

How deep is your love? B cell reset in autoimmune diseases

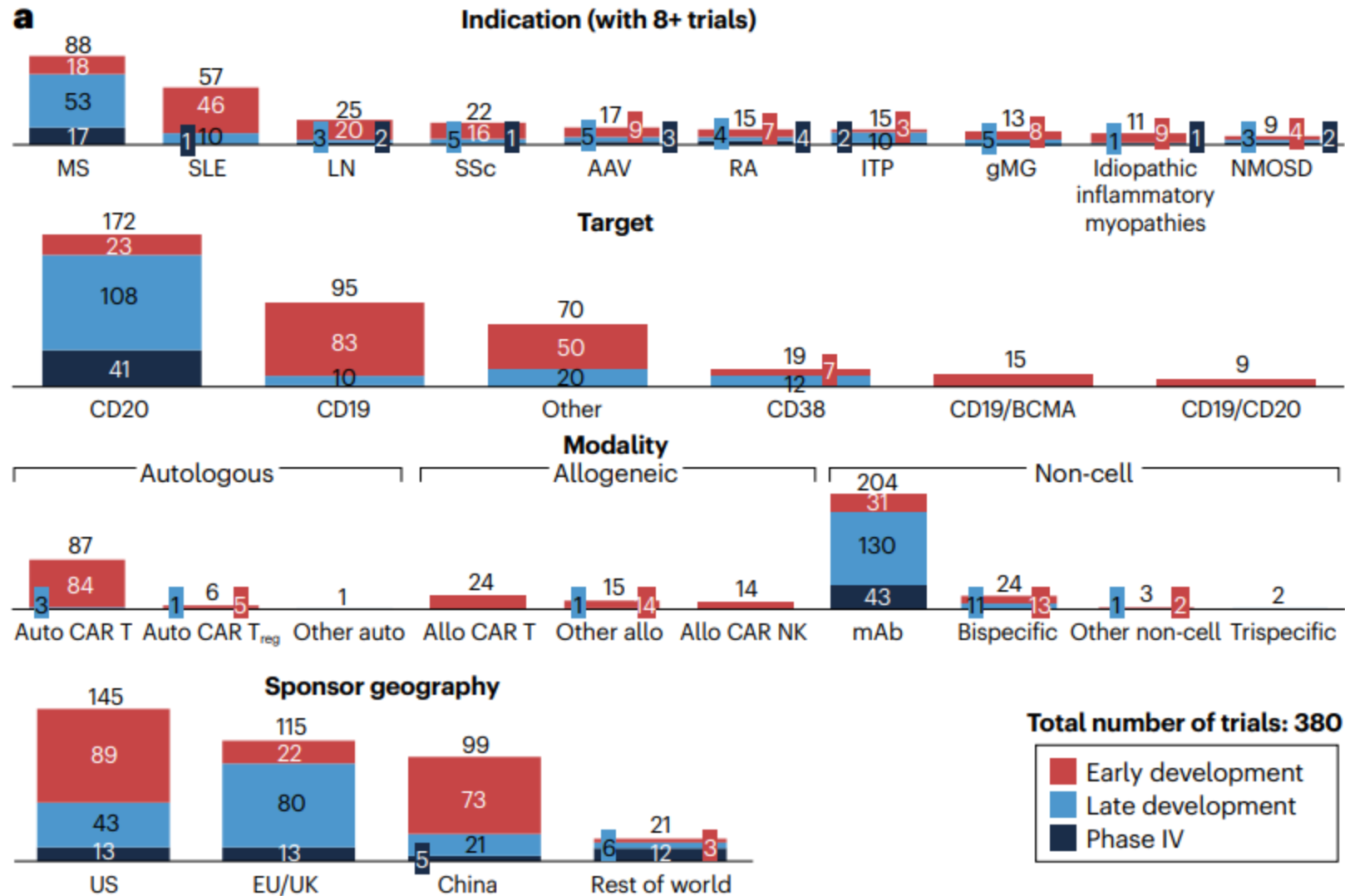


Cell Coast 2025 Debate:

Bispecific antibodies (Castaneda) or
CAR T cells (Jain) for autoimmune
disease?

Michael D. Jain, Moffitt Cancer Center
17 Oct. 2025

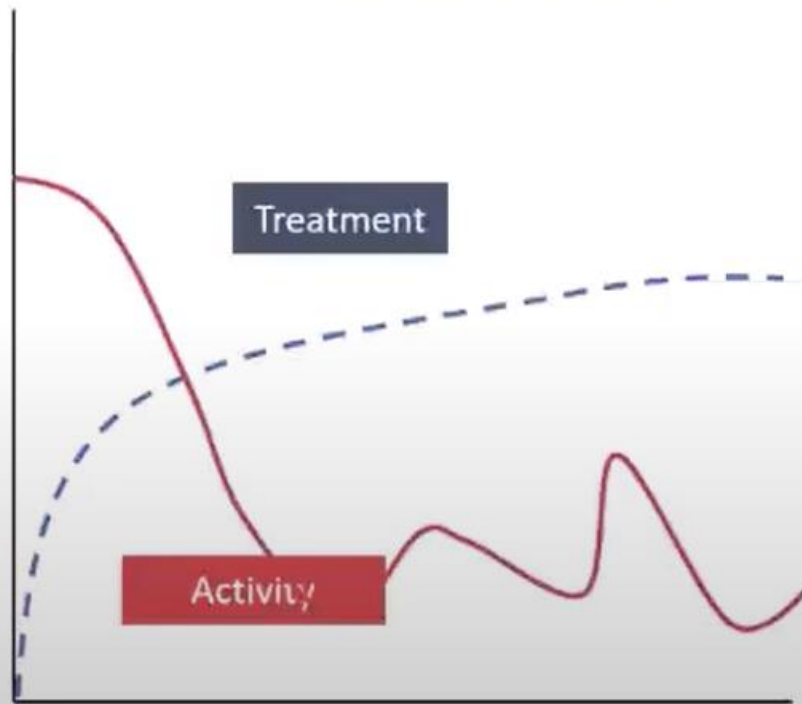
The race to reset autoimmune diseases



Restoring health- from suppression to cure?

