Memorial Sloan Kettering Cancer Center

CAR T cell therapy for brain tumors

Bench to bedside to bench

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2/25/2026

1

CAR T Cells and CNS Malignancies

- Current trials: efficacy and toxicity signal
- Challenges
- Paper discussion
- Translational examples: bench to bedside to bench

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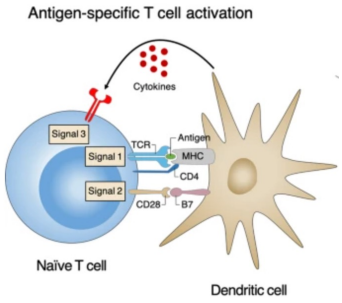
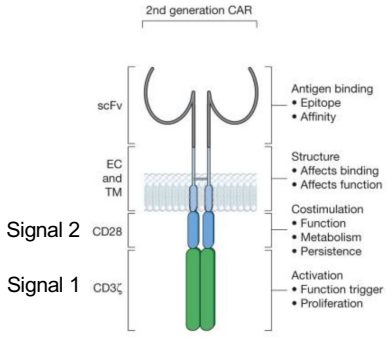
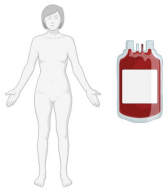
2

CAR T cell basics





Apheresis



CAR transduction and expansion

Infusion following lymphodepleting chemotherapy

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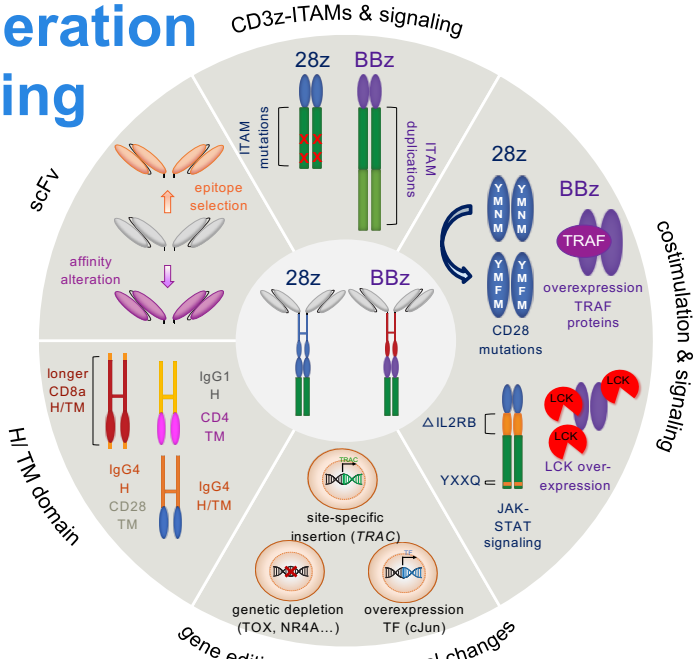
3

Next generation engineering



Feucht and Sadelain, IOTECH 2020

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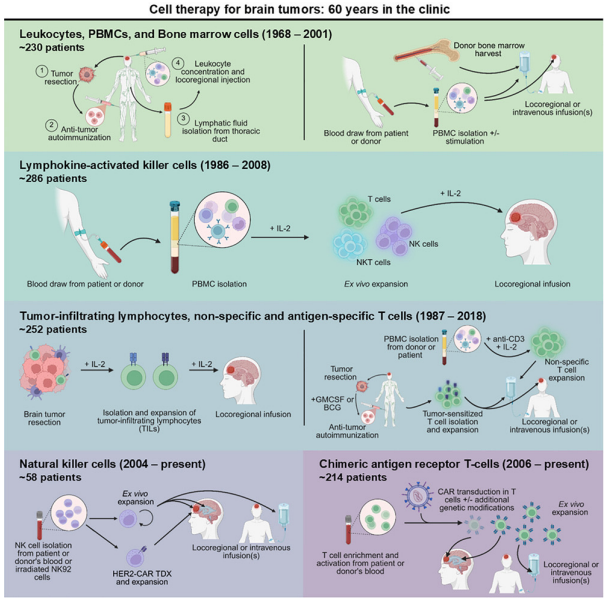
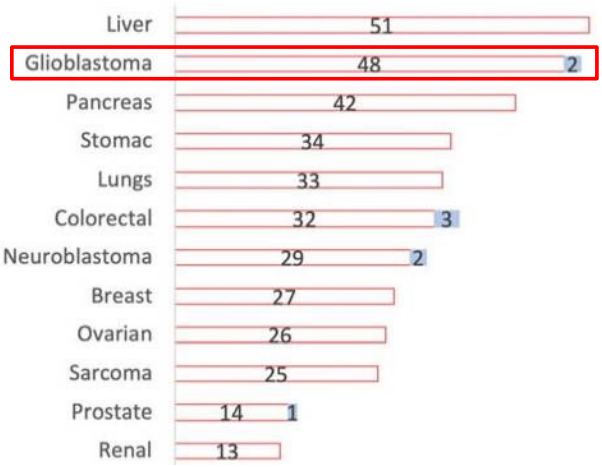
Cell therapy and CNS malignancies



Mehta et al., Cell Rep Med 2026

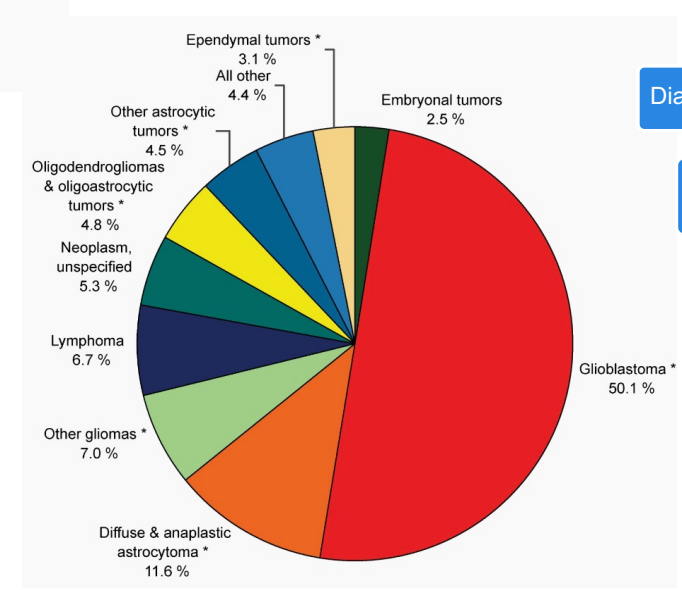
Number of CAR T cell clinical trials for solid tumors



