

Application of CAR-T cell therapy in clinical practice

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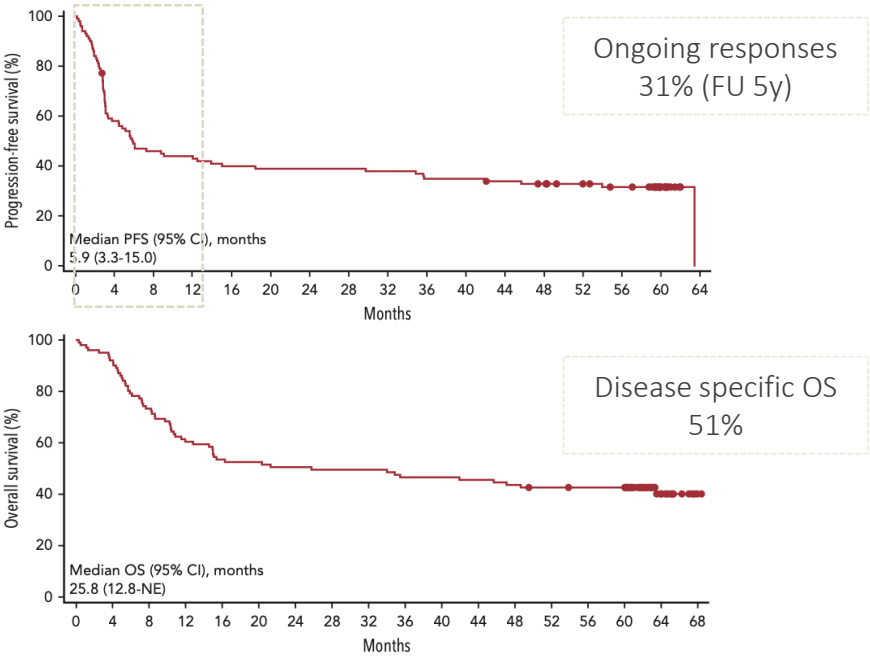
EMA APPROVED INDICATIONS FOR CAR-T CELLS

Axi-cel	Brexu-cel	Ide-cel	Liso-cel
Tisa-cel			Cilta-cel
2018	2020	2021	2022
3L+ DLBCL HGL	3L+ MCL	4L+ MM	3L+ FL
3L+ PMBCL			4L+ FL
Paediatric & AYA 3L+ ALL			2L+ DLBCL
			3L+ DLBCL 3L+ PMBCL
			4L+ MM