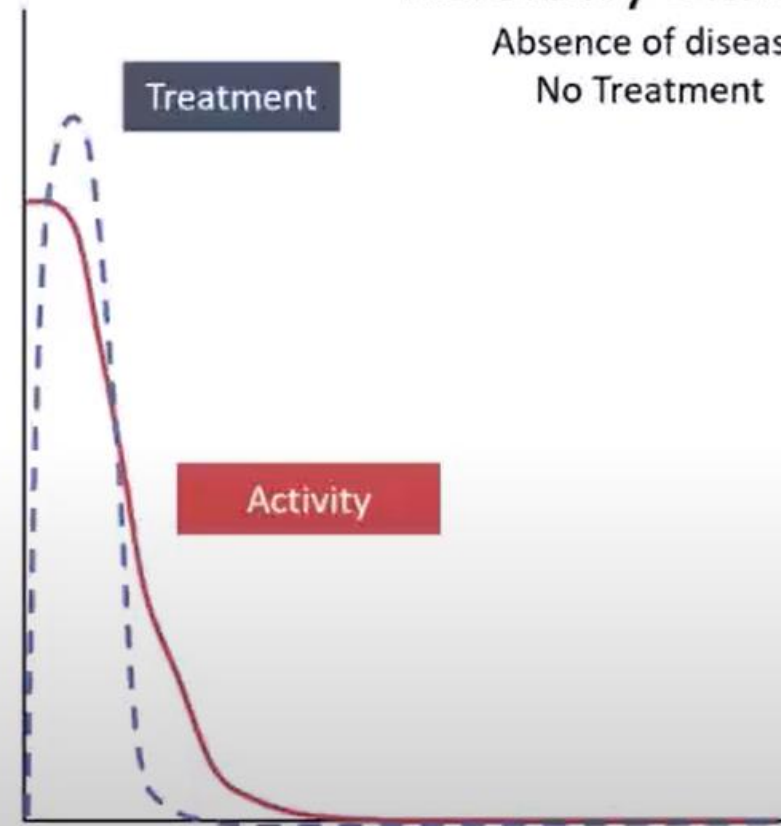
Traditional Scenario

Suppression of disease
Continuous Treatment



Visionary Scenario

Absence of disease
No Treatment

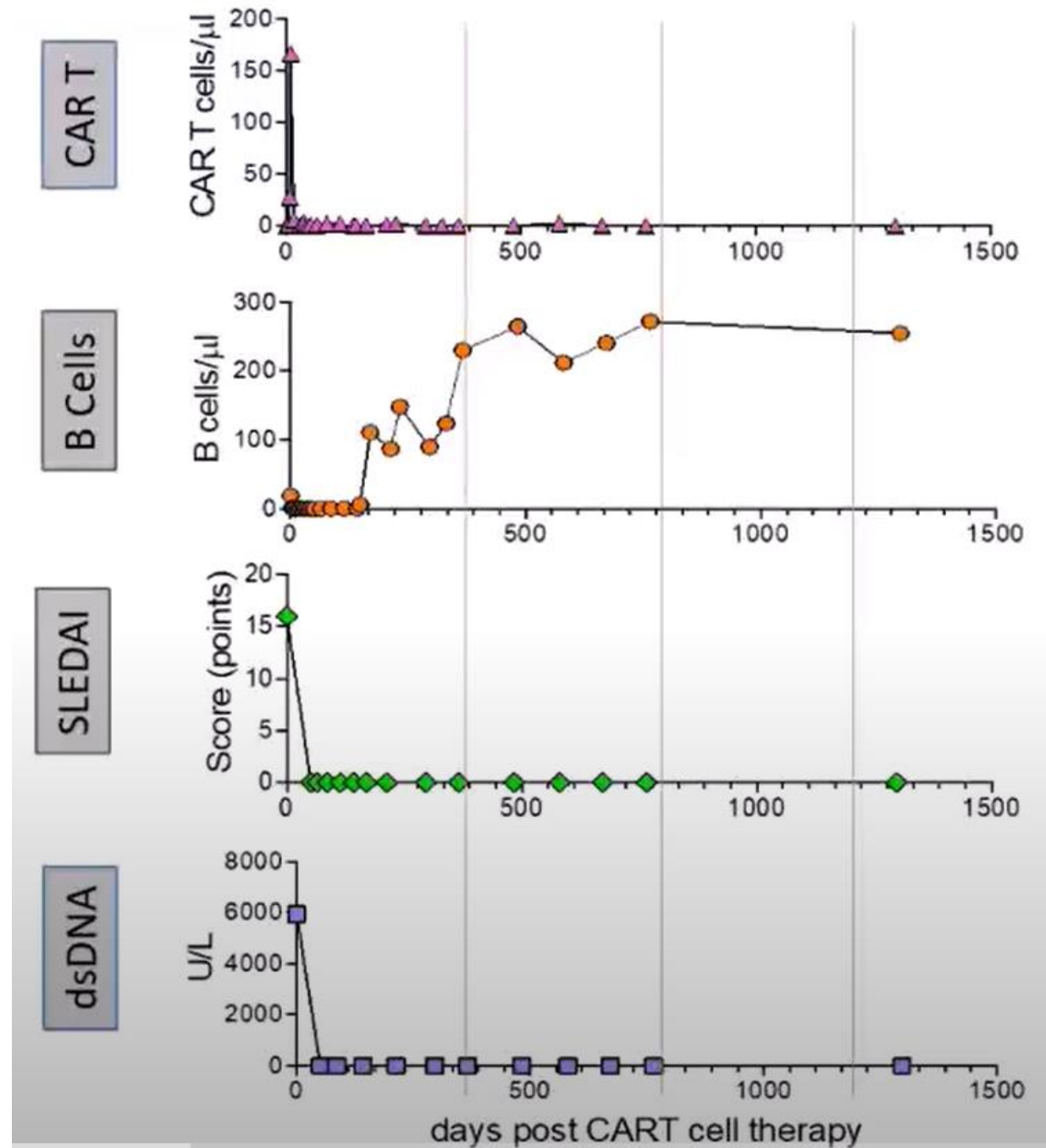


Why is it called an
“immune reset”?

