CAR T-cell therapy

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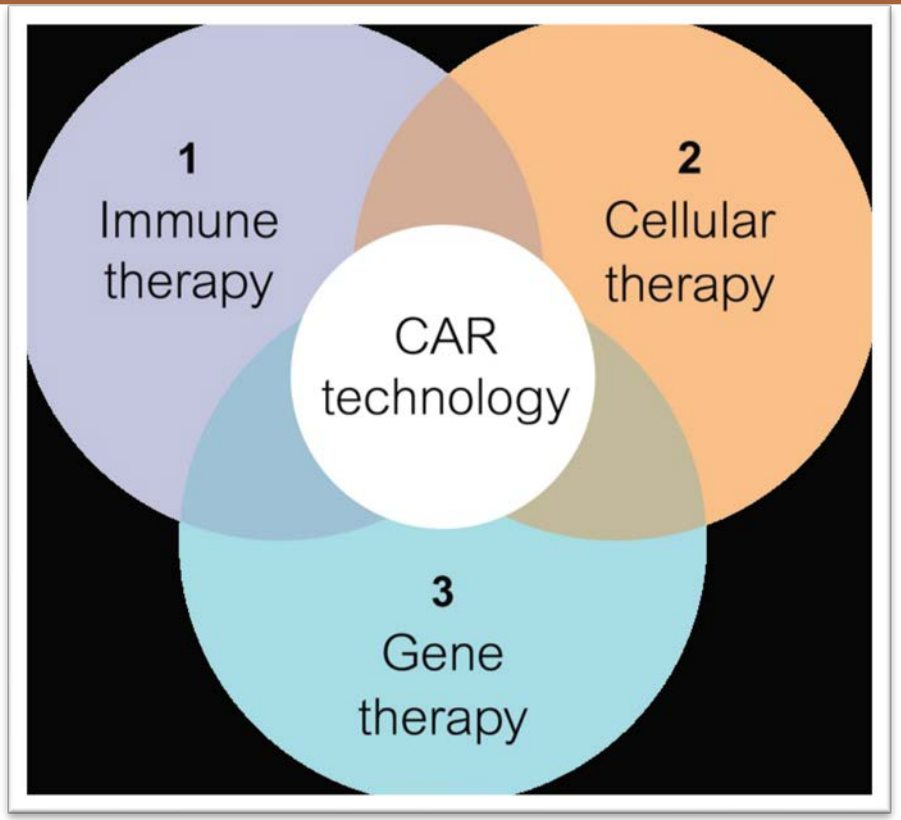
CAR T cells are at the intersection of 3 Innovative Technologies

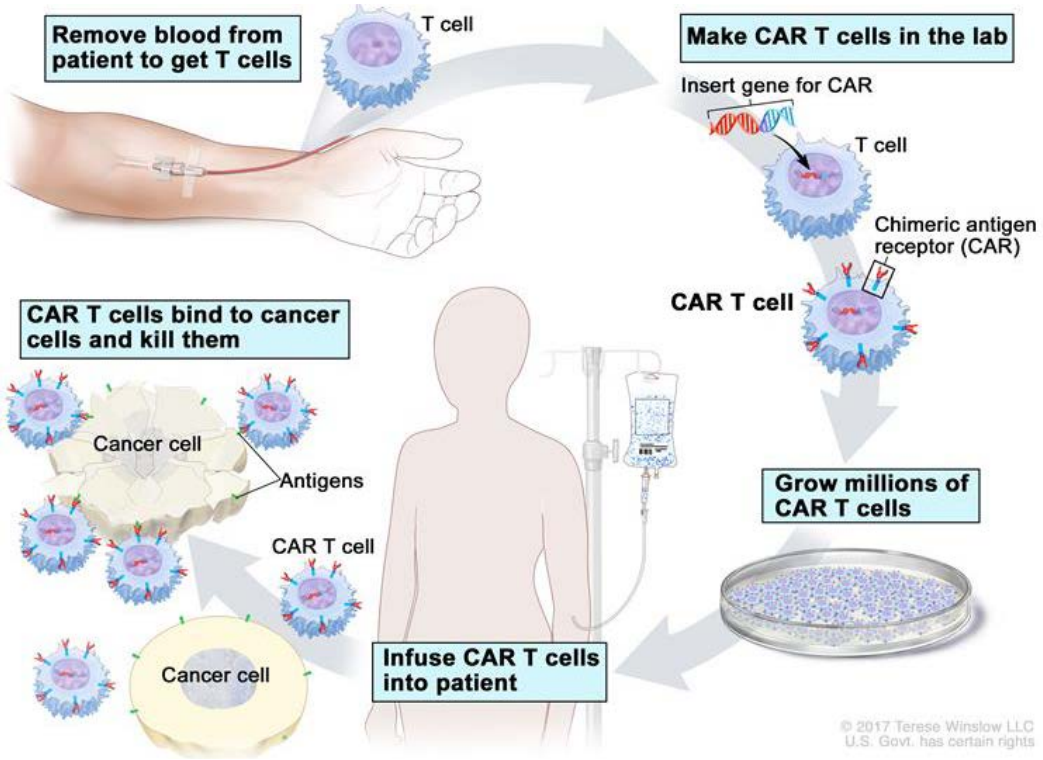
1. Immune therapy
Control and influence an individual's own immune system
2. Cellular therapy
CAR T Cells Produced From the Patient's Own Cells
3. Gene therapy
Inserting genes into a patient's cells, causing them to express a new CAR protein



Porter DL et al. J Cancer. 2019;2(1):331-332

CAR T-Cell Treatment Is Individualized

CAR T Cells Produced From the Patient's Own Cells



Current CAR T-cell therapies are engineered for each individual recipient

To create CAR T cells, T cells must be collected from the patient's tissue, tumor, or blood

T cells are then processed in manufacturer's lab to add an engineered antibody that is specific to the disease target

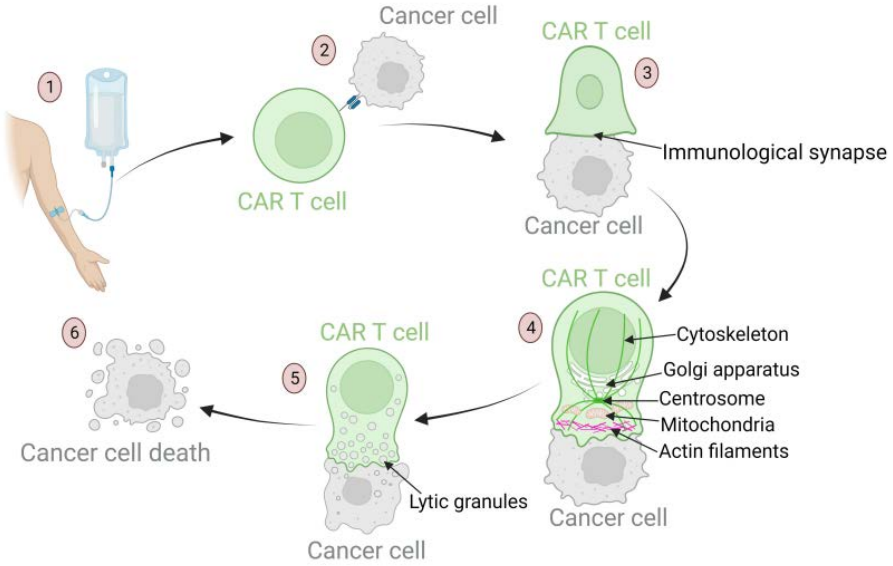
NIH. CAR-T cell therapy. www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy. Accessed October 7, 2019..

Definition of CAR T-cell therapy

CAR-T cells - autologous T cells engineered to express a surface receptor to target a specific (auto)antigen.

Current CAR T-cell therapies DO NOT recognise and attack tumor-specific antigens but kill specifically defined patient‘s own cell type

Aim – depletion of (auto)antigen positive cells, e.g. CD19-targeting CAR-T kill patient‘s own B cells expressing CD19 (pathogenic and healthy cells); in future non-depleting CAR Treg for autoimmunity?

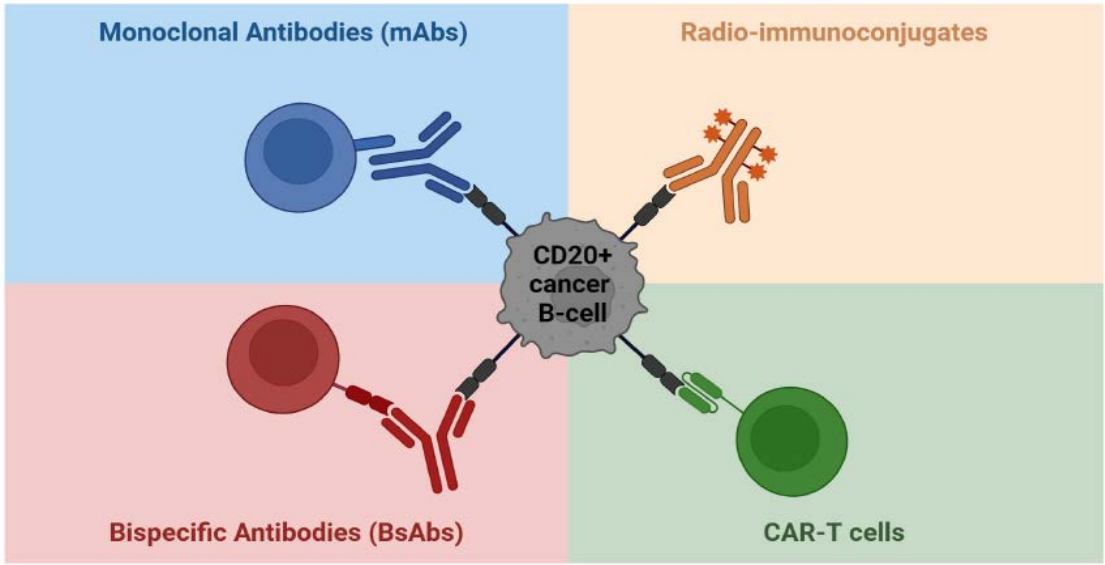


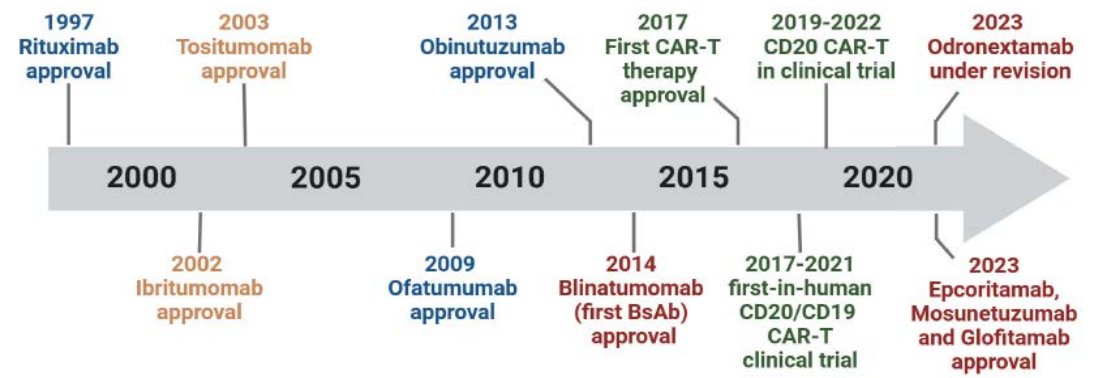
Levstek L, Janžič L, Ihan A, Kopitar AN. Front. Immunol. 2024;15:1378944

CAR T-cell therapy vs. antibody therapies vs. bispecific T-cell engager (BiTE) therapies

CAR T-cell therapy is similar to existing antibody therapies (e.g., Rituximab - a chimeric (mouse/human) monoclonal antibody against the protein CD20. Similar mechanism of action because they both have antigen targets on B cells and cause B-cell depletion.
CAR-T: long-term depletion (years) with single-dose; tissue-hidden cells; complement-independent lysis

Also can be compared to bispecific T-cell engager (BiTE) therapies (e.g., blinatumomab – CD19/CD3) Both therapies rely on the engagement of T cells with malignant cells Adverse events can be similar to those associated with CAR T cells.
CAR-T: long-term depletion (years) with single-dose