CLINICAL IMPACT OF CAR-T CELL THERAPY

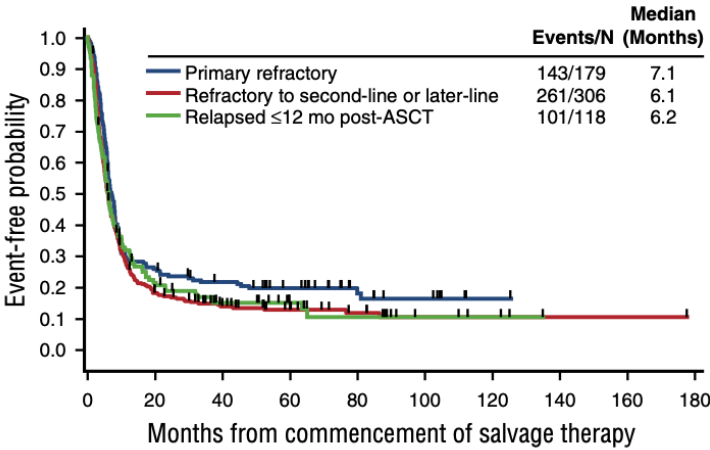
DIFFUSE LARGE B CELL LYMPHOMA

ZUMA-1: phase 2 axi-cel in RR DLBCL



Median OS: ~26 months

SCHOLAR-1: refractory or relapsed at ≤12 months from ASCT



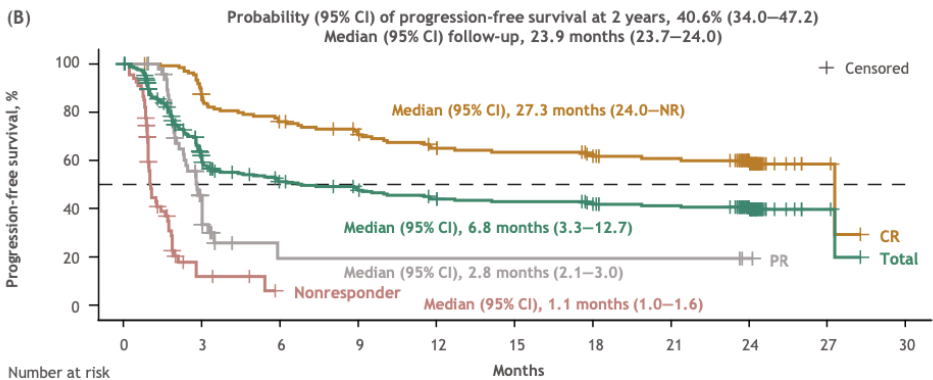
Median OS: ~6 months

CLINICAL IMPACT OF CAR-T CELL THERAPY

DIFFUSE LARGE B CELL LYMPHOMA

1. OTHER CAR-T CELLS

TRANSCEND NHL-001: phase 1 liso-cel in RR DLBCL



Median OS: ~27 months

2. REAL WORLD DATA

	RWE	ZUMA-1
Number of patients	2754	101
ORR CR (%)	73 51	83 58
mPFS (months)	7.3	5.9
mOS (months)	19.5	25.8
CRS total G ≥3 (%)	86 8	93 11
ICANs: total G≥3 (%)	48 19	64 30

Included a significant proportion of patients that did not fulfill inclusion criteria for ZUMA-1

LYMPHOID NEOPLASIA

CME Article

Real-world experience of CAR T-cell therapy in older patients with relapsed/refractory diffuse large B-cell lymphoma

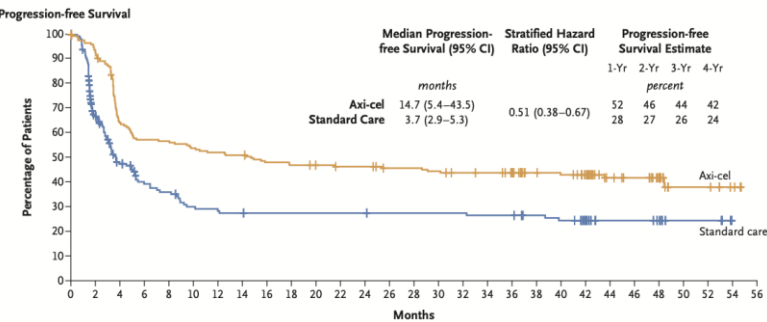
Dai Chihara,¹ Laura Liao,² Joseph Tkacz,³ Anjali Franco,³ Benjamin Lewing,³ Karl M. Kilgore,³ Loretta J. Nastoupil,¹ and Lei Chen²

CLINICAL IMPACT OF CAR-T CELL THERAPY

DIFFUSE LARGE B CELL LYMPHOMA

3. SECOND LINE TREATMENT

ZUMA 7: phase 3 axi-cel vs ASCT in DLBCL, refractory or relapsed < 12 months after 1st line