Deep B cell
depletion, followed
by rapid recovery.

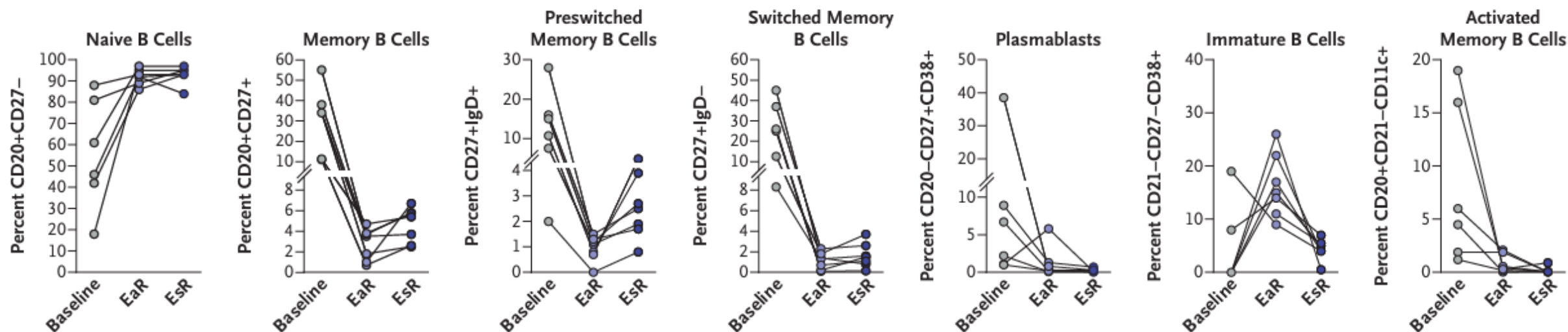
Auto-antibodies
remain negative.

G. Schett; based on Schett et al. NEJM 2021



After CAR T, B cells are “reset”

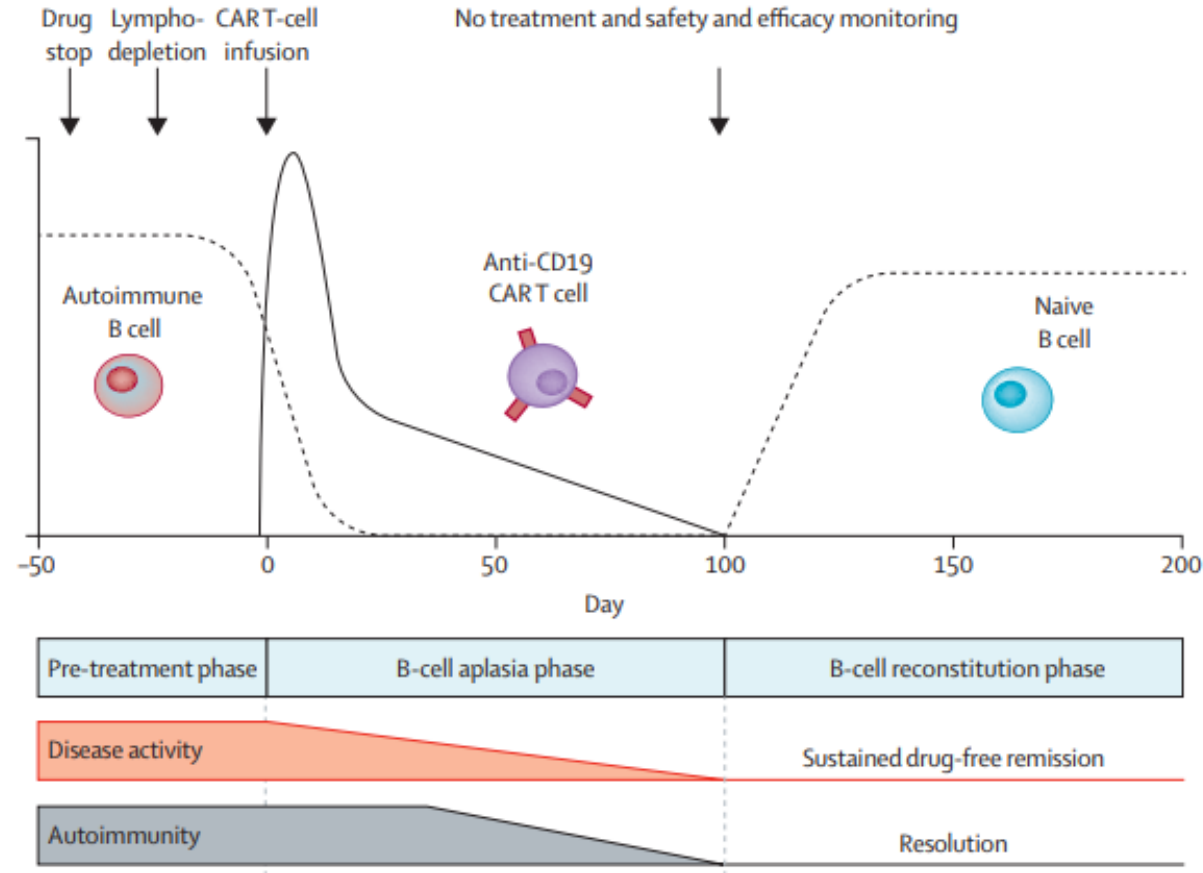
A Patients with SLE with More than 1 Yr of Follow-up after CD19 CAR T-Cell Therapy (N=6)