Wang et al., Cancers 2023

5

Glioblastoma (GBM): mOS 14-16 months



Ostrom et al., Neuro-oncology 2022

Diagnosis, neurosurgery

Tumor irradiation (6 weeks) with daily temozolomide

Monthly temozolomide

Recurrence
- NO STANDARD OF CARE
- Re-irradiation
- Re-operation
- Change in chemotherapy regimen
- Clinical trial

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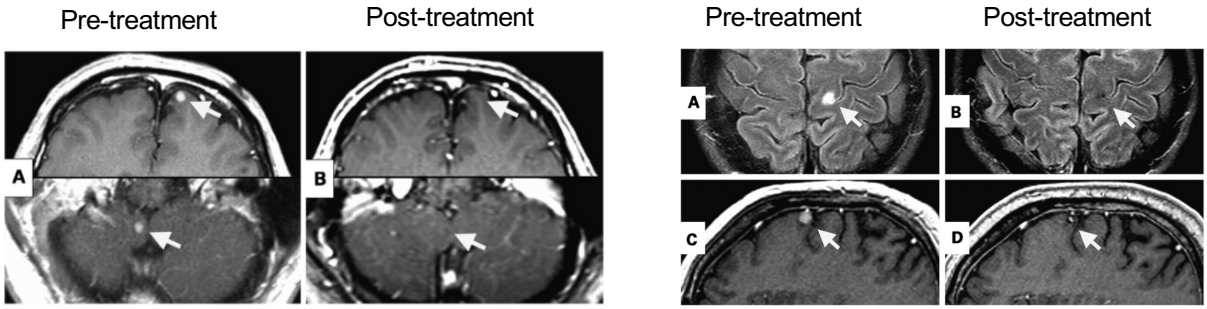
Adoptive T Cell Therapies Mediate Regression of Melanoma Brain Metastases



Tumor infiltrating lymphocytes

T cell receptor targeting gp-100 or MART-1

13/17 (77%) ORR
7/17 (41%) CR

Hong et al., Clin Cancer Res 2010

7

CAR T cells mediate tumor regression in CNS lymphoma

Study	Institution	Disease	Product	Responses
Epperla et al., Br J Haematol 2024	CIBMTR	136 SCNSL	Tisa-cel (60%) Axi-cel (33%) Liso-cel (6%)	**53% CR** **2yr PFS 21%**
Mercadal et al., Haematol 2025	CIBMTR	24 PCNSL	Tisa-cel (88%) Axi-cel (12%)	**46% CR** **1yr PFS 48%** **2yr PFS 28%**
Choquet et al., AJH 2024	LOC network, France	25 PCNSL	Tisa-cel (64%) Axi-cel (36%)	**64% CR** **1yr and 2yr PFS 43%** mPFS 8.4 vs. 3 mos (historical controls)
Cook et al., Blood Adv 2023	Meta-analysis	128 PCNSL 98 SCNSL	PCNSL: 63% Tisa SCNSL: 50% Axi	**PCNSL: 56% CR** **SCNSL: 47% CR** **6mo PFS 37%**

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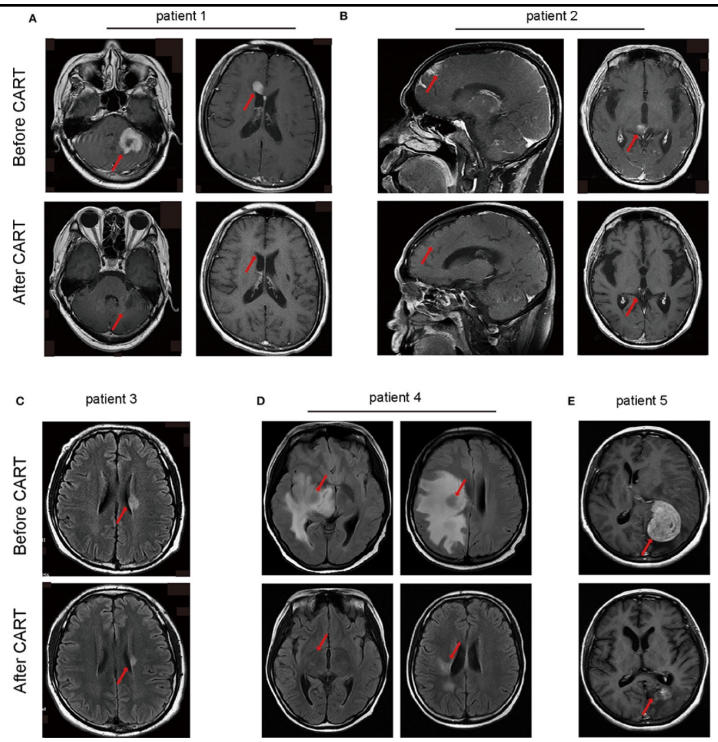

Li et al.,
Front Oncol 2020

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IL13RA2-targeting CAR T cells mediate regression of GBM with leptomeningeal involvement

