

CAR T-Cell Therapy: Multiple Myeloma

Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



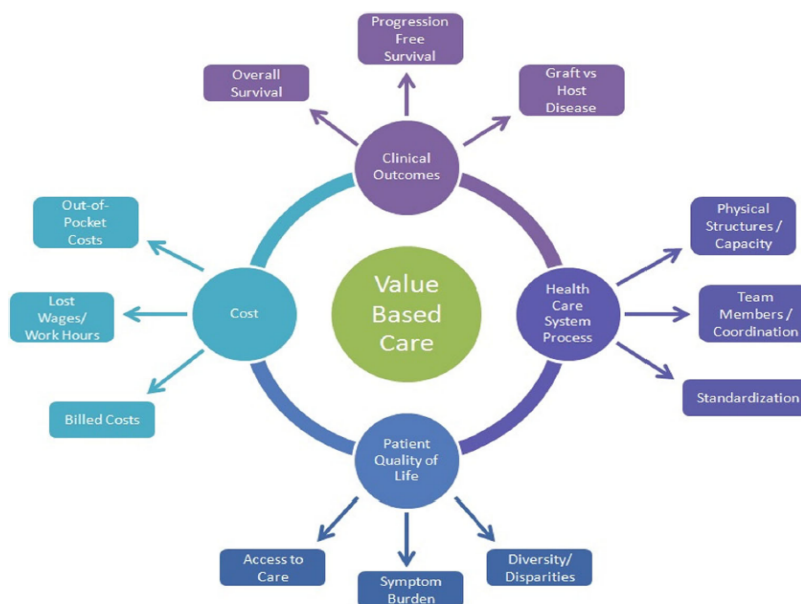
Gunjan Shah, MD, MS
Memorial Sloan Kettering Cancer Center