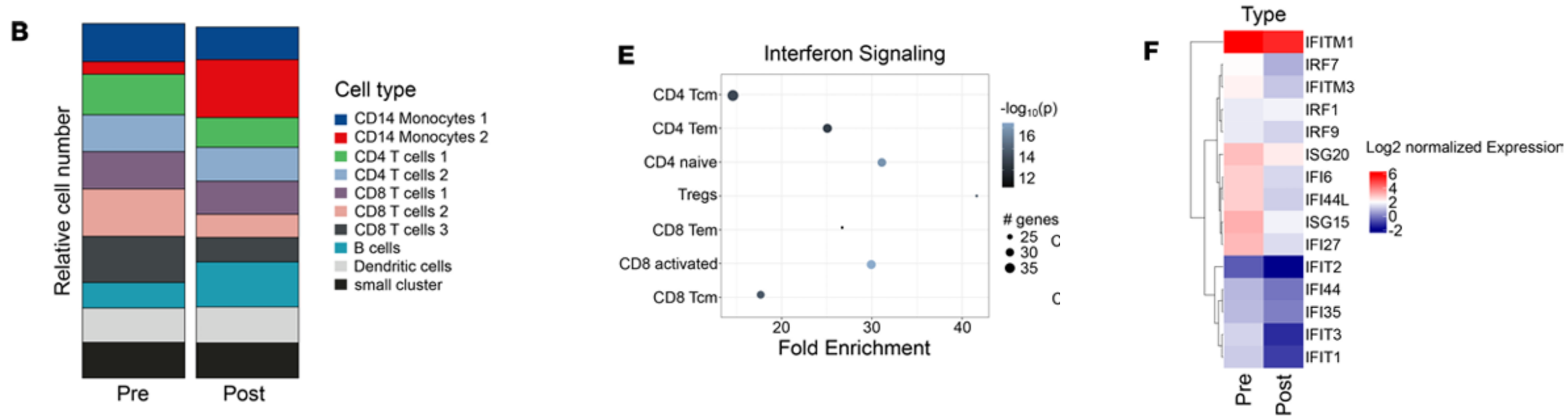
EaR = “early reconstitution” (4 months after CAR T).

EsR = “established reconstitution” (1 year after CAR T).

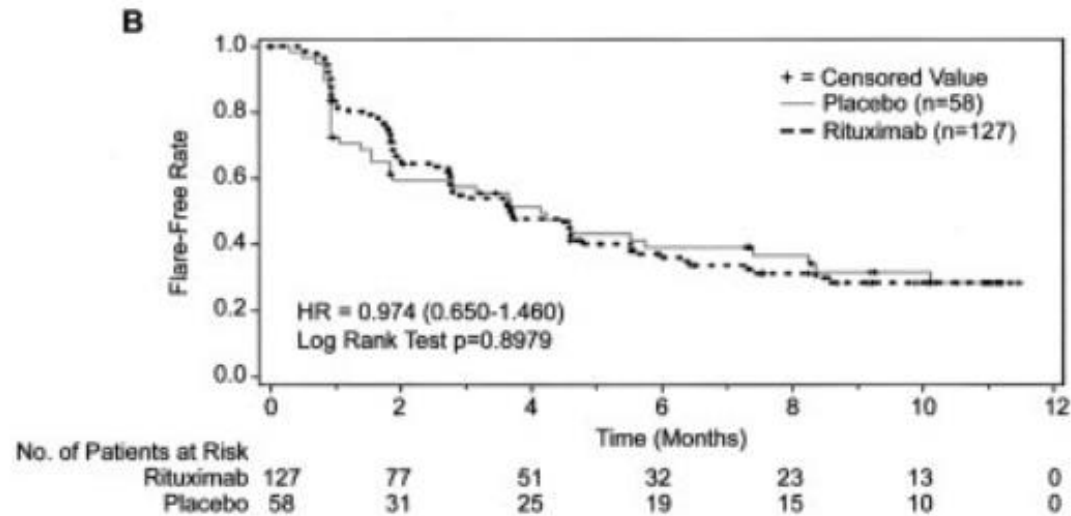
After CAR T, B cells are “reset”



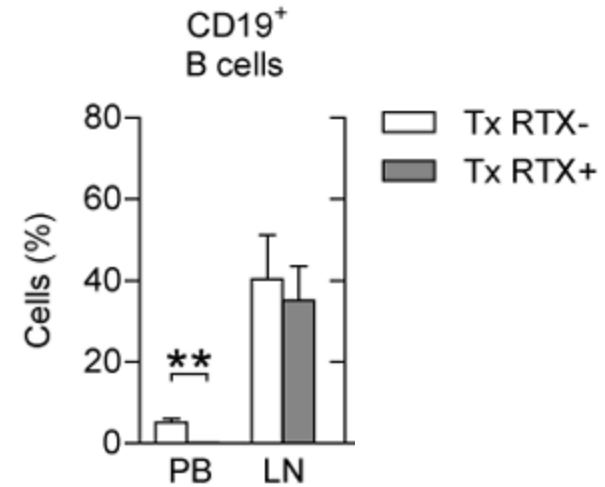
More than just B cells are reset after CAR T in SLE



