
Response assessment: 1 month after infusion

First regulatory approval



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Regulatory Issues: EMA

The European Medicines Agency Review of Kymriah (Tisagenlecleucel) for the Treatment of Acute Lymphoblastic Leukemia and Diffuse Large B-Cell Lymphoma

Sahra Ali,[d] Rune Kjeken,[e] Christiane Niederlaender,[f] Greg Markey,[f] Therese S. Saunders,[a,e] Mona Opsata,[a,e] Kristine Moltu,[a,e] Bjørn Bremnes,[a,e] Eirik Grønevik,[a,e] Martine Muusse,[a,e] Gro D. Håkonsen,[a,e] Venke Skibeli,[a,e] Maria Elisabeth Kalland,[a,e] Ingrid Wang,[a,e] Ingebjørg Buajordet,[a,e] Ania Urbaniak,[a,e] John Johnston,[f] Khadija Rantell,[f] Essam Kerwash,[f] Martina Schuessler-Lenz,[b,g] Tomas Salmonson,[a,h] Jonas Bergh,[c,i,j] Christian Gisselbrecht,[c,k] Kyriaki Tzogani,[d] Irene Papadouli,[d] Francesco Pignatti[d]

[a]Committee for Medicinal Products for Human Use, [b]Committee for Advanced Therapies, [c]Scientific Advisory Group, and [d]European Medicines Agency, Amsterdam, The Netherlands; [e]Norwegian Medicines Agency, Oslo, Norway; [f]Medicines and Healthcare Products Regulatory Agency, London, United Kingdom; [g]Paul-Ehrlich-Institut, Langen, Germany; [h]Medical Products Agency, Uppsala, Sweden; [i]Department of Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden; [j]Karolinska University Hospital BioClinicum, New Karolinska Hospital, Solna, Sweden; [k]Institut d'Hématologie, Hôpital Saint Louis, Paris, France

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Acute lymphoblastic leukemia • Diffuse large B-cell lymphoma • Chimeric antigen receptor • Kymriah (Tisagenlecleucel, CTL019) • Replication-competent lentivirus • Cytokine release syndrome

The Oncologist Feb 2020

The supporting trials

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia

S.L. Maude, T.W. Laetsch, J. Buechner, S. Rives, M. Boyer, H. Bittencourt, P. Bader, M.R. Verneris, H.E. Stefanski, G.D. Myers, M. Qayed, B. De Moerloose, H. Hiramatsu, K. Schlis, K.L. Davis, P.L. Martin, E.R. Nemecek, G.A. Yanik, C. Peters, A. Baruchel, N. Boissel, F. Mechinaud, A. Balduzzi, J. Krueger, C.H. June, B.L. Levine, P. Wood, T. Taran, M. Leung, K.T. Mueller, Y. Zhang, K. Sen, D. Lebwohl, M.A. Pulsipher, and S.A. Grupp

ABSTRACT

BACKGROUND

In a single-center phase 1–2a study, the anti-CD19 chimeric antigen receptor (CAR) T-cell therapy tisagenlecleucel produced high rates of complete remission and was associated with serious but mainly reversible toxic effects in children and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL).

ELIANA Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Stephen J. Schuster, M.D., Michael R. Bishop, M.D., Constantine S. Tam, M.D., Edmund K. Waller, M.D., Ph.D., Peter Borchmann, M.D., Joseph P. McGuirk, D.O., Ulrich Jäger, M.D., Samantha Jaglowski, M.D., Charalambos Andreadis, M.D., Jason R. Westin, M.D., Isabelle Fleury, M.D., Veronika Bachanova, M.D., Ph.D., S. Ronan Foley, M.D., P. Joy Ho, M.B., B.S., D.Phil., Stephan Mielke, M.D., John M. Magenau, M.D., Harald Holte, M.D., Ph.D., Serafino Pantano, Ph.D., Lida B. Pacaud, M.D., Rakesh Awasthi, Ph.D., Jufen Chu, Ph.D., Özlem Anak, M.D., Gilles Salles, M.D., Ph.D., and Richard T. Maziarz, M.D., for the JULIET Investigators*

ABSTRACT

BACKGROUND

Patients with diffuse large B-cell lymphoma that is refractory to primary and second-line therapies or that has relapsed after stem-cell transplantation have a poor prognosis. The chimeric antigen receptor (CAR) T-cell therapy tisagenlecleucel targets and eliminates CD19-expressing B cells and showed efficacy against B-cell lymphomas in a single-center, phase 2a study.

JULIET Trial

UMM UNIVERSITÄTSMEDIZIN MANNHEIM

Medizinische Fakultät Mannheim der Universität Heidelberg

Universitätsklinikum Mannheim

JULIET STUDY

- A Phase II, Single Arm, multicenter trial to determine the efficacy and safety of CTL019 in adult patients with relapsed or refractory Diffuse Large B-cell Lymphoma
- 27 sites in 10 countries
- Patients must have received at least 2 lines of therapy
- Primary end point was best overall response rate (combined percentage of patients with complete and partial response)

JULIET study…..

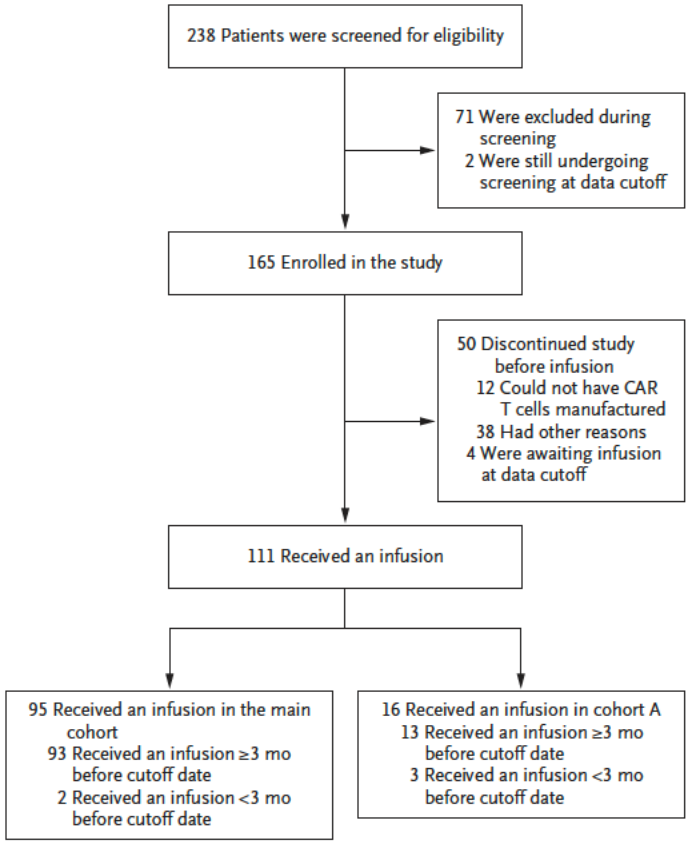
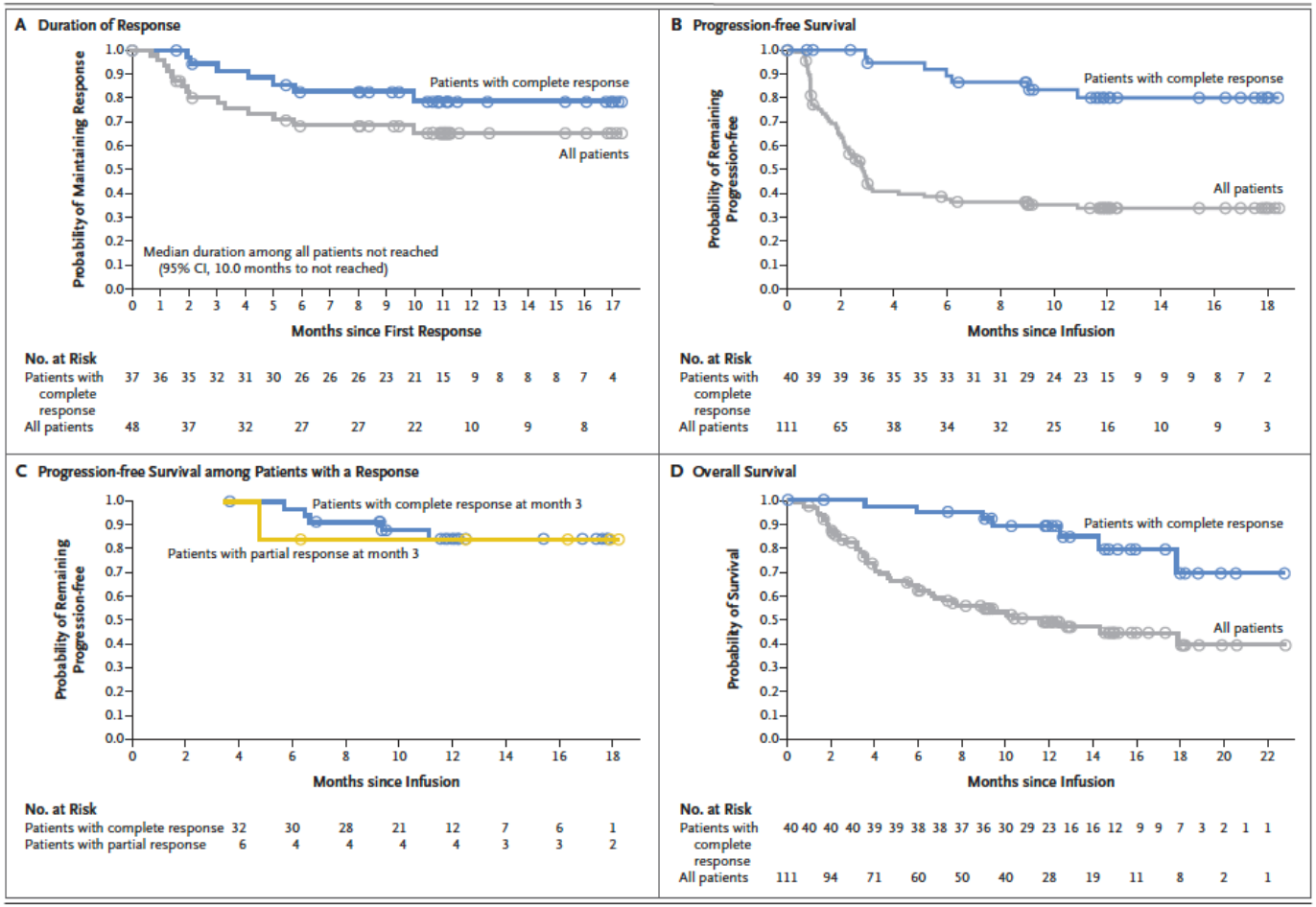


Table 1. Demographic and Clinical Characteristics of the Patients in the Full Analysis Set at Baseline.*

Characteristic	Patients (N = 111)
Median age (range) — yr	56 (22–76)
Age ≥65 yr — no. (%)	25 (23)
ECOG performance status — no. (%)†	
0	61 (55)
1	50 (45)
Disease stage at study entry — no. (%)‡	
Stage I	8 (7)
Stage II	19 (17)
Stage III	22 (20)
Stage IV	62 (56)
Bone marrow involvement at study entry — no. (%)	8 (7)
Diagnosis on central histologic review — no. (%)	
Diffuse large B-cell lymphoma, not otherwise specified	88 (79)
Transformed follicular lymphoma	21 (19)
Other	2 (2)
Double- or triple-hit rearrangement: *MYC* plus *BCL2*, *BCL6*, or both — no./total no. (%)§	19/70 (27)
Cell of origin of cancer — no. (%)	
Germinal center B-cell type	63 (57)
Non–germinal center B-cell type	45 (41)
Missing data	3 (3)
No. of previous lines of antineoplastic therapy — no. (%)¶	
1	5 (5)
2	49 (44)
3	34 (31)
4–6	23 (21)
Relapse after last therapy — no. (%)‖	50 (45)
Refractory diffuse large B-cell lymphoma — no. (%)**	61 (55)
Previous autologous hematopoietic stem-cell transplantation — no. (%)	54 (49)

