4th MEETING ON
INNOVATIVE IMMUNOTHERAPIES
FOR LYMPHOID MALIGNANCIES

Presidents
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Società Italiana di Ematologia

# Clinical Results CAR-T for DLBCL: What's Next?

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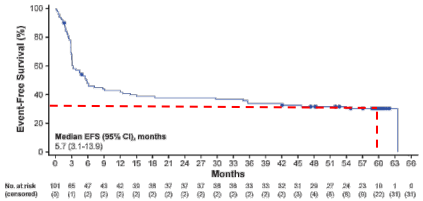
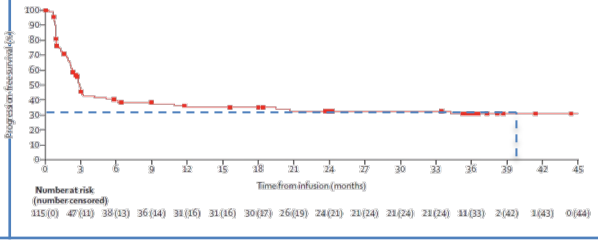
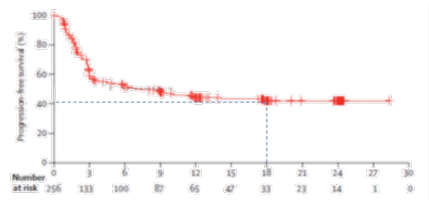
# Disclosures of Stephen J. Schuster

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
|---|---|---|---|---|---|---|---|
| AbbVie | | | | | | X | |
| ADC Therapeutics | | | | | | X | |
| AstraZeneca | X | | X | | | X | |
| BeiGene | | | | | | X | |
| BioNTech | | | X | | | | |
| BMS | X | | | | | X | |
| Caribou Bio | | | X | | | X | |
| Genentech/Roche | X | | | | | X | |
| Genmab | X | | X | | | X | |
| Incyte | | | X | | | | |
| Janssen | | | | | | X | |
| Novartis | X | | X | | | X | |
| Vittoria Bio | | | | | | X | |

# Large B-cell lymphomas: the remaining unmet need

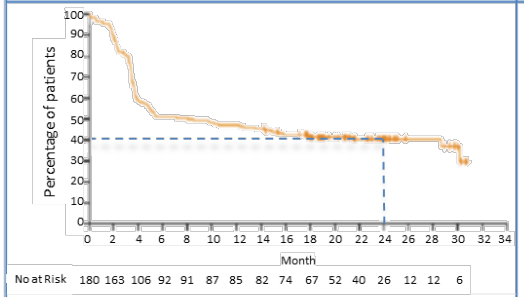
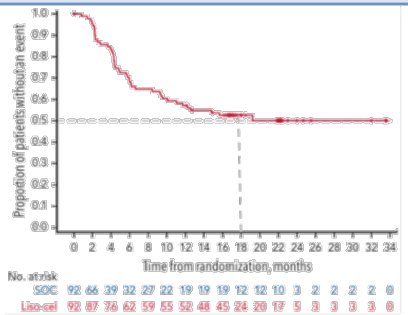
## ~ 2/3 of patients fail to achieve durable responses with clinically available CAR-T products as 3rd-line therapy

| Axicabtagene ciloleucel[1] | Tisagenlecleucel[2] | Lisocabtagene maraleucel[3] |
|---|---|---|
| **ZUMA-1**[1]: axi-cel as ≥ 3rd-line therapy for LBCL<br>N = 101<br>Median follow-up: 63.1 months<br>**Estimated 5-year EFS: 30.3%** | **JULIET**[2]: tisa-cel as > 3rd-line therapy for LBCL<br>N = 115<br>Median follow-up: 40·3 months<br>**Estimated 40-month PFS:~30%** | **TRANSCEND**[3]: liso-cel as ≥ 3rd-line therapy LBCL<br>N = 256<br>Median follow-up: 12.3 months<br>**Estimated 18-month PFS: 42.1%** |
|  |  |  |

[1]Neelapu SS, et al. Blood. 2023; Epub ahead of print; [2]Schuster SJ, et al. Lancet Oncol 2021;22(10):1403-1415; [3]Abramson J, et al. Lancet. 2020;396(10254):839-852.