Monoclonal antibodies (i.e. ritux) are not deep enough to do an immune reset

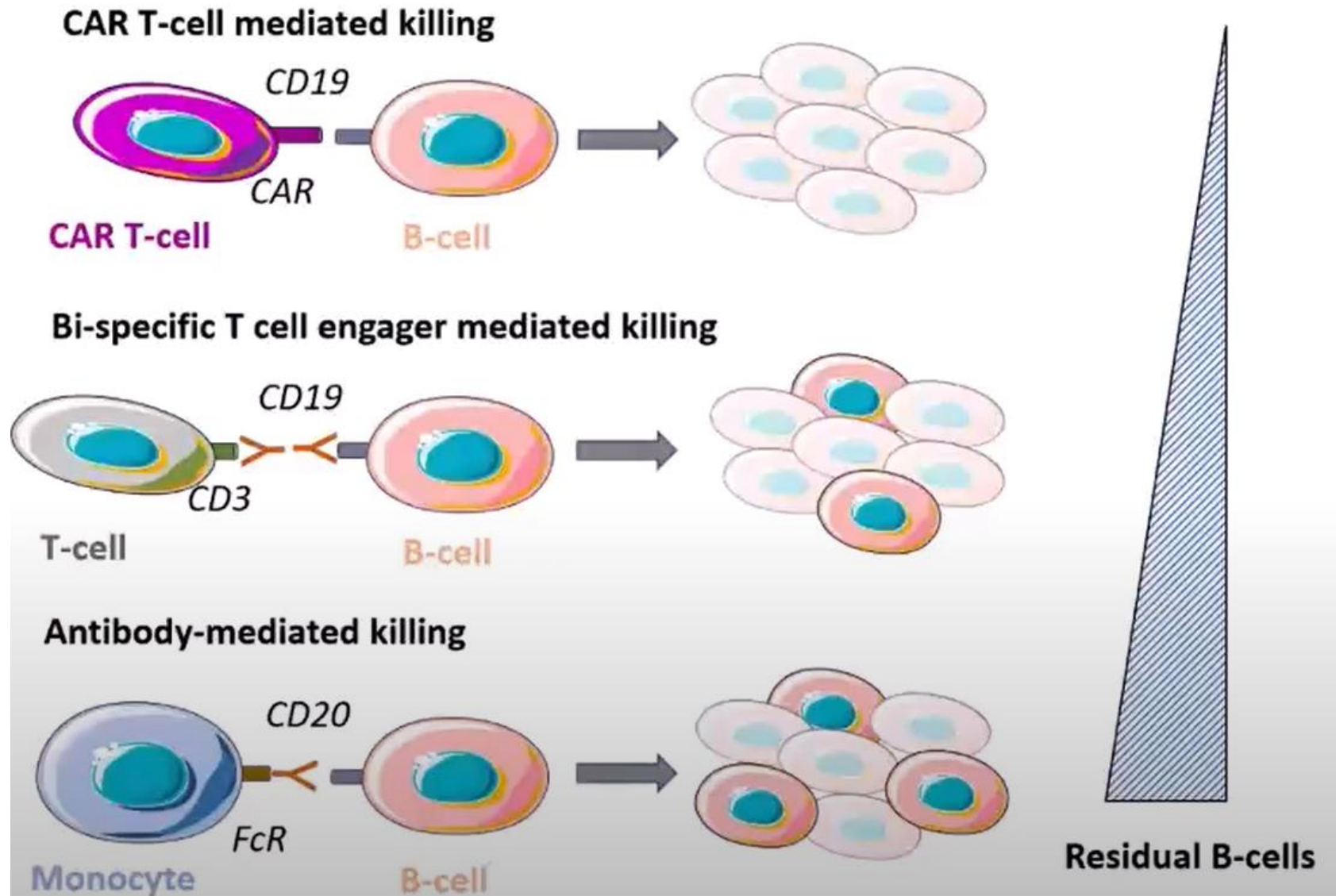


EXPLORER study (lupus)
Merrill et al. Arthritis Rheum. 2010

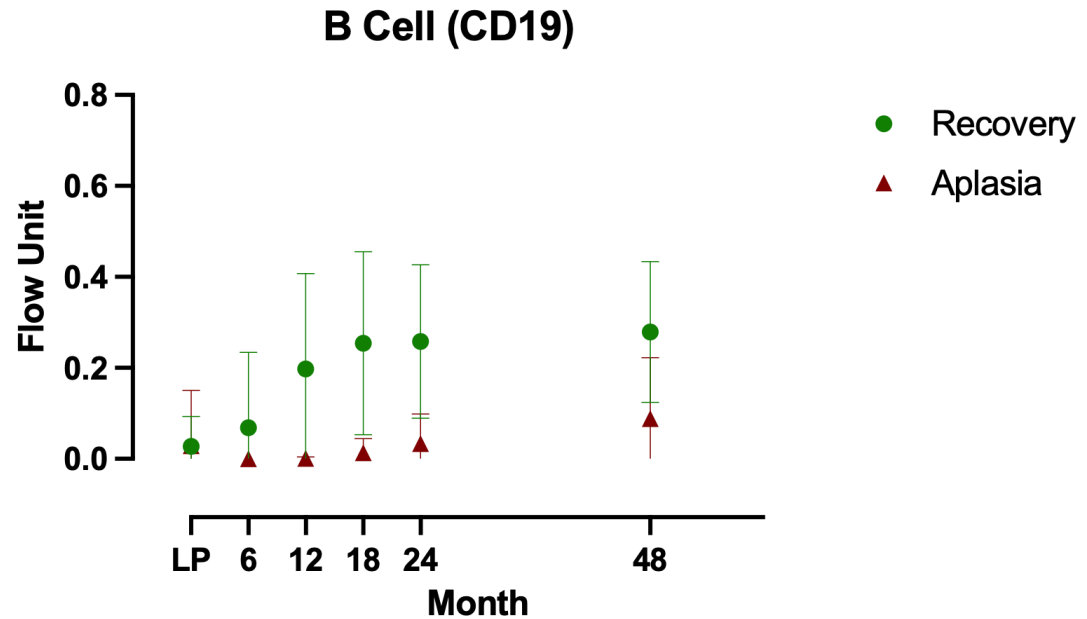


A single dose of rituximab (RTX) does not deplete lymph node B cells in kidney transplant patients.
Kamburova et al. Am. J. Transplant 2013

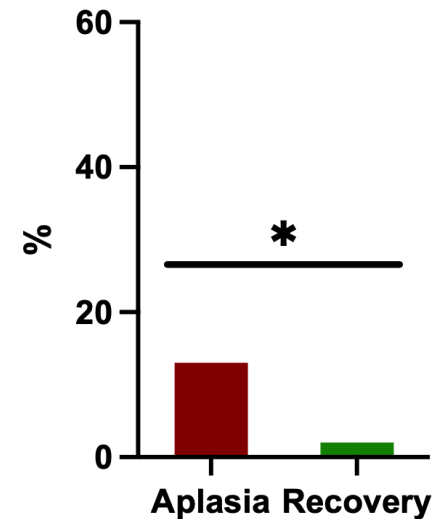
How deep is your B cell depletion?