Schuster et al., NEJM 2019

Duration of response, PFS and OS



Best overall response

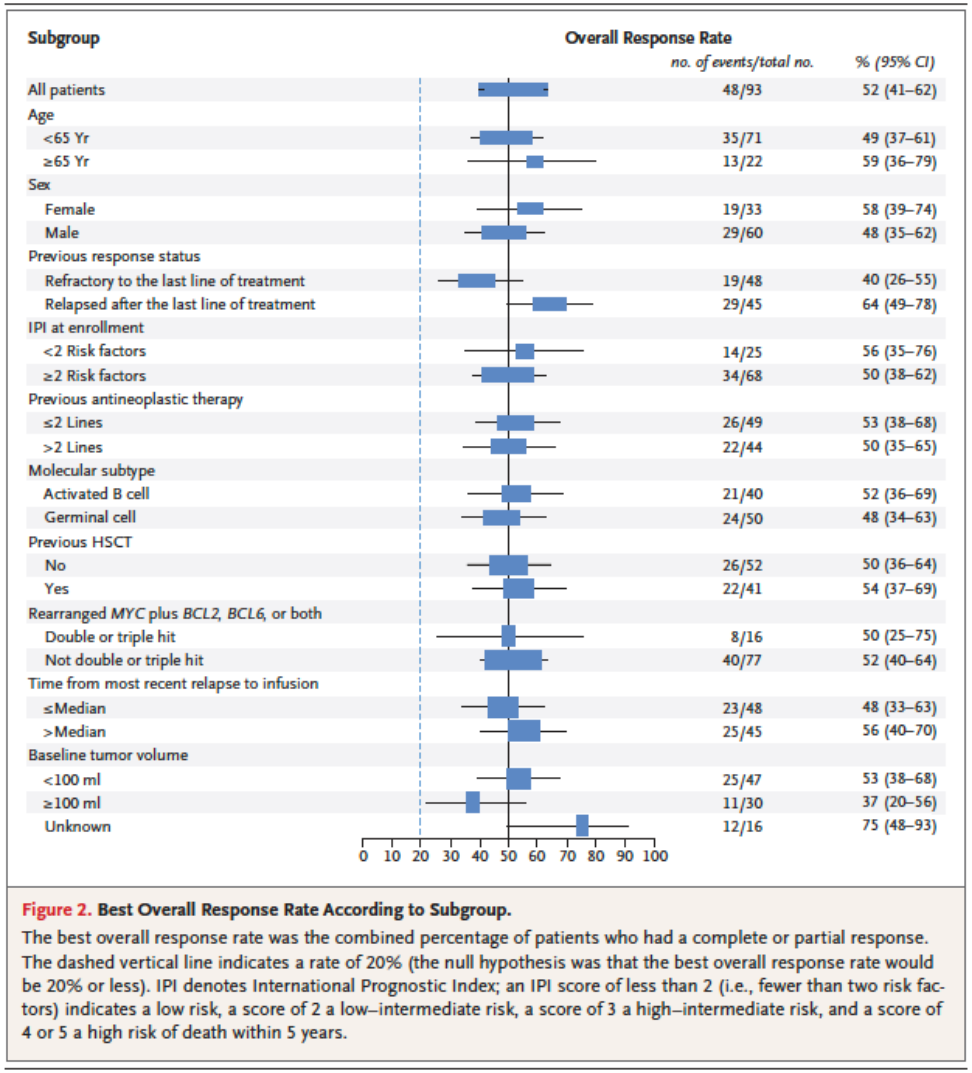


Figure 2. Best Overall Response Rate According to Subgroup.

The best overall response rate was the combined percentage of patients who had a complete or partial response. The dashed vertical line indicates a rate of 20% (the null hypothesis was that the best overall response rate would be 20% or less). IPI denotes International Prognostic Index; an IPI score of less than 2 (i.e., fewer than two risk factors) indicates a low risk, a score of 2 a low–intermediate risk, a score of 3 a high–intermediate risk, and a score of 4 or 5 a high risk of death within 5 years.

Schuster et al., NEJM 2019

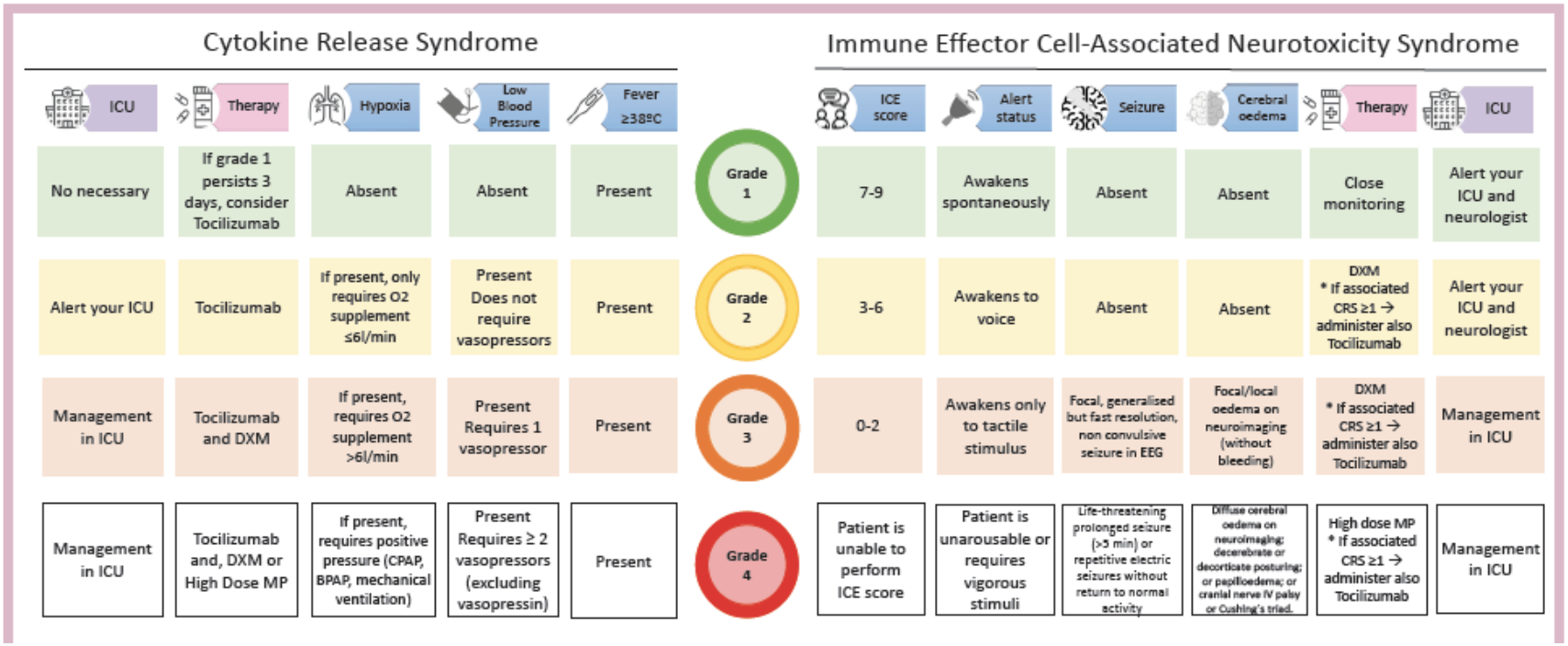
Adverse Events

Table 2. Overall Safety of Tisagenlecleucel.*

Type of Adverse Event	Patients with Any Event (N=111)	Patients with Events Starting ≤8 Wk after Infusion (N=111)	Patients with Events Starting >8 Wk after Infusion (N=96)
		number of patients (percent)	
Any adverse event	111 (100)	111 (100)	69 (72)
Adverse event suspected to be related to study drug	99 (89)	96 (86)	30 (31)
Serious adverse event	72 (65)	55 (50)	30 (31)
Serious adverse event suspected to be related to study drug	52 (47)	46 (41)	9 (9)
Grade 3 or 4 adverse event	99 (89)	94 (85)	47 (49)
Grade 3 or 4 adverse event suspected to be related to study drug	70 (63)	64 (58)	21 (22)
Adverse events of special interest†			
Cytokine release syndrome‡			
Any grade		64 (58)	0
Grade 3		15 (14)	0
Grade 4		9 (8)	0
Infection			
Any grade		38 (34)	37 (39)
Grade 3		20 (18)	13 (14)
Grade 4		2 (2)	4 (4)
Cytopenia not resolved by day 28§			
Any grade		49 (44)	NA
Grade 3		18 (16)	NA
Grade 4		18 (16)	NA
Neurologic event¶			
Any grade		23 (21)	5 (5)
Grade 3		8 (7)	3 (3)
Grade 4		5 (5)	0
Febrile neutropenia			
Any grade		17 (15)	2 (2)
Grade 3		14 (13)	1 (1)
Grade 4		2 (2)	1 (1)
Tumor lysis syndrome			
Any grade		1 (1)	0
Grade 3		1 (1)	0
Grade 4		0	0

Schuster et al., NEJM 2019

CRS & ICANS: Grading and Therapy: ASTCT



Cytokine Release Syndrome						Immune Effector Cell-Associated Neurotoxicity Syndrome					
ICU	Therapy	Hypoxia	Low Blood Pressure	Fever ≥38ºC		ICE score	Alert status	Seizure	Cerebral oedema	Therapy	ICU
No necessary	If grade 1 persists 3 days, consider Tocilizumab	Absent	Absent	Present	Grade 1	7-9	Awakens spontaneously	Absent	Absent	Close monitoring	Alert your ICU and neurologist
Alert your ICU	Tocilizumab	If present, only requires O2 supplement ≤6l/min	Present Does not require vasopressors	Present	Grade 2	3-6	Awakens to voice	Absent	Absent	DXM * If associated CRS ≥1 → administer also Tocilizumab	Alert your ICU and neurologist
Management in ICU	Tocilizumab and DXM	If present, requires O2 supplement >6l/min	Present Requires 1 vasopressor	Present	Grade 3	0-2	Awakens only to tactile stimulus	Focal, generalised but fast resolution, non convulsive seizure in EEG	Focal/local oedema on neuroimaging (without bleeding)	DXM * If associated CRS ≥1 → administer also Tocilizumab	Management in ICU
Management in ICU	Tocilizumab and, DXM or High Dose MP	If present, requires positive pressure (CPAP, BPAP, mechanical ventilation)	Present Requires ≥ 2 vasopressors (excluding vasopressin)	Present	Grade 4	Patient is unable to perform ICE score	Patient is unarousable or requires vigorous stimuli	Life-threatening prolonged seizure (>5 min) or repetitive electric seizures without return to normal activity	Diffuse cerebral oedema on neuroimaging; decerebrate or decorticate posturing; or papilloedema; or cranial nerve IV palsy or Cushing's triad.	High dose MP * If associated CRS ≥1 → administer also Tocilizumab	Management in ICU

Yanez et al., ESMO/BMJ 2020

Expanding the horizon

ORIGINAL ARTICLE

KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma

M. Wang, J. Munoz, A. Goy, F.L. Locke, C.A. Jacobson, B.T. Hill, J.M. Timmerman, H. Holmes, S. Jaglowski, I.W. Flinn, P.A. McSweeney, D.B. Miklos, J.M. Pagel, M.-J. Kersten, N. Milpied, H. Fung, M.S. Topp, R. Houot, A. Beitinjaneh, W. Peng, L. Zheng, J.M. Rossi, R.K. Jain, A.V. Rao, and P.M. Reagan