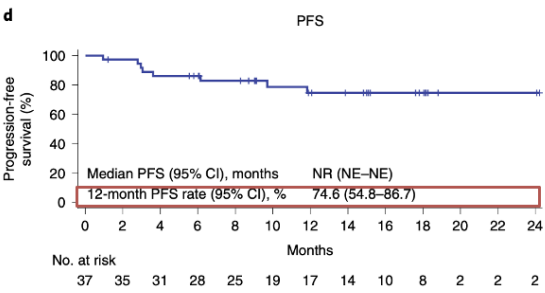
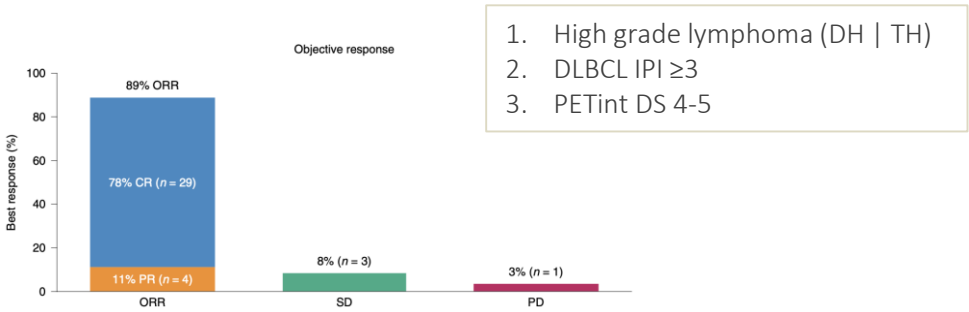
Median OS NR vs 31m | 4y OS 55% vs 46%

Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study

Alison Sehgal, Daanish Hoda, Peter A Riedell, Nilanjan Ghosh, Mehdi Hamadani, Gerhard C Hildebrandt, John E Godwin, Patrick M Reagan, Nina Wagner-Johnston, James Essell, Rajneesh Nath, Scott R Solomon, Rebecca Champion, Edward Licitra, Suzanne Fanning, Neel Gupta, Ronald Dubowy, Aleco D'Andrea, Lei Wang, Ken Ogasawara, Jerill Thorpe, Leo I Gordon