# Large B-cell lymphomas: the remaining unmet need

## As 2nd-line, ~1/2 of patients have disease progression or need new lymphoma treatment by 2 years after available CAR-T products

| Axicabtagene ciloleucel[1] | Lisocabtagene maraleucel[2] |
|---|---|
| **ZUMA-7**[1]: axi-cel as ≥ 2nd-line therapy for r/r LBCL<br>N = 180<br>Median follow-up: 24.9 months<br>**Estimated 24-month EFS: 41% (95% CI, 33-48)** | **TRANSFORM**[2]: liso-cel as ≥ 2nd-line therapy for r/r LBCL<br>N = 92<br>Median follow-up: 17.5 months<br>**Estimated 18-month EFS: 52.6% (95% CI, 42.3-62.9)** |
|  |  |

***So, do we need a new car?***

[1]Locke FL, et al. N Engl J Med. 2022;386(7):640-654; [2]Abramson, et al. Blood. 2023;141(14):1675-1684.

*The question is,*

**"How can we improve these results?"**

*The easy answer is,*

**"Treat patients who are likely to respond**

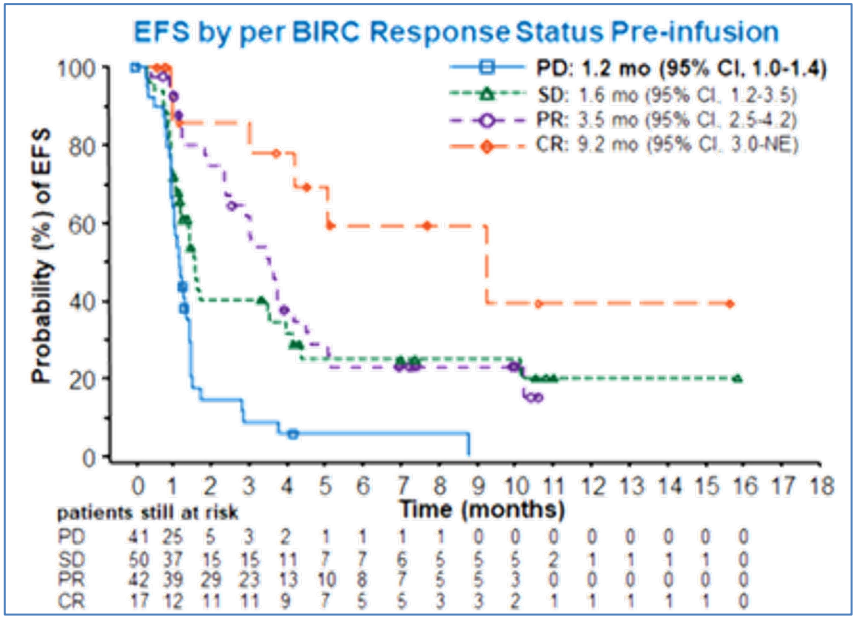
**and treat those destined to fail on clinical trials."**

*The next question is,*

**"So, how do we identify patients destined to fail CAR-T."**

# Patient characteristics impact outcome: Disease Control

- **Disease status at the time of CAR-T infusion impacts best response and EFS**
  - **Data from the BELINDA trial: tisagenlecleucel vs SOC**




**Multivariate Logistic Regression Model for Post-Infusion Best Overall Response (CR/PR vs SD/PD/UNK) in Arm A (second-line CAR-T)**

| | Odds Ratio Estimates | | |
|---|---|---|---|
| Variable | Point Estimate | 95% Wald Confidence Limits | |
| CR/PR before infusion vs. SD/PD before infusion at mean cell dose | 7.75 | 3.23 | 18.62 |

**The odds ratio is the odds of having a best overall response of CR/PR vs. SD/PD/UNK; *i.e.*, an odds ratio >1 means patients are more likely to have a best overall response of CR/PR.**

**EFS time is relative to date of tisagenlecleucel infusion; median time from pre-infusion disease assessment to infusion was 10 days (range, 2-57; Q1-Q3, 8-15).**
**EFS events defined as PD/SD after day 71 from randomization or death at any time.**