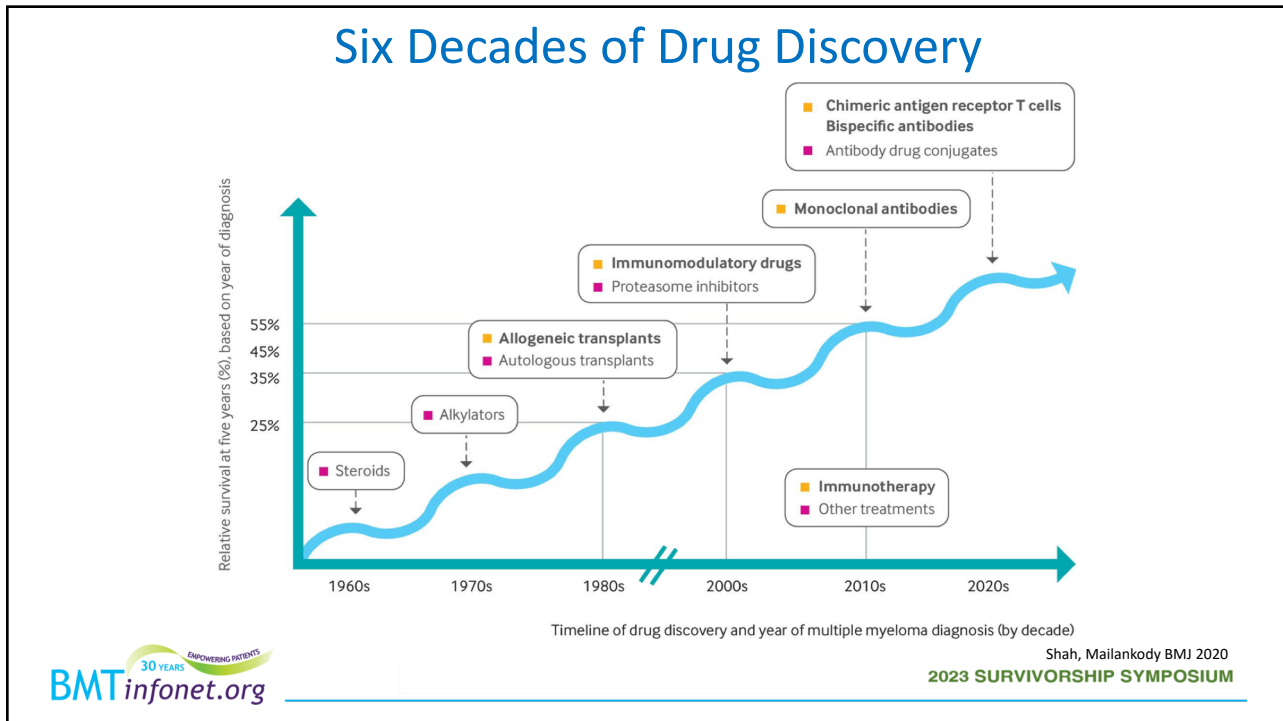
Disclosures

- Research Funding: Janssen, Amgen, BMS, Beyond Spring
- DSMB: Arcellx

Take Home Points

- Two commercially available CAR T cells for multiple myeloma (MM)
- Timing of therapy depends on prior treatments and approvals (expected to become earlier over time)
- Cytokine release syndrome (CRS) and neurotoxicity (ICANS) important toxicities, but also infections
- Many options for therapy






Philosophy of Treatment

Effectiveness

- How quick
- How likely
- For how long



Safety

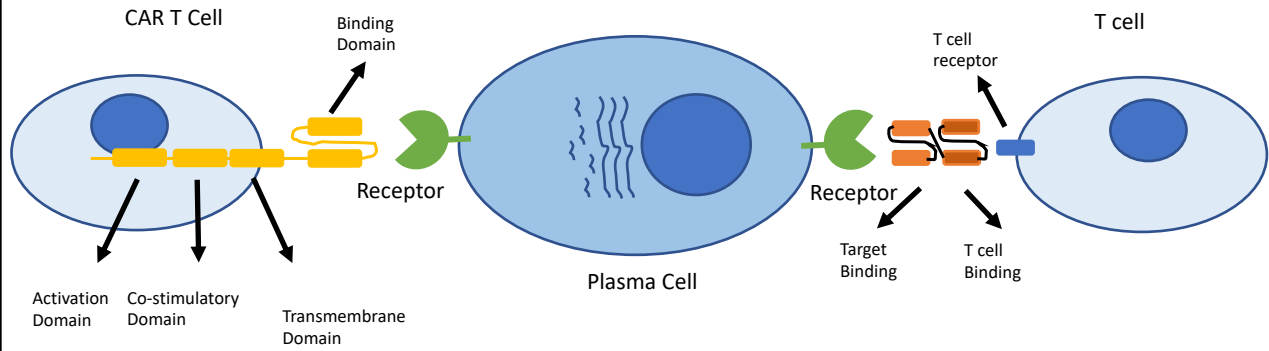
- Short-term risks
- Long-term risks

Impact on later decisions

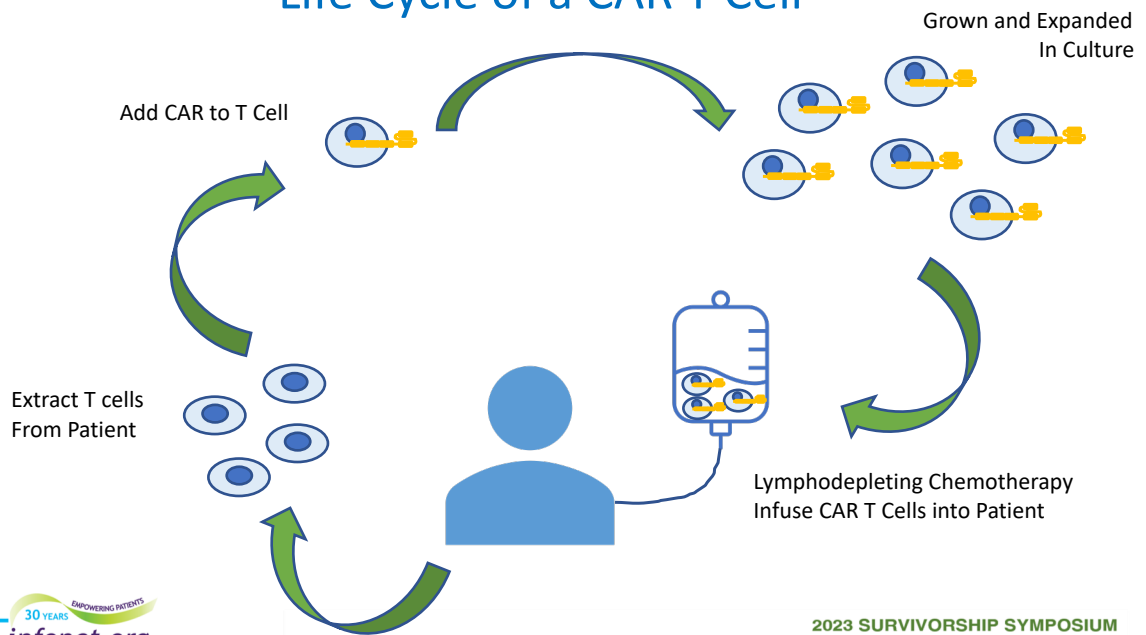
- One time only?
- Limit choices down the road?