4. FIRST LINE TREATMENT

ZUMA 12: phase 2 axi-cel for 1st line treatment of high risk LBCL

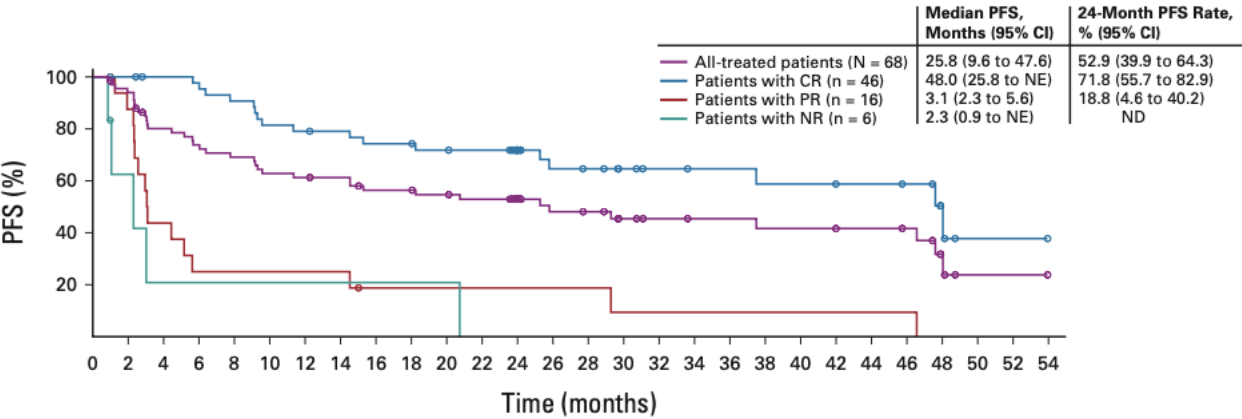


ZUMA 23: ongoing phase 3 axi-cel vs SoC for 1st line treatment of high risk LBCL

CLINICAL IMPACT OF CAR-T CELL THERAPY

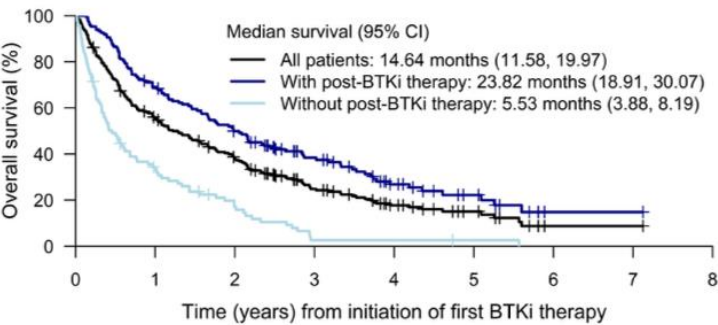
MANTLE CELL LYMPHOMA

ZUMA-2: phase 2 brexucabtagene autoleucel in RR MCL



Median OS: ~47 months

SCHOLAR-2: MCL RR > 2L



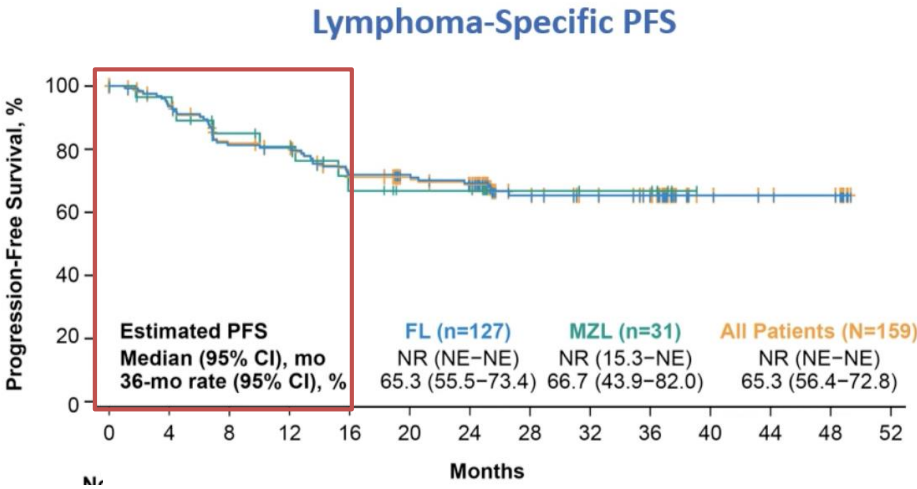
Median OS: ~15 months