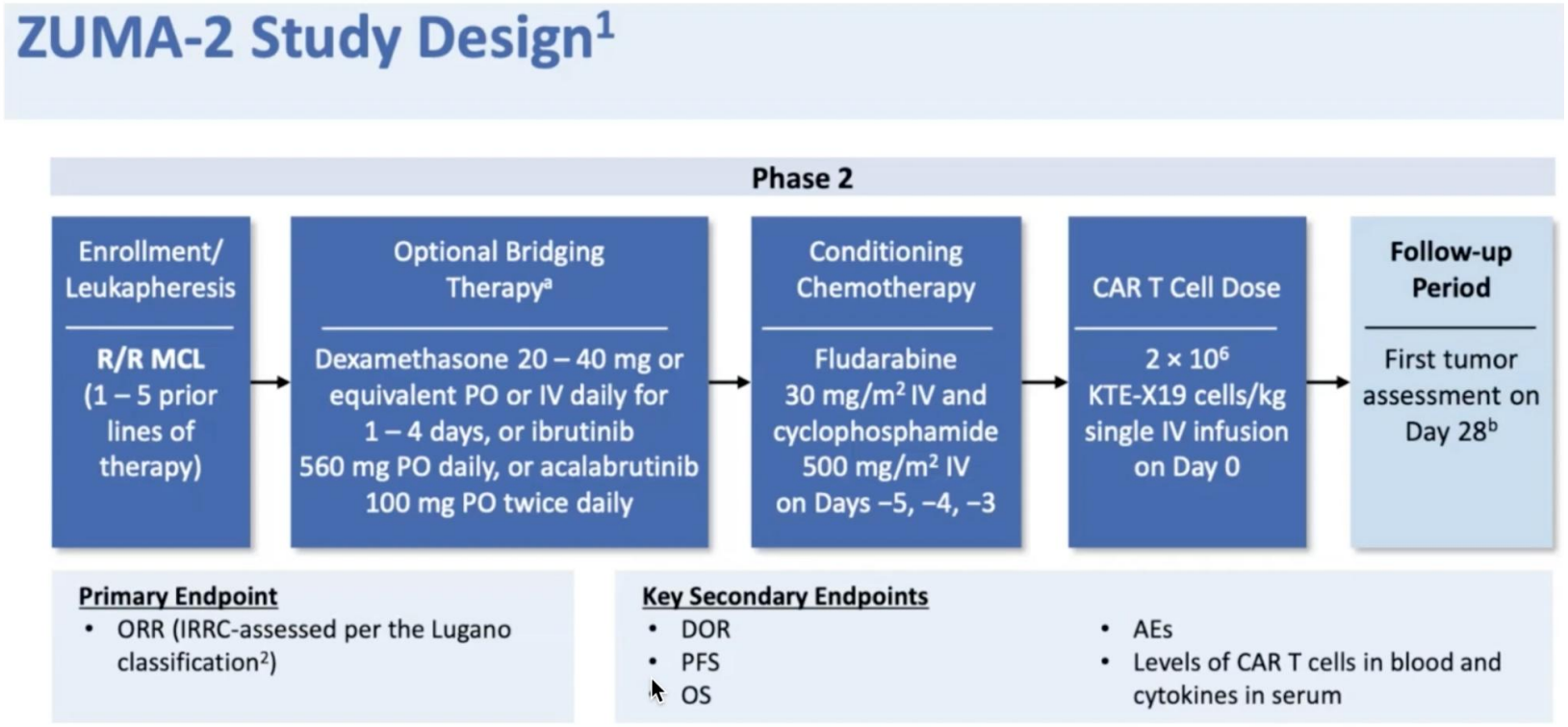
ABSTRACT

BACKGROUND

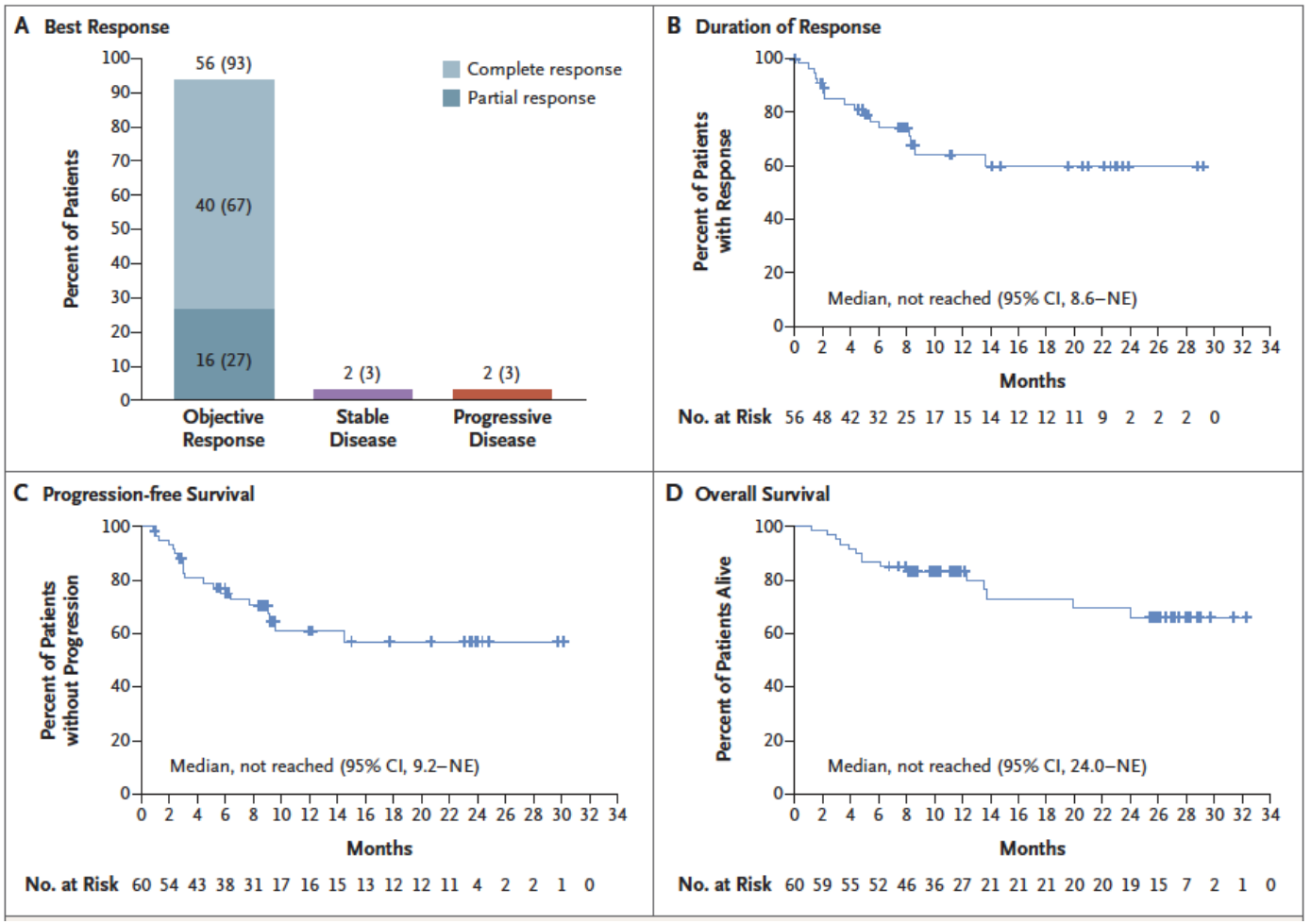
Patients with relapsed or refractory mantle-cell lymphoma who have disease progression during or after the receipt of Bruton's tyrosine kinase (BTK) inhibitor therapy have a poor prognosis. KTE-X19, an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, may have benefit in patients with relapsed or refractory mantle-cell lymphoma.

ZUMA 2 Trial: Mantle Cell Lymphoma

ZUMA 2


ZUMA-2 Study Design[1]
Phase 2
Enrollment/ Leukapheresis
R/R MCL (1 – 5 prior lines of therapy)
Optional Bridging Therapy[a]
Dexamethasone 20 – 40 mg or equivalent PO or IV daily for 1 – 4 days, or ibrutinib 560 mg PO daily, or acalabrutinib 100 mg PO twice daily
Conditioning Chemotherapy
Fludarabine 30 mg/m² IV and cyclophosphamide 500 mg/m² IV on Days −5, −4, −3
CAR T Cell Dose
2 × 10⁶ KTE-X19 cells/kg single IV infusion on Day 0
Follow-up Period
First tumor assessment on Day 28[b]
Primary Endpoint
• ORR (IRRC-assessed per the Lugano classification[2])
Key Secondary Endpoints
• DOR
• PFS
• OS
• AEs
• Levels of CAR T cells in blood and cytokines in serum

ZUMA 2


A Best Response
Percent of Patients
Complete response
Partial response
56 (93)
40 (67)
16 (27)
2 (3)
2 (3)
Objective Response
Stable Disease
Progressive Disease
B Duration of Response
Percent of Patients with Response
Median, not reached (95% CI, 8.6–NE)
Months
No. at Risk 56 48 42 32 25 17 15 14 12 12 11 9 2 2 2 0
C Progression-free Survival
Percent of Patients without Progression
Median, not reached (95% CI, 9.2–NE)
Months
No. at Risk 60 54 43 38 31 17 16 15 13 12 12 11 4 2 2 1 0
D Overall Survival
Percent of Patients Alive
Median, not reached (95% CI, 24.0–NE)
Months
No. at Risk 60 59 55 52 46 36 27 21 21 21 20 20 19 15 7 2 1 0

Expanding the horizon

Articles

Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial

Caron A Jacobson, Julio C Chavez, Alison R Sehgal, Basem M William, Javier Munoz, Gilles Salles, Pashna N Munshi, Carla Casulo, David G Maloney, Sven de Vos, Ran Reshef, Lori A Leslie, Ibrahim Yakoub-Agha, Olalekan O Oluwole, Henry Chi Hang Fung, Joseph Rosenblatt, John M Rossi, Lovely Goyal, Vicki Plaks, Yin Yang, Remus Vezan, Mauro P Avanzi, Sattva S Neelapu

Summary

Background Most patients with advanced-stage indolent non-Hodgkin lymphoma have multiple relapses. We assessed axicabtagene ciloleucel autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy in relapsed or refractory indolent non-Hodgkin lymphoma.

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ZUMA 5 Trial: Follicular Lymphoma and Marginal Zone Lymphoma

Expanding the horizon

nature medicine

FOCUS | ARTICLES

https://doi.org/10.1038/s41591-022-01731-4

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OPEN

Axicabtagene ciloleucel as first-line therapy in high-risk large B-cell lymphoma: the phase 2 ZUMA-12 trial

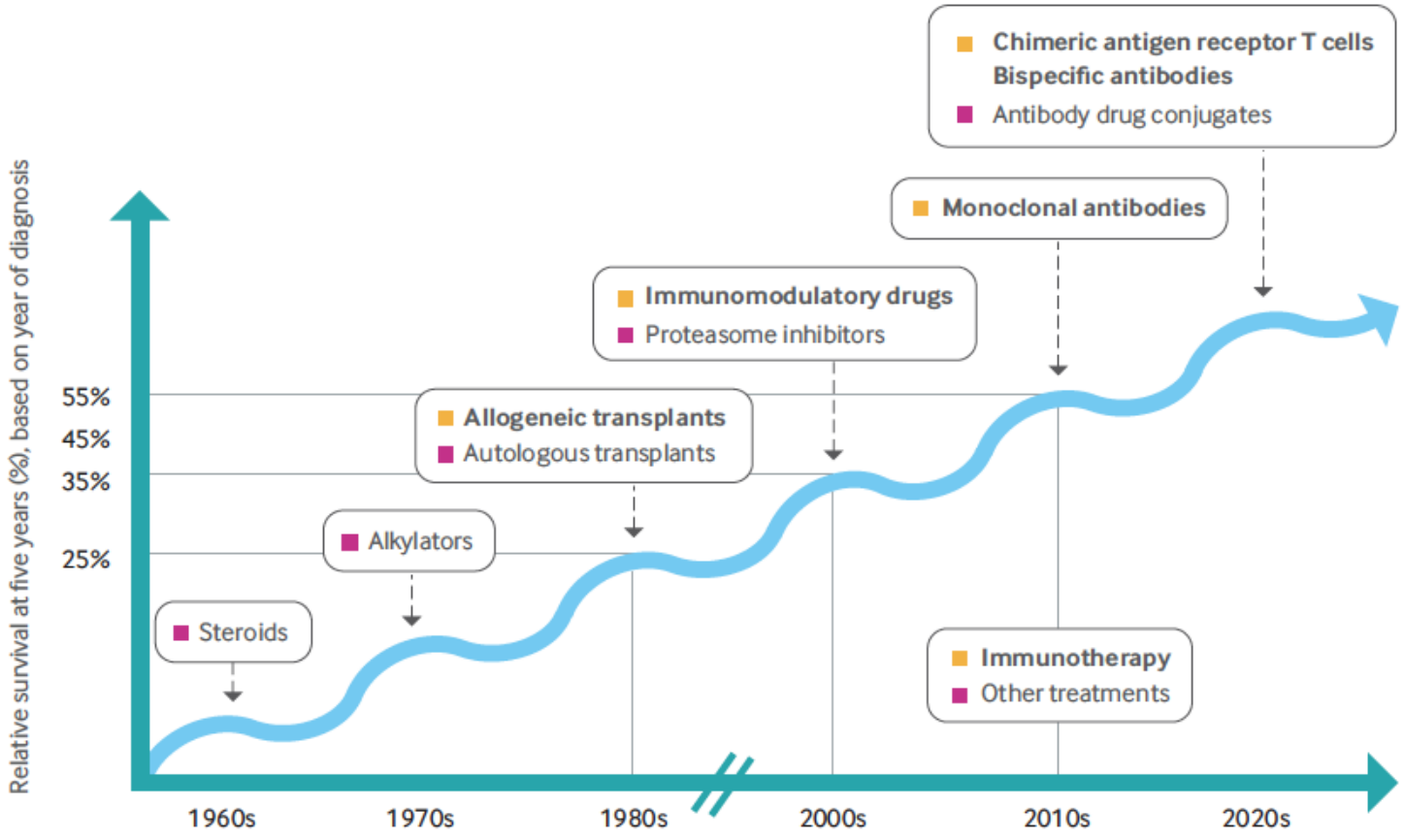
Sattva S. Neelapu[1✉], Michael Dickinson[2], Javier Munoz[3], Matthew L. Ulrickson[3], Catherine Thieblemont[4,5], Olalekan O. Oluwole[6], Alex F. Herrera[7], Chaitra S. Ujjani[8], Yi Lin[9], Peter A. Riedell[10], Natasha Kekre[11], Sven de Vos[12], Christine Lui[13], Francesca Milletti[13], Jinghui Dong[13], Hairong Xu[13] and Julio C. Chavez[14]