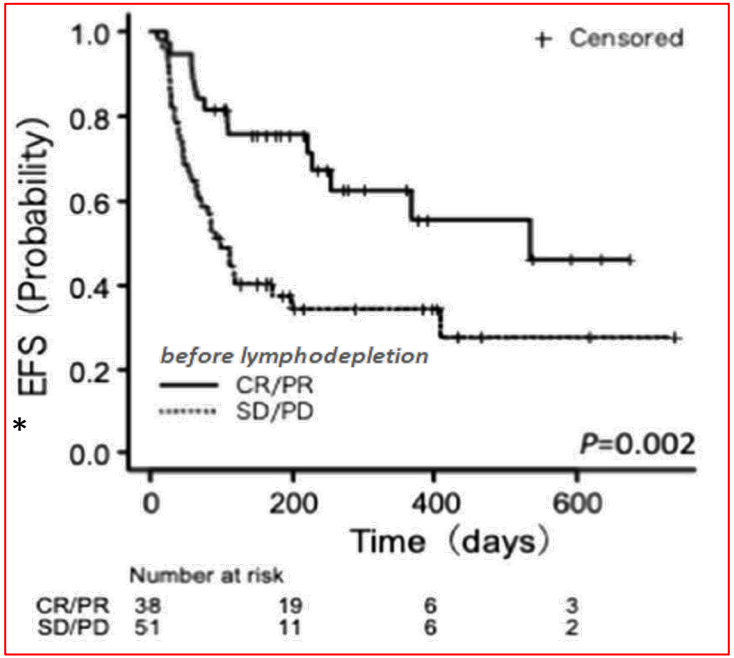
PD = progressive disease; SD = stable disease; PR = partial response; CR = complete response

Bishop *et al.* N Engl J Med. 2021 Dec 14. Epub

# Patient characteristics impact outcome: Disease Control

- **Disease status at the time of CAR-T infusion impacts best response and EFS**
  - **Real-world data from Japan for tisagenlecleucel in r/r LBCL**

**Event-free survival after tisagenlecleucel by disease status *after* bridging therapy and *before* lymphodepletion**




***EFS defined as the period from infusion to either progression or death**

[1]Goto H, et al. Int J Clin Oncol. 2023;28:816–826.

# Patient characteristics impact outcome: Serum LDH

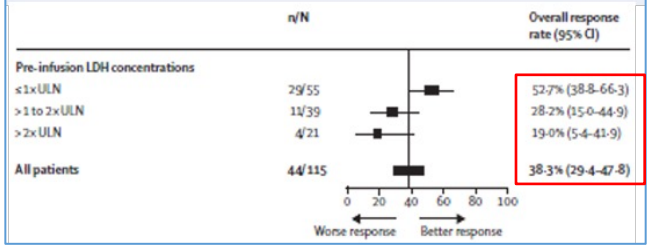
- **Pre-infusion serum LDH impacts response to CAR-T and survival outcome**
  - **Data from the JULIET trial: Phase 2 trial of tisagenlecleucel in r/r LBCL**

**Multivariable analysis ***

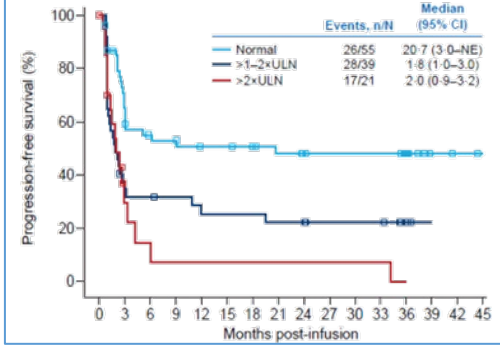
| Predictive Factors from Univariable Analysis | Responders/Patients | Odds Ratio (95% CI) |
|---|---|---|
| LDH | | |
| ≤ x ULN | 29/55 | 2.74 (0.71-10.56) |
| >2 x ULN | 4/21 | |
| >1 - 2 x ULN | 11/39 | 0.97 (0.23-4.06) |
| >2 x ULN | 4/21 | |

*Lab analytes are defined as the closest time before or on the day of infusion (93% of values were obtained on the day of infusion)