CLINICAL IMPACT OF CAR-T CELL THERAPY

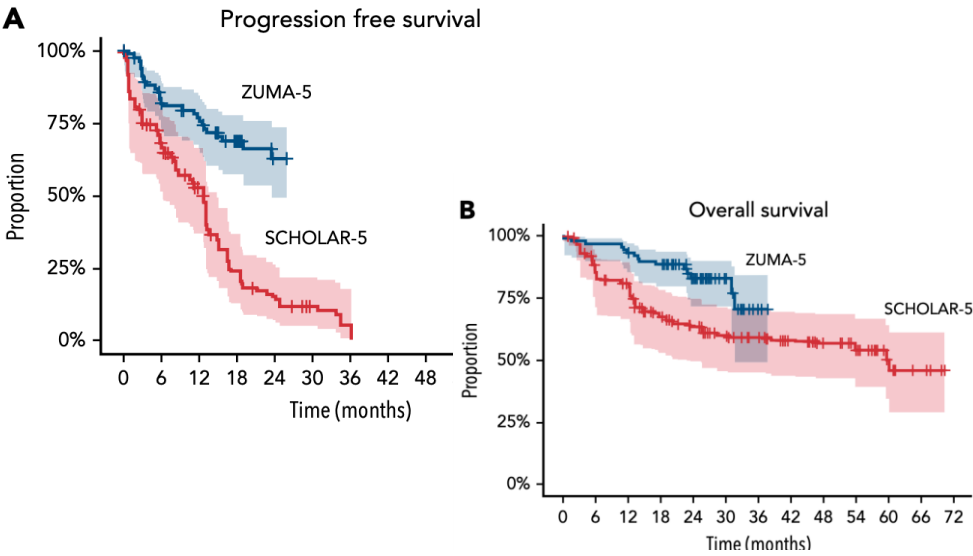
FOLLICULAR LYMPHOMA

ZUMA-5: phase 2 axicabtagene ciloleucel in RR FL

SCHOLAR-5: FL RR > 2L



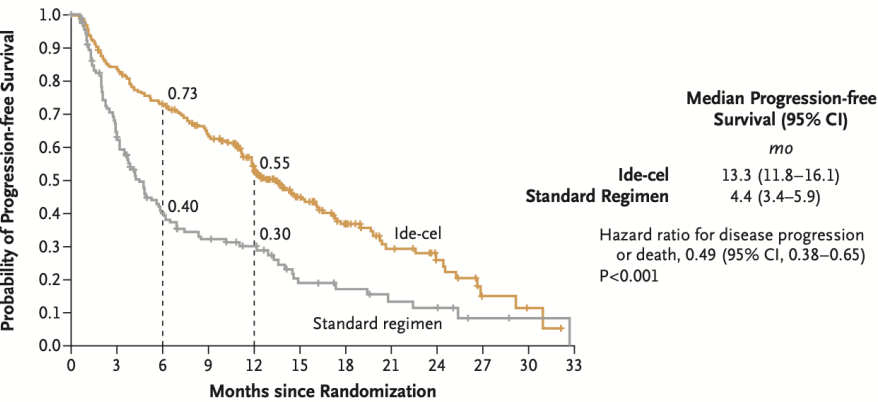
Median OS NR



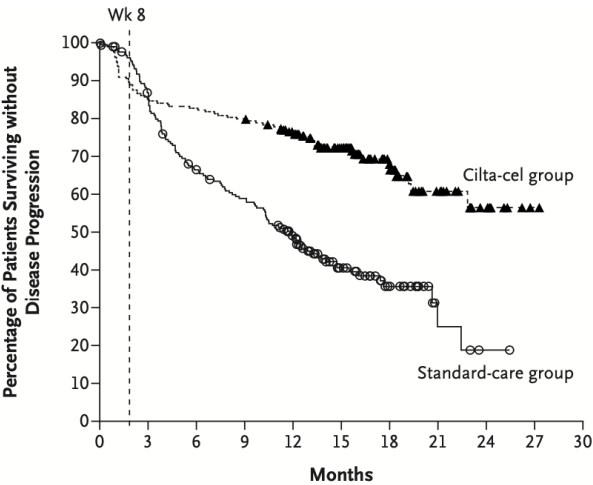
CLINICAL IMPACT OF CAR-T CELL THERAPY

MULTIPLE MYELOMA

KarMma-3 : phase 3 ide-cel vs SoC in triple-class–exposed RR MM

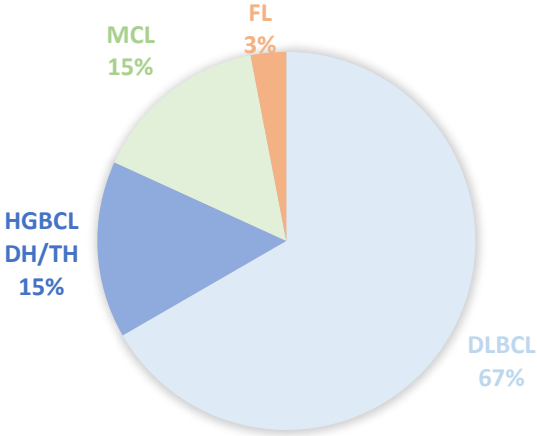


CARTITUDE-4: phase 3 cilta-cel vs SoC in lenalidomide-refractory MM