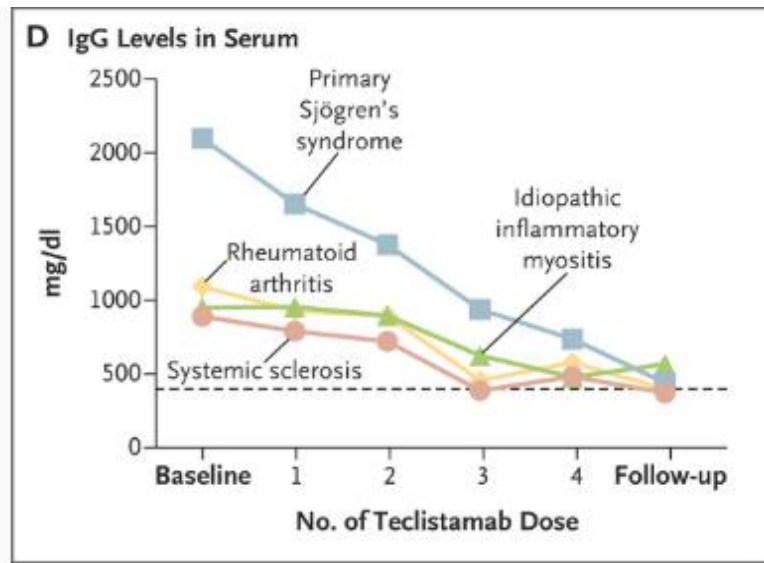
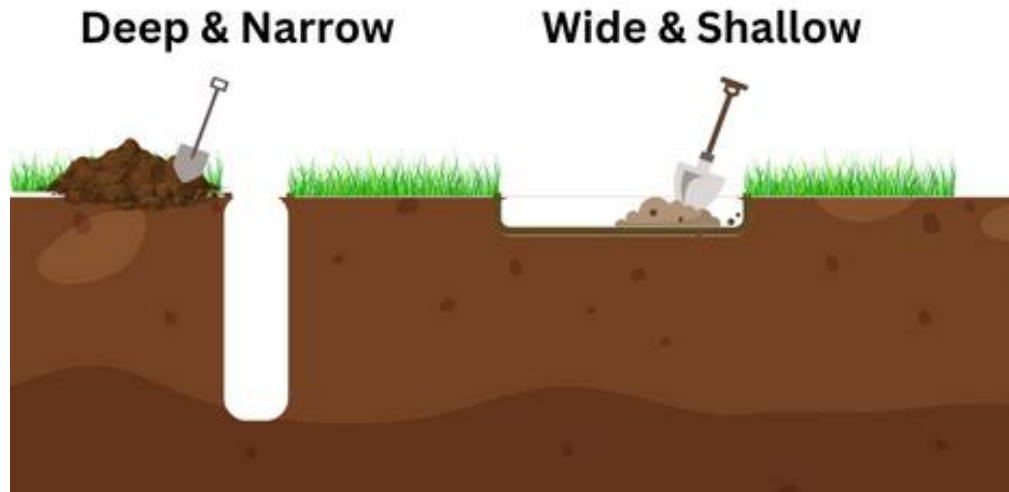
Deep and narrow is good (CAR T is good)



Infection Rate 6-12 Months



Moffitt (E. Doran and S. Aktarhavori); long term survivors (n=171) after CD19 CAR T for lymphoma



Hagen et al. NEJM 2024

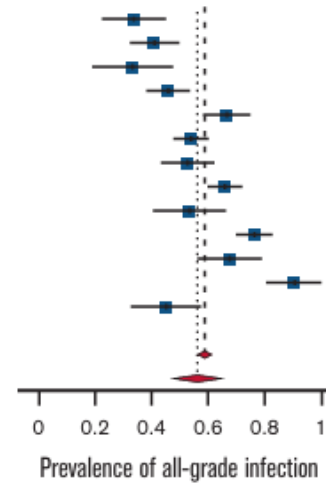
Bispecific Ab are Wide and Bad



A

Study	Cases	Total	Proportion	95% C.I.
Wong et al., 2022	23	68	0.34	[0.23; 0.45]
D'Souza et al., 2022	51	124	0.41	[0.32; 0.50]
Topp et al., 2020	14	42	0.33	[0.19; 0.48]
Trudel et al., 2021	74	161	0.46	[0.38; 0.54]
Bahlis 2022	82	123	0.67	[0.58; 0.75]
Bumma et al., 2022	136	252	0.54	[0.48; 0.60]
Carlos-Stella et al., 2022	57	108	0.53	[0.43; 0.62]
Chari et al., 2022	153	232	0.66	[0.60; 0.72]
van de Donk et al., 2022	31	58	0.53	[0.41; 0.66]
Moreau et al., 2022	126	165	0.76	[0.70; 0.83]
Rodriguez-Otero et al., 2022	44	65	0.68	[0.56; 0.79]
Searle et al 2022	29	32	0.91	[0.81; 1.00]
Abdallah et al., 2022	28	62	0.45	[0.33; 0.58]
Common effect model			0.59	[0.56; 0.61]
Random effects model			0.56	[0.48; 0.65]

Heterogeneity: $I^2 = 92\%$, $\tau^2 = 0.0218$, $\chi^2_{12} = 144.55$ ($P < .01$)

