Autologous CART cell therapies:

What does the future look like?

Bart Jacobs, PhD
Asscociate Director Medical Affairs Benelux, Gilead/Kite

Kite by the Numbers…

31,000+
Patients Treated
(Clinical & Commercial Patients)

2
Global Commercial
Products on Market

5
Approved Indications
in CAR T-cell Therapy*

4,000+
Employees

90,000+
Square Meters of Cell Therapy
Manufacturing and R&D Space

30
Countries
with Reimbursed Product

(Data on File as of 08/2025; References available)
*Approved indication number varies per market

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Kite: Leading Cell Therapy Manufacturing Capabilities


California

Amsterdam

Maryland

Process development - to move from lab to clinic

Internal vector manufacturing capability

Clinical manufacturing capability

Commercial manufacturing on a global scale

Vertically integrated, dedicated cell therapy manufacturing network

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Kite's continuous investment in CAR T manufacturing

	First 2 years	Latest 2 years
Date range (with final lot disposition available)	September 6, 2018-September 5, 2020	September 6, 2020-September 5, 2022
Patients registered on Kite Konnect® and leukapheresed[a]	1155	2546
Median turnaround time[b] (range), days	25 (19-127)	19 (16-38)
Delivery success rate (n/N lots), %	96% (1072/1115)	99% (2398/2432)
Manufacturing success rate (n/N lots), %	95% (1069/1123)	96% (2449/2560)

[a] Includes patients from the European Union, United Kingdom, Switzerland, and Israel. [b] Based on primary peripheral blood mononuclear cell (PBMC) process. A frozen PBMC process was used in the first 2 years of experience, and a fresh apheresis material process was used in the latest 2 years of experience.

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Van De Wiel et al. EBMT 2023

Opportunities to Deliver Therapies More Efficiently

Example

1	**TAT Reduction**	Approval of 5-day manufacturing reduces overall TAT by 2 days in the U.S.[1]
2	**Automation**	Manufacturing automation and quality control (QC) automation in development
3	**Innovation**	Rapid manufacturing assets are in the pipeline and are expected to further reduce manufacturing time

- Deliver quality, speed & reliability
- Time to treatment is a critical factor for patients
- Gives certainty to treating physician
- Eases logistics for all stakeholders

1. Data on file: Kite Pharma, Inc., as of 08/2025

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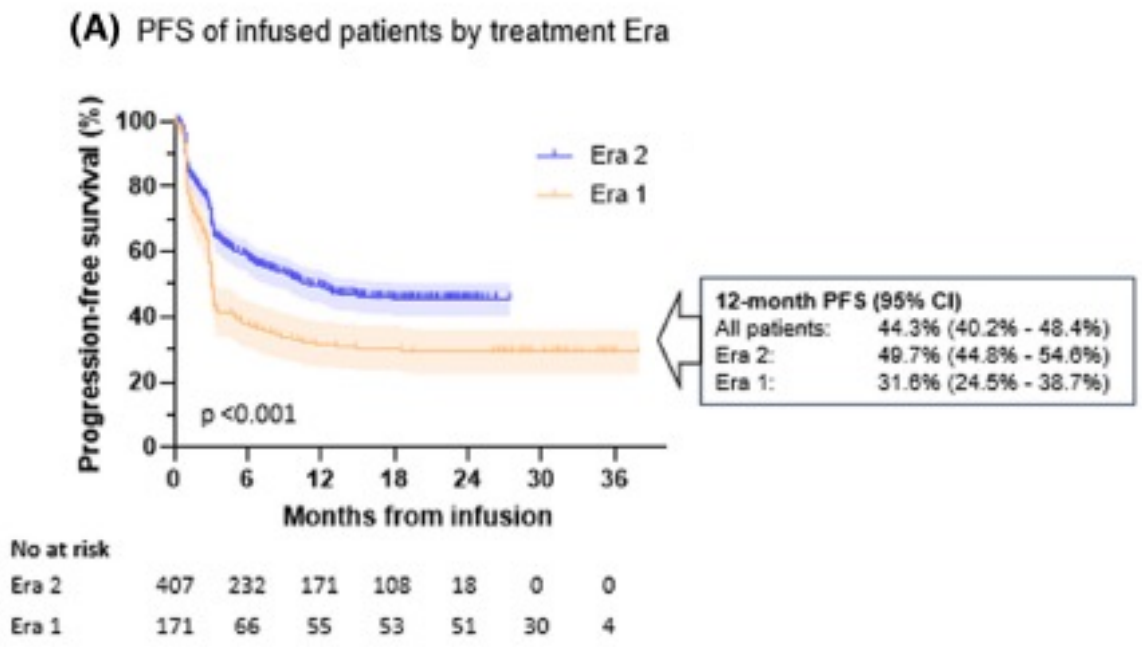
What have we learned clinically?