High-risk large B-cell lymphoma (LBCL) has poor outcomes with standard first-line chemoimmunotherapy. In the phase 2, multicenter, single-arm ZUMA-12 study (ClinicalTrials.gov NCT03761056) we evaluated axicabtagene ciloleucel (axi-cel), an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, as part of first-line treatment in 40 patients with high-risk LBCL. This trial has completed accrual. The primary outcome was complete response rate (CRR). Secondary outcomes were objective response rate (ORR), duration of response (DOR), event-free survival (EFS), progression-free survival (PFS), overall survival (OS), assessment of safety, central nervous system (CNS) relapse and blood levels of CAR T cells and cytokines. The primary endpoint in efficacy-evaluable patients ($n = 37$) was met, with 78% CRR (95% confidence interval (CI), 62–90) and 89% ORR (95% CI, 75–97). As of 17 May 2021 (median follow-up, 15.9 months), 73% of patients remained in objective response; median DOR, EFS and PFS were not reached. Grade ≥3 cytokine release syndrome (CRS) and neurologic events occurred in three patients (8%) and nine patients (23%), respectively. There were no treatment-related grade 5 events. Robust CAR T-cell expansion occurred in all patients with a median time to peak of 8 days. We conclude that axi-cel is highly effective as part of first-line therapy for high-risk LBCL, with a manageable safety profile.

ZUMA 12 Trial: LBCL First line

New Indications

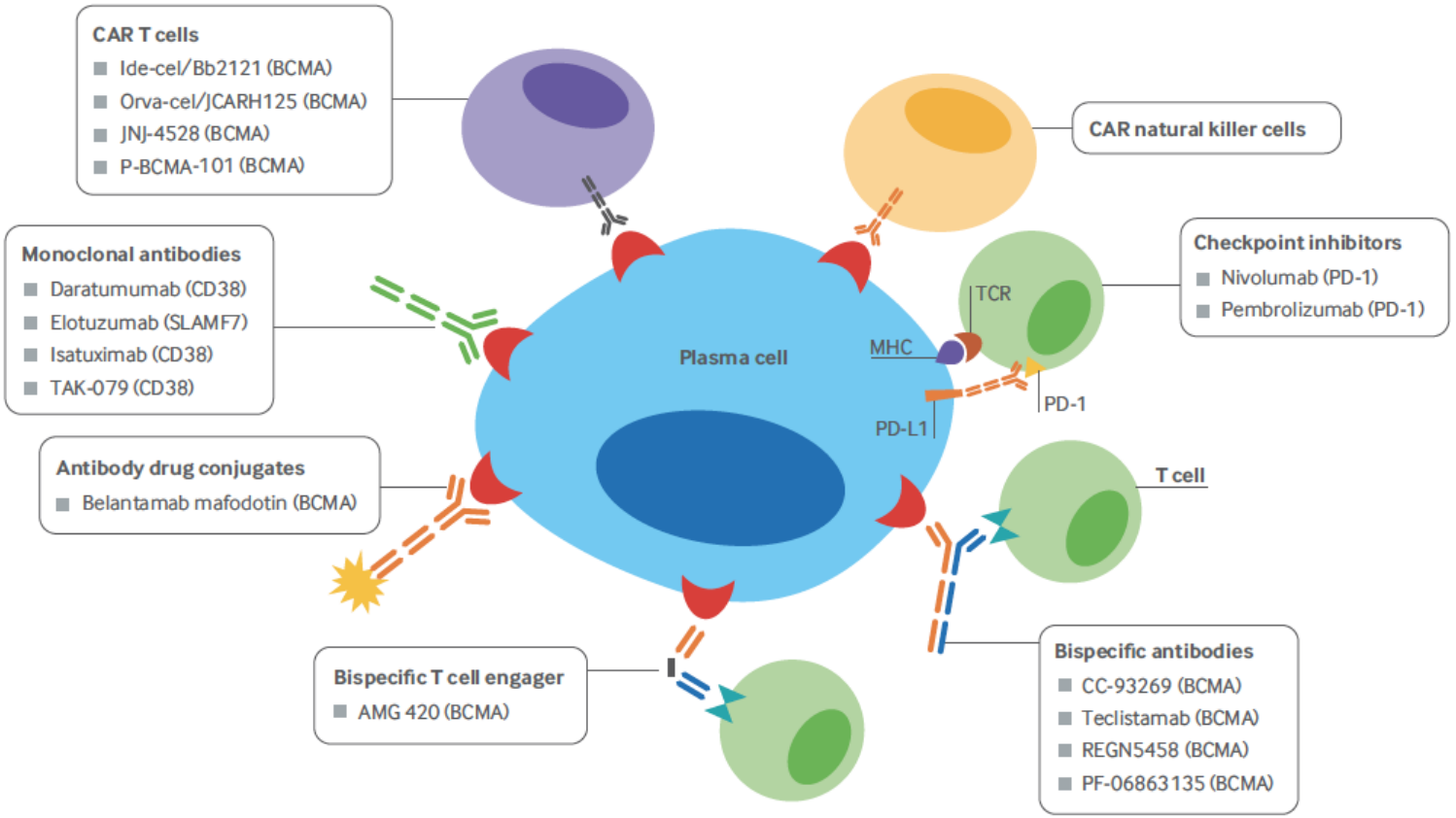
Multiple Myeloma



Timeline of drug discovery and year of multiple myeloma diagnosis (by decade)

Shah and Mailankody, BMJ 2020

Immunotherapeutic approaches to treat Myeloma



Shah and Mailankody, BMJ 2020

KarMMa and CARTITUDE Trials

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma

Nikhil C. Munshi, M.D., Larry D. Anderson, Jr., M.D., Ph.D., Nina Shah, M.D., Deepu Madduri, M.D., Jesús Berdeja, M.D., Sagar Lonial, M.D., Noopur Raje, M.D., Yi Lin, M.D., Ph.D., David Siegel, M.D., Ph.D., Albert Oriol, M.D., Philippe Moreau, M.D., Ibrahim Yakoub-Agha, M.D., Ph.D., Michel Delforge, M.D., Michele Cavo, M.D., Hermann Einsele, M.D., Hartmut Goldschmidt, M.D., Katja Weisel, M.D., Alessandro Rambaldi, M.D., Donna Reece, M.D., Fabio Petrocca, M.D., Monica Massaro, M.P.H., Jamie N. Connarn, Ph.D., Shari Kaiser, Ph.D., Payal Patel, Ph.D., Liping Huang, Ph.D., Timothy B. Campbell, M.D., Ph.D., Kristen Hege, M.D., and Jesús San-Miguel, M.D., Ph.D.

ABSTRACT

BACKGROUND

Idecabtagene vicleucel (ide-cel, also called bb2121), a B-cell maturation antigen–directed chimeric antigen receptor (CAR) T-cell therapy, has shown clinical activity with expected CAR T-cell toxic effects in patients with relapsed and refractory multiple myeloma.

METHODS

In this phase 2 study, we sought to confirm the efficacy and safety of ide-cel in patients with relapsed and refractory myeloma. Patients with disease after at least three previous regimens including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody were enrolled. Patients received ide-cel target doses of 150×10^6 to 450×10^6 CAR-positive (CAR+) T cells. The primary end point was an overall response (partial response or better); a key secondary end point was a complete response or better (comprising complete and stringent complete responses).

Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study

Jesus G Berdeja, Deepu Madduri*, Saad Z Usmani, Andrzej Jakubowiak, Mounzer Agha, Adam D Cohen, A Keith Stewart, Parameswaran Hari, Myo Htut, Alexander Lesokhin, Abhinav Deol, Nikhil C Munshi, Elizabeth O'Donnell, David Avigan, Indrajeet Singh, Enrique Zudaire, Tzu-Min Yeh, Alicia J Allred, Yunsi Olyslager, Arnob Banerjee, Carolyn C Jackson, Jenna D Goldberg, Jordan M Schecter, William Deraedt, Sen Hong Zhuang, Jeffrey Infante, Dong Geng, Xiaoling Wu, Marlene J Carrasco-Alfonso, Muhammad Akram, Farah Hossain, Syed Rizvi, Frank Fan, Yi Lin†, Thomas Martin†, Sundar Jagannath†*