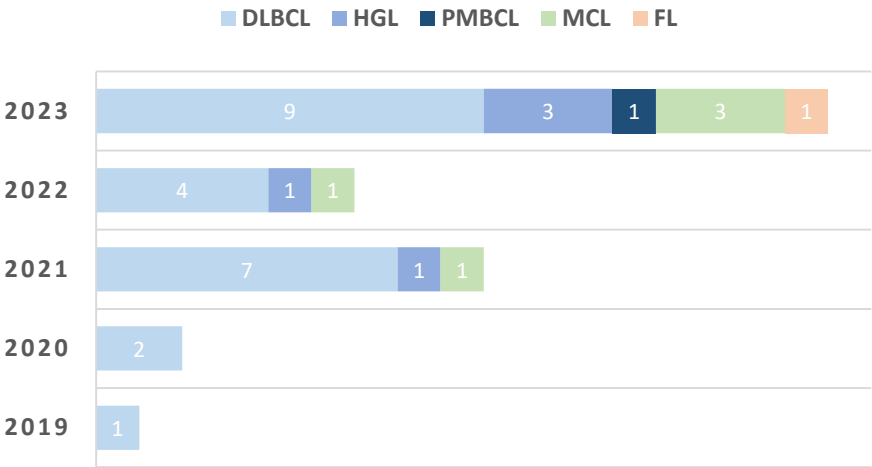


IPO LISBON EXPERIENCE WITH CAR-T CELL THERAPY

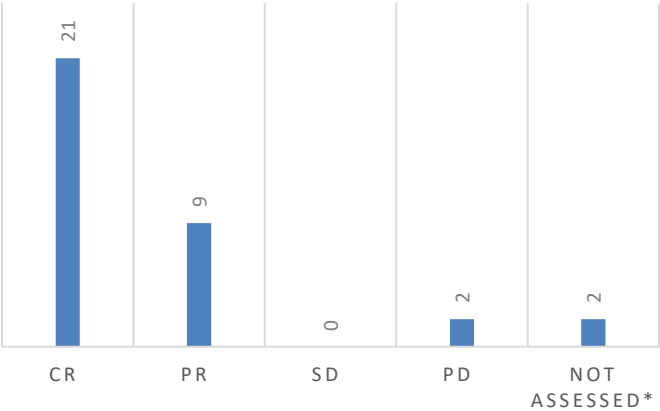
Axicel	Brexucel	Tisacel	Axicel
Nov 2019	Aug 2021	Jun 2022	Mar 2023
3L+ DLBCL	3L+ MCL	3L+ DLBCL	4L+ FL
3L+ PMBCL			



IPO LISBON EXPERIENCE WITH CAR-T CELL THERAPY

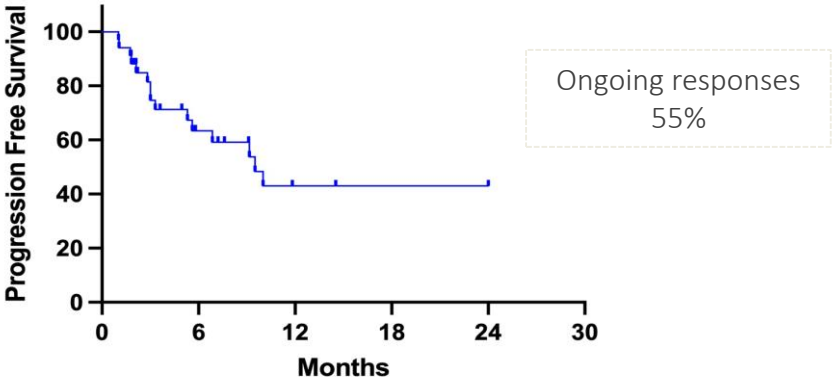


Best Overall Response



	Toxicity
Number of patients	34
CRS total G ≥3	82% 15%
ICANs: total G≥3	29% 12%
Tocilizumab, %	76%
Steroids, %	44%
ICU admission	21% (median 5d)