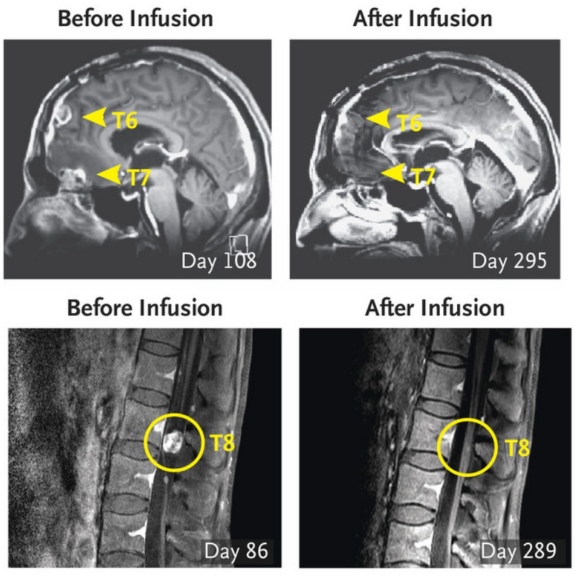
6 weekly doses into resection cavity with SD

↓

Progression at 1.5 months

↓

10 doses intraventricularly with CR for 6 months

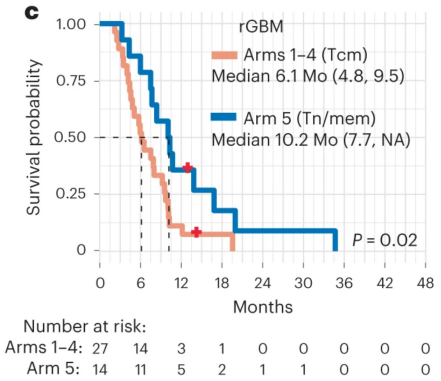


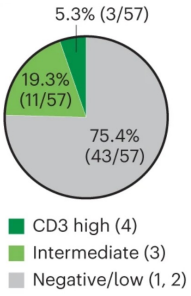
Brown et al., NEJM 2016

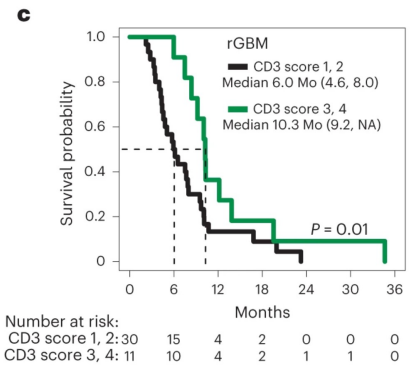
10

Locoregional delivery of IL13RA2-targeting CAR T cells for rHGG: tumor responses

- No additional objective responses in IDH-wt rGBM patients



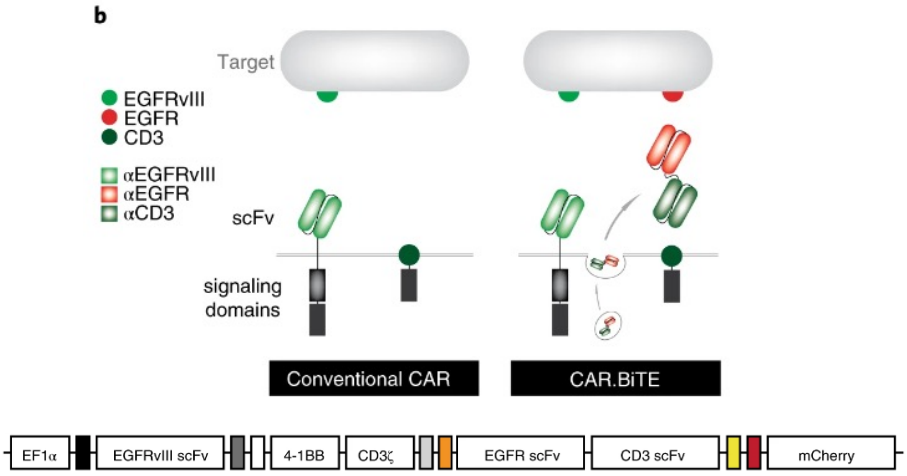




Brown et al., Nat Med 2024

11

EGFRvIII targeting CAR T cells secreting an EGFR BiTE for the treatment of GBM



Choi et al., Nat Biotech 2019

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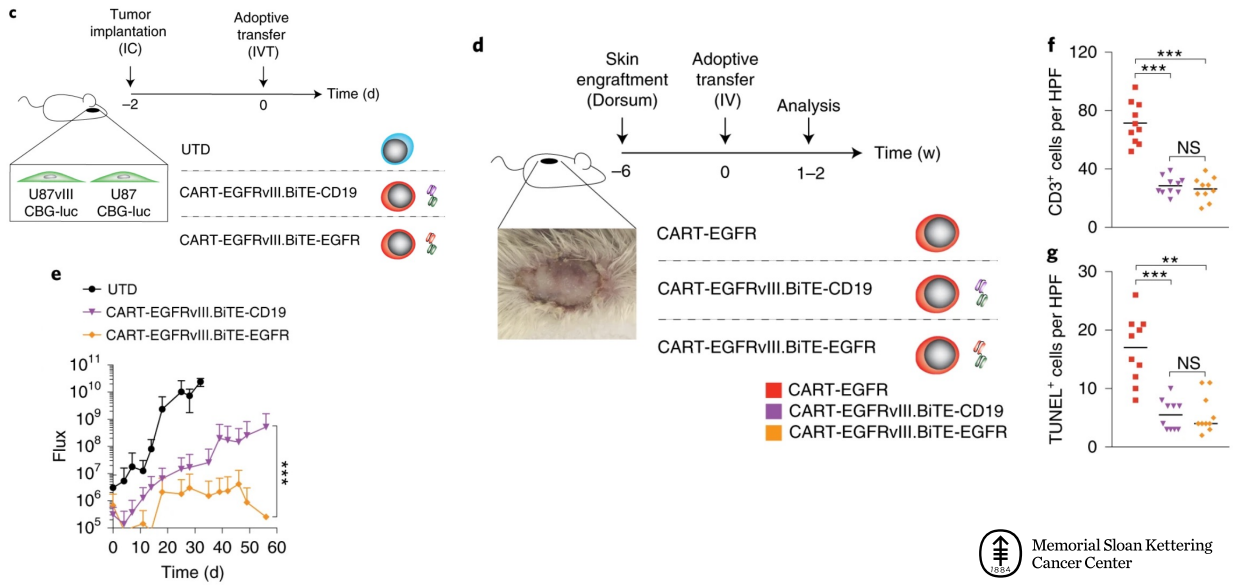
BiTE-secreting CARs display efficacy and safety against heterogenous tumors