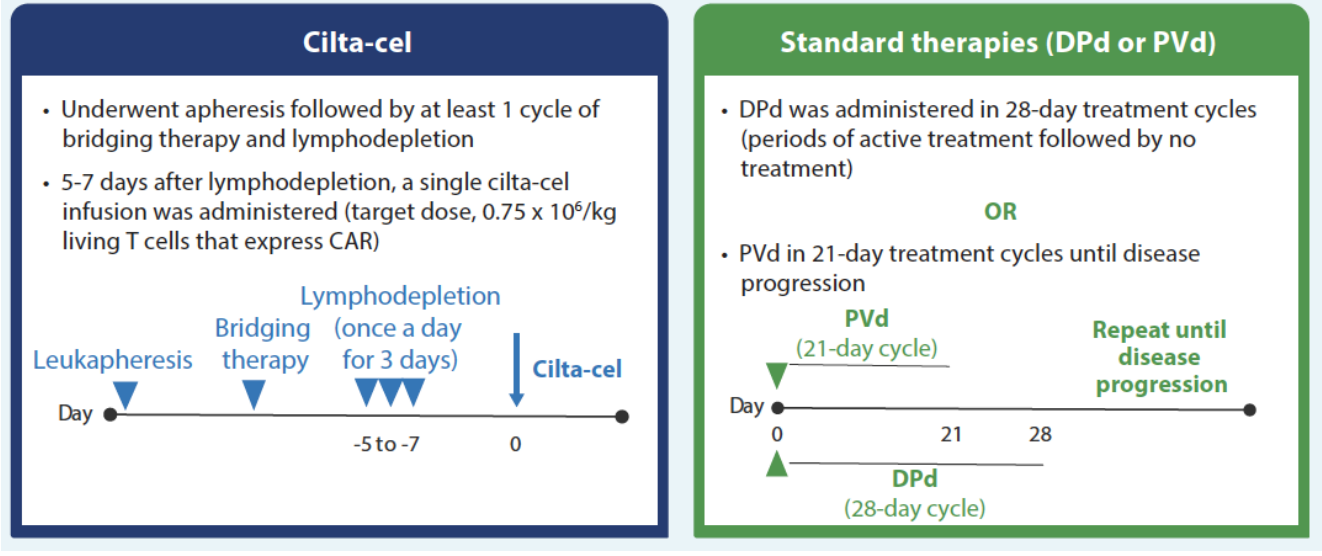
Summary

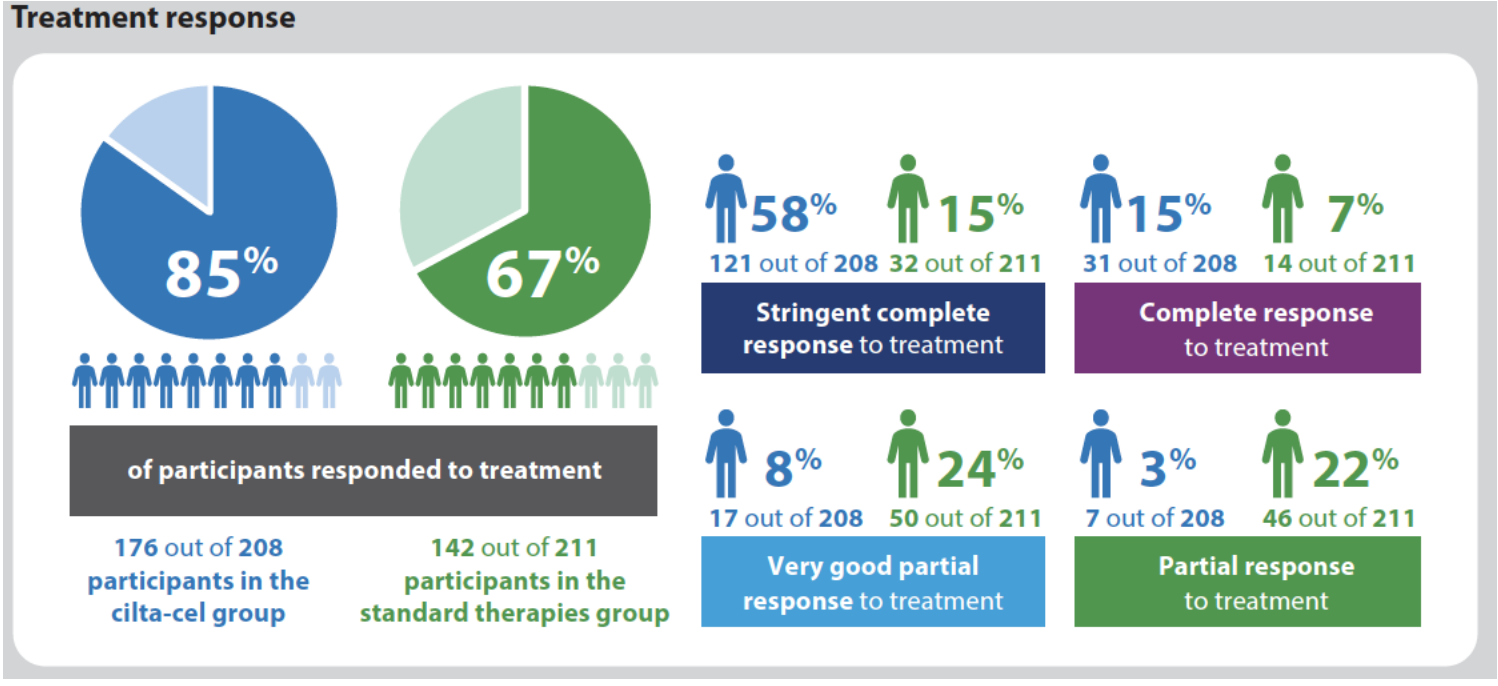
Background CARTITUDE-1 aimed to assess the safety and clinical activity of ciltacabtagene autoleucel (cilta-cel), a chimeric antigen receptor T-cell therapy with two B-cell maturation antigen-targeting single-domain antibodies, in patients with relapsed or refractory multiple myeloma with poor prognosis.

Methods This single-arm, open-label, phase 1b/2 study done at 16 centres in the USA enrolled patients aged 18 years or older with a diagnosis of multiple myeloma and an Eastern Cooperative Oncology Group performance status score of 0 or 1, who received 3 or more previous lines of therapy or were double-refractory to a proteasome inhibitor and an immunomodulatory drug, and had received a proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody. A single cilta-cel infusion (target dose $0{\cdot}75 \times 10^6$ CAR-positive viable T cells per kg) was administered 5–7 days after start of lymphodepletion. The primary endpoints were safety and confirmation of the recommended phase 2 dose (phase 1b), and overall response rate (phase 2) in all patients who received treatment. Key secondary endpoints were duration of response and progression-free survival. This trial is registered with ClinicalTrials.gov, NCT03548207.

Findings Between July 16, 2018, and Oct 7, 2019, 113 patients were enrolled. 97 patients (29 in phase 1b and 68 in phase 2) received a cilta-cel infusion at the recommended phase 2 dose of $0{\cdot}75 \times 10^6$ CAR-positive viable T cells per kg. As of the Sept 1, 2020 clinical cutoff, median follow-up was 12·4 months (IQR 10·6–15·2). 97 patients with a median of six previous therapies received cilta-cel. Overall response rate was 97% (95% CI 91·2–99·4; 94 of 97 patients); 65 (67%) achieved stringent complete response; time to first response was 1 month (IQR 0·9–1·0). Responses deepened over time. Median duration of response was not reached (95% CI 15·9–not estimable), neither was progression-free survival (16·8–not estimable). The 12-month progression-free rate was 77% (95% CI 66·0–84·3)

CARTITUDE-4 Trial





CARTITUDE-4 Trial

In the CARTITUDE-4 study, treatment with cilta-cel reduced the risk of multiple myeloma progression and death by 59% compared to standard therapies. The median time before the disease progressed was 11.8 months in patients receiving standard therapies, but the median time for patients on cilta-cel was 16 months and still counting at last report.

Cilta-cel is now approved for use after just one prior line of therapy, which includes some of the most used treatments for myeloma such as a proteosome inhibitor like bortezomib (Velcade®) and an immunomodulator drug like lenalidomide (Revlimid®).

KarMMa-3 Trial

386 people took part in the study
- Aged 18 years or older
- Had relapsed or refractory multiple myeloma
- Had received between 2 and 4 previous treatments for their multiple myeloma
- Cancer had gotten worse after last treatment

254 people randomly assigned to receive ide-cel → **225** of these people received ide-cel

132 people randomly assigned to receive a standard treatment → **126** of these people received a standard treatment as decided by their doctor

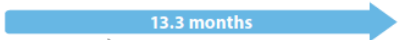
People who were randomly assigned to a treatment group were included in the study analysis, whether or not they received study medication

Effect of study treatment on survival and response

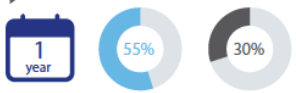
For people who received ide-cel (254 participants) and people who received the standard of care regimen (132 participants).

Progression-free survival

The amount of time alive and without the cancer getting worse after treatment was longer for people receiving ide-cel



After 1 year, 55% of patients receiving ide-cel and 30% of patients on the standard of care regimen were surviving without their cancer getting worse



Overall response rate

The percentage of people who responded to treatment was higher in the ide-cel group than the standard of care regimen group	71% / 42%
People with a stringent complete response, meaning cancer has decreased during or after treatment and is not currently detectable by all tests	35% / 5%
People with a complete response, meaning cancer has decreased during or after treatment and is not detectable by most tests but may still be present in the bone marrow	3% / 1%
People with a very good partial response or partial response, meaning cancer has decreased in size or severity during or after treatment, but is still present	33% / 36%

Duration of response

The amount of time that the person's cancer continued to respond to treatment without the cancer getting worse (or the person died) was longer for people receiving ide-cel

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Medizinische Fakultät Mannheim der Universität Heidelberg

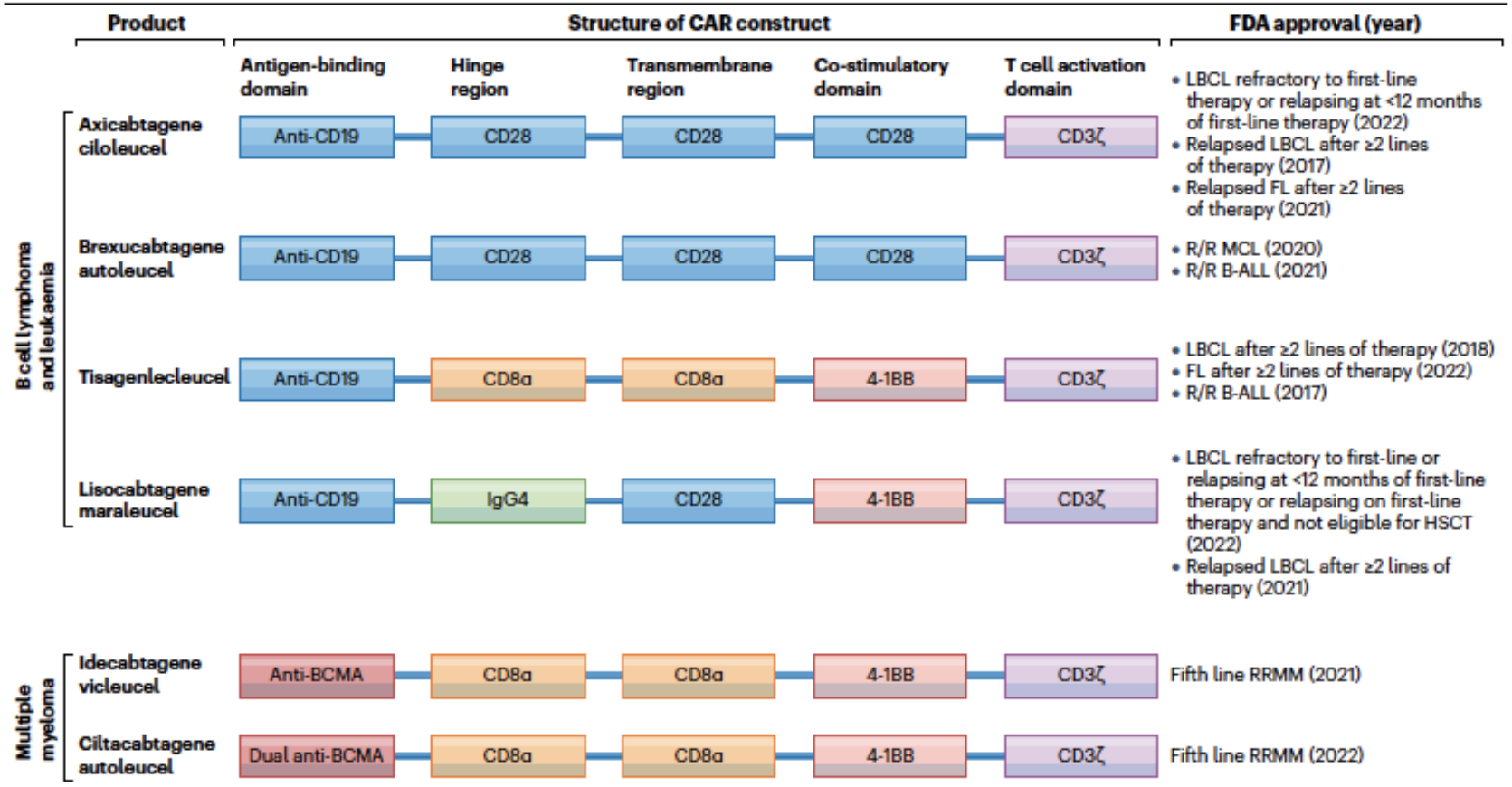
Universitätsklinikum Mannheim

KarMMa-3 Trial

- In KarMMA-3, ide-cel tripled progression-free survival time compared to standard treatments, from 4.4 months to 13.3 months. Most patients (71%) treated with ide-cel responded to treatment and 39% had a complete response, which means no cancer could be detected. The response in these patients lasted for a median of 20 months.

- Ide-cel is now approved for use in patients who received at least two prior lines of treatment, including a proteosome inhibitor, an immunomodulator and an anti-CD38 antibody like daratumumab (Darzalex®) or isatuximab (Sarclisa®), which can be used in combination with one another.

FDA Approved CAR-T Cell Therapies



Cappell and Kochenderfer, Nature Reviews Clinical Oncology 2023

EMA Approved CAR-T Cell Therapies

Anti CD19

Tisagenlecleucel (tisa-cell, Novartis, KYMRIAH)

- -r/r DLBCL (3rd line)
- -r/r Follicular Lymphoma (3rd line)
- -r/r ALL <26 yrs

Axicabtagen ciloleucel (axi-cel, Gilead, YESCARTA)

- -DLBCL/PMBCL (2./3. Linne)
- -r/r Follicular Lymphoma (4. Line)

Brexucabtagen autoleucel (brexu-cel, Gilead, TECARTUS)

- -r/r MCL (3.Line after BTKI
- -r/r ALL >25 yrs

Lisocabtagen maraleucel (liso-cel, BMS, BREYANZI)

- -DLBCL/HGBCL/PMBCL/FL 3B (2./3. Line)

EMA Approved CAR-T Cell Therapies

Anti BCMA

Idecabtagene vicleucel (ide-cel, BMS, ABECMA)

- -Multiple Myeloma (3. Line after PI, IMID & anti CD38 Antibody)

Ciltacabtagene autoleucel (cilta-cel, Janssen, CARVYKTI)