IPO CAR-T patients with lymphoma



NOVEL TARGETS AND INDICATIONS FOR CAR-T CELL THERAPY

Clinical trial identifier	Antigen	Disease	Estimated enrollment (participants)	Start date	Estimated completion date	Source	Conditioning regimen	Phase	Location
NCT04627740	ALPP	Ovarian and endometrial cancer	20	December 1, 2020	December 31, 2023	Autologous	Flu / Cy	I/II	Not provided
NCT03958656	CS1	Multiple myeloma	13	June 13, 2019	January 19, 2021	Autologous	Flu / Cy	I	United States
NCT04142619	(SLAMF7)	R/R multiple myeloma	18	November 21, 2019	November 1, 2022	Allogeneic	–	I	United States
NCT03159819	CLDN18.2	Pancreatic and gastric adenocarcinoma	24	April 1, 2017	December 31, 2021	Autologous	–	Not Applicable	China
NCT04467853		Gastric cancer	34	September 21, 2020	November 2024	Autologous	Flu / Cy	I	China
NCT03393936	AXL	Renal cell carcinoma	66	March 26, 2018	March 30, 2035	Autologous	Flu / Cy	I/II	China
NCT04151186	ROR2	Advanced solid tumors	72	November 20, 2019	November 20, 2021	–	–	Not Applicable	China
NCT04420754	TM4SF1	Anaplastic thyroid cancer	24	September 28, 2020	June 2024	Autologous	–	I	United States
NCT02311621	ICAM-1	Neuroblastoma, ganglioneuroblastoma	40	November 25, 2014	November 2037	Autologous	–	I	United States
NCT03829540	L1CAM (CD171)	T-cell lymphoma, T-cell leukemia	20	June 18, 2019	December 2037	Autologous	–	I	United States
NCT03081910	CD4	T-cell acute lymphoblastic lymphoma, non-Hodgkin T-cell lymphoma	42	November 1, 2017	September 1, 2039	Autologous	Flu / Cy	I	United States
NCT04599556	CD5	Acute leukemia and lymphoma	108	October 2020	December 2023	–	–	I/II	China
NCT03690011	CD7	T-cell acute lymphoblastic lymphoma, T-cell acute lymphoblastic leukemia, non-Hodgkin T-cell lymphoma	21	September 1, 2021	May 1, 2038	Autologous	Flu / Cy	I	United States
NCT04430530	CD10	CD19-negative B-cell malignancies	100	June 1, 2020	December 31, 2023	–	–	I/II	China
NCT04348643	CD38	Lung, colorectal, liver, pancreatic, gastric, and breast cancer	40	February 20, 2020	April 30, 2023	–	–	I/II	China
NCT03904069	CEA	R/R acute myeloid leukemia	40	March 15, 2022	May 9, 2029	Autologous	–	I	United States
NCT02830724	FLT3	Pancreatic, renal cell, ovarian, and breast cancer, melanoma	2	April 6, 2017	January 1, 2028	Autologous	Flu / Cy	I/II	United States
NCT04288726	CD70	Hodgkin lymphoma	18	September 16, 2020	June 1, 2037	Allogeneic	–	I	United States
NCT04136275	CD30	Leukemia and B-cell, T-cell, and Non-Hodgkin lymphoma	18	June 19, 2020	September 30, 2024	Autologous	–	I	United States
NCT04045847	CD37	Glioblastoma	31	May 30, 2019	May 30, 2022	Autologous	–	I (early phase)	China
	CD147								

CHALLENGES OF CAR-T CELL THERAPY

How to deliver CAR-T cell therapy to all possible candidates?

- Financial burden
- Complexity of the procedure

Referral

Apheresis

Bridging

Lymphodepletion Infusion

Post infusion surveillance

Long term FU

Internal and other
peripheral hospitals

- Slot availability
- Apheresis procedure

- Need for disease control
during CAR-T cell
manufacturing

- Need for hospital admission
- Risk of CRS and ICANs
- Risk of infection

- Prolonged B cell aplasia
- Susceptibility to infections
- Risk of relapse

- Need for constant monitoring → Caregiver training
- Social and psychological support

Multidisciplinary team: hematology, immunohemotherapy, intensive care, neurology, radiology, pharmacy

Trained nursing staff and caregivers

Patient selection is key for optimization of CAR-T therapy

Novel strategies are needed to reduce costs and optimize the procedure: locally produced CARTs? Allogeneic CARTs?



Thank you for your attention!