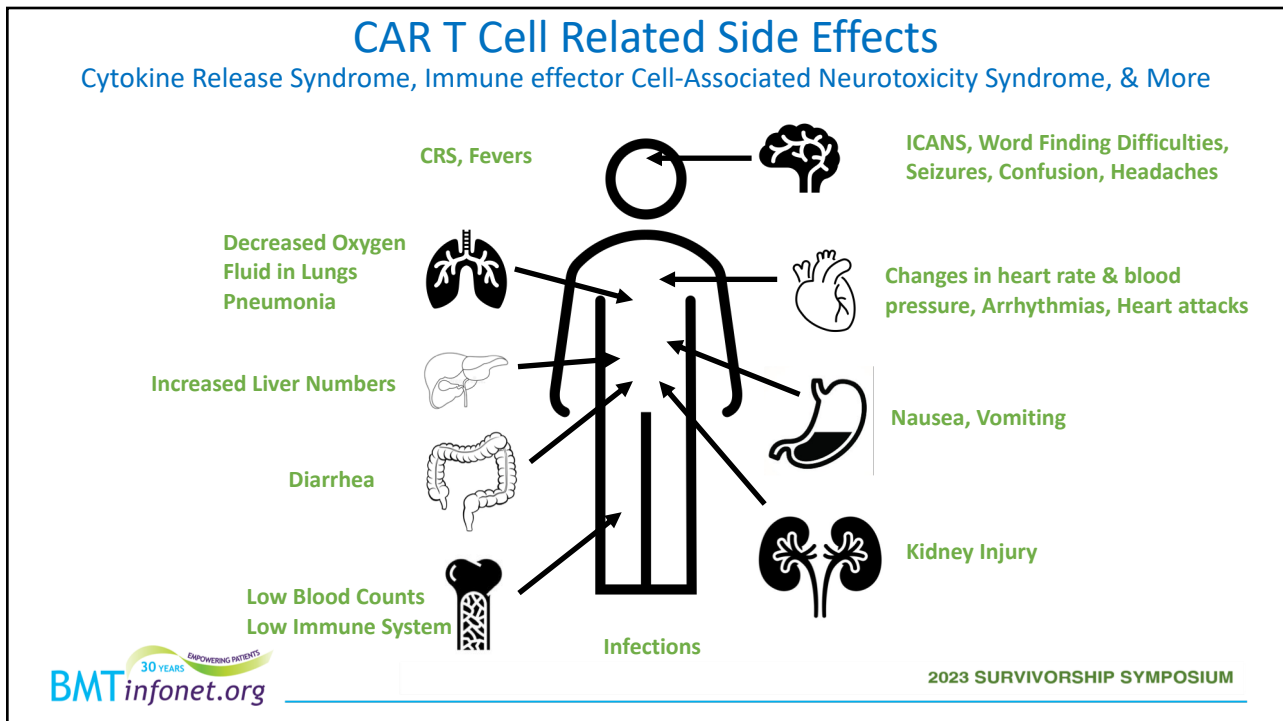
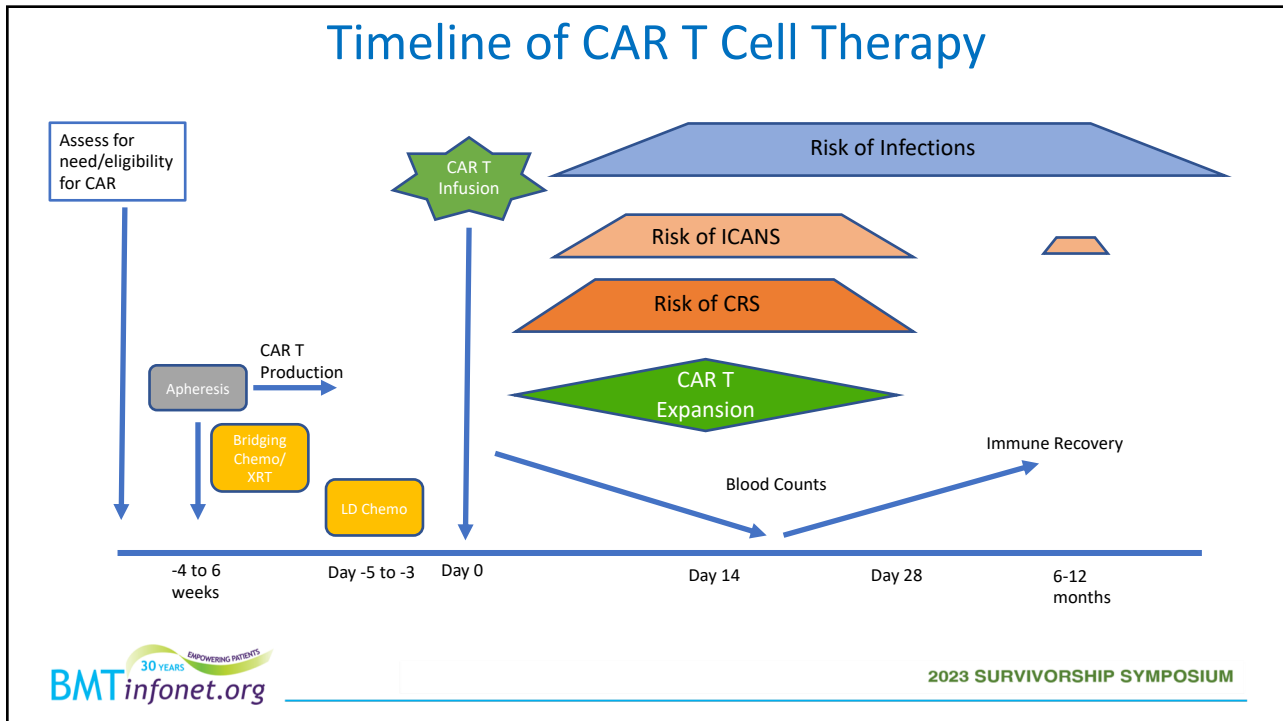
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