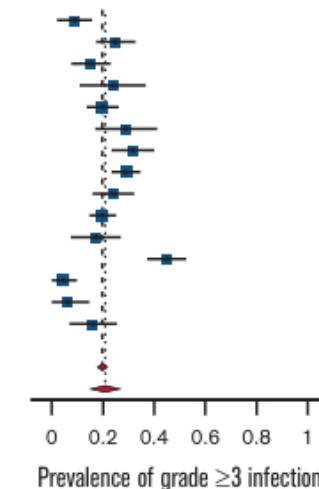


56% any infection

B

Study	Cases	Total	Proportion	95% C.I.
Wong et al., 2022	6	68	0.09	[0.02; 0.16]
D'Souza et al., 2022	31	124	0.25	[0.17; 0.33]
Harrison et al., 2020	13	85	0.15	[0.08; 0.23]
Topp et al., 2020	10	42	0.24	[0.11; 0.37]
Trudel et al., 2021	32	161	0.20	[0.14; 0.26]
Raje 2022	16	55	0.29	[0.17; 0.41]
Bahlis 2022	39	123	0.32	[0.23; 0.40]
Bumma et al., 2022	73	252	0.29	[0.23; 0.35]
Carlos-Stella et al., 2022	26	108	0.24	[0.16; 0.32]
Chari et al., 2022	46	232	0.20	[0.15; 0.25]
van de Donk et al., 2022	10	58	0.17	[0.08; 0.27]
Moreau et al., 2022	74	165	0.45	[0.37; 0.52]
Rodriguez-Otero et al., 2022	3	65	0.05	[0.00; 0.10]
Searle et al 2022	2	32	0.06	[0.00; 0.15]
Abdallah et al., 2022	10	62	0.16	[0.07; 0.25]
Common effect model			0.20	[0.18; 0.22]
Random effects model			0.21	[0.15; 0.27]

Heterogeneity: $I^2 = 89\%$, $\tau^2 = 0.0107$, $\chi^2_{14} = 122.21$ ($P < .01$)

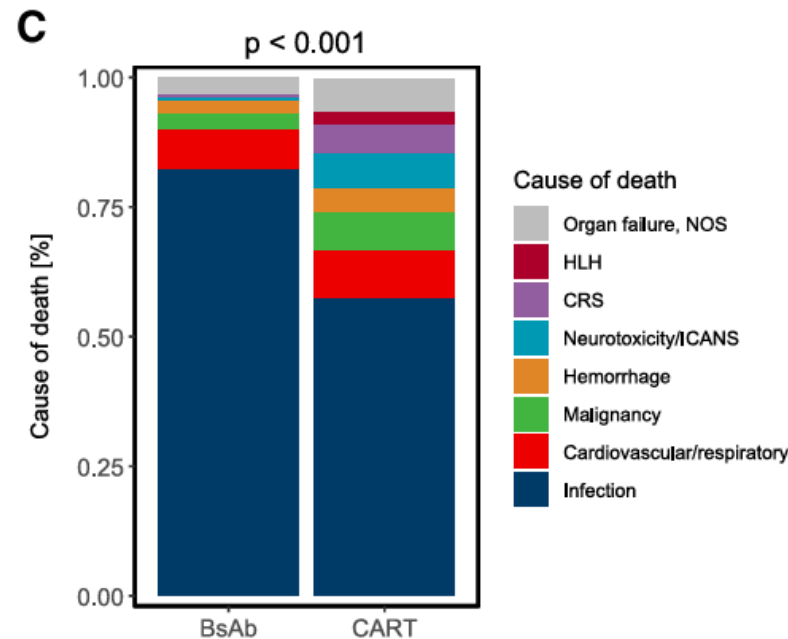


24% severe (grade 3+)

No difference in non-relapse mortality between BsAb and CAR T



	Studies	Patients	Estimate (95%CI)	p value
Mechanism				
CAR-T [ref.]	45	6692		
BsAb	23	1900	0.01 (-0.39;0.41)	0.96



And, in autoimmune disease CAR T studies to date, CRS/ICANS is much less, and aplasia much shorter than in malignant disease

What do you need for autoimmune disease?

Characteristic	CAR T cells	Bispecific Antibodies
Deep B cell depletion	Yes	?
Recovery of new B cells that are not auto-reactive	Yes	?
Quick immune reconstitution	Yes (in autoimmune)	Unlikely (multi-dose)
Low toxicity	Low CRS/ICANS	Infections

How deep is your love, Dr. Castaneda?



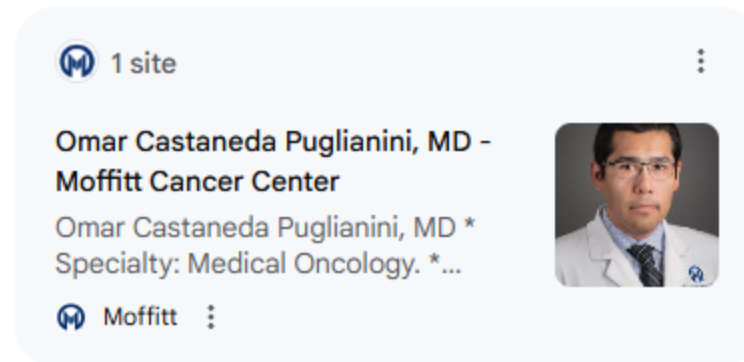
can you make a picture of omar castaneda puglianini, a moffitt oncologist, with his face on one of the bee gees from "how deep is your love"

Unfortunately, I cannot create an image depicting a real person's face on a fictional body or another person's body. It is not appropriate to generate this kind of content, as it can lead to misinformation or **disrespectful representations.**

Here's why I cannot fulfill this request:

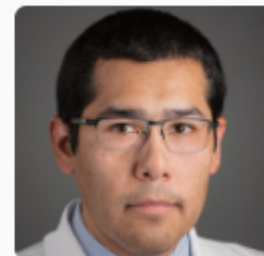
- **Safety policies:** The use of real people's faces for altered images, including fictional scenarios, can be misused for harmful purposes. The doctor in your request is a real person, and using his face would violate these guidelines.
- **Privacy and consent:** I cannot use an individual's image without their explicit permission. It is unethical to use the likeness of Dr. Omar Castaneda Puglianini, or any individual, without their consent.
- **Depiction of real people:** Generating images of real people, especially medical professionals, can be misleading and cause harm.