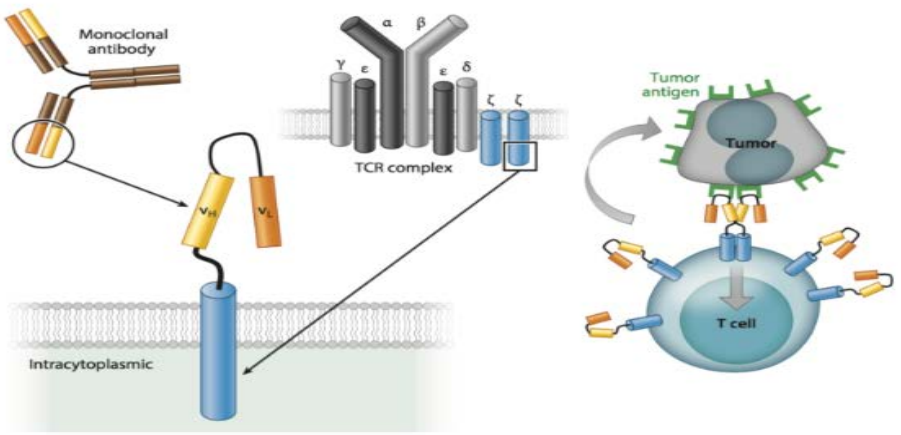


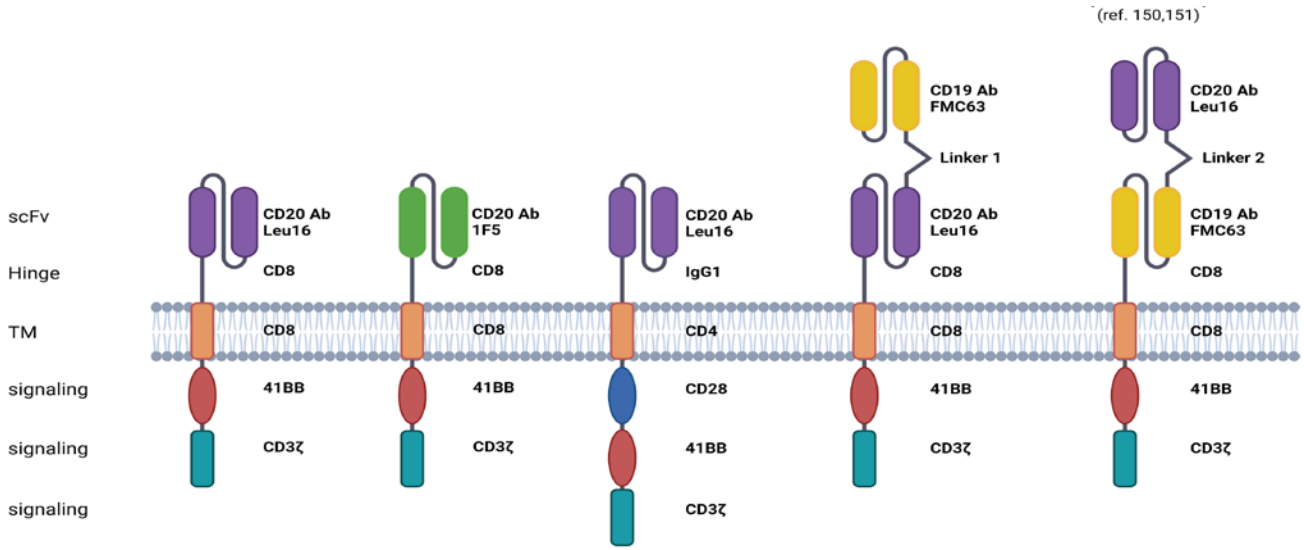
Dabkowska A, Domka K and Firczuk M 2024; Front. Immunol. 15:1363102

Chimeric antigen receptor (CAR)

Chimeric antigen receptors (CARs) are proteins that incorporate an antigen recognition domain, costimulatory domains, and T-cell activation domains (TCR zeta-chain - CD3ζ).

T cells genetically modified to express CARs specifically recognize and eliminate malignant cells expressing a target antigen (CD19, BCMA, CD30 etc)



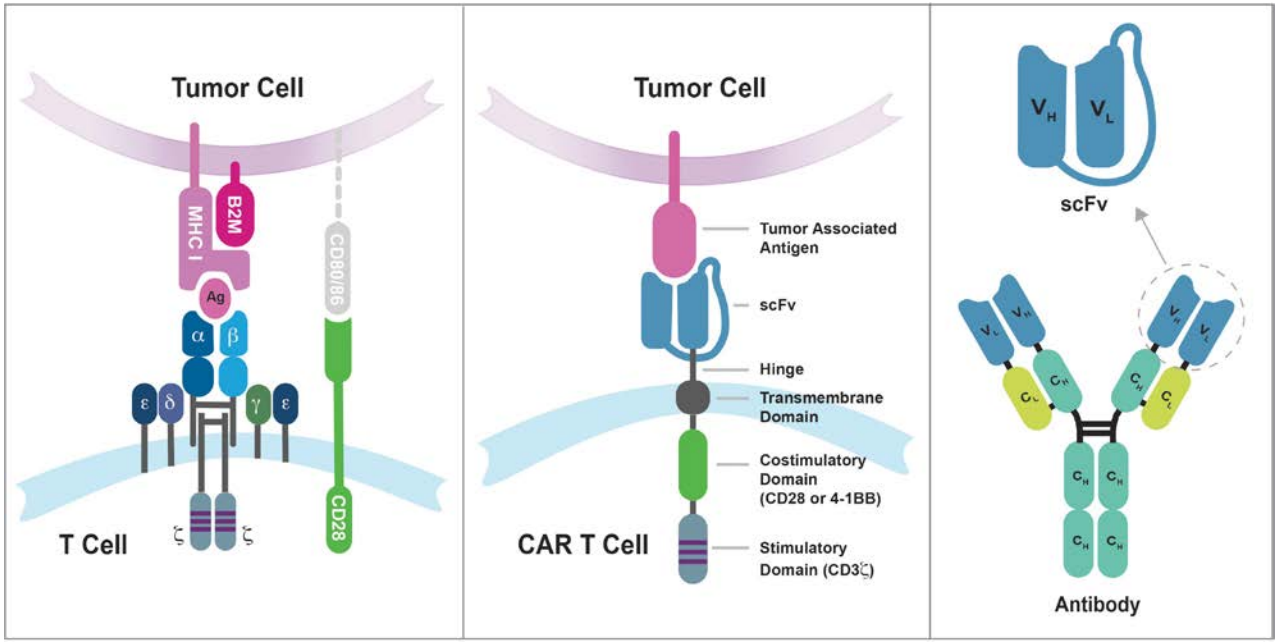


Mitra A, Barua A, Huang L(2023) Front. Immunol. 14:1188049

The differences in antigen recognition between conventional TCRs and synthetic CARs

Due to tolerance mechanisms, a patient can not produce TCR to eliminate own cells (e.g. CD19+ B cells)

Engineered single-chain variable fragment (scFv) derived from a monoclonal antibody may serve as surrogate TCR to recognise and kill patient‘s own cells



(A) TCR recognition of antigens is restricted by MHC complex molecules, and the suboptimal efficiency of cancer cell killing by conventional T cells may be due in part to the lack of CD80/86 expression on tumor cells.
(B) Synthetic CARs recognize tumor-associated antigens on the surface of cancer cells through the single-chain variable fragment (scFv) domain – non MHC restricted. These interactions then activate both the CD3-mediated primary signal and the CD28/4-1BB-mediated secondary signal in T cells.
(C) The scFv domain is derived from a monoclonal antibody and consists of the variable regions from the heavy chain (VH) and light chain (VL) linked by a flexible linker sequence.

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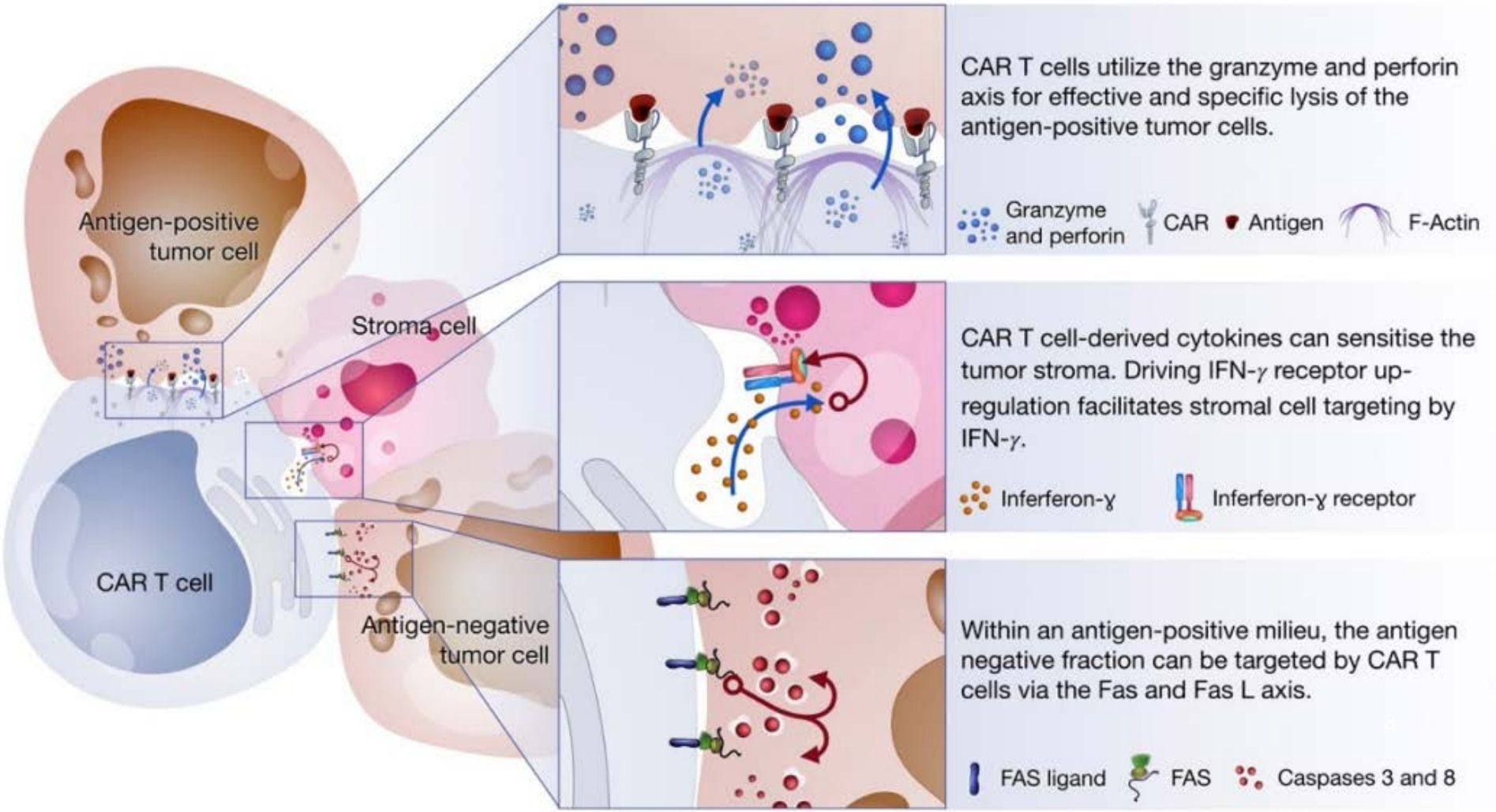
CAR T-Cell Therapy Mechanism of Action



Causes lysis of antigen-positive tumor cell. Modulates tumor microenvironment by sensitizing tumor stroma. Causes lysis of antigen-negative tumor cells through apoptotic mechanisms

Advantages of CAR T-Cell Therapy

CAR T cells retain long-term "graft"-versus-tumor effect

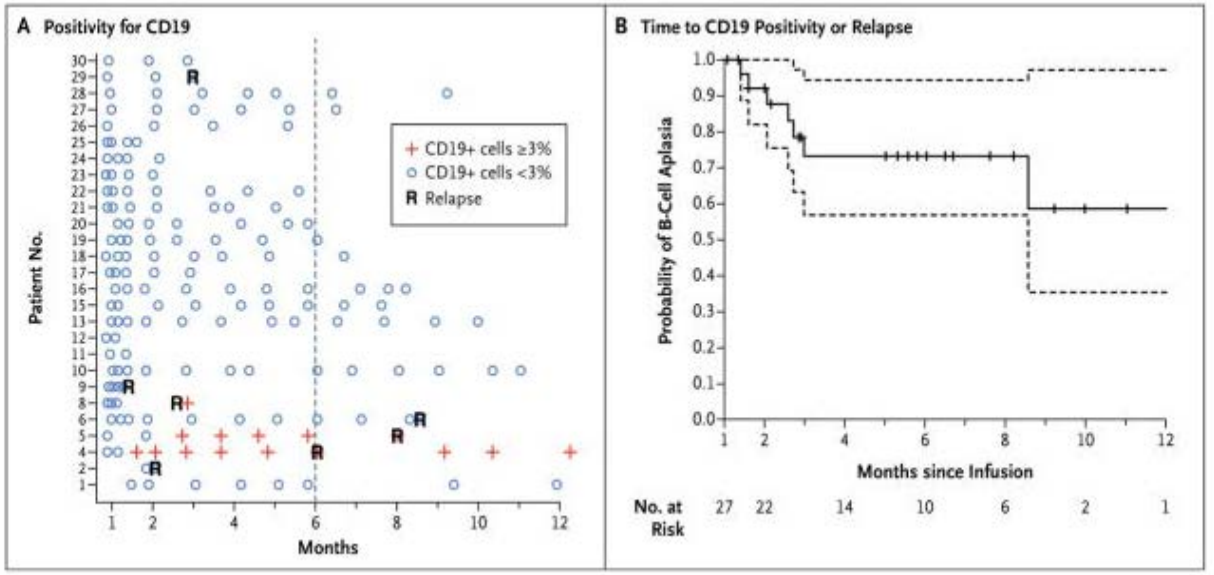
HLA-independent antigen recognition, therefore universal application

Rapid generation of tumor specific T-cells

Active in both CD4+ and CD8+ T-cells

Because it utilizes the patient's own cells, there are no graft-versus-host complications

Target antigens include proteins, carbohydrates, and glycolipids



B-cell aplasia can be used as a measure of CAR-T (CD19) function
B-cell aplasia occurred in all the patients who had a response and persisted for up to 1 year after CTL019 cells were no longer detectable by means of flow cytometry.