Improved outcomes of large B-cell lymphoma patients treated with CD19 CAR T in the UK over time

S. Boyle[1] | C. Roddie[2,3] | M. O'Reilly[2] | T. Menne[4] | J. Norman[5] | A. Gibb[6] | S. Lugthart[7] | S. Chaganti[8] | C. Gonzalez Arias[9] | C. Jones[10] | A. Latif[11] | B. J. Uttenthal[12] | F. Seymour[13] | W. Osborne[4] | D. Springell[2] | P. Hardefeldt[1] | D. Yallop[1] | E. Thoulouli[5] | A. Bloor[14] | C. Besley[7] | A. Mathew[8] | D. Burns[8] | K. Cwynarski[2] | R. Sanderson[1] | A. Kuhnl[1]

2019 vs 2020-2021



Boyle et al. Br. J Hematology 2023

What have we learned clinically?

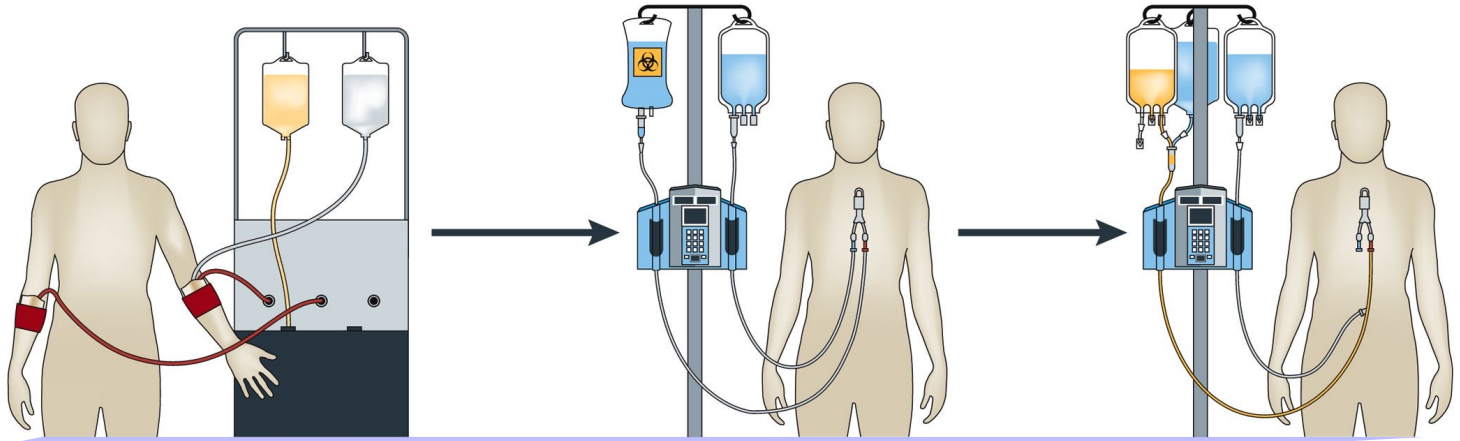
- **Clear Patient selection**
  - Ineligibility based on comorbidities
- **Improved manufacturing:**
  - Shorter production and Vein-to-vein times (cooperation with centers)
  - Reduced out-of-specification rates
- **Better utilization of Holding and Bridging therapy**
  - patients arrive in better condition at day of infusion
- **More experience with toxicity management:**
  - earlier interventions and long term follow-up (infections)

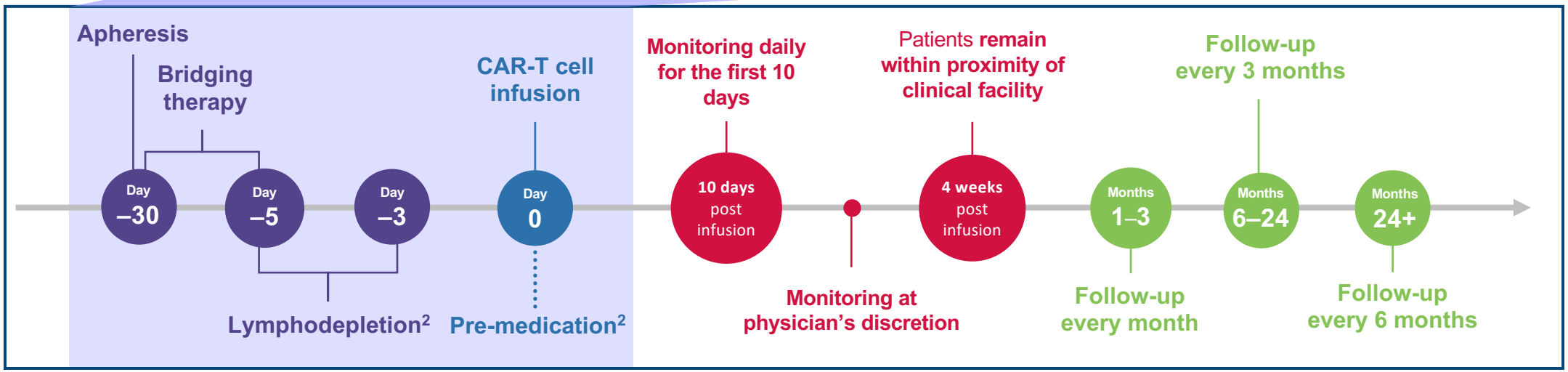
Can we still improve the Patient Journey ?