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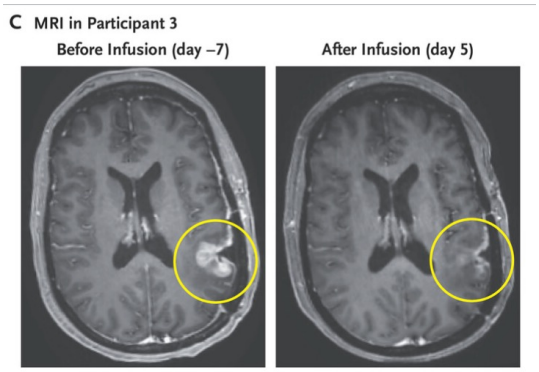
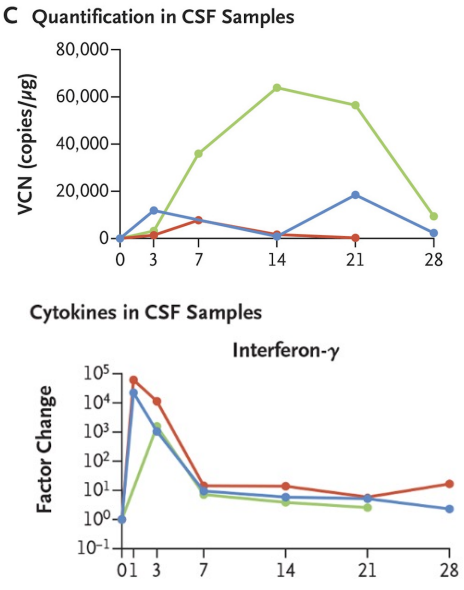
Three of three patients had objective responses at a low dose of CAR T cells, but relapsed

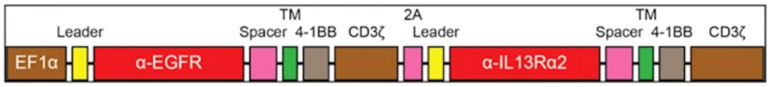


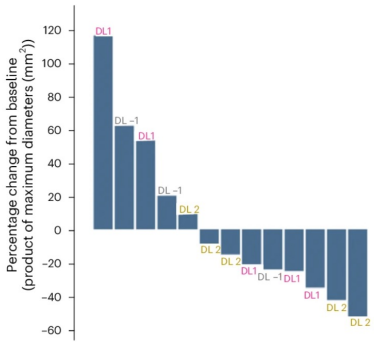
Choi et al., NEJM 2024

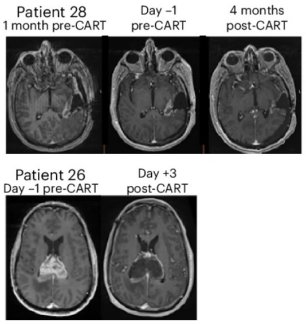


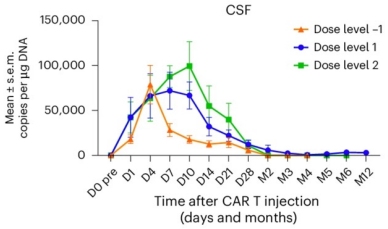
14

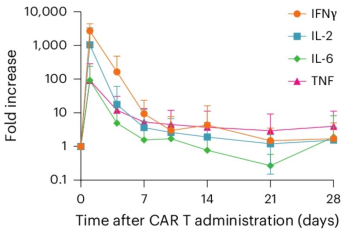
EGFR(806) and IL13Rα2-targeting dual CAR T cells can reduce tumor size, but lack durability











Bagley et al., Nat Med 2024, 2025

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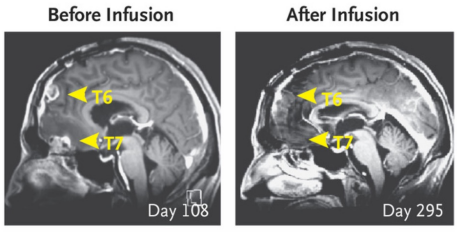
15

Recent trials with an additional layer of cell engineering report more consistent tumor responses in GBM, but they are transient

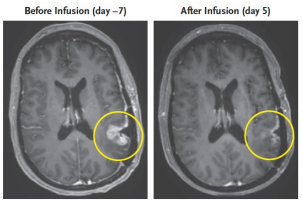
Conventional CAR

IL13Rα2-BBz CAR
Decreased tumor size:
1 of 41 IDH-wt rGBM pts



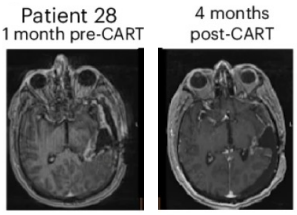
Brown et al., *NEJM* 2016
Brown et al., *Nat Med* 2024