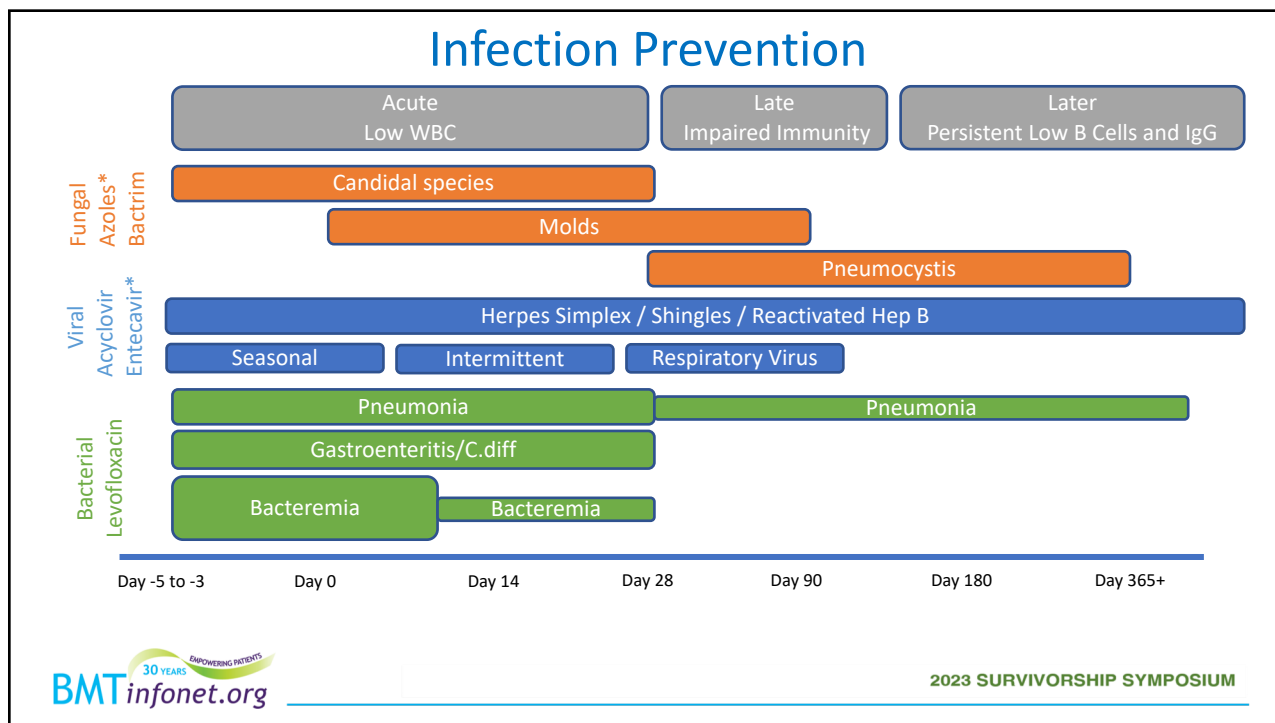
CAR T Cell vs Bispecific T Cell Engager