Leukapheresis[1] (PBMC collection)

Conditioning chemotherapy[1] (Lympodepletion)

CAR-T cell infusion[1] (following pre-medication)





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1. Brudno, J. et Kochenderfer, J.; Nat Rev Clin Onc, 2017
2. As defined per current product SmPC

Currently used lymphodepleting/conditioning regimens (26 variants) – (1)

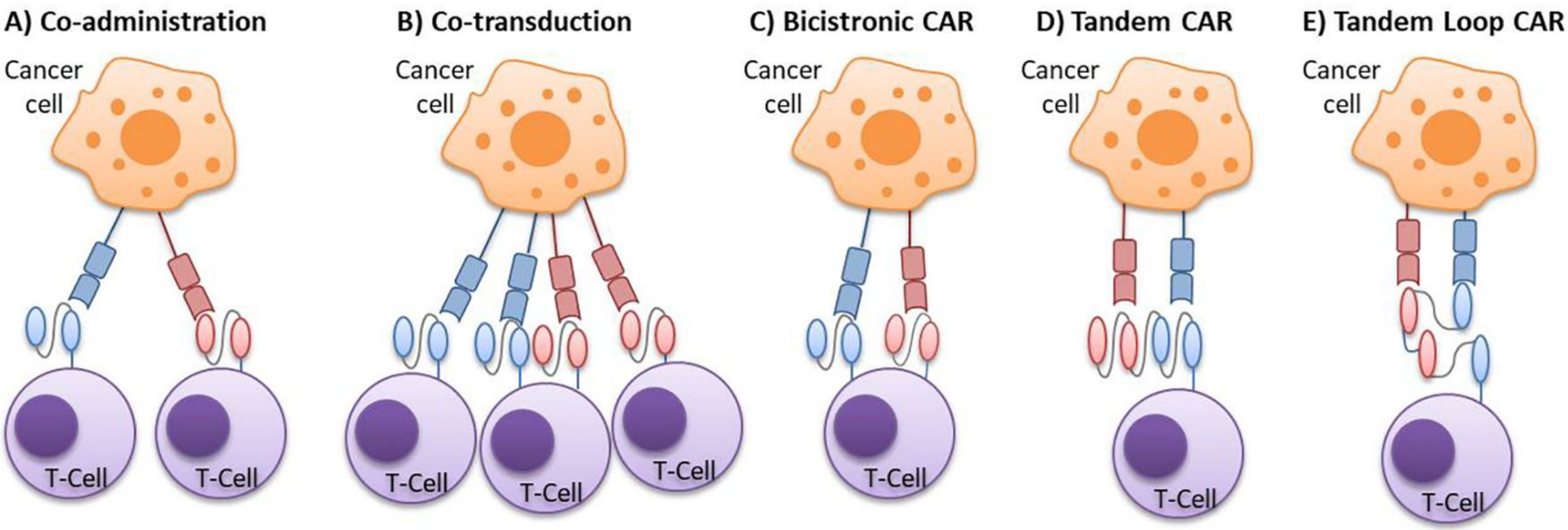
Lymphodepletion Regimen	Dose (mg)	Dose total (mg)	Days	Timing	Comments / Reference	Variant
Fludarabine/ Cyclophosphamide	25/250/m²	75/750/m²	3	day -6 to -2	JULIET, PORTIA studies	1a
Fludarabine/ Cyclophosphamide	25/250/m²	75/750/m²	3	day -7 to -2	NCT05445011	1b
Fludarabine/ Cyclophosphamide	25/250/m²	75/750/m²	3	day -4 to -1	iPD1 CD19 eCAR T cells NCT03208556	1c
Fludarabine/ Cyclophosphamide	25/250/m²	75/750/m²	3	day -3 to -1	Anti-EGFRvIII CAR T Cells NCT02844062 NCT02937844	1d
Fludarabine/ Cyclophosphamide	25/300/m²	75/900/m²	3	day -5 to -3	CD19 CAR-T NCT05326243 CAR7-T Cells NCT04823091	2a
Fludarabine/ Cyclophosphamide	25/250/m²	75/750/m²	3		CI-135 CAR-T cells NCT05266950 JWCAR029 NCT05727683	2b
Fludarabine/ Cyclophosphamide	30/250/m²	90/750/m²	3	day -5 to -3	NCT05326243 Dual CD33/CLL1 CAR T Cells NCT05248685 CD5 CAR T cells NCT05032599 CT125B NCT05487495	3
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3	day-6 to -4	Varnimcabtagene autoleucel (ARI-0001), Cesnicabtagene autoleucel (ARI0002h), TranspoCART	4a
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3	day -7 to -5	ciltacabtagene autoleucel CARTITUDE-1	4b
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3	day -4 to -2	Idecabtagene vicleucel KarMMa huCART NCT03054298	4c
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3	day -6 to -4	Lisocabtagene maraleucel TRANSCEND	4d
Fludarabine/ Cyclophosphamide	30/300/m²	90/300/m²	3,1	day -5 to -3, Day -6	ISIKOK-19 NCT04206943	4e
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3	CART 2-14d after LD	CAR.B7-H3 NCT04670068 ATLCAR.CD128 NCT03672318 NCT05634785 ATLCAR.CD30	4f
Fludarabine/ Cyclophosphamide	30/300/m²	90/900/m²	3		Anti-BCMA CAR-T Cell NCT04637269 CD19 and CD22 Dual-targeted CAR-T Cells NCT04303247 Anti-CD19 Allo-CAR-T Cells NCT04516551	4?
Fludarabine/ Cyclophosphamide	30/500/m²	90/1000/m²	3,2	day-5 to -3	ZUMA-7 OPBG PBCAR20A NCT04030195	5a
Fludarabine/ Cyclophosphamide	30/500/m²	90/1500/m²	3	day -5 to -3	Axicabtagene Ciloleucel Routine, ZUMA-1, CARTITUDE, KaRRMa, JCAR017/TRANSCEND, MB-CART20.1, MB-CART2019.1 (lymphoma)	5b
Fludarabine/ Cyclophosphamide	30/500/m²	90/1500/m²	3	day -7 to -5	Bexucabtagene autoleucel ZUMA - 2	5c
Fludarabine/ Cyclophosphamide	30/500/m²	90/1500/m²	3	CART 2-14d after LD	NCT02690545 NCT02917083	5d
Fludarabine/ Cyclophosphamide	30/500/m²	90/1500/m²	3	day -4 to -2	NCT02443831 CARPALL UF-KURE19 NCT05400109 CARTinNS NCT04561557 CT125A cells NCT04767308	5e
Fludarabine/ Cyclophosphamide	30/500/m²	120/1000/m²	4,2	Completed at day -2	NCT05010564 TRICAR-ALL ELIANA NCT03321123	5f