With a follow-up period 24 months 90% rate of complete remission among patients who received CTL019 for ALL that was relapsed or refractory. Relapses were associated with either lack of CTL019 persistence or CD19 escape variants.

N Engl J Med. 2014 Oct 16; 371(16): 1507–1517

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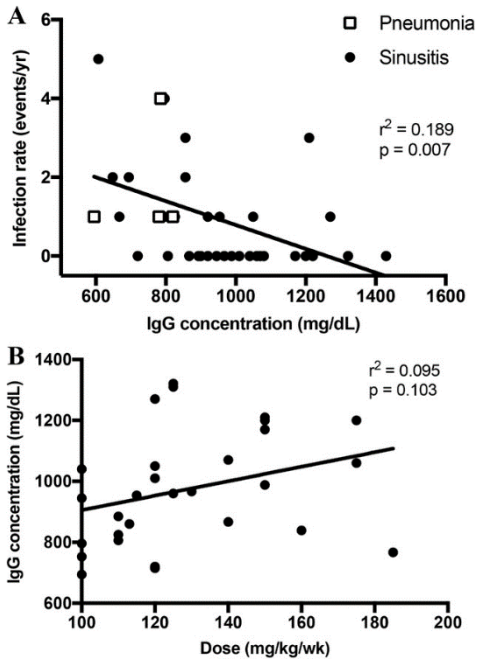
Subcutaneous immunoglobulin replacement following CD19-specific chimeric antigen receptor T-cell therapy for B-cell acute lymphoblastic leukemia in pediatric patients

Danielle E. Arnold, Shannon L. Maude, Colleen A. Callahan, Amanda M. DiNofia, Stephan A. Grupp, Jennifer R. Heimall



Patients successfully treated with CAR T-cell therapy are expected to demonstrate B-cell aplasia and associated agammaglobulinemia, and immunoglobulin replacement has been used for these patients.

26 (93%) patients had undetectable CD19+ B-cell counts. Twenty-five (89%) patients had undetectable IgA levels, and no patient had detectable IgM levels.

Based on results from our cohort, we recommend maintaining IgG levels > 1000 mg/dL and monitoring IgG levels on a routine basis to ensure adequate replacement.

Pediatr Blood Cancer.2020;67:e28092

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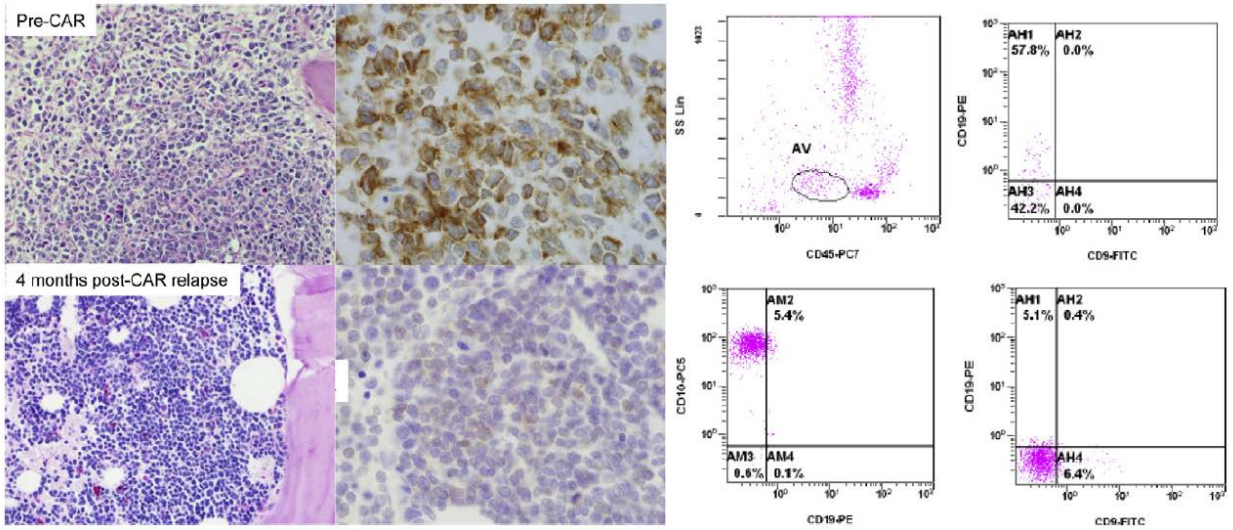

Fig. 3. CD19-negative relapse with loss of surface CD19 but retained cytoplasmic expression.

CD19-positive relapses - loss of CAR T-cell function and return of the pre-CAR clone, mostly within a year of infusion (T cell fitness, immunogenicity to murine components of the CAR); first re-apperance of normal B cells, then re-apperance tumor B cells (relaps)

CD19-negative relapses - occur despite ongoing B-cell aplasia. Comparison of pre-CAR and post-CAR immunophenotype showed that only CD19 expression was different—in most of the cases the immune repertoires of the malignant cells were identical; no normal B cells, expanded tumor B cells (CD19-) - relaps

Clin Lab Med 41 (2021) 325–339

Advantages of CAR T-Cell Therapy

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Rapid generation of tumor specific T-cells (2-4 weeks)

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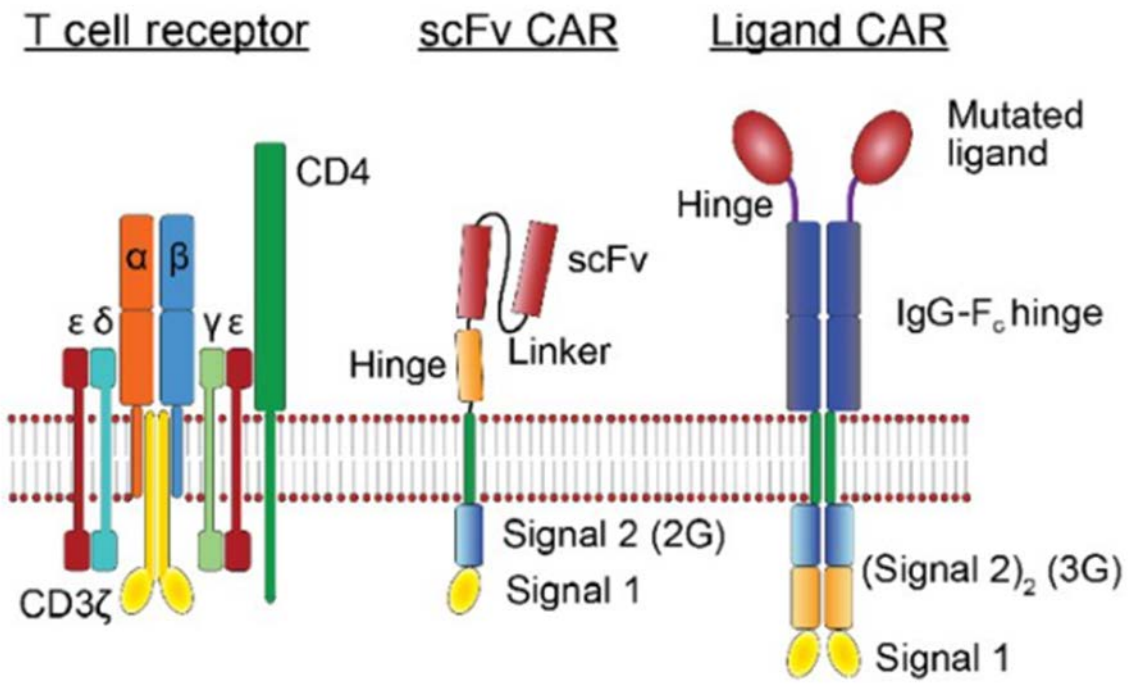

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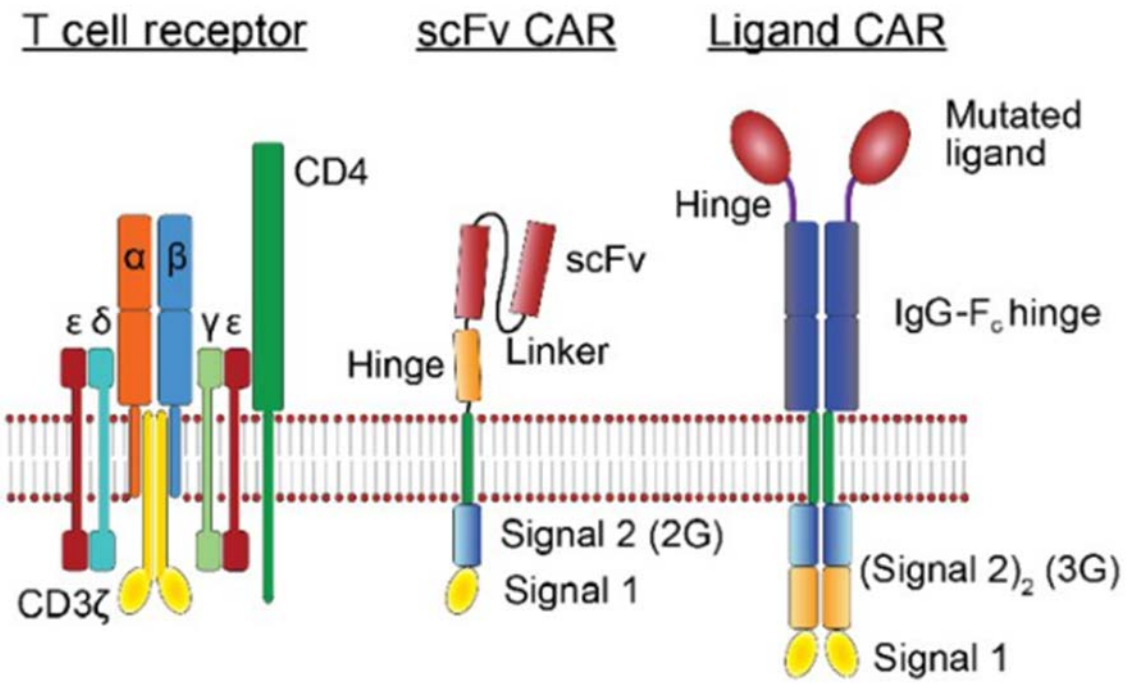

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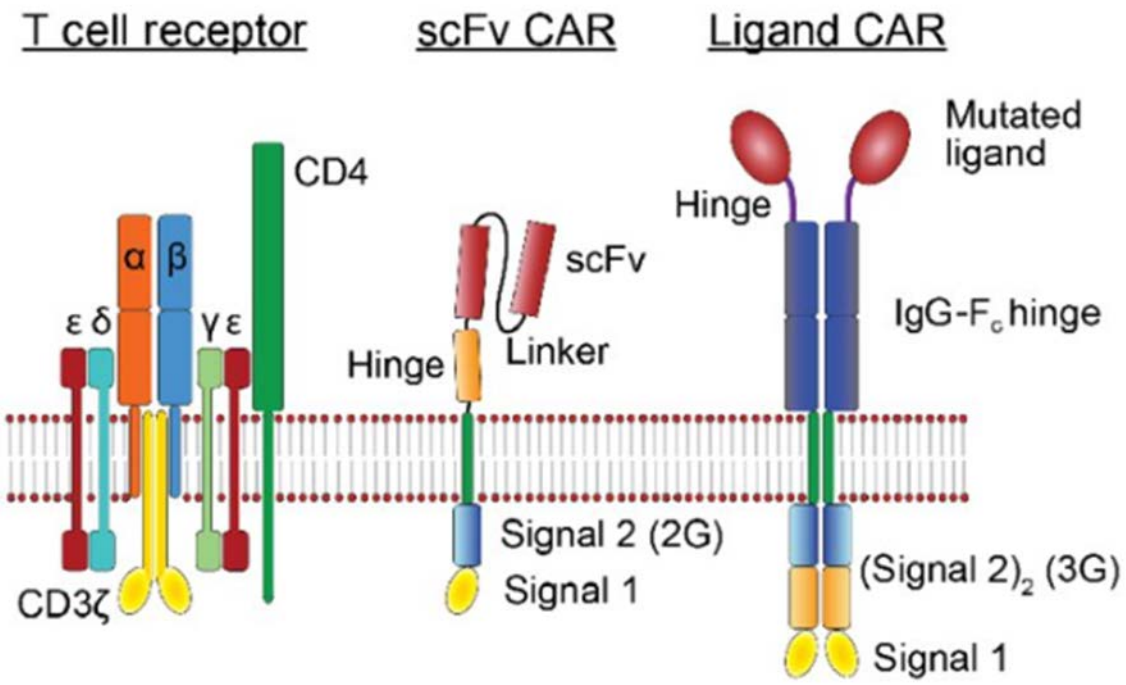