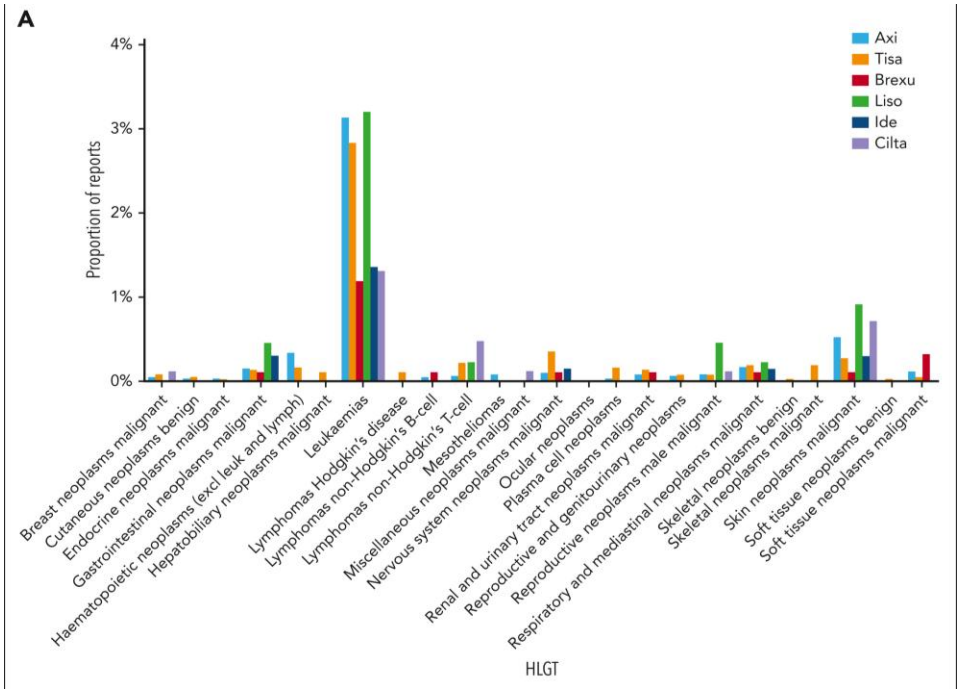
- -Multiple Myeloma (2. Line after PI & IMID)

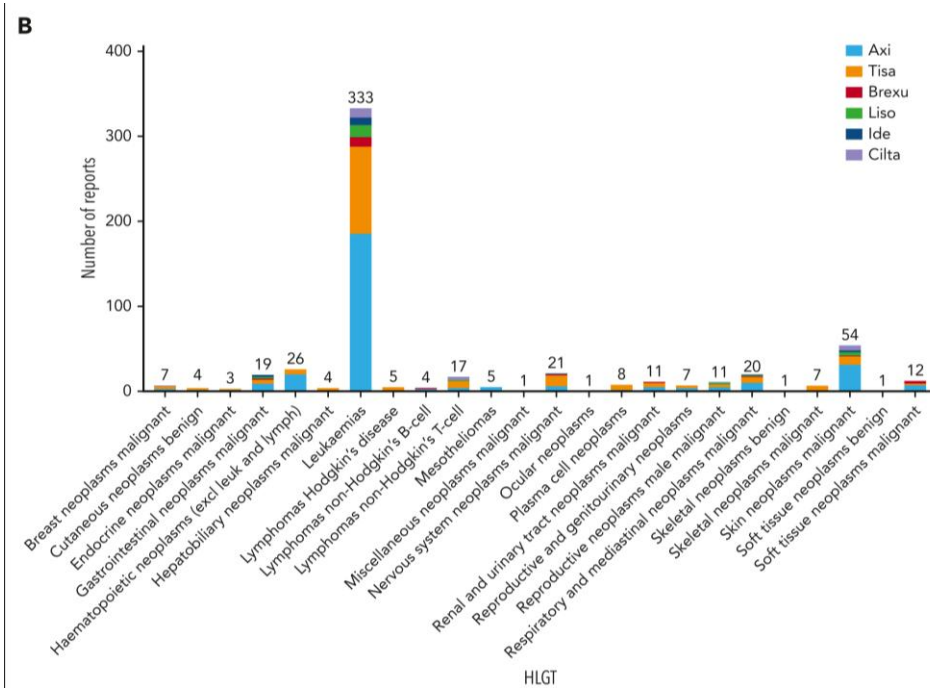
Table 1 | Long-term outcomes of patients with B cell lymphoma and/or CLL/SLL receiving CD19-targeted CAR T cells

Study (year of publication)	CAR product and trial phase	Cancer types (*n*)	Median follow-up (range)	ORR and CRR	PFS or EFS	DOR in responding patients
Chong et al. (2021)[31]	Tisagenlecleucel, single-centre case series	DLBCL (24); FL (14)	61 months	ORR: 66%; CRR: 55%	31% PFS at 5 years for DLBCL; 43% PFS at 5 years for FL	60% remained in response at 5 years
Jacobson et al. (2021)[32]	Axicabtagene ciloleucel, multicentre phase I/II	DLBCL (77); PMBCL (8); tFL (16)[9]	51 months	ORR: 74%; CRR: 54%[67]	Median EFS: 5.7 months, with 24-month EFS of 38%	NR
Cappell et al. (2020)[16]	FMC63-28Z[a], single-centre phase I	DLBCL/PMBCL (28); indL (8); CLL/SLL (7)	42 months (1–123 months)	ORR: 81%; CRR: 58%	Median EFS: 55 months	76% of patients with a CR remained in response at last follow-up with a DOR ranging from 43 to 113 months
Schuster et al. (2021)[33]	Tisagenlecleucel, multicentre phase II	DLBCL, HGBCL or tFL (115)	40 months (IQR 38–44 months)	ORR: 53%; CRR: 39%	Median PFS: 2.9 months; median EFS: 2.8 months	Median DOR: not estimable
Hirayama et al. (2019)[34]	Lisocabtagene maraleucel, single-centre phase I/II	tFL (13) and FL (8)	38 months for patients with tFL and 24 months for those with FL	ORR: NR for FL and 46% for tFL; CRR: 88% for FL and 46% for tFL	Median PFS: 1.4 months in tFL cohort; NR for FL cohort	All patients with FL with a CR remained in remission at a median follow-up duration of 24 months (range 5–37 months)
Wang et al. (2023)[35]	Brexucabtagene autoleucel, multicentre phase II	MCL (68)	36 months (26–56 months)	ORR: 91%; CRR: 68%	Median PFS: 26 months	Median DOR: 47 months in patients with a CR
Frey et al. (2020)[36]	CART-19, single-centre phase II	CLL (38)	32 months (2–75 months)	ORR: 44%; CRR: 28%	Median PFS: 1 month in all patients; 40 months in those with CR	4/9 (44%) of patients with a CR had disease relapse
Abramson et al. (2021)[37]	Lisocabtagene maraleucel, multicentre phase I	LBCL (270)	All patients had ≥24 months of follow-up data; median NR	ORR: 73%; CRR: 53%	Median PFS: 6.8 months	Median DOR: 26 months in those with a CR
Locke et al. (2022)[23b]	Axicabtagene ciloleucel, multicentre phase III	DLBCL (126); HGBCL (31); NR (18); other (5)	25 months	ORR: 83%; CRR: 65%	Median PFS: 15 months	Median DOR: 27 months
Siddiqi et al. (2022)[38]	Lisocabtagene maraleucel, multicentre phase I	CLL/SLL (23)	24 months	ORR: 82%; CRR: 45%	Median PFS: 18 months	Median DOR: not reached

Cappell and Kochenderfer, Nature Reviews Clinical Oncology 2023

Second malignancies





Elsallab et al.,Second primary malignancies after commercial CAR T-cell therapy: analysis of the FDA Adverse Events Reporting System, Blood, 2024

Real world examples

Patient 1

- 65 year old female
- Mantle cell-lymphoma with peripheral blood lymphocytosis ED 7/2022
- - Ann Arbor Stage IVB (Involvement: LN li hilär (1,5 cm), Liver hilus (2,6 cm), splenomegaly 23x 9x 15 cm with spontaneous bleeding , Ki67 80%, BM Infiltration 80-90 %)
- - 28.7.2022 Tumorboard: alternating cycles 3xR-CHOP, 3xR-DHAP with autologous SCT, followed by 3 year maintenace with Rituximab
- 19.8.- 24.11: 2022 3 cycles R-CHOP and 3 cycles R-DHAP
- 9.12.2022 CT Thorax - Pelvis complete remission, No lymphadenopathy, No Splenomegaly,
- 13.12.2022 Bonemarrow: cytologically and histologically no lymphoma

Real world examples: Patient 1

- 19.01.2023: High dose-chemotherapy with BEAM und autologous SCT - 3/2023-
- 9/23 Rituximab-Ibrutinib- Maintenace
- - 9/23 Relapse with isolated meningiosis lymphomatosa initial 700
- cells/ul in CSF
- BM/FACS/CT No sign of disease outside the CNS
- - 19.9./21.9/23.9./25.9.23: ith Triple-Therapy with Ara-C (40 mg), Dexamethasone (4mg) und MTX 15 mg,
- 28.9.23: LP # No sign of lymphoma
- - 27.10.2023 T-Cell-apheresis for the production of Tecartus
- - 5.12.23 CAR-T-Cell-Therapie with Brexucabtagen-Autoleucel (Tecartus);
- Complications: CRS max. Grade I (fever), ICANS Grade I (ICE-Score 8 points), Tocilizumab 4 x 500 mg, Dexamethason
- - 26.3.24: LP # No signs of meningiosis lymphomatosa
- - 4.4.2024 Total body CT, complete remission

Real world examples

- Patient 2
- 27 year old female
- DLBCL Stage IVA ED 06/2023
- Manifestation 06/2023: HWK 7, supraclavicular LN R, ant. mediastinum, Os ilium L, dorsal acetabulum bds., proximal humerus R, adrenal glands bds.
- 16.06.2023 CT cervical spine: compression fracture C7 mit Beteiligung der Hinterkante
- 21.06.2023 C7-vertebral body replacement, Histology (UKHD): ED aggressives B- Cell-Lymphoma
- 30.06.2023 Bonemarrrow: No affectation
- 03.07.2023 CT Hals-Becken: cervical soft tissue asymmetry with excess soft tissue on the right submandibular side DD submandibular gland associated, irregular enlarged thymus
- 04.07.2023 cranial MRT : No lymphoma
- 05.07.2023 •Cryopreservation of 50% of one ovary, cyst removal on the left side 07/06/2023
- 11.07.2023 PET-CT : As above
- 07/2023- 10/2023 C1-C5 Pola-R-CHP
- 06.09.2023 MRT Hals/Thorax/Abdomen: Almost complete regression of mediastinal lymphoma mass, residual changes in renal parenchyma on both sides. In cases of renal lymphoma, constant visualization of bone foci, but without evidence of relevant diffusion disorder (non-viable).
- 18.10.2023 cranial MRT : No lymphoma (Headache and Vomitting)