Lickefett B, et al.. Front Immunol. 2023

Other Clinical areas of improvement

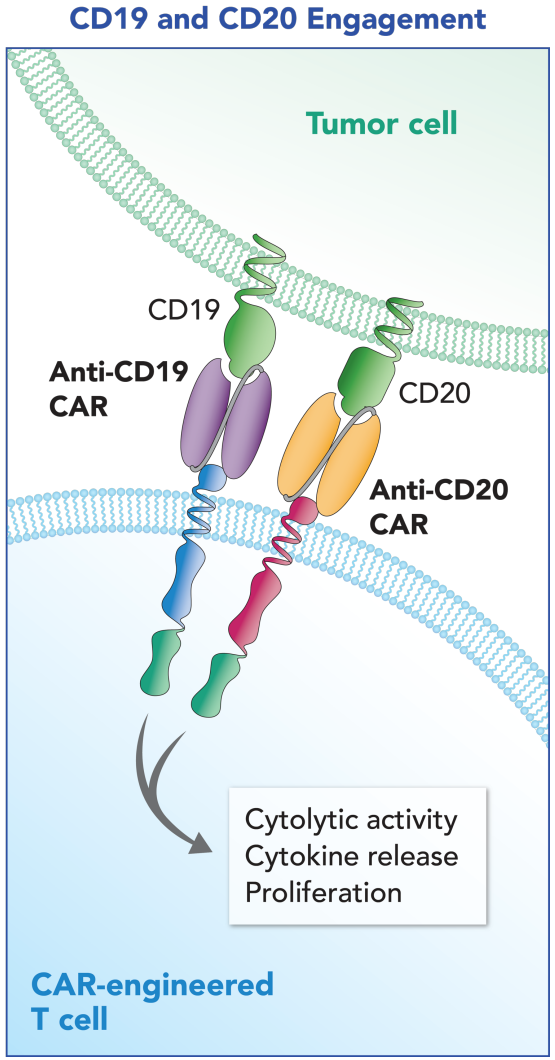
- Bridging therapy:
  - Better reduction of disease = better outcomes?
    - Optimal use of bridging regimens, incl. Radiotherapy
- Optimize toxicity management & outpatient delivery
- Improved CAR T cell products
  - ~30% of patients with relapse downregulate target (CD19) expression