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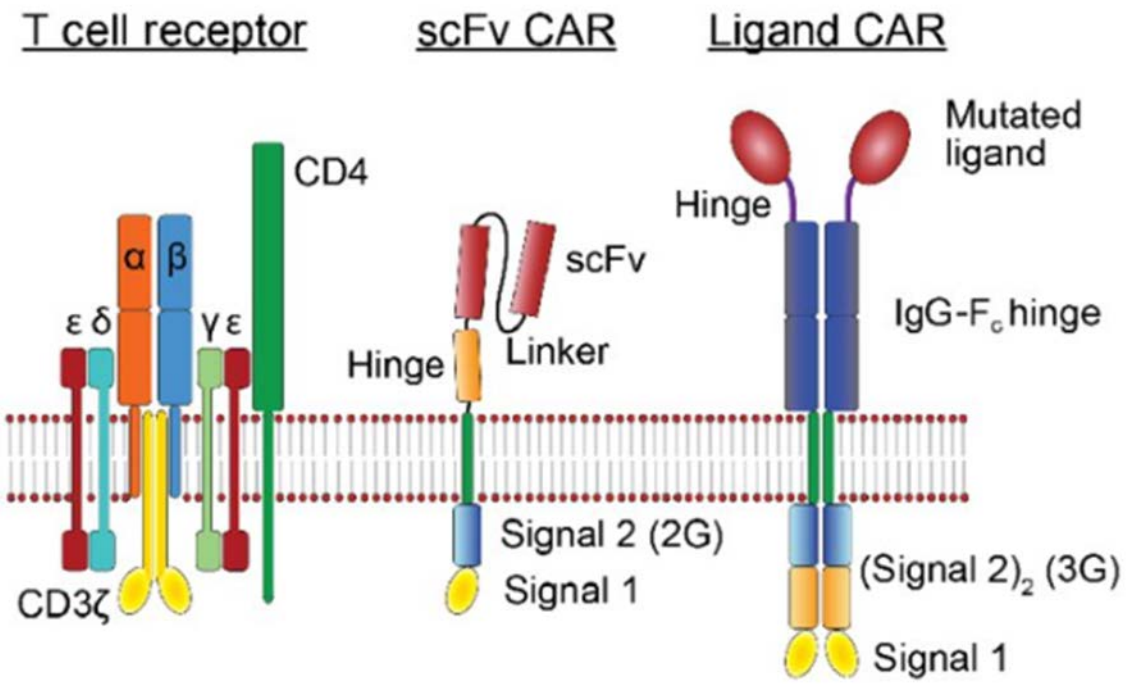

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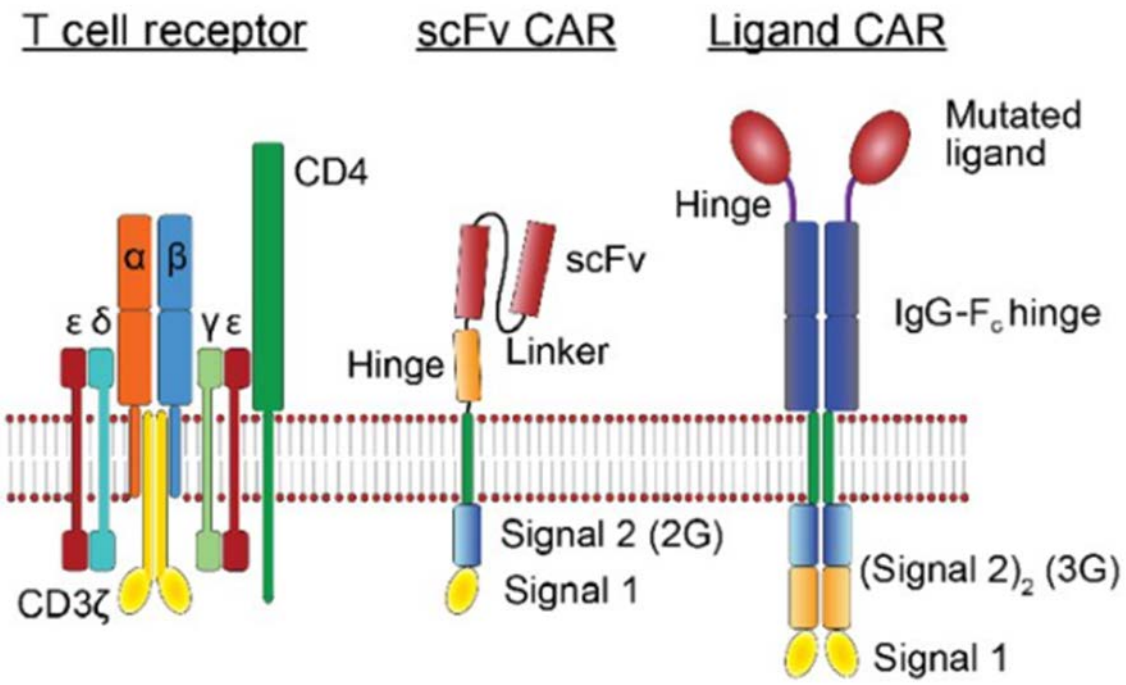

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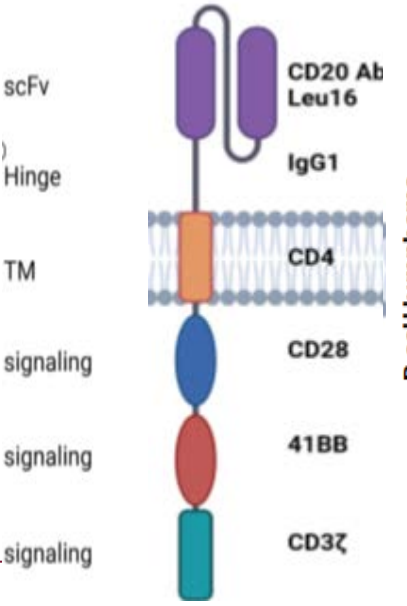
CAR-T cell products approved in the European Union (EMA)

CAR-T expressing an anti-CD19 chimeric antigen receptor (CAR)

Kymriah (tisagenlecleucel),
Yescarta (axicabtagene ciloleucel),
Tecartus (brexucabtagene autoleucel),
Breyanzi (lisocabtagene maraleucel)

CD19 expression is restricted to B-cells and possibly follicular dendritic cells
CD19 is not expressed on pluripotent bone marrow stem cells
CD19 is expressed on the surface of most B-cell malignancies
Antibodies against CD19 inhibit growth of tumor cells



B cell lymphoma and leukaemia

Product	Structure of CAR construct					FDA approval (year)
	Antigen-binding domain	Hinge region	Transmembrane region	Co-stimulatory domain	T cell activation domain	
Axicabtagene ciloleucel	Anti-CD19	CD28	CD28	CD28	CD3ζ	• LBCL refractory to first-line therapy or relapsing at <12 months of first-line therapy (2022) • Relapsed LBCL after ≥2 lines of therapy (2017) • Relapsed FL after ≥2 lines of therapy (2021)
Brexucabtagene autoleucel	Anti-CD19	CD28	CD28	CD28	CD3ζ	• R/R MCL (2020) • R/R B-ALL (2021)
Tisagenlecleucel	Anti-CD19	CD8α	CD8α	4-1BB	CD3ζ	• LBCL after ≥2 lines of therapy (2018) • FL after ≥2 lines of therapy (2022) • R/R B-ALL (2017)
Lisocabtagene maraleucel	Anti-CD19	IgG4	CD28	4-1BB	CD3ζ	• LBCL refractory to first-line or relapsing at <12 months of first-line therapy or relapsing on first-line therapy and not eligible for HSCT (2022) • Relapsed LBCL after ≥2 lines of therapy (2021)

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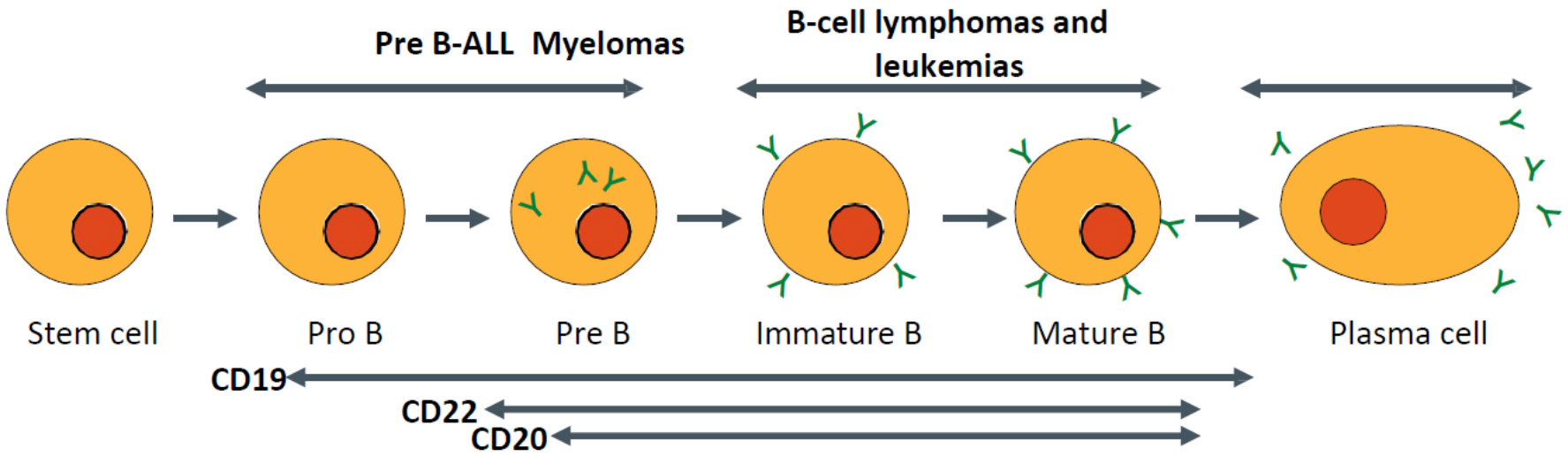


Bellino S, La Salvia A, Cometa MF and Botta R (2023) Front. Pharmacol. 14:1200808

CAR-T cell products approved in the European Union

CAR-T expressing an anti-BCMA (B-cell maturation antigen) expressed on the surface of normal and malignant plasma cells

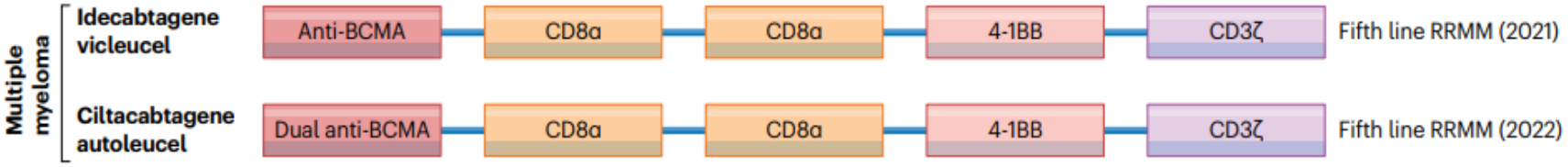
Abecma (idecabtagene vicleucel)

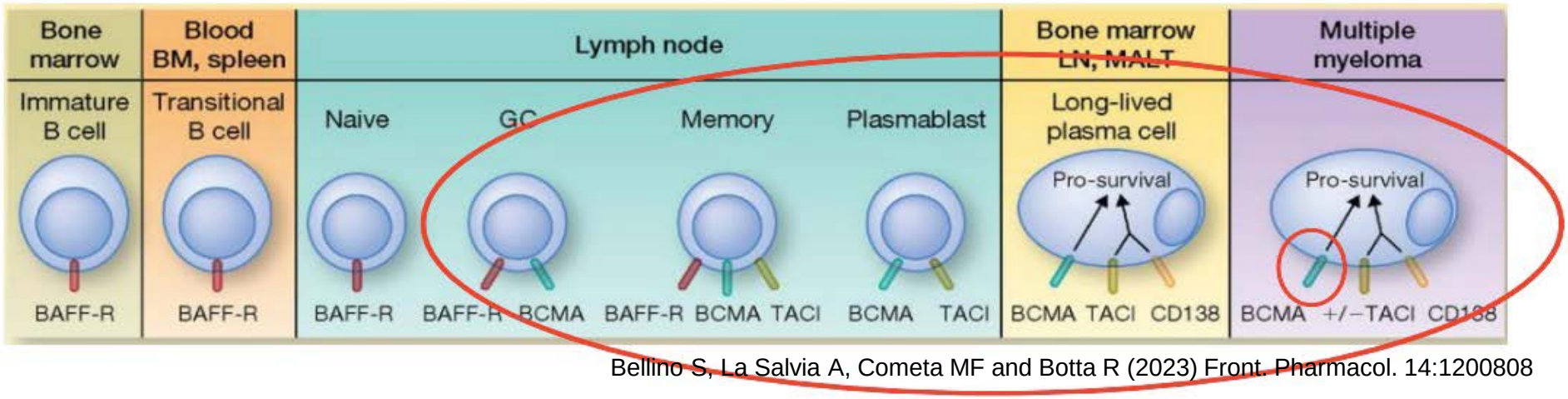
Carvykti (ciltacabtagene autoleucel)

BCMA as a target for multiple myeloma

B cell maturation antigen - member of the TNF receptor superfamily

- Binds 2 ligands (BAFF and APRIL)
- Expression largely restricted to plasma cells and B mature cells
- Expressed nearly universally on multiple myeloma cells





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CAR T-Cell therapy is not yet approved for first-line treatment

As a result, there are no studies that compare the effectiveness of different antitumor therapies (chemotherapy, monoclonal antibodies, CAR-T, bispecific antibodies) in the same stage of the disease and in the same patient condition.