Conventional CAR + one layer of engineering



EGFRvIII-BBz CAR + EGFR BiTE
Decreased tumor size:
3 of 3 IDH-wt rGBM pts

Choi et al., *NEJM* 2024

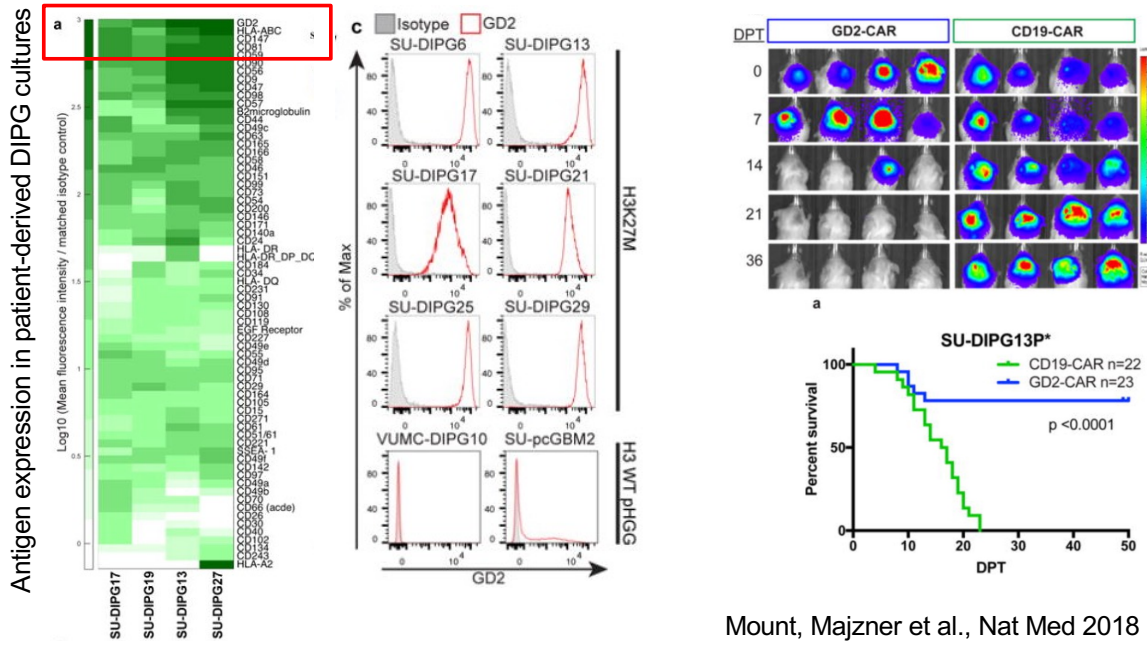


EGFR806-BBz + IL13Rα2-BBz CAR
Decreased tumor size:
8 of 13 IDH-wt rGBM pts

Bagley et al., *Nat Med* 2025

16

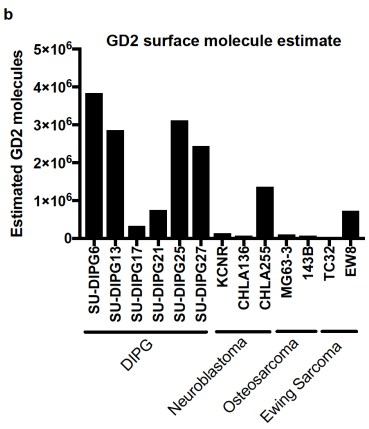
GD2 targeted CAR T cells for DIPG



Mount, Majzner et al., Nat Med 2018

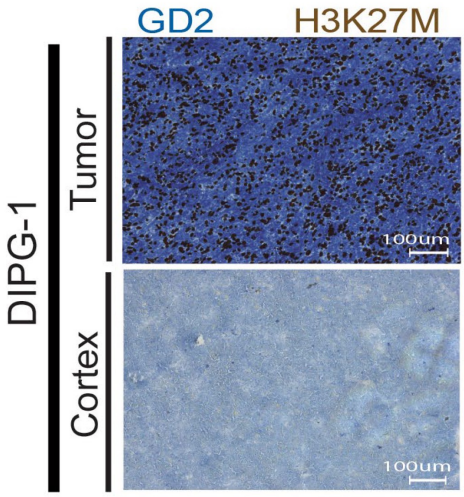
17

GD2 targeted CAR T cells for DIPG



500,000 to 4,000,000
GD2 molecules/cell

Mount, Majzner et al., Nat Med 2018

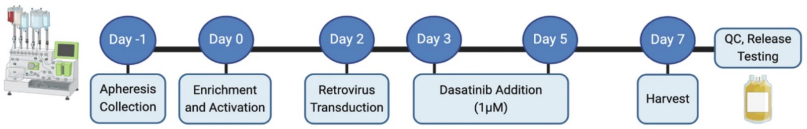


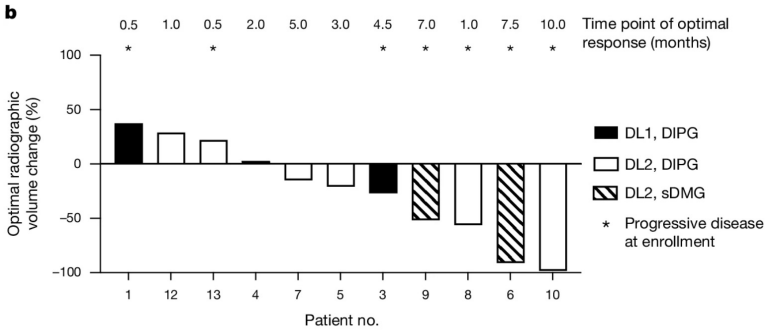
Therapeutic window

Majzner, Ramakrishna et al., Nature 2022

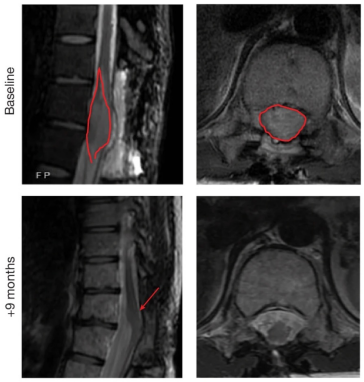
18

GD2 CAR T cells mediate tumor responses and neurologic improvement in DIPG/DMG

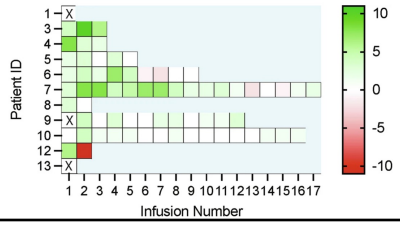




Monje et al., Nat Med 2024



Clinical improvement score



19

Correlatives

- Paper discussion

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20

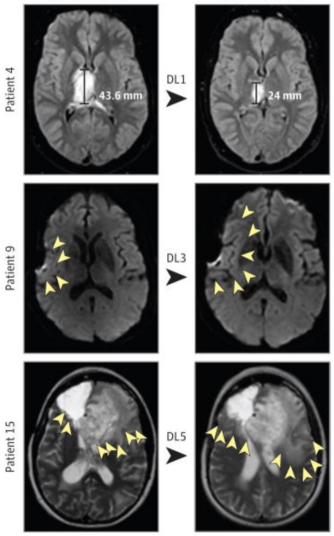