Life Cycle of a CAR T Cell







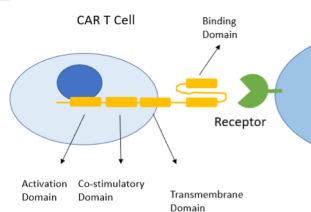
FDA Approved CAR T Cells

Generic Name	Brand Name	Target Antigen	Targeted Disease	Patient Population
Tisagenlecleucel	Kymriah	CD19	B-cell acute lymphoblastic leukemia (ALL)	Children and young adults with refractory or relapsed B-cell ALL
			B-cell non-Hodgkin lymphoma (NHL) <i>DLBCL, FL</i>	Adults with relapsed or refractory B-cell NHL <i>3rd Line</i>
Axicabtagene ciloleucel	Yescarta	CD19	B-cell non-Hodgkin lymphoma (NHL)	Adults with relapsed or refractory B-cell NHL <i>2nd and 3rd Line</i>
			Follicular lymphoma	Adults with relapsed or refractory follicular lymphoma
Brexucabtagene autoleucel	Tecartus	CD19	Mantle cell lymphoma (MCL)	Adults with relapsed or refractory MCL
			B-cell acute lymphoblastic leukemia (ALL)	Adults with refractory or relapsed B-cell ALL
Lisocabtagene maraleucel	Breyanzi	CD19	B-cell non-Hodgkin lymphoma (NHL) <i>DLBCL, FL3B</i>	Adults with relapsed or refractory B-cell NHL <i>2nd and 3rd Line</i>
Idecabtagene vicleucel	Abecma	BCMA	Multiple myeloma	Adults with relapsed or refractory multiple myeloma
Ciltacabtagene autoleucel	Carvykti	BCMA	Multiple myeloma	Adults with relapsed or refractory multiple myeloma

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Myeloma CAR T Cells Approved

Idecabtagene (Abecma)	Ciltacabtagene (Carvykti)
Autologous	Autologous
Anti-BCMA Binding Domain	Anti-BCMA Binding Domain
4-1BB Costimulatory Domain	4-1BB Costimulatory Domain
CD3Zeta Signaling Domain	CD3Zeta Signaling Domain
	Two BCMA Targeting Sites
Approved after 4+ Lines of Therapy	Approved after 4+ Lines of Therapy



Response Rates and Outcomes

	Idecabtagene (Abecma)	Ciltacabtagene (Carvykti)	Teclistamab (Tecvayli)
Cell Dose	150-450 million	0.75 million/kg	NA
Median Follow-up	14.7 mo	18 mo	14.1 mo
Response: Overall/Complete	73% 33%	98% 80%	63% 39%
Duration of Response	10.7 mo	21.8 mo	18.4 mo
Progression Free Survival	8.8 mo	>27 mo	11.3 mo