1) Multi-target CAR T therapy



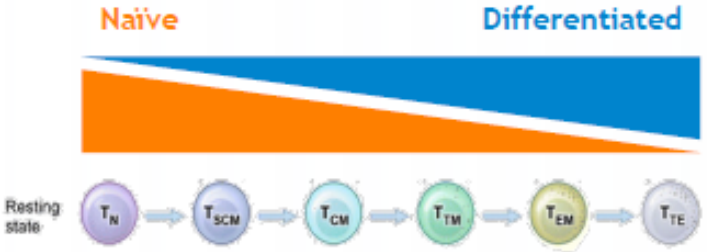
Gomez-Melero et al Front. Immunol. 2025

Kite's Bicystronic Anti-CD19/CD20 CAR Mechanism of Action

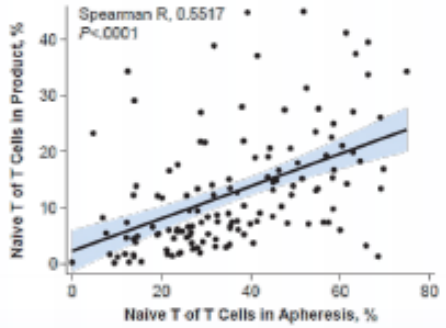


1. Murakami J, et al. ASH 2024. Abstract 3481.

Translational Learning Applied to Next Gen CAR T



Naïve T-cells result in better expansion into memory T-cells

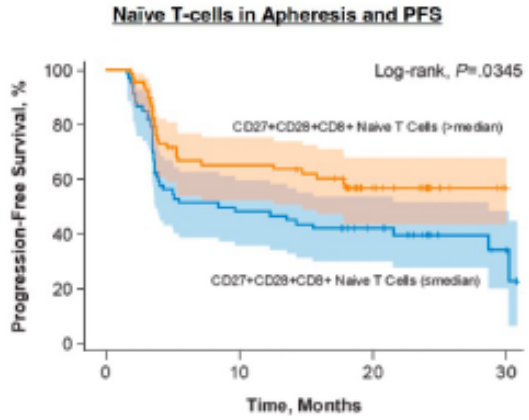


Higher proportion of naïve T-cells in apheresis result in higher proportion of naïve T-cells in product

Similarly, T-cells with poor qualities could impact product

RESULTS FROM ZUMA-7

Higher naïve T-cells in Apheresis result in better clinical outcomes



Fine-tuning T-cell inputs to develop improved CAR T product for select T-cell qualities based on translational research

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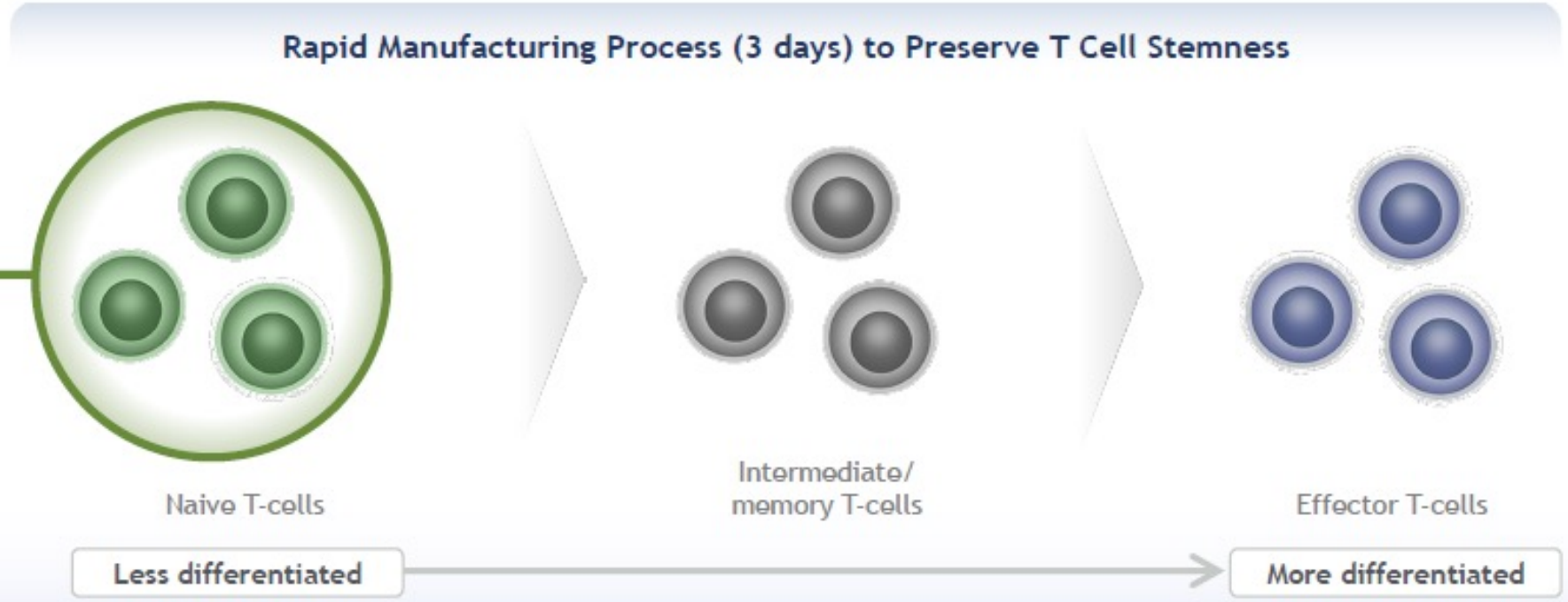
KITE-753:CD19/CD20 Dual-targeting Fast Manufacturing