Toxicity attributable to CAR T cells

CNSL	Other CNS tumors		
Similar to systemic lymphoma	Cytokine release syndrome	Neurologic events: headaches, seizures	Tumor inflammation associated neurotoxicity (TIAN)
	Generally low-grade	Generally low-grade	Thus far either non-life threatening or reversible
			Treatment: CSF removal, steroids, anakinra

21

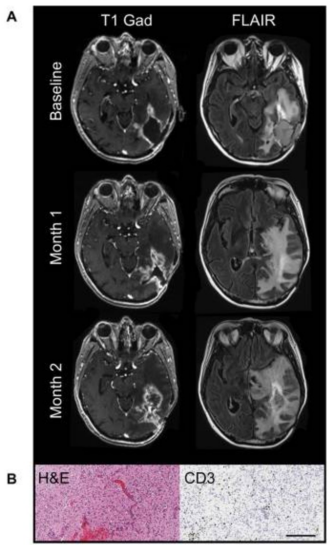
Glioma inflammation following treatment

HER2-28z



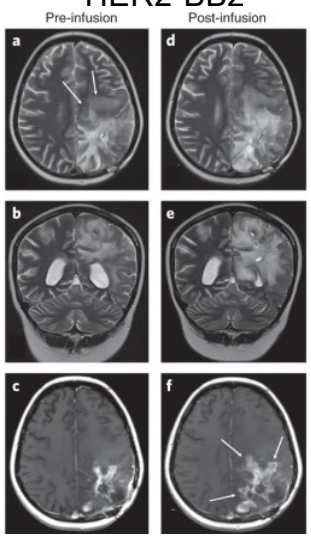
Ahmed et al., JAMA Oncol 2017

EGFRvIII-BBz



O'Rourke et al., Sci Transl Med 2017

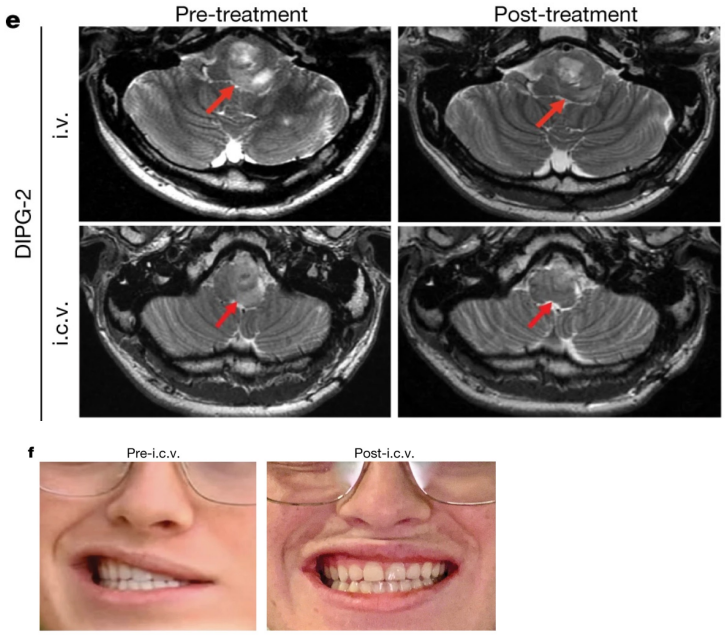
HER2-BBz



Vitanza et al., Nat Med 2021

22

DIPG inflammation following Ommaya infusion

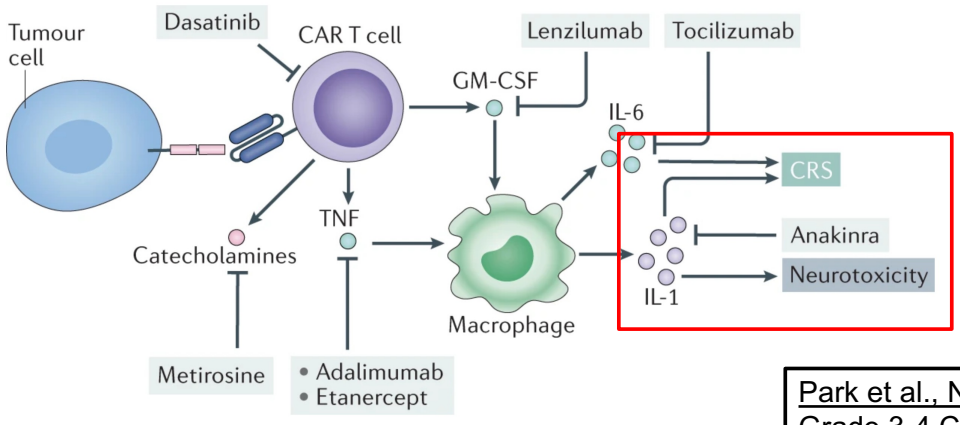


- Recurrence 2-3 months after IV infusion
- Ommaya infusion
  - D1: Tmax 40 C
  - D2: somnolence, CN3 palsy
    - ICP 34 due to obstructive hydro
    - Immediate improvement w CSF removal
    - Hypertonics, anakinra, steroids
    - 2d CSF drainage with Ommaya
    - 4d steroids
  - D14: improved MRI and neuro exam