Patient 2

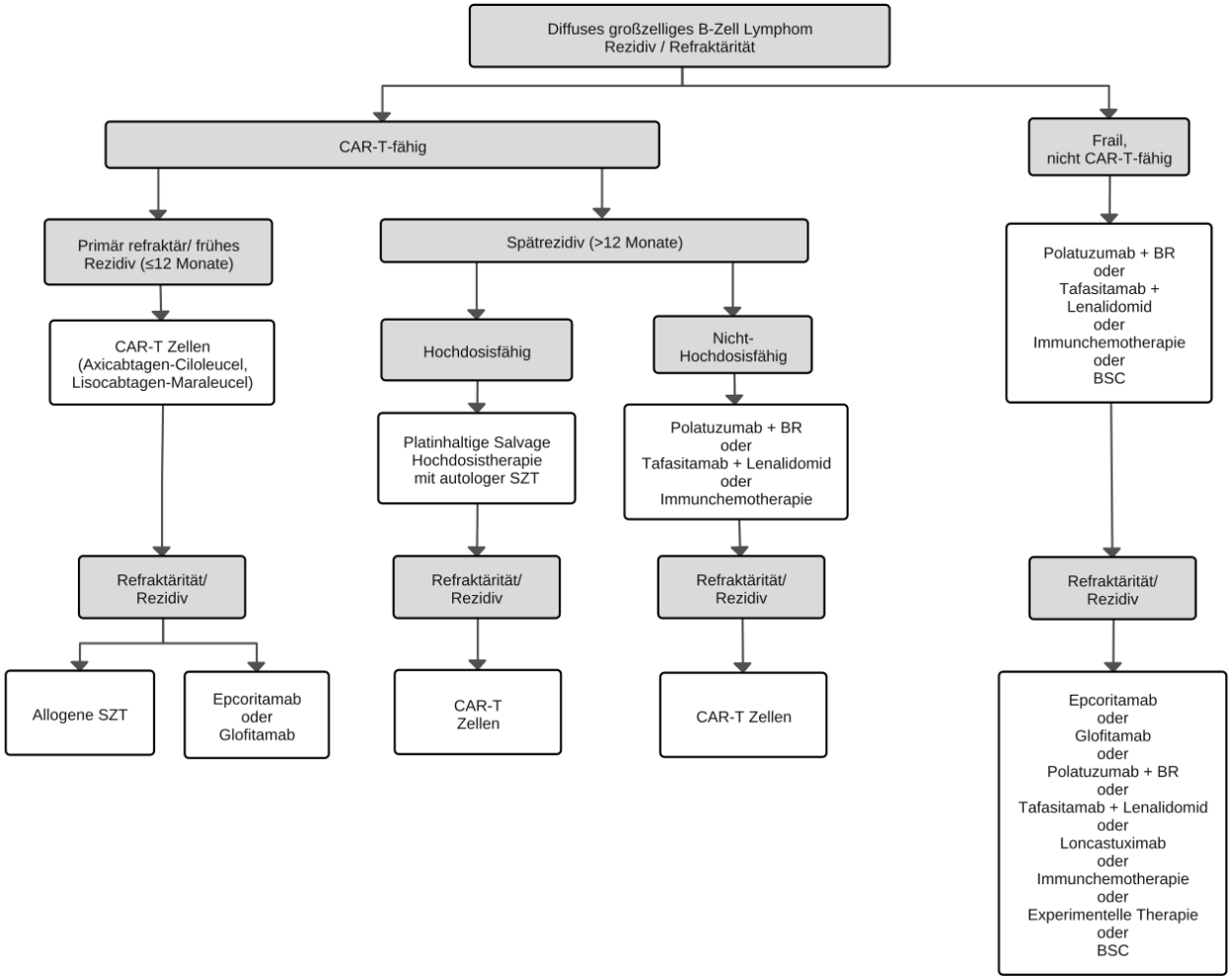
- 20.10.2023 Liquor: Pleocytosis with atypical lymphatic cells, V. a. Meningeosis
- Lymphomatosa
- 11-.12.2023 : R-MATRIX C1-C3
- 29.12.2023 MRT (cranium + total spine: Progress, neu parenchymal lesions
- 04.01.2024 Tumorboard: Progress CNS-affectation; procedere: LP, Neuro- Oncoboard,
- CAR-T-Cell-Therapy mit Yescarta
- 04.01.2024 CSF: no evidence of lymphoma
- 10.01.2024 Neuro-oncology Tumorboard: aim for biopsy confirmation
- 19.01.2024: Resection of the mass on the right frontal side : Histology DLBCL
- 30.01.2024 Progress with new CNS symptoms, meningeosis lymphomatosa, i.th. Triple-Therapy
- 06.02.2024 T-cell-apheresis for Yescarta.
- 07.02.2024: Beginn Bridging-Therapy with Rituximab 375 mg/m² d0, Lenalidomid 25 mg/day d1- 10, Ibrutinib 560 mg/d1-14

Patient 2

- 04.03.2024 CAR-T-Cell-Therapie mit Axicabtagene ciloleucel (Yescarta®); Complications: CRS Grade II, ICANS Grade II, Neutropenic fever
- 06.04.24 Encepahlopathy after CAR-T-Cell-Therapie Symptome: Myoclonus in right hand, speech disorder
- 06.04.24: LP, no lymphoma involvement
- 10.04.2024 cMRT No reliable evidence of lymphoma progression with continued known cerebral changes with perifocal edema, other lesions regressive. DD CAR-T cell activity
- 26.04.2024 cMRT Lymphoma progression with hemiparesis
- 14.05.2024 Autologous stem cell transplantation after conditioning with rituximab, carmustine, etoposide, and thiotepa
- 06/2024 Very good clinical response, largely symptom-free neurologically, cMRT; very good PR
- 24.07.2024 Allogeneic related HLA 10/10 matched peripheral blood stem cell transplantation after cranial boost with 12 Gy and conditioning with TBI 8 Gy and fludarabine; GvHD prophylaxis: Tac, MMF; donor: sister
- Last update 01/2026: Complete remission

Onkopedia Guidelines

Rezidivtherapie bei diffusem großzelligem B-Zell-Lymphom (erstes und nachfolgende Rezidive)



Legende:
BSC: best supportive care.
Die Beschreibung der Therapieprotokolle findet sich im zugehörigen Dokument „Medikamentöse Tumortherapie“

Solid Tumors

nature cancer

Article

https://doi.org/10.1038/s43018-024-00749-6

Autologous HER2-specific CAR T cells after lymphodepletion for advanced sarcoma: a phase 1 trial

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Check for updates

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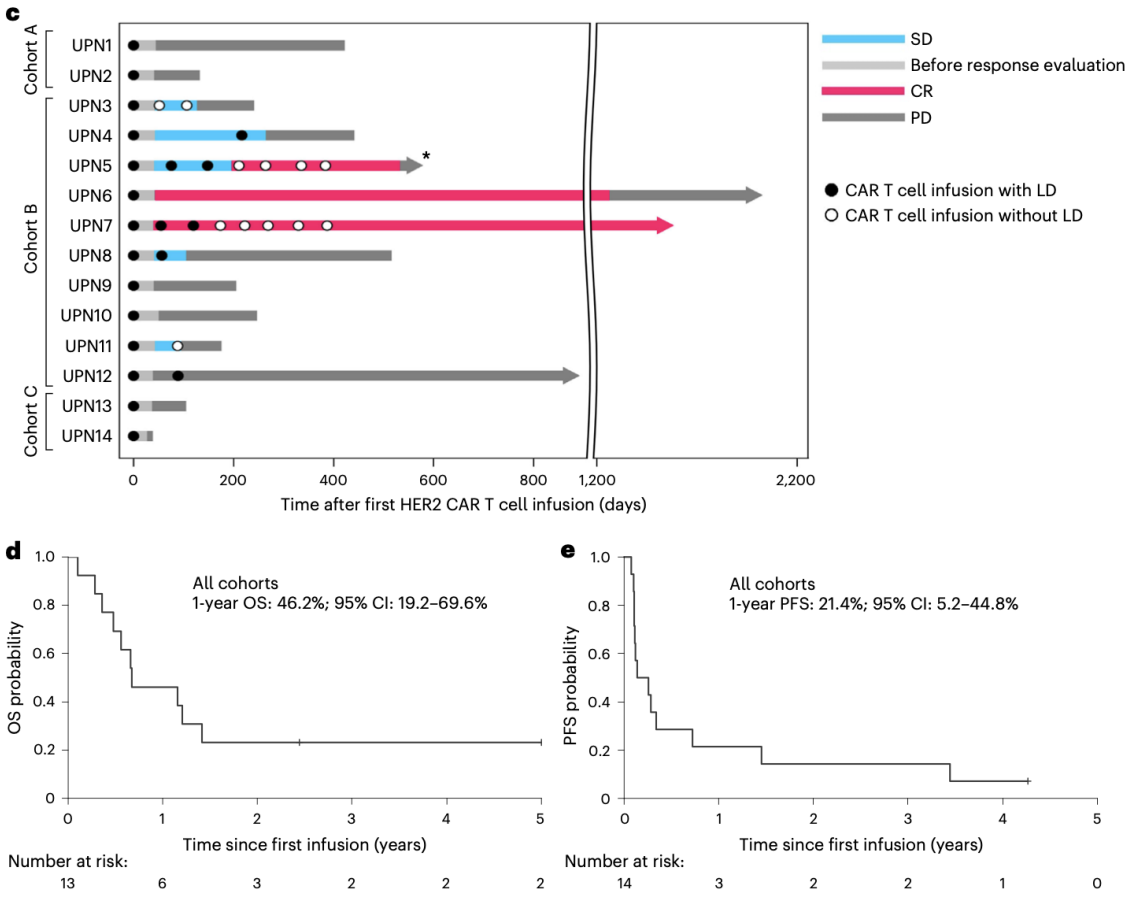
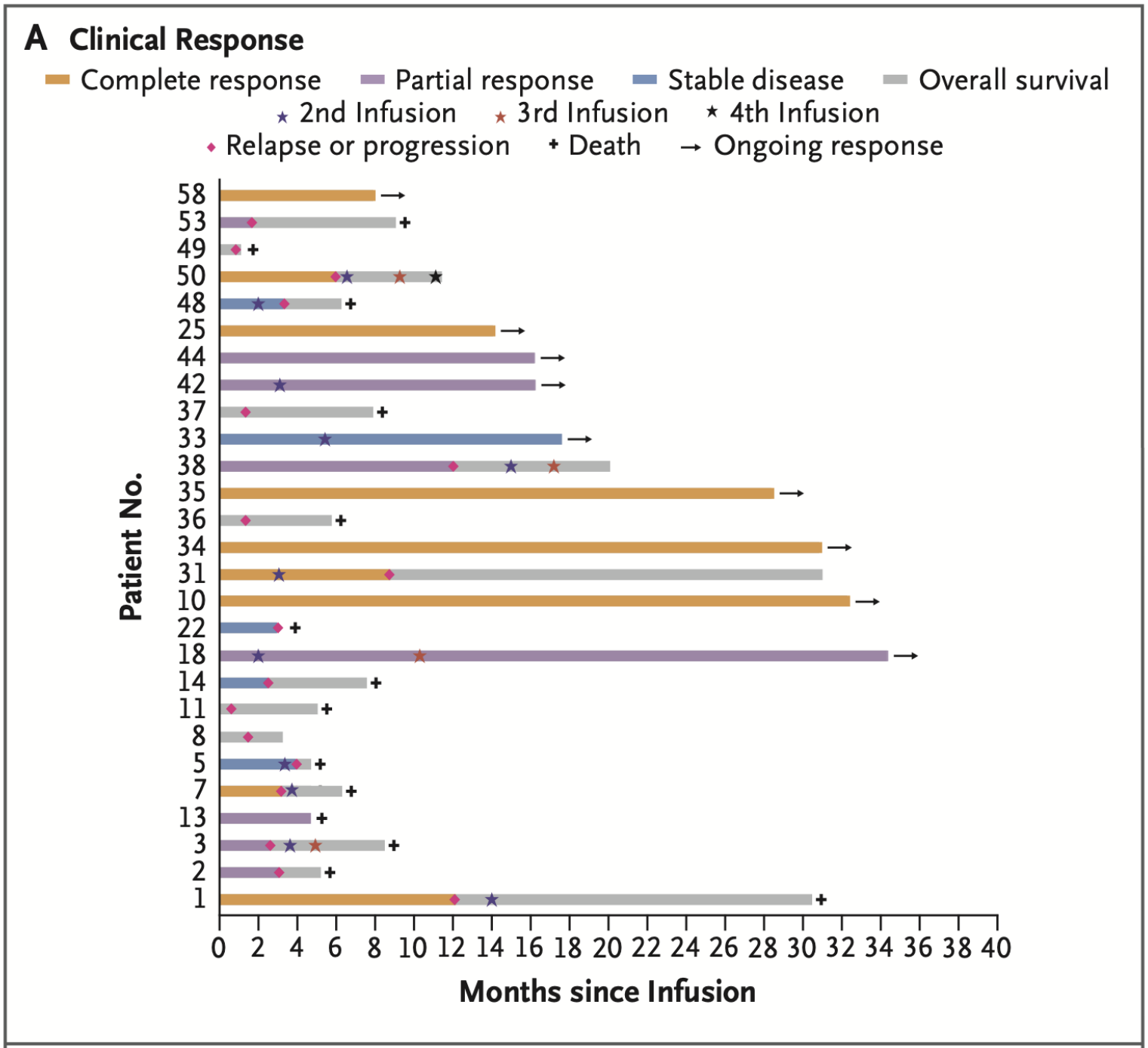

c
Cohort A
Cohort B
Cohort C
UPN1
UPN2
UPN3
UPN4
UPN5
UPN6
UPN7
UPN8
UPN9
UPN10
UPN11
UPN12
UPN13
UPN14
*
0
200
400
600
800
1,200
2,200
Time after first HER2 CAR T cell infusion (days)
SD
Before response evaluation
CR
PD
CAR T cell infusion with LD
CAR T cell infusion without LD
d
All cohorts
1-year OS: 46.2%; 95% CI: 19.2–69.6%
OS probability
1.0
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
Time since first infusion (years)
Number at risk:
13
6
3
2
2
2
e
All cohorts
1-year PFS: 21.4%; 95% CI: 5.2–44.8%
PFS probability
1.0
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
Time since first infusion (years)
Number at risk:
14
3
2
2
1
0