Key Unmet Need: Speed to treatment especially for those with very aggressive lymphomas

Kite's rapid and enhanced manufacturing process harvests the product early to enrich a more naive, less differentiated T-cell population



Potential Benefits

Improved product potency - demonstrates enhanced efficacy in preclinical studies with the potential for a lower dose in the clinic

Enables increased manufacturing success, reduced turn-around-time and reduced cost of goods - reduced average turnaround time to 3 days

Exploits the benefits of 2 different costim domains and thus the combined functional output - rescue CD19 negative relapsed patients and prevent CD19 antigen escape

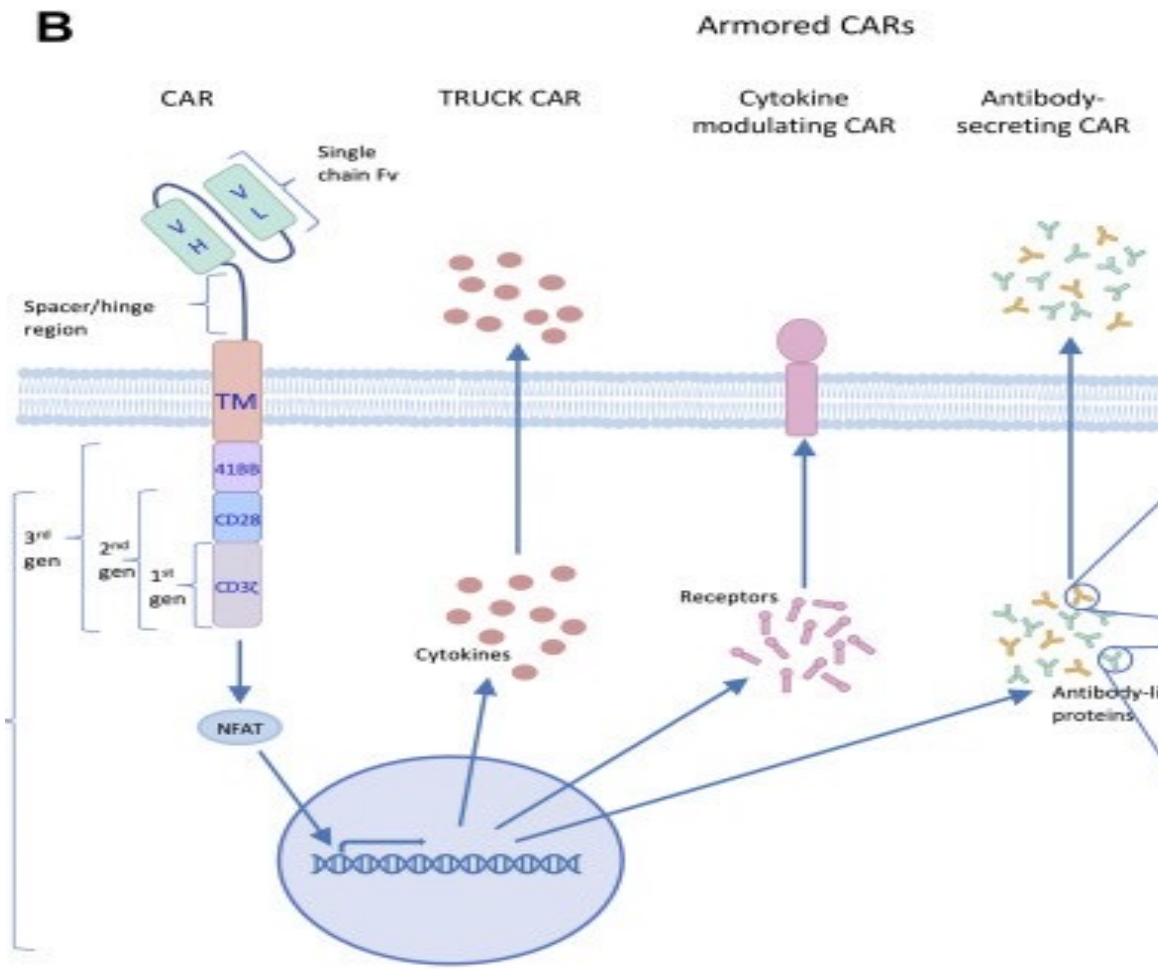
2) Armored CARs – TRUCKs

Regular CAR T

Armored CAR T

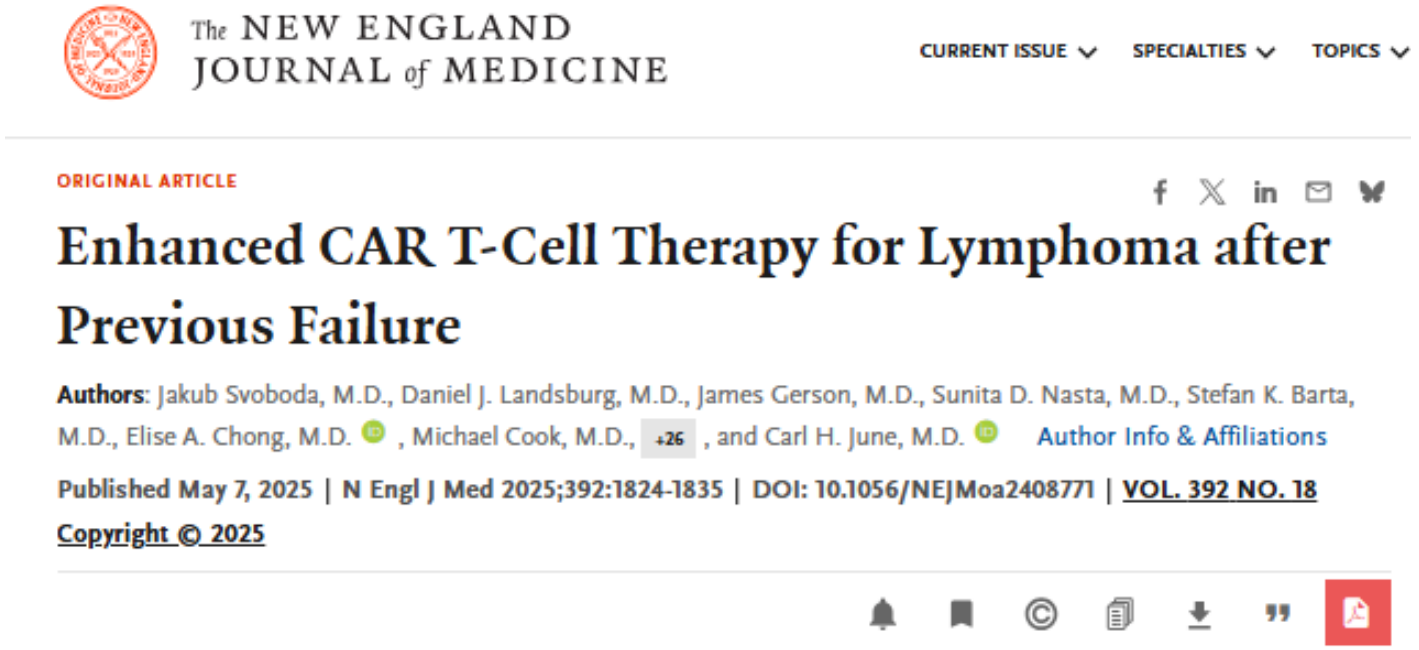
Carcopino et al. Immuno-Oncology and Technology 2024

Armored CAR T therapies



Carcopino et al. Immuno-Oncology and Technology 2024

IL18-Armored CAR in pretreated lymphoma



The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Enhanced CAR T-Cell Therapy for Lymphoma after Previous Failure