Given that success requires intact T-cell population, it has been postulated that earlier therapy may result in a more robust therapeutic results compared with use as salvage treatment after chemotherapy failure
Anecdotal clinician reports seem to indicate that patients with extensive chemotherapy exposure may have difficulty producing a viable product (CD19-positive relapses)

Tisagenlecleucel (Kymriah®) has been approved by the US Food and Drug Administration (FDA) since 2017 for the treatment of:

- Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (B-ALL) that is either refractory or in a second or later relapse
- Adult patients with relapsed or refractory large B-cell lymphoma–after two or more lines of systemic therapy—including: diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma (FL)
- Adult patients with relapsed or refractory FL after two or more lines of systemic therapy

CAR T-cell clinical trials (clinicaltrials.gov)

May allow enrollment of patients who do not meet FDA/EMA approval criteria and who might not otherwise be candidates for therapy

May offer patients treatment with a CAR T-cell product targeted to an alternative antigen (i.e., not CD19 or BCMA)

Clinical trials currently exist to allow patients to receive FDA/EMA-approved product that fails to meet manufacturing specifications

Manufacturing hurdles continue to persist, which affect the number of viable T cells delivered in any given dose of CAR T-cell product

Clinical trials may offer patients the possibility of receiving CAR T-cell therapy earlier in their disease course

Multiple Myeloma
- CD38
- BCMA
- CD19
- CS1

Breast Cancer
- ROR1
- TnMUC1
- CD70
- MNC2-CAR44 (targets MUC1)

Lung Cancer
- ROR1
- TnMUC1
- Mesothelin

Prostate Cancer
- PSMA
- PSCA

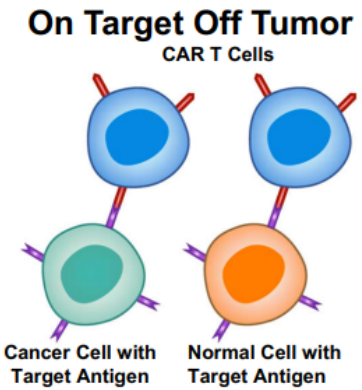
Clinical trial challenges: on-target off-tumor effects

CAR-T targeted tumor antigens are often also expressed on normal tissues at varying levels.

Especially solid tumor antigens are often also expressed on multiple normal tissues at varying levels.

Antigen selection is crucial in CAR design to limit “on-target off-tumor” toxicity. In solid tumors, a solution may be targeting of tumor-restricted post-translational modifications such as overexpressed truncated O-glycans: Tn (GalNAcα1-O-Ser/T and sialyl-Tn (STn)

(NeuAcα2–6-GalNAcα1-O-Ser/T



Antigen	Hematologic Malignancy	Potential Normal Tissue Impacted
CD5	T-ALL, T-cell lymphoma	Normal T cells
CD7	T-ALL, T-cell lymphoma	Normal T cells
CD19	ALL, CLL, NHL	Normal B cells
CD20	ALL, CLL, NHL	Normal B cells
CD22	B cell leukemias; B-cell lymphomas	Normal B cells
Igκ	CLL, NHL, myeloma	Normal B cells
ROR1	CLL, NHL	Pancreas parathyroid, adipose (fat) tissue
CD30	NHL, HL	Resting CD8 T cells
CD33	AML	Multipotent myeloid precursors, unipotent colony-forming cells, and maturing granulocytes and monocytes
CLL-1	AML	Peripheral blood leukocytes and in the spleen
CD138	Myeloma	Precursor and plasma B cells, epithelia
CD123	AML	Bone marrow myeloid progenitors, B cells, mast cells, monocytes, macrophages, endothelial cells
BCMA	Myeloma	B cells

Blood Cancer Journal (2021) 11:69

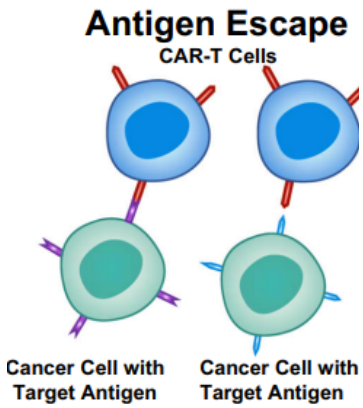
Clinical trial challenges: antigen escape

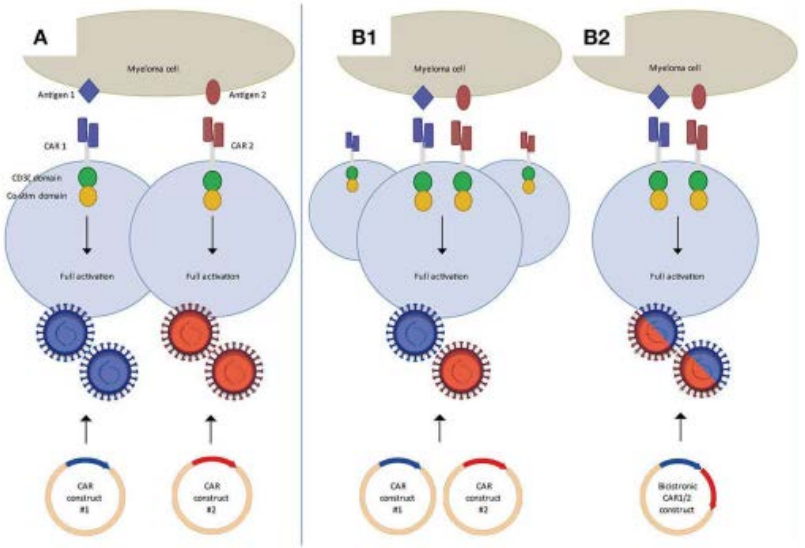
CAR-T cells, althought present, display no tumor supression due to partial or complete loss of target antigen expression by tumor cells.

SOLUTION: Targeting multiple antigens (dual or tandem CARs)

Hematologic tumors: CD19/CD22 targeted CARs for treatment of ALL/DLBCL and CD19/BCMA targeted for multiple myeloma

Solid tumors: HER2 /IL13Ra2 (glioblastoma) and HER2/MUC1 (breast cancer) CARs produce superior antitumor responses compared to single target therapy





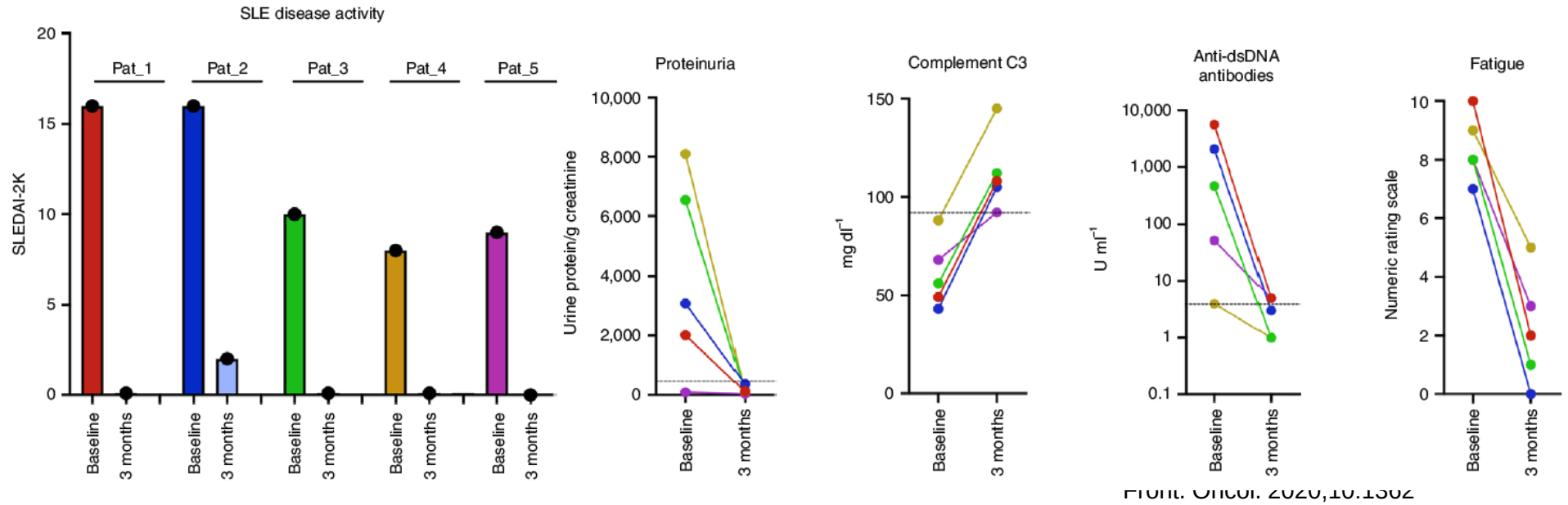
(A) Mixture of two pools of single CAR T-cells in which each pool targets a different antigen. These can be co-infused or sequentially infused into a patient. (B) Two CARs targeting distinct antigens expressed on one T-cell through the use of co-transduction (B1) or a bicistronic vector (B2).

Front. Oncol. 2020;10:1362

Clinical trial oportunities: autoimmune diseases

Anti-CD19 CAR T cell therapy for refractory systemic lupus erythematosus. Nat Med 28, 2124–2132 (2022)

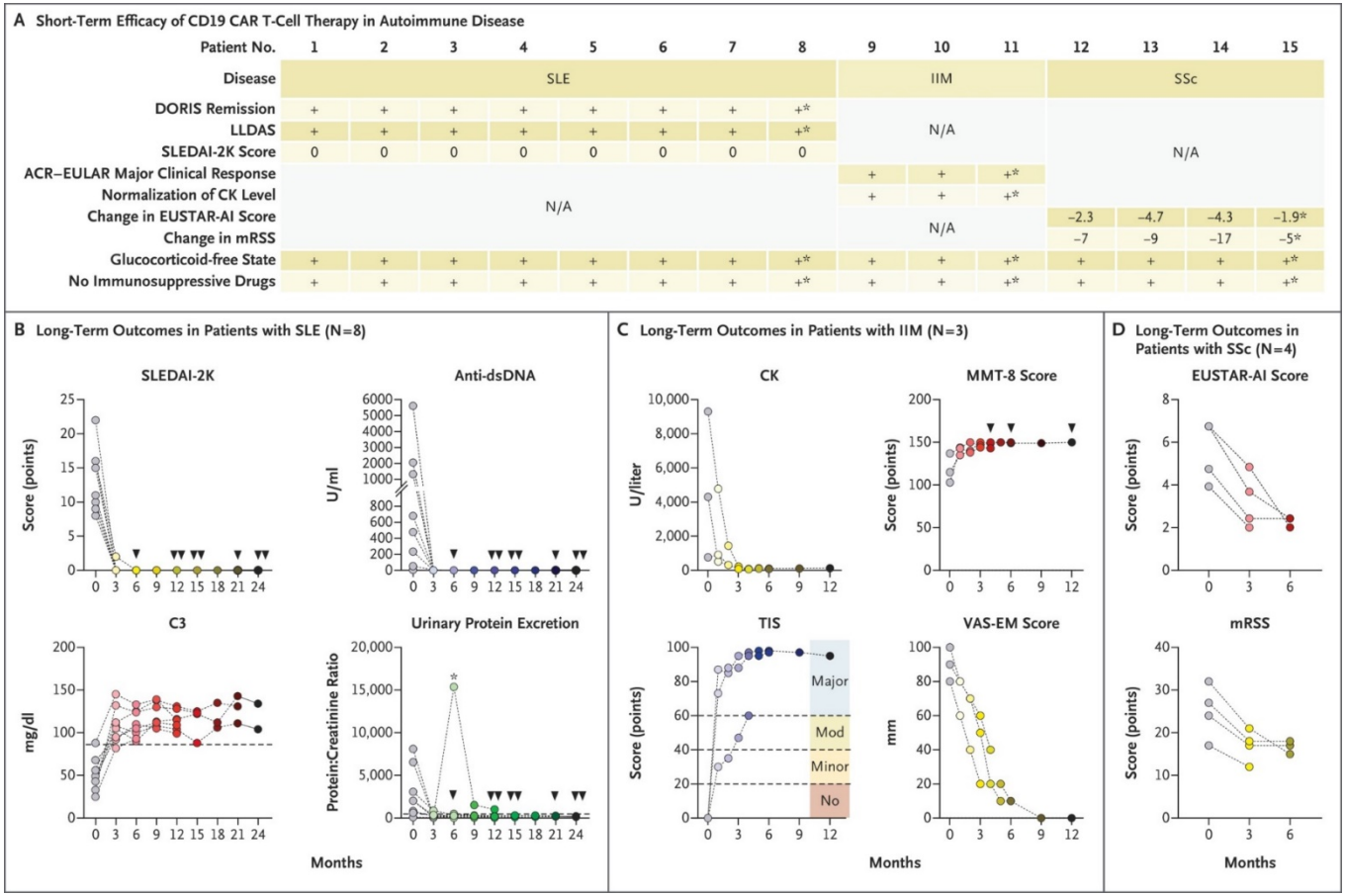
SLE refractory to several immunosuppressive drug treatments were enrolled in a compassionate-use CAR T cell program. Remission of SLE according to DORIS criteria was achieved in all five patients after 3 months. Drug-free remission was maintained during longer follow-up (median (range) of 8 (12) months 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.



Front. Oncol. 2020;10:1362

Clinical Efficacy of CD19 CAR T-Cell Therapy in Autoimmune Disease

All the patients had a decrease in the score on the EUSTAR activity index. Immunosuppressive therapy was completely stopped in all the patients.