Majzner, Ramakrishna et al., Nature 2022

23

IL-1Ra (Anakinra) and toxicity management



Park et al., Nat Med 2023
Grade 3-4 CRS: 6%
Grade 3-4 ICANS: 10%

Giavridis et al., Nat Med 2018
Morris et al., Nat Rev Immunol 2021

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24

Challenges

- Antigen heterogeneity
- Immunosuppressive Microenvironment
- Trafficking

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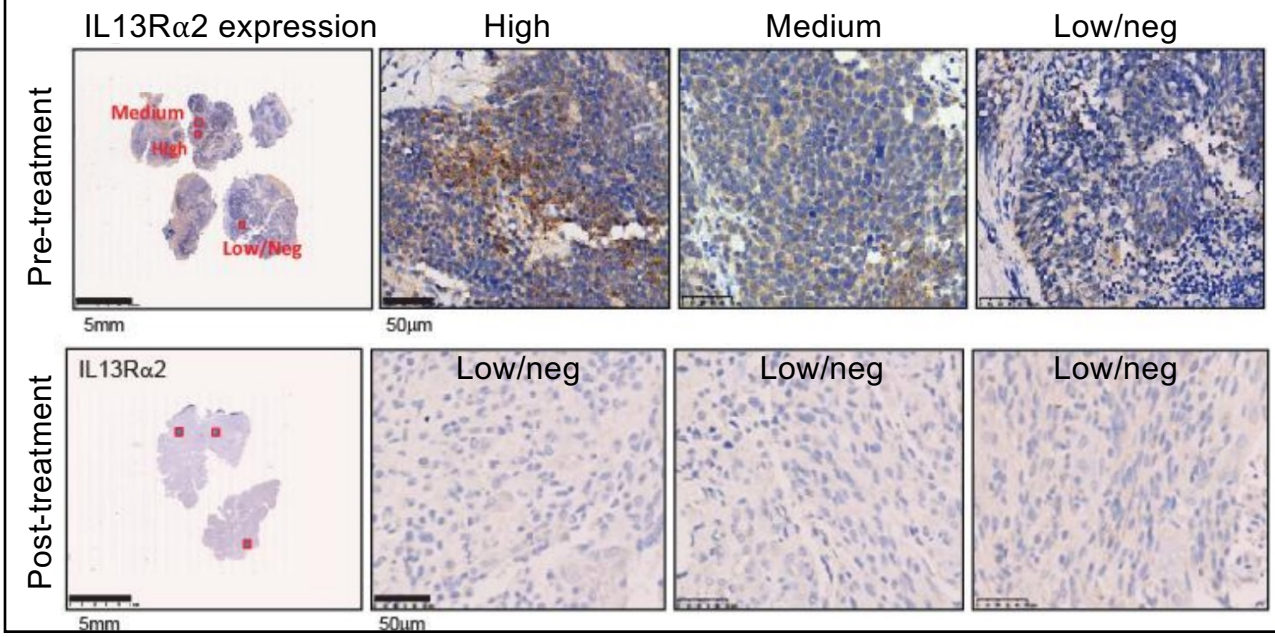
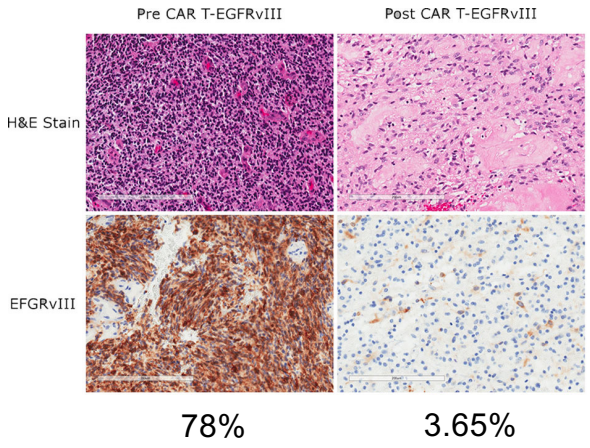
Challenges: Heterogeneity

Brown et al., NEJM 2016



26

Challenges: Heterogeneity



Durgin et al., Front Oncol 2021

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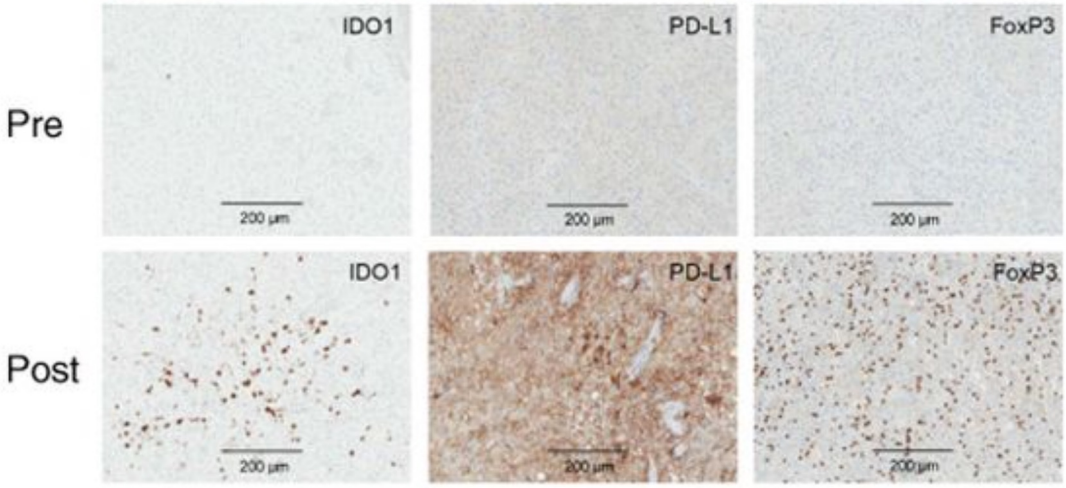
27