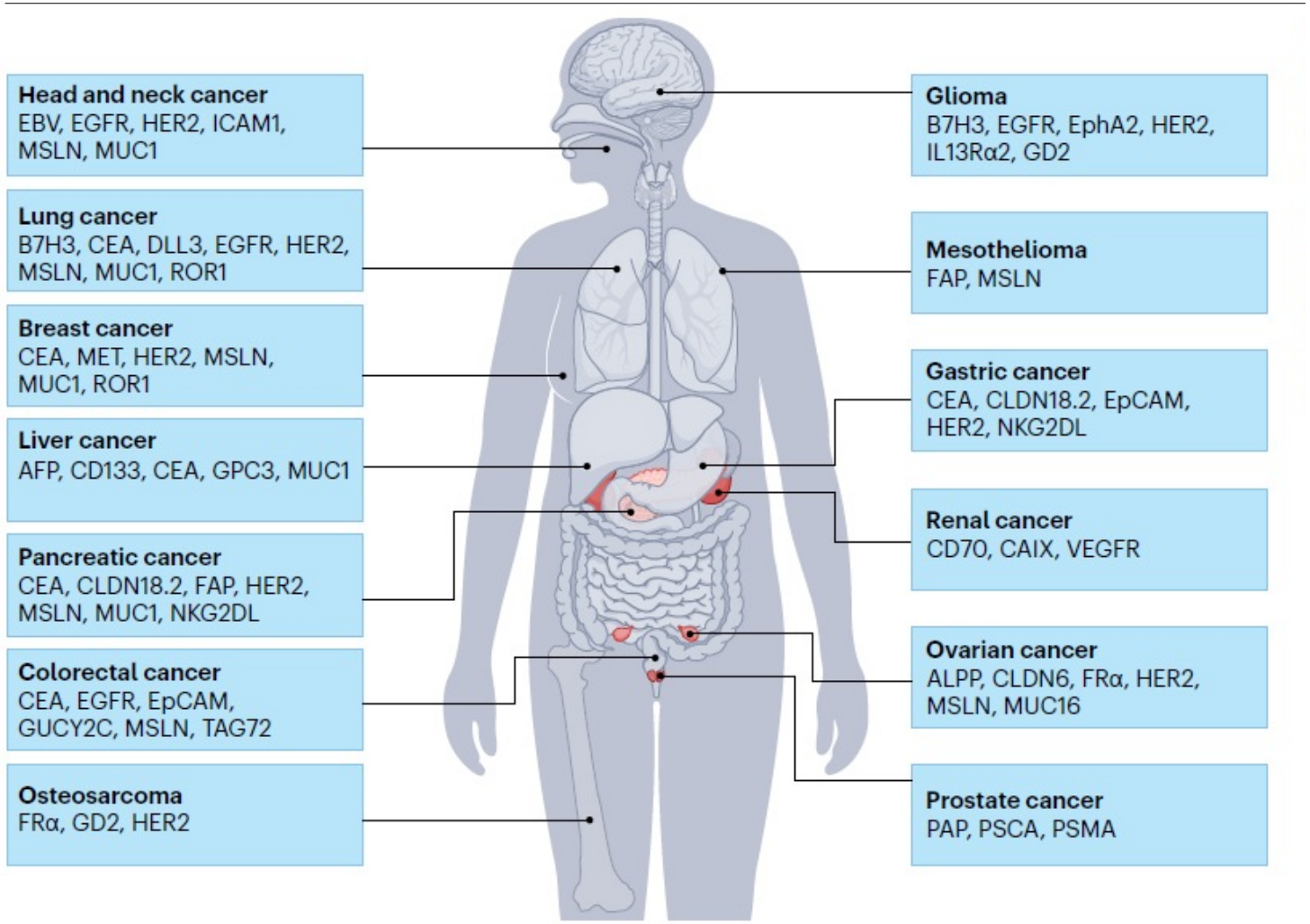
Authors: Jakub Svoboda, M.D., Daniel J. Landsburg, M.D., James Gerson, M.D., Sunita D. Nasta, M.D., Stefan K. Barta, M.D., Elise A. Chong, M.D., Michael Cook, M.D., +26, and Carl H. June, M.D. Author Info & Affiliations

Published May 7, 2025 | N Engl J Med 2025;392:1824-1835 | DOI: 10.1056/NEJMoa2408771 | VOL. 392 NO. 18

Svoboda et al. NEJM 2025

3) Considerations for CAR T cell therapy in solid tumors

3) Emerging Targets for CAR T cell therapy in Solid tumors



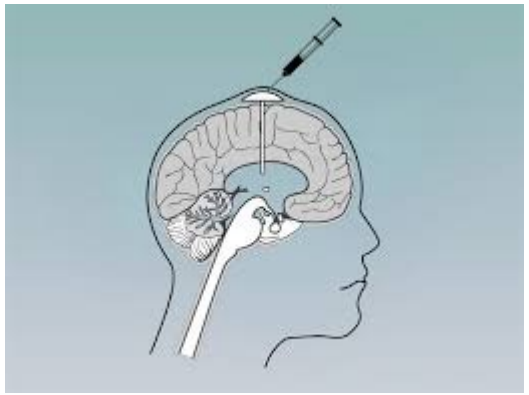
Li et al. Nat Rev Clin Oncol 2025

Early signals in glioblastoma

HEALTH & MEDICINE | JUNE 1, 2025

Dual-target CAR T-cell therapy slows growth of aggressive brain cancer

Researchers from Penn Medicine have demonstrated encouraging tumor reductions rarely seen in recurrent glioblastoma following phase I clinical trials.



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Bagley et al. Nature Medicine 2025

Conclusion