A Short-Term Efficacy of CD19 CAR T-Cell Therapy in Autoimmune Disease

Patient No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Disease	SLE								IIM			SSc			
DORIS Remission	+	+	+	+	+	+	+	+*							
LLDAS	+	+	+	+	+	+	+	+*	N/A						
SLEDAI-2K Score	0	0	0	0	0	0	0	0				N/A			
ACR–EULAR Major Clinical Response									+	+	+*				
Normalization of CK Level									+	+	+*				
Change in EUSTAR-AI Score	N/A											−2.3	−4.7	−4.3	−1.9*
Change in mRSS									N/A			−7	−9	−17	−5*
Glucocorticoid-free State	+	+	+	+	+	+	+	+*	+	+	+*	+	+	+	+*
No Immunosuppressive Drugs	+	+	+	+	+	+	+	+*	+	+	+*	+	+	+	+*

Müller F et al. N Engl J Med2024;390:687-700

Clinical Efficacy of CD19 CAR T-Cell Therapy in Autoimmune Disease

15 patients with severe SLE (8 patients), idiopathic inflammatory myositis (3 patients), or systemic sclerosis (4 patients) who received a single infusion of CD19 chimeric antigen receptor (CAR) T cells after preconditioning with fludarabine and cyclophosphamide. Efficacy up to 2 years after CAR T-cell infusion was assessed by means of Definition of Remission in SLE (DORIS) remission criteria

The median follow-up was 15 months (range, 4 to 29). The mean (±SD) duration of B-cell aplasia was 112±47 days. All the patients with SLE had DORIS remission, all the patients with idiopathic inflammatory myositis had an ACR–EULAR major clinical response, and all the patients with systemic sclerosis had a decrease in the score on the EUSTAR activity index. Immunosuppressive therapy was completely stopped in all the patients.

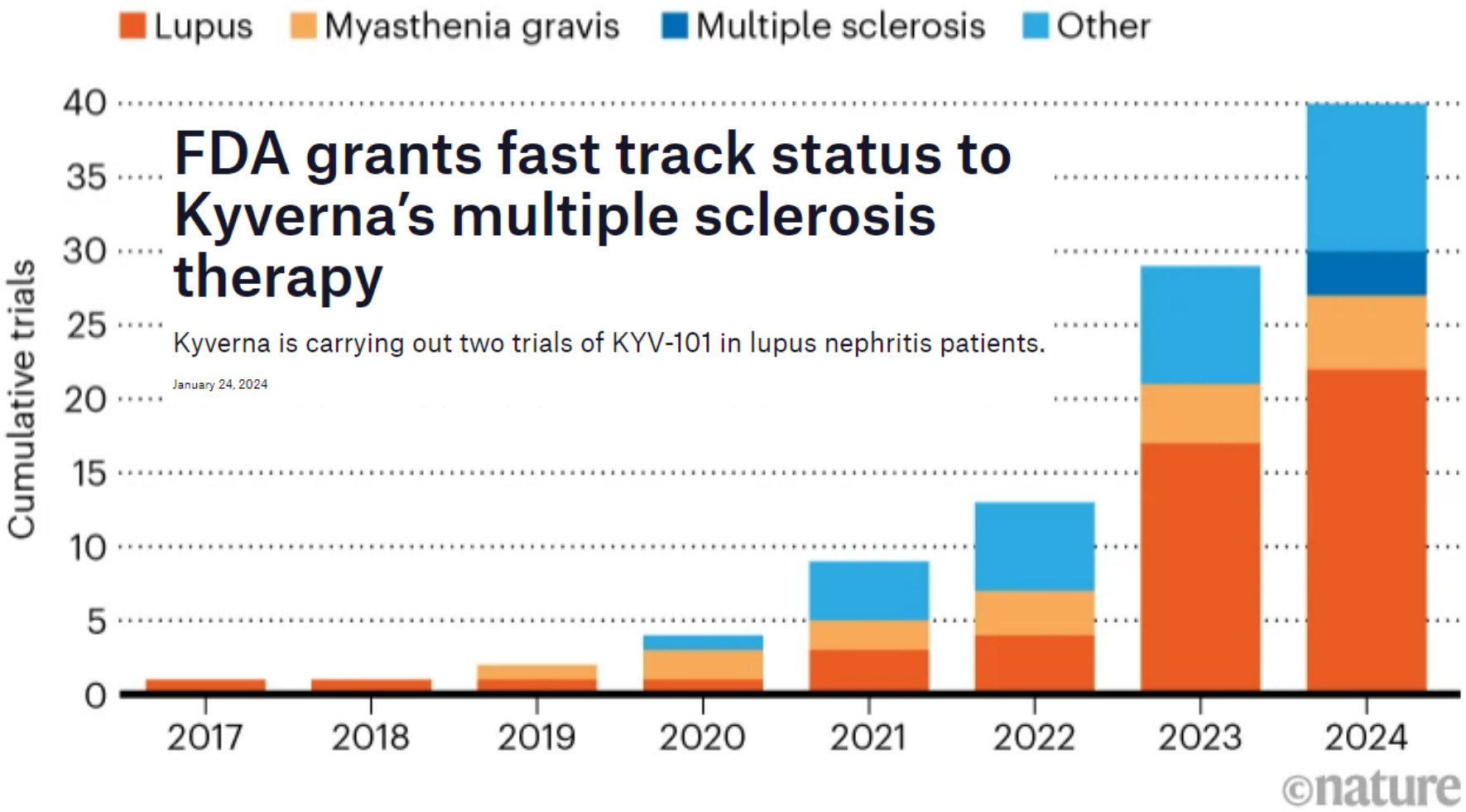
Grade 1 cytokine release syndrome occurred in 10 patients. One patient each had grade 2 cytokine release syndrome, grade 1 immune effector cell–associated neurotoxicity syndrome, and pneumonia that resulted in hospitalization.

CD19 CAR T-cell transfer appeared to be feasible, safe, and efficacious in three different autoimmune diseases, providing rationale for further controlled clinical trials.

Müller F et al. N Engl J Med2024;390:687-700

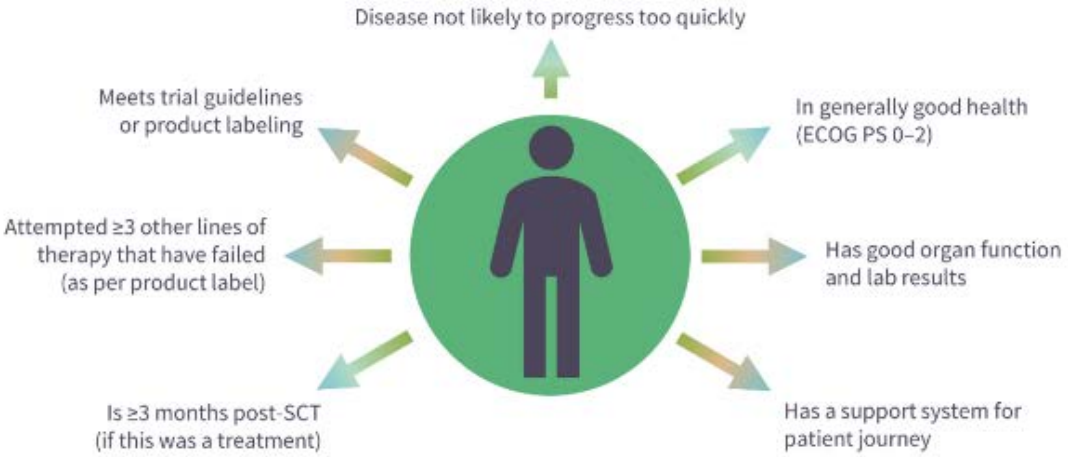
ENLISTING IMMUNE CELLS TO TREAT AUTOIMMUNE DISEASE

The number of clinical trials of CAR T cells — engineered immune cells — used to treat autoimmune disorders has grown rapidly over the past seven years. Testing of CAR-T therapy for the autoimmune disorder lupus accounts for the bulk of the trials.



Patient Eligibility for CAR T-Cell Therapy

- Neurological, cardiac, pulmonary, hepatic, and renal function per oncologist approval
- No uncontrolled infections
- Cannot have acute GVHD
- Bulky disease, disease impacting organ function may benefit from debulking with chemotherapy prior to initiation of CAR T-cell products
- Patients must have sufficient organ reserve to tolerate lymphodepleting therapy, typically cyclophosphamide and fludarabine
- Because neurotoxicity and delirium are components of CAR T-cell toxicity, some institutions consider psychiatric screening



https://medicalpolicies.amerigroup.com/medicalpolicies/policies/mp_pw_d052641.htm. Accessed October 10, 2019. 4. Hayden PJ, et al. *Curr Res Transl Med*. 2019;67:79-88.

T-Cell Harvest

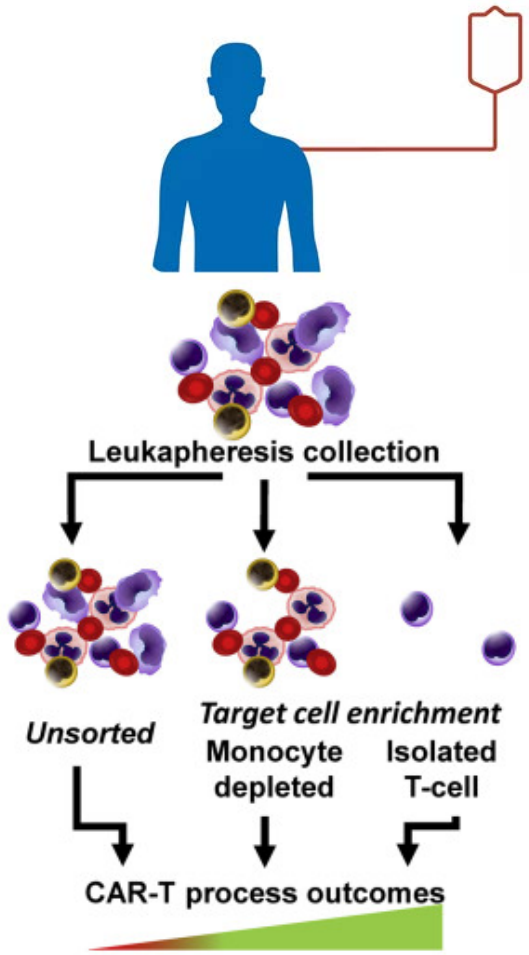
Patient must first enroll with eligible center to establish care

- Pretreatment workup will be conducted to establish patient reserve
- May include: PFT, stress testing, echo, MRI/CT, BMA, LP, etc

T cells harvested either by biopsy or apheresis

- Sample may be found to be insufficient at various times in harvest and creation process
  - Insufficient quantity of T cells recovered
  - Insufficient expansion after modification
- Sample quality may depend on prior chemotherapy exposure and degree of immunodeficiency

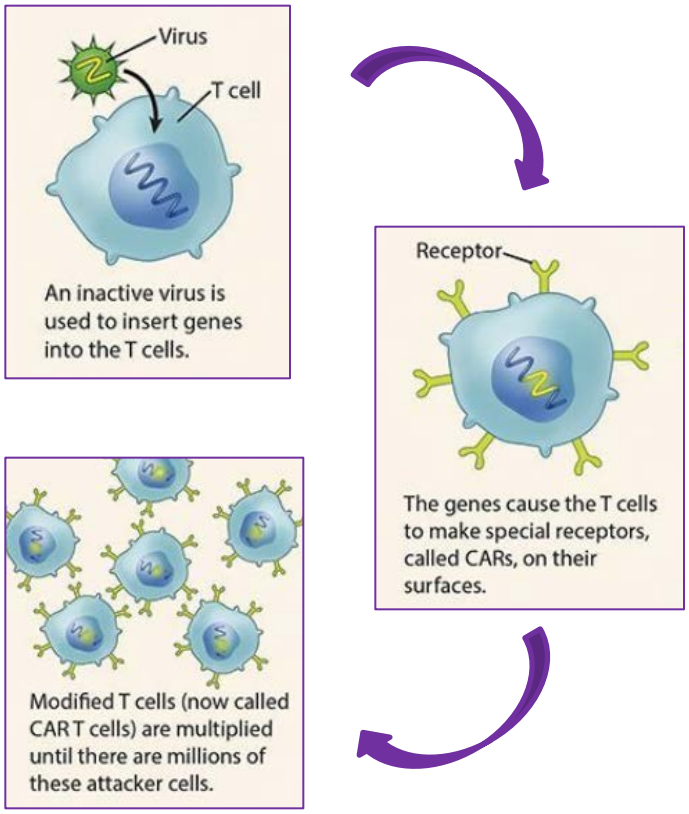
After isolating endogenous T cells from patient, cells are delivered to manufacturing lab for cell and processing



Zou Y, et al. *J Hematol Oncol*. 2018;11:130.

BMA, bone marrow aspirate; echo, echocardiogram; LP, lumbar puncture; PFT, pulmonary function testing.