The NEW ENGLAND JOURNAL of MEDICINE

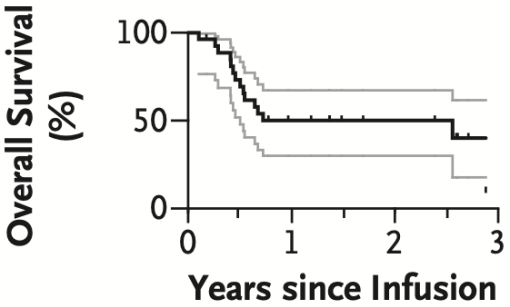
ORIGINAL ARTICLE

GD2-CART01 for Relapsed or Refractory High-Risk Neuroblastoma

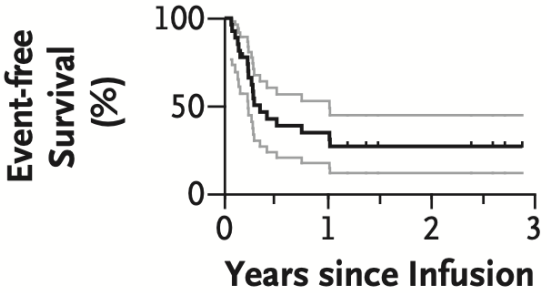
F. Del Bufalo, B. De Angelis, I. Caruana, G. Del Baldo, M.A. De Ioris, A. Serra, A. Mastronuzzi, M.G. Cefalo, D. Pagliara, M. Amicucci, G. Li Pira, G. Leone, V. Bertaina, M. Sinibaldi, S. Di Cecca, M. Guercio, Z. Abbaszadeh, L. Iaffaldano, M. Gunetti, S. Iacovelli, R. Bugianesi, S. Macchia, M. Algeri, P. Merli, F. Galaverna, R. Abbas, M.C. Garganese, M.F. Villani, G.S. Colafati, F. Bonetti, M. Rabusin, K. Perruccio, V. Folsi, C. Quintarelli, and F. Locatelli, for the Precision Medicine Team–IRCCS Ospedale Pediatrico Bambino Gesù*


A Clinical Response
Complete response
Partial response
Stable disease
Overall survival
2nd Infusion
3rd Infusion
4th Infusion
Relapse or progression
Death
Ongoing response
Patient No.
58
53
49
50
48
25
44
42
37
33
38
35
36
34
31
10
22
18
14
11
8
5
7
13
3
2
1
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40
Months since Infusion

B Entire Cohort

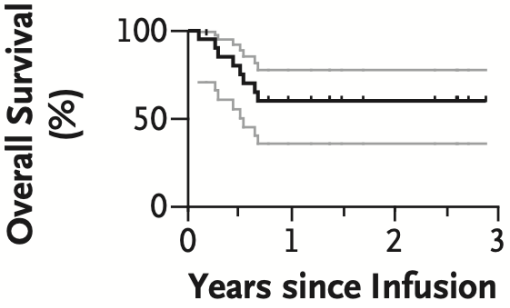


No. at Risk 27 19 12 8 7 3

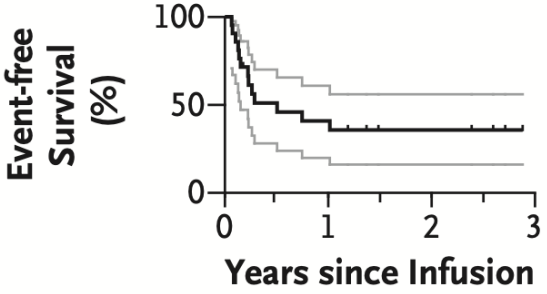


No. at Risk 27 11 9 5 5 4

C Patients Who Received Recommended Dose

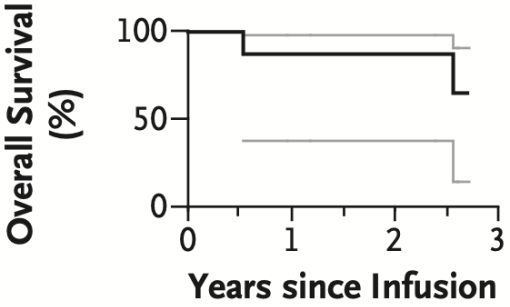


No. at Risk 21 17 11 7 6 5

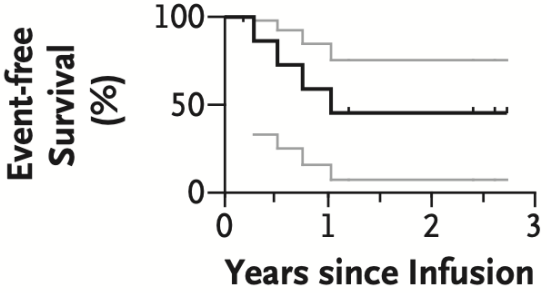


No. at Risk 21 11 9 5 5 4

D Patients with Complete Response



No. at Risk 9 8 7 6 5 5



No. at Risk 9 8 6 4 3 3

CAR-T cell Trials for solid tumors

- NCT06101082/NCT06658951/NCT04684459: **anti-HER 2-CAR-T cells for HER2+ malignancies**
- NCT07266311/NCT06084286/NCT05620732/NCT06134960/NCT05583201/NCT03874897/NCT05472857/NCT06782425: **Claudin18.2 Positive Solid Tumors**
- NCT07152236/NCT05341492/NCT06825455/NCT04483778/NCT04897321: **B7H3 Positive Solid Tumors**
- NCT06010862/NCT07179692/NCT06126406/NCT06006390/NCT07250386/NCT07250386/:NCT06043466 **CEA-positive advanced/metastatic solid tumors**
- NCT05518253/NCT05468190/NCT05947487: **CD70-positive Advanced/Metastatic Solid Tumors**
- NCT05783089: **MSLN-targeted CAR-T Cells in Solid Tumors**
- NCT06501183/NCT06937567: **CDH17-positive Advanced Malignant Solid Tumors**
- NCT05779917/NCT04981691/NCT03545815: **Mesothelin/GPC3/GUCY2C**
- NCT06865664: **FGFR4**
- NCT02107963: **GD2+ Solid Tumors**
- NCT02587689: **MUC1+ Advanced Refractory Solid Tumors**
- NCT07224568/NCT07242417: **GPC3**

Autoimmune Diseases

ARTICLES
https://doi.org/10.1038/s41591-022-02017-5
nature medicine

Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus

Andreas Mackensen[1,2,8], Fabian Müller[1,2,8], Dimitrios Mougiakakos[1,2,3,8], Sebastian Böltz[2,4], Artur Wilhelm[2,4], Michael Aigner[1,2], Simon Völkl[1,2], David Simon[2,4], Arnd Kleyer[2,4], Luis Munoz[2,4], Sascha Kretschmann[1,2], Soraya Kharboutli[1,2], Regina Gary[1,2], Hannah Reimann[1,2], Wolf Rösler[1,2], Stefan Uderhardt[2,4], Holger Bang[5], Martin Herrmann[2,4], Arif Bülent Ekici[6], Christian Buettner[6], Katharina Marie Habenicht[7], Thomas H. Winkler[7], Gerhard Krönke[2,4,8] and Georg Schett[2,4,8] ✉

Systemic lupus erythematosus (SLE) is a life-threatening autoimmune disease characterized by adaptive immune system activation, formation of double-stranded DNA autoantibodies and organ inflammation. Five patients with SLE (four women and one man) with a median (range) age of 22 (6) years, median (range) disease duration of 4 (8) years and active disease (median (range) SLE disease activity index Systemic Lupus Erythematosus Disease Activity Index: 16 (8)) refractory to several immunosuppressive drug treatments were enrolled in a compassionate-use chimeric antigen receptor (CAR) T cell program. Autologous T cells from patients with SLE were transduced with a lentiviral anti-CD19 CAR vector, expanded and reinfused at a dose of 1×10^6 CAR T cells per kg body weight into the patients after lymphodepletion with fludarabine and cyclophosphamide. CAR T cells expanded in vivo, led to deep depletion of B cells, improvement of clinical symptoms and normalization of laboratory parameters including seroconversion of anti-double-stranded DNA antibodies. Remission of SLE according to DORIS criteria was achieved in all five patients after 3 months and the median (range) Systemic Lupus Erythematosus Disease Activity Index score after 3 months was 0 (2). Drug-free remission was maintained during longer follow-up (median (range) of 8 (12) months after CAR T cell administration) and even after the reappearance of B cells, which was observed after a mean (±s.d.) of 110 ± 32 d after CAR T cell treatment. Reappearing B cells were naïve and showed non-class-switched B cell receptors. CAR T cell treatment was well tolerated with only mild cytokine-release syndrome. These data suggest that CD19 CAR T cell transfer is feasible, tolerable and highly effective in SLE.

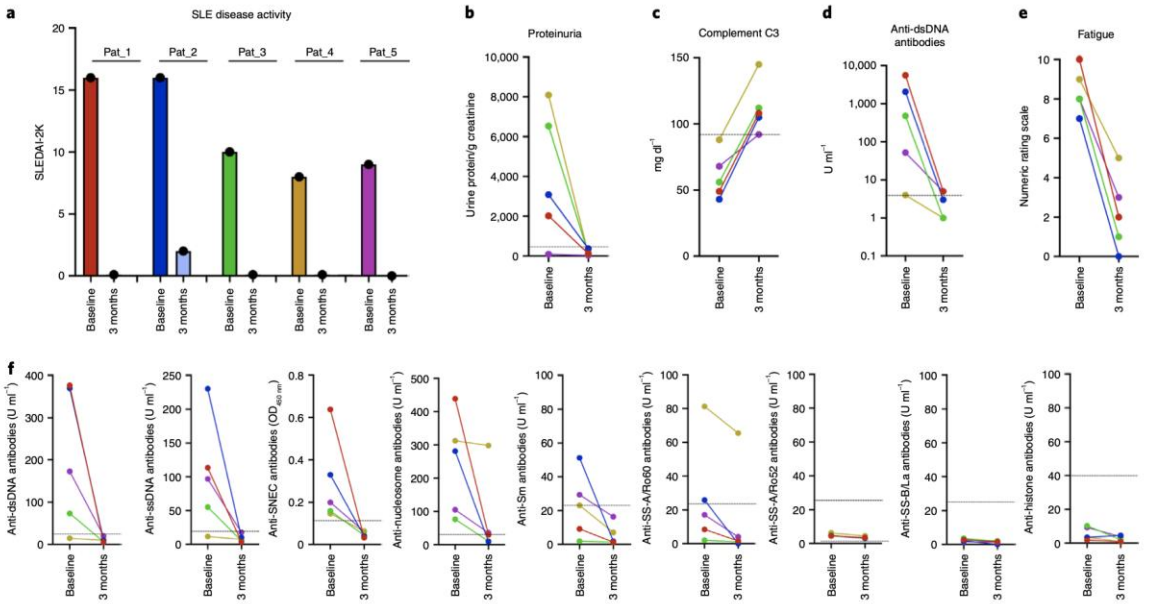


Fig. 3 | Effects of CAR T cell treatment on the activity of systemic lupus erythematosus. a, SLEDAI-2K scores at baseline and 3 months after CAR T cell administration ($N=5$). **b**, Proteinuria at baseline and 3 months after CAR T cell administration ($N=5$). **c**, Complement factor C3 levels at baseline and 3 months after CAR T cell administration ($N=5$). **d**, Anti-dsDNA antibodies assessed by radioimmunoassay at baseline and 3 months after CAR T cell administration ($N=5$). **e**, Fatigue measured by numerical rating scale (0–10) at baseline and 3 months after CAR T cell administration ($N=5$). **f**, ELISA-based quantification of antibodies against double stranded (ds) DNA, single stranded (ss) DNA, secondary necrotic cells (SNECs), nucleosomes, Smith (Sm) antigen, Sjogren's syndrome (SS)-A/Ro60, SS-A/Ro52 and SS-B/La antigens and histones at baseline and 3 months after CAR T cell administration ($N=5$).

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Case Report

CD19-targeted chimeric antigen receptor T cell therapy in two patients with multiple sclerosis

Felix Fischbach,[1,6] Johanna Richter,[2,6] Lena Kristina Pfeffer,[1,6] Boris Fehse,[2] Susanna Carolina Berger,[2] Stefanie Reinhardt,[1] Jens Kuhle,[3] Anita Badbaran,[2] Kristin Rathje,[2] Nico Gagelmann,[2] Dominic Borie,[4] Johan Seibel,[5] Francis Ayuk,[2] Manuel A. Friese,[1] Christoph Heesen,[1,*] and Nicolaus Kröger[2,7,*]

Summary

- CAR-T cell Therapy is a promising alternative for patients with relapsed/refractory lymphomas and leukemias.
- In myeloma, CAR-T cell therapy has demonstrated remarkable outcomes
- CAR-T cell persistence is associated with longer remission
- CRS is the most common adverse event

Summary

- Not immediately available, a bridging therapy is almost always required
- Limited success in solid Tumors
- Promising results in autoimmune diseases
- EXPENSIVE

Emily Whitehead

PHOTO: EMILY WHITEHEAD FOUNDATION

Thank you for your attention