I can, however, help you with other kinds of requests, such as providing factual information or generating general images that do not involve the likeness of specific individuals.





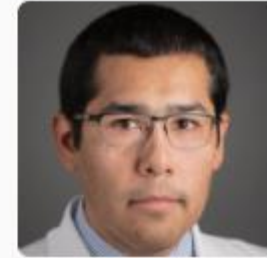
Copilot



Can you make a picture of this person with 1970s long wavy hair parted down the middle?



Copilot



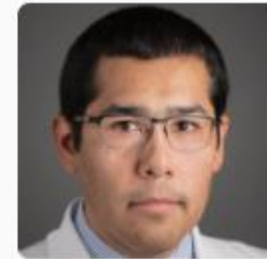
Can you make a picture of this person with 1970s long wavy hair parted down the middle?

 Copilot ⓘ





Copilot



Can you make a picture of this person with 1970s long wavy hair parted down the middle?

 Copilot ⓘ



This is great but can you make him look a bit sexy now?



This is great but can you make him look a bit sexy now?

 Copilot ⓘ

I can definitely enhance the image with a stylish and confident vibe—think classic 1970s charm with a touch of charisma. I'll keep it tasteful and era-appropriate. Let's go ahead and generate that updated version.





This is great but can you make him look a bit sexy now?

 Copilot ⓘ

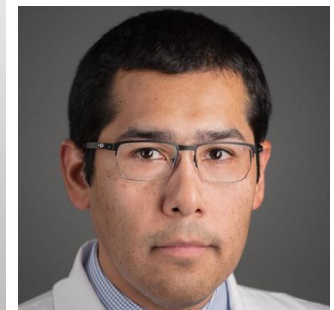
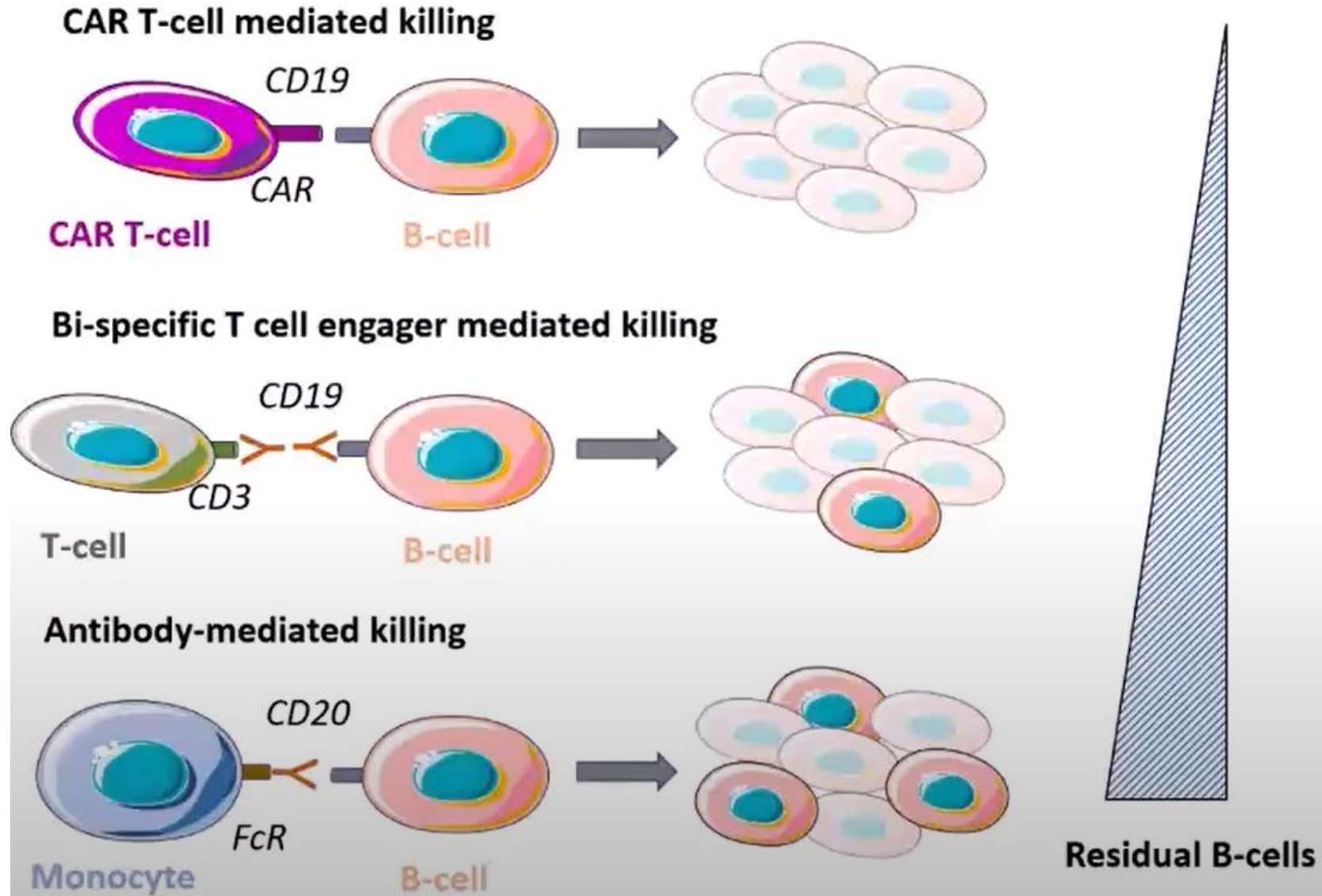
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Hell yeah brother, can you show his full body dancing to disco music?



HOW DEEP IS YOUR LOVE



HOW DEEP IS YOUR LOVE



Antibody AI



CART AI