Cell Engineering and Expansion



Manufacturing process involves use of modified viral vector, such as lentivirus or γ-retrovirus, to insert specific genetic sequences to produce antibody expression

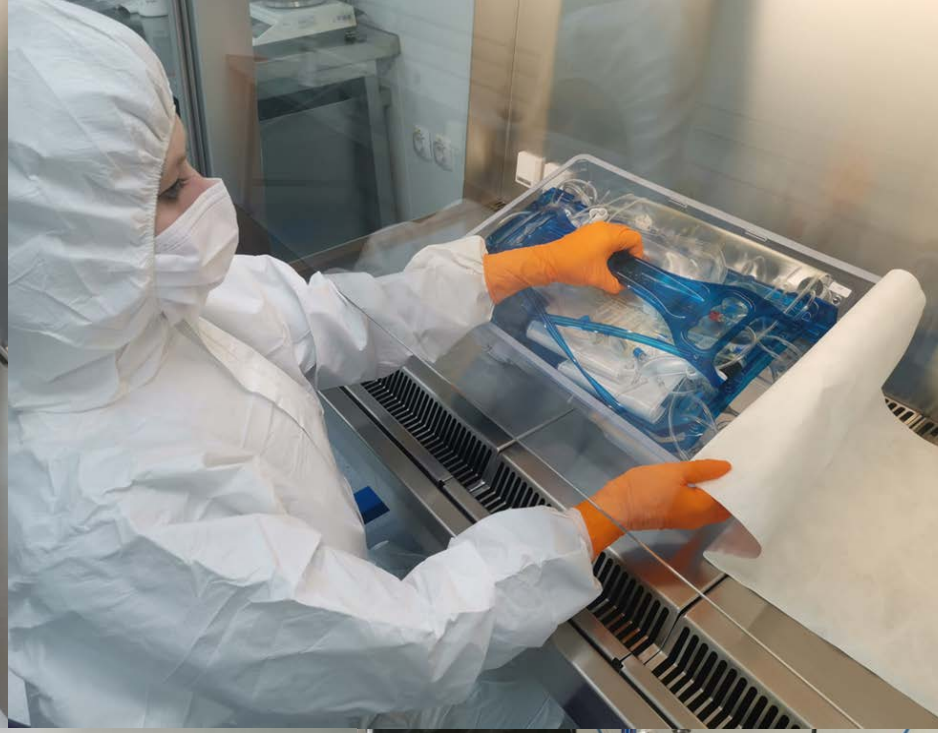
- Each viral vector is manufactured specifically for the product of interest
- Viral vectors are incapable of causing disease, though long-term observation is lacking

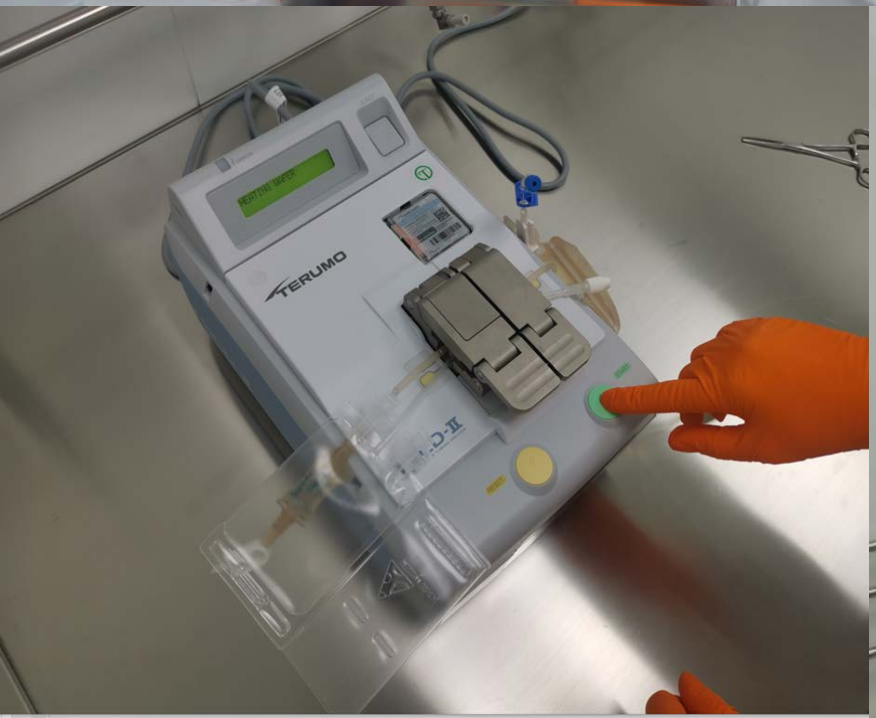
T cells are also modified to expand population in vitro and in vivo

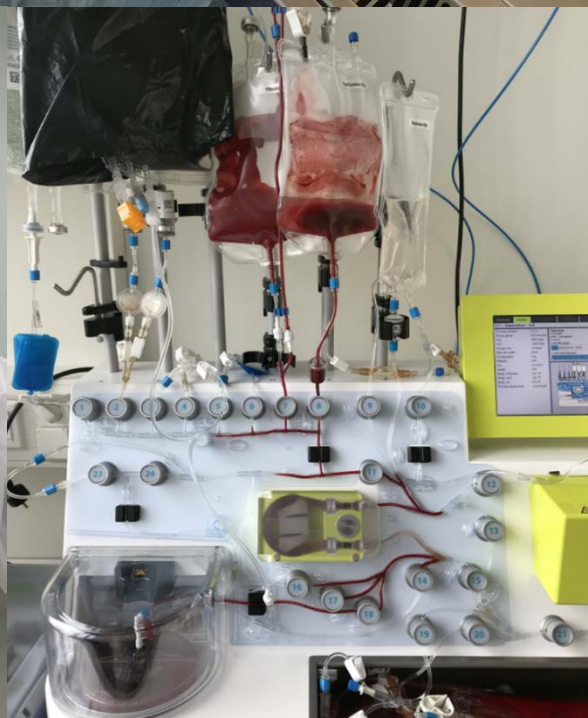
Different products are expanded to different specifications

- Clinical trials may target specific cell populations
- Development of regulations on cell count and viability has led to “generic” product

. Zhang C, et al. *Biomark Res*. 2017;5:22..



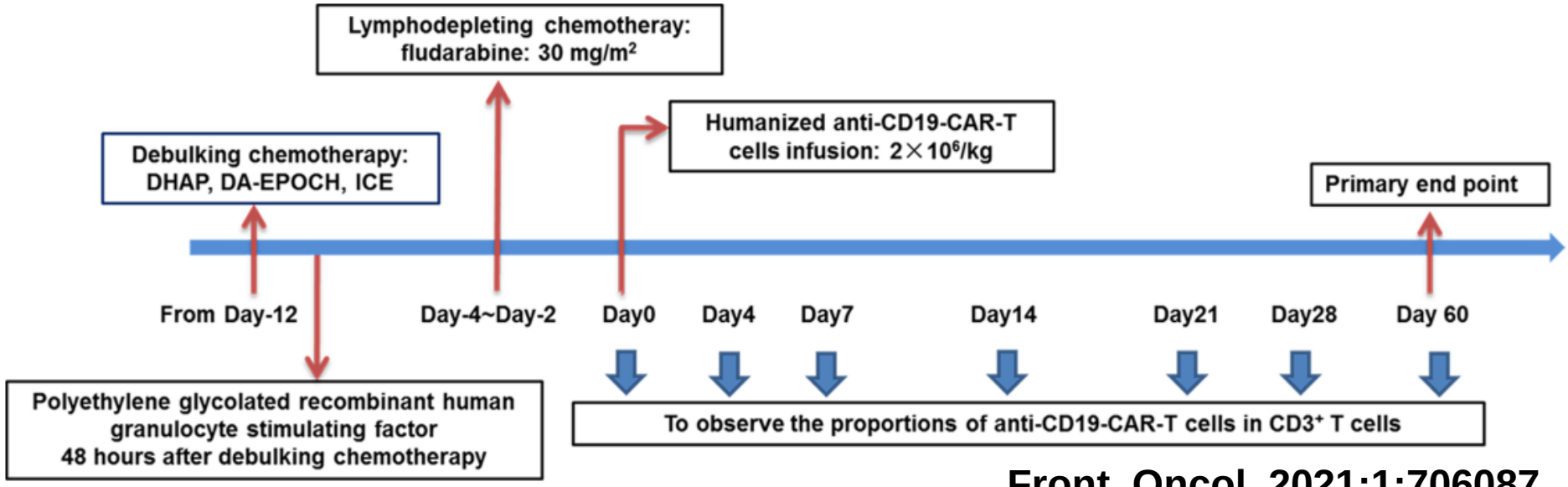

TERUMO



Debulking
- chemotherapy to decrease disease burden

To decrease circulating cells to reduce likelihood of tumor lysis syndrome or CRS because patients with bulky disease or excessive blasts in marrow are significantly at higher CRS risk. Typically use a standard regimen (e.g., ICE, EPOCH, hyper-CVAD), even if disease was previously refractory or chemotherapy resistant

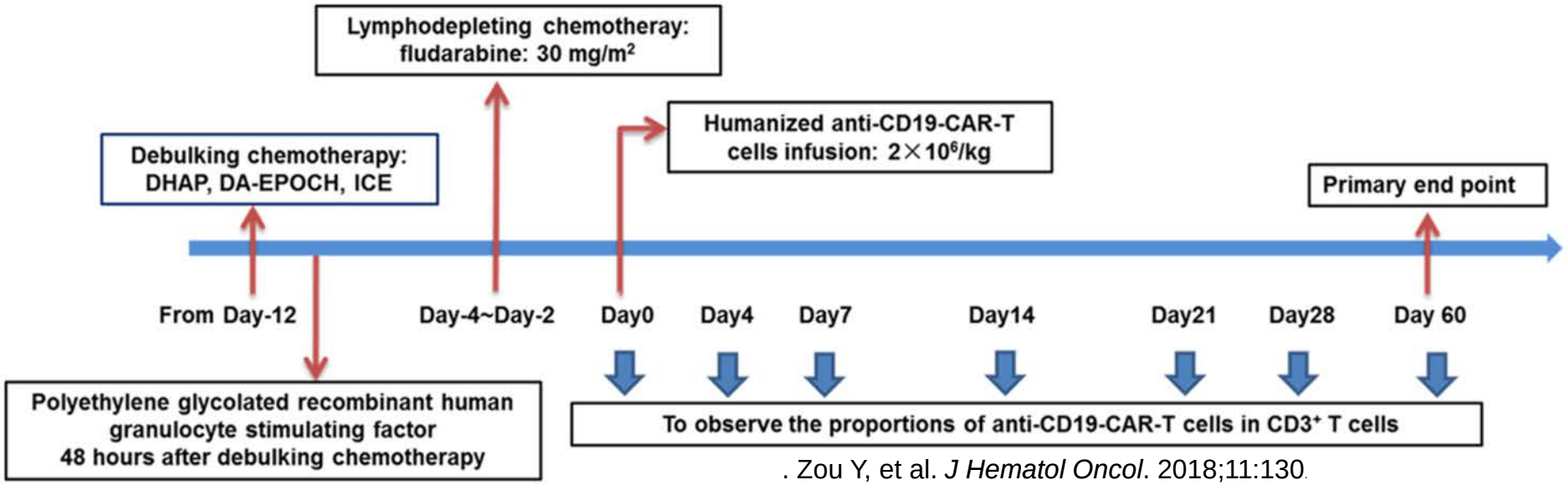
EPOCH, etoposide phosphate, prednisone, vincristine sulfate, cyclophosphamide, and doxorubicin hydrochloride; ICE, ifosfamide, carboplatin, and etoposide; hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone.



Front. Oncol. 2021;1:706087

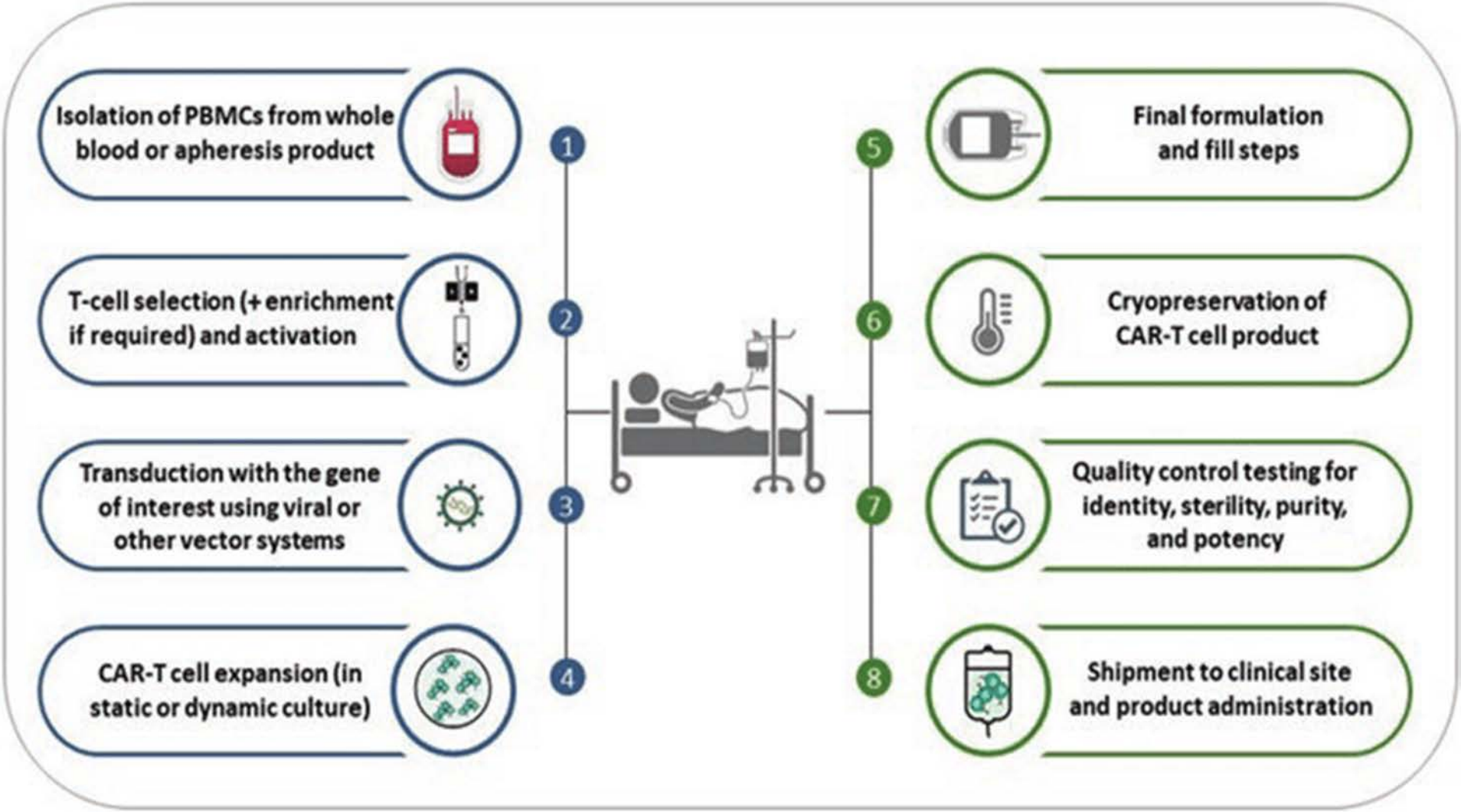
Lymphodepletion
- to reduce endogenous nonengineered T cells and improve response to CAR T-cell therapy

Lymphodepletion is a chemotherapy step prior to infusion of cell product, can be repeated if necessary due to delays. Utilizes conventional chemotherapy - cyclophosphamide and fludarabine. Bendamustine approved as alternative.May be omitted if pancytopenic under specific product guidelines
Not a myeloablative regimen, as this is not a stem cell transplant



. Zou Y, et al. *J Hematol Oncol*. 2018;11:130.