*Cannot be directly compared as data from individual trials with different patients

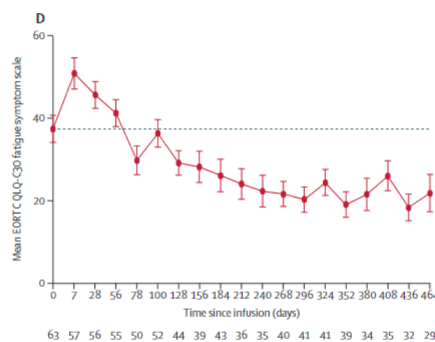
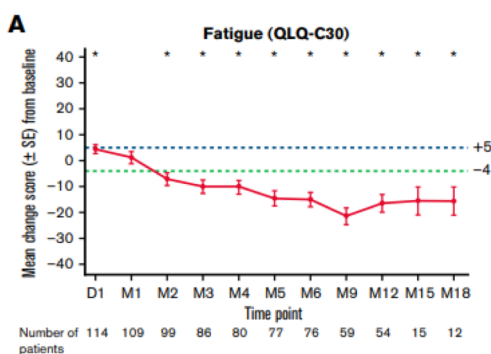
Reported Toxicities in Clinical Trials

	Idecabtagene (Abecma)		Ciltacabtagene (Carvykti)		Teclistamab (Tecvayli)	
	Any Grade	Grade 3-4	Any Grade	Grade 3-4	Any Grade	Grade 3-4
Cytokine Release Syndrome (CRS)	84%	5%	95%	4%	72%	0.6%
Time to Onset	1 day		7 days		2 days	
Duration	5 days		4 days		2 days	
Neurotoxicity (ICANS)	18%	3%	21%	9%	14.5%	0.6%
Time to Onset	2 days		8 days		NA	
Duration	3 days		4 days		NA	

*Cannot be directly compared as data from individual trials with different patients

*Delayed neurotoxicity seen with both products very rarely (unknown cause)

Patient Reported Outcomes - Fatigue



Idecabtagene (Abecma)

Ciltacabtagene (Carvykti)

Cost and Virtual Comparisons Lots of Assumptions

	Study	F/U	ORR	IIT ORR	PFS	Intervention Cost	Non-Intervention Cost	Total Cost	QALY Gained
Ide-Cel	KarMMa	13.3 mo	73%	63%	8.6mo	\$466,000	\$180,000	\$646,000	2.24
Cilta-Cel	CARTITUDE-1	18 mo	98%	75%	>18mo	\$445,000	\$164,000	\$609,000	3.1
Usual Care	MAMMOTH	10.6 mo		31%	3.4mo	\$153,000	\$123,000	\$276,000	1.08

	Comparator	Cost Difference	QALY Difference	Cost per QALY Gained	Cost per PFS Month Gain
Ide-Cel	Usual Care	\$370,000	1.16	\$319,000	\$35,000
Cilta-Cel	Usual Care	\$333,000	2.02	\$165,000	\$17,000

Selected Ongoing/Upcoming Studies


Idescabtagene		Ciltacabtagene	
KarMMa-2	Phase 2, RR/Early Relapse	CARTITUDE-2	Phase 2, RR/Early Relapse
KarMMa-3	Phase 3, SOC vs CAR	CARTITUDE-4	Phase 3, SOC vs CAR
KarMMa-4	Phase 1, Newly Diagnosed	CARTITUDE-6	Randomized HCT vs CAR
BMT CTN 1902	Post HCT with Suboptimal Response		

- *Toxicity Prevention
- *Improve Response
- *Other Targets
- *Two Targets
- *Allogeneic (Donor)

Concerns Related to CAR T Therapy

- Insurance approval timing – need for quick therapy
- Manufacturing Slot Availability
- Logistics– Staying close to the Center
- Access – approvals in different countries, only at certain centers (ICU, CRS/ICANS management)

Which Treatment is Right When?

	ASCT	CART	Bispecifics Ab
Data			
Cost	\$\$	\$\$\$\$	\$\$\$
Manufacturing Concerns	No	Yes	No
Available Globally	Yes		
Non-relapse Deaths	Low		
Long-term Safety Data	Yes	No	No

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