Challenges: Immunosuppressive Microenvironment



O'Rourke et al., Sci Transl Med 2017

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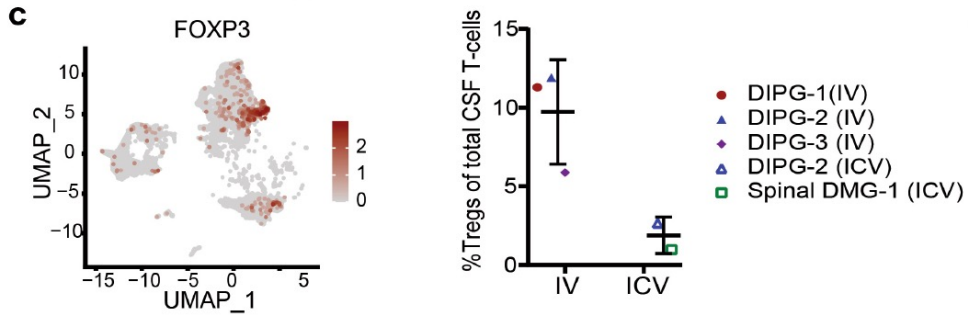
28

Challenges: Immunosuppressive Microenvironment



Majzner, Ramakrishna, et al., Nature 2022

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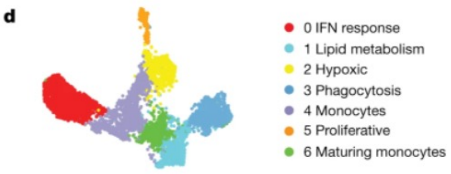
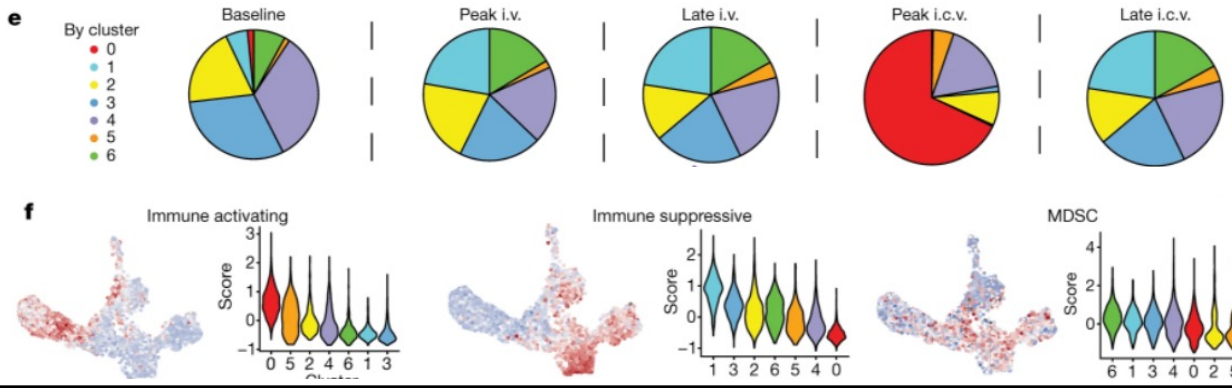
29

Challenges: Immunosuppressive Microenvironment

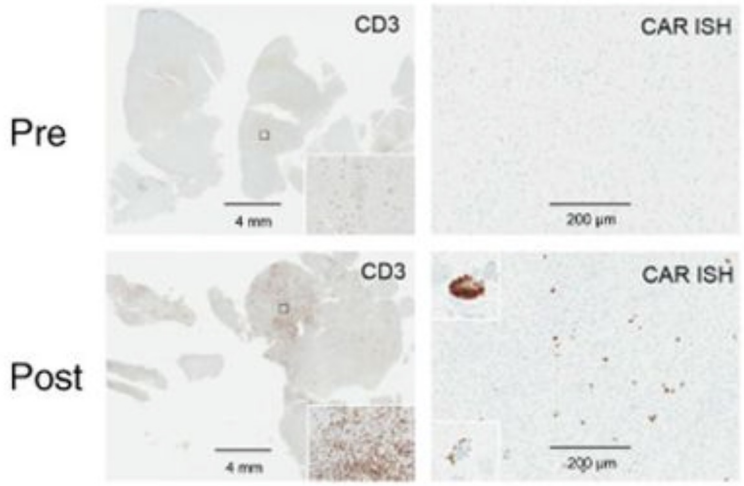


Majzner, Ramakrishna, et al., Nature 2022



30

Challenges: Trafficking



O'Rourke et al., Sci Transl Med 2017

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31

Clinical Trials of CAR T Cells for Brain Tumors: General Summary

All data are from Phase I trials

Toxicity attributable to CAR T cells

- Generally low-grade CRS and neurologic events
- Tumor inflammation
- Generally non-life threatening or reversible

Objective radiographic responses

- Less frequent and transient in GBM
- Common for CNSL, occur for DIPG, but durability remains an issue

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32

Break

- Questions

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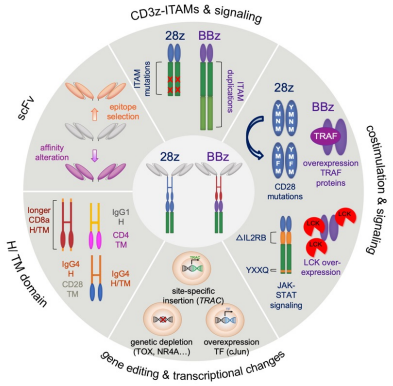
33

Developing a successful CAR T cell therapy for CNS tumors: bench to bedside to bench



Human Disease Challenges
↕
Cell Engineering Tools

Clinical trial
Correlatives
Biological validation

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34