Cell Delivery
currently takes 2 to 4 wk “vein-to-vein”



Common Adverse Events Associated With CAR T-Cell Therapy

Common Adverse Events

- Toxicity associated with classical cytotoxic chemotherapy in debulking and lymphodepleting regimens
  - Nausea, vomiting, alopecia, anorexia, myelosuppression, etc
- Unique side effect profiles due to cytokine release and neurotoxicity

Neurotoxicity

- Occurred in 40% to 57% within 8 weeks of infusion[1,2]
- Typically occurred during or shortly after CRS[1]
- Considered manageable and reversible, but can be life-threatening or fatal[2]

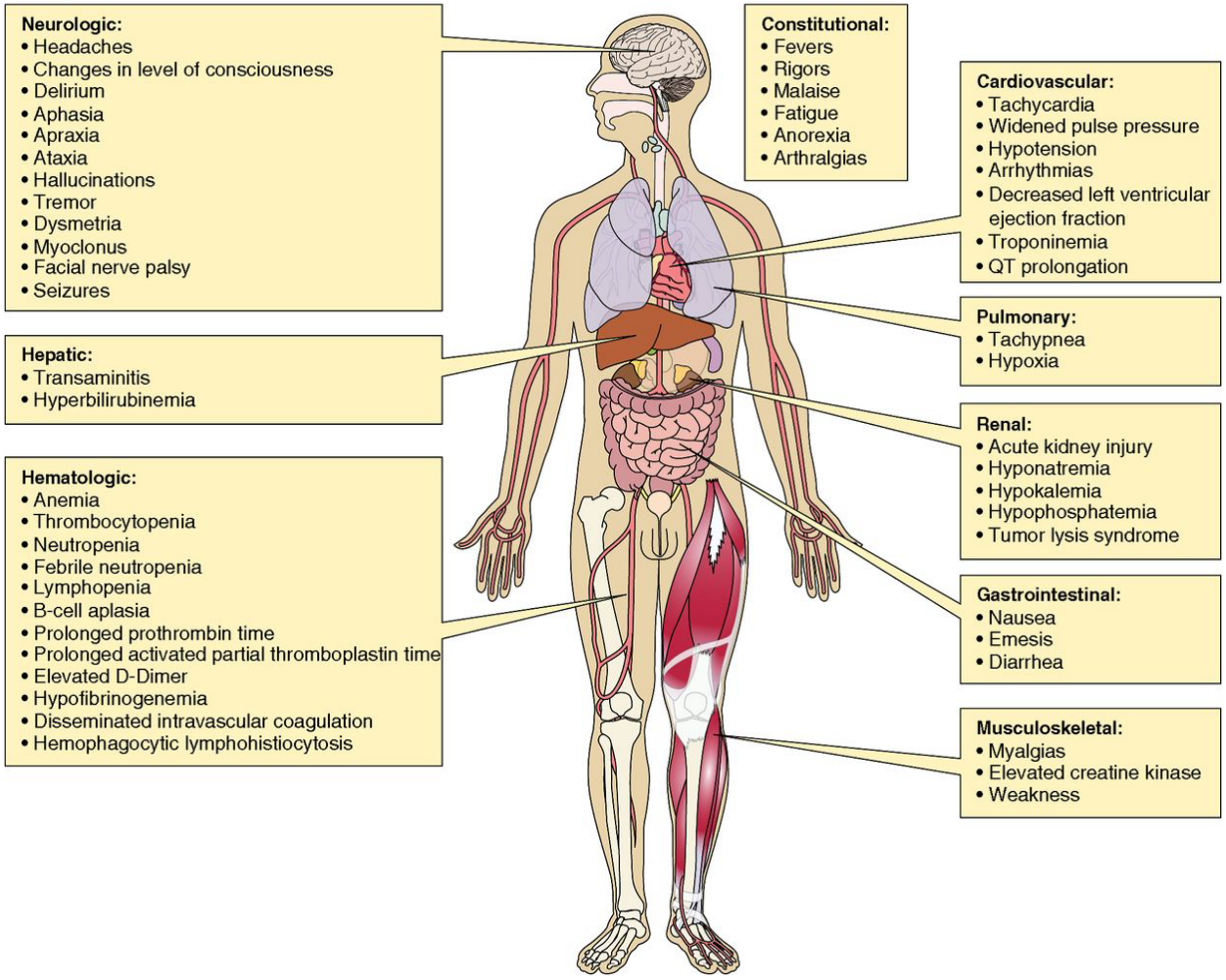
Cytokine Release Syndrome

- Occurred in 77% to 94% of patients in clinical trials[1,2]
- Median time to onset was 3 days[1]
- Median duration was 8 days[1]
- Considered manageable and reversible with early recognition and intervention, but potentially fatal

Locke FL, et al. *Lancet Oncol*. 2019;20:31-42.

CRS: Symptoms

Common symptoms of CRS
- Fever
- Chills
- Hypotension
- Tachypnea and shortness of breath
- Acute kidney injury
- Hepatoxicity
- Myelosuppression
  - Beyond 28 days in approximately 30% of patients
- Coagulopathy



Brudno JN, Kochenderfer JN. *Blood*. 2016;127:3321-30.

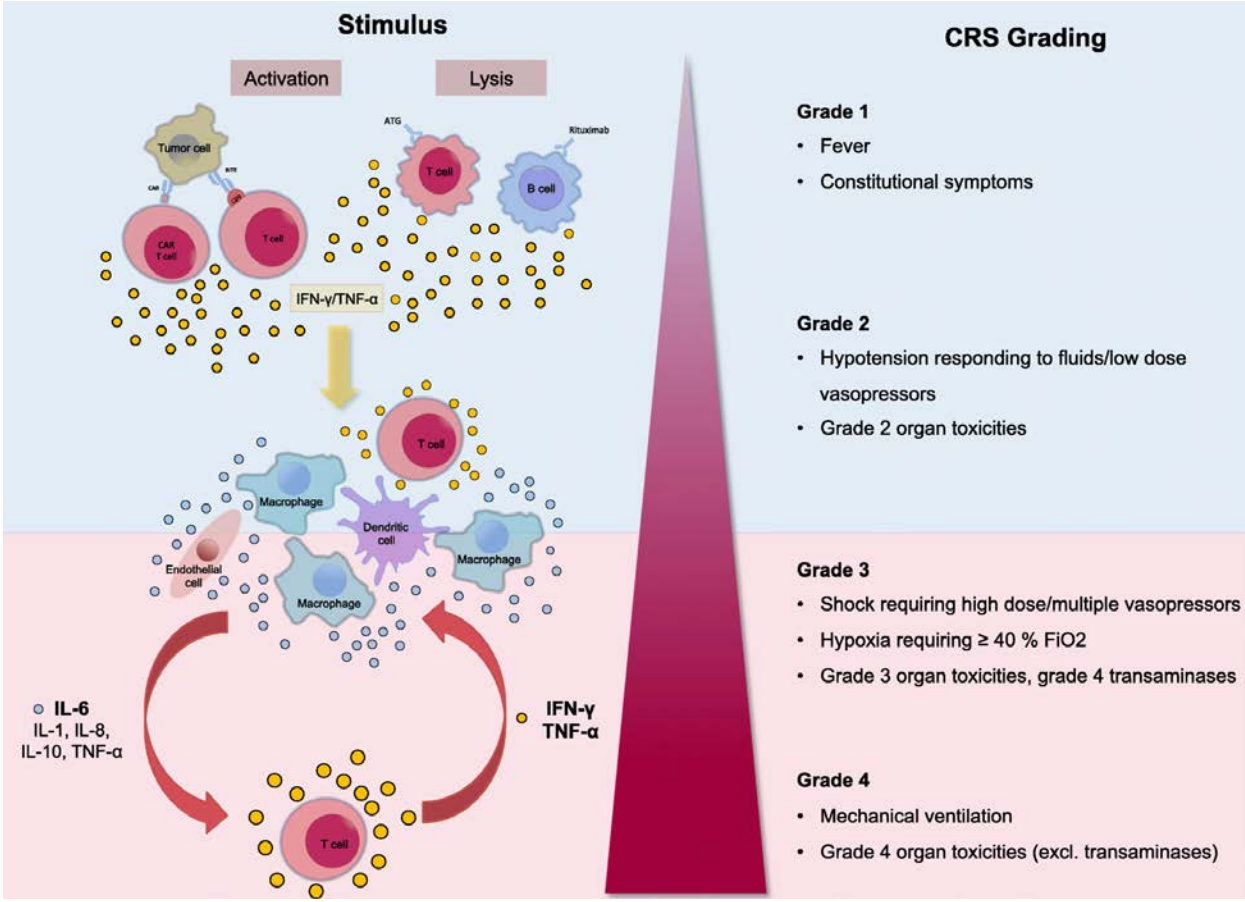
CRS: Mechanism and Grading

Systemic inflammatory response associated with immune activation

- High degree of circulating IL molecules, specifically IL-6

Grading currently based on symptoms, organ toxicities, and supportive care required

Currently, there are multiple grading systems, but there is work toward creating a consensus grading



. Riegler LL, et al. *Ther Clin Risk Manag*. 2019;15:323-35.

Treatment of CRS

Tocilizumab is the only FDA-approved agent for the treatment of CRS

- Both FDA-approved CAR T-cell products require that 2 vials of tocilizumab per patient are on hand prior to CAR T-cell infusion
- Blocks IL-6 receptor
- Used to treat moderate to severe CRS

Dexamethasone or methylprednisolone for severe CRS or failure of tociluzumab

Siltuximab

- Less extensively studied and not part of REMS
- Binds to circulating IL-6

Anakinra

- Even less studied than siltuximab
- Binds to IL-1 receptor

Mahmoudjafari Z, et al. *Biol Blood Marrow* Transplant. 2019;25:26-33.

Neurotoxicity

- Encompasses a spectrum of CNS toxicity
  - Including: confusion or delirium, paranoia, aphasia, somnolence, seizures, insomnia, encephalopathy, and death[1,2]
- Wide range of time to onset
  - 48 hr to 4 wk[3,4]
- Treated with supportive care through management of any concurrent CRS
- Dexamethasone or methylprednisolone per product algorithms or clinical trial design[3,4]
- Tocilizumab when concurrent with CRS
- Lack of imaging does not rule out CAR T-cell neurotoxicity
  - Cerebral edema a late sign with very poor prognosis
- Antiepileptics may be utilized per institutional standard, although not required by current REMS
- Limit driving, heavy machinery, dangerous activities, etc for approximately 4 to 6 wk
  - Can be individualized based on concern for CNS toxicity
- Provide extensive caregiver education

Gust J, et al. *CNS Drugs*. 2018;32:1091-101.

Long-Term Follow-Up

- Monitoring by caregivers for delayed CRS and neurotoxicity
- Clinic and laboratory follow-up for prolonged or delayed cytopenias
- Antibiotic prophylaxis for neutropenia and trimethoprim-sulfamethoxazole for pneumocystis jiroveci pneumonia prophylaxis
- Hypogammaglobulinemia, secondary to B-cell depletion by CD19-targeted CAR-T products, may be treated per clinic preference or reserved for patients with recurrent infections or other risk factors
- Antiepileptic prophylaxis per clinic protocols
- Disease specific monitoring for relapse
- T cell–specific monitoring, albeit unclear significance at this time

Doan A, Pulsipher MA. *Pediatric Blood Cancer*. 2018;65:e26914.

Conclusions

- CAR T-cell therapy represents new and novel management strategy for the treatment of B-cell malignancies, hematologic and solid tumors, autoimmune diseases.
- Awareness of the current treatment landscape, including the clinical trial landscape, is critical to effectively manage patient expectations and direct patients to appropriate therapy.
- Although CAR T-cell treatment is neither a conventional chemotherapy nor a hematopoietic stem cell transplant, it can be used in conjunction with either or both to manage aggressive disease.
- The side effects of CAR T cells are unique and require practitioner and institution experience and expertise to provide early and effective intervention.

Thank You!!

Univerza v Ljubljani