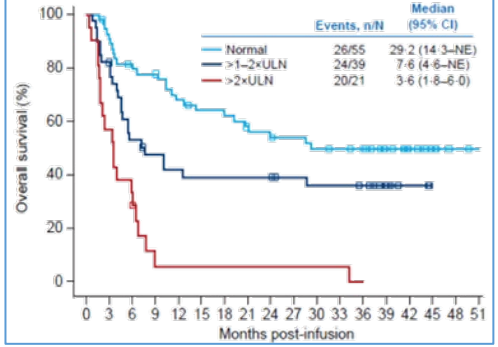
**Overall best response rates by pre-infusion LDH**




**Progression-free survival by LDH**



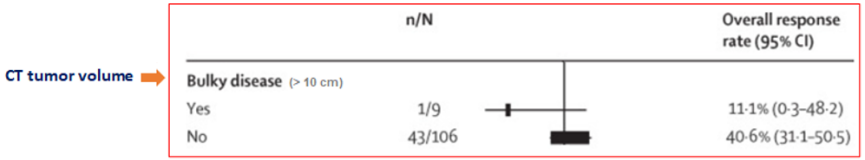

**Overall survival by LDH**



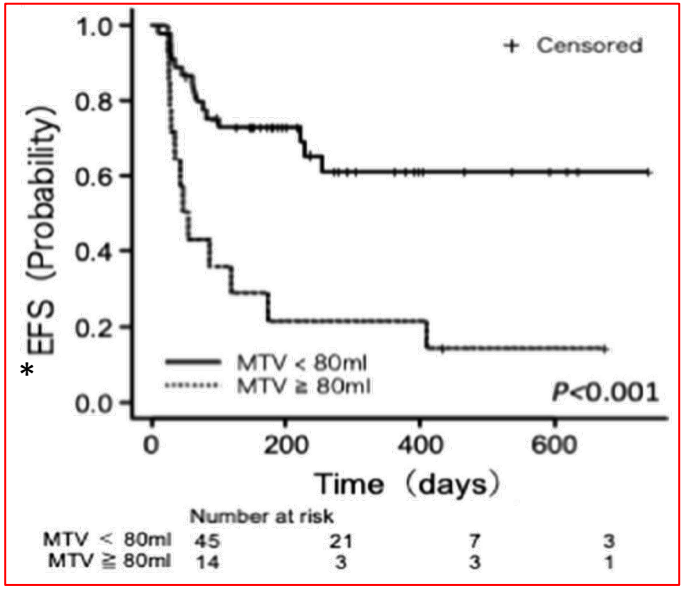

Schuster SJ, *et al*. Lancet Oncol. 2021;22(10):1403-1415.

# Patient characteristics impact outcome: Tumor Volume

- **Tumor bulk and its impact on response *("size matters")*[1]**
  - **Data from JULIET trial: Phase 2 trial of tisagenlecleucel in r/r LBCL**




- **MTV Data for tisagenlecleucel in r/r LBCL[2]**
  - **Real-world evidence from Japan**




*** EFS defined as the period from infusion to either progression or death**

MTV, metabolic tumor volume, EFS, event-free survival

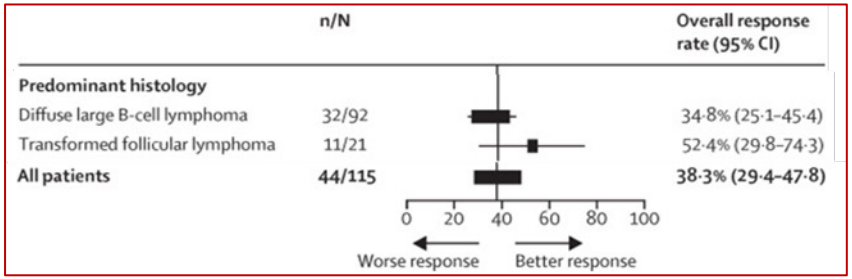
[1]Schuster SJ, *et al*. Lancet Oncol. 2021;22(10):1403-1415.

[2]Goto H, et al. Int J Clin Oncol. 2023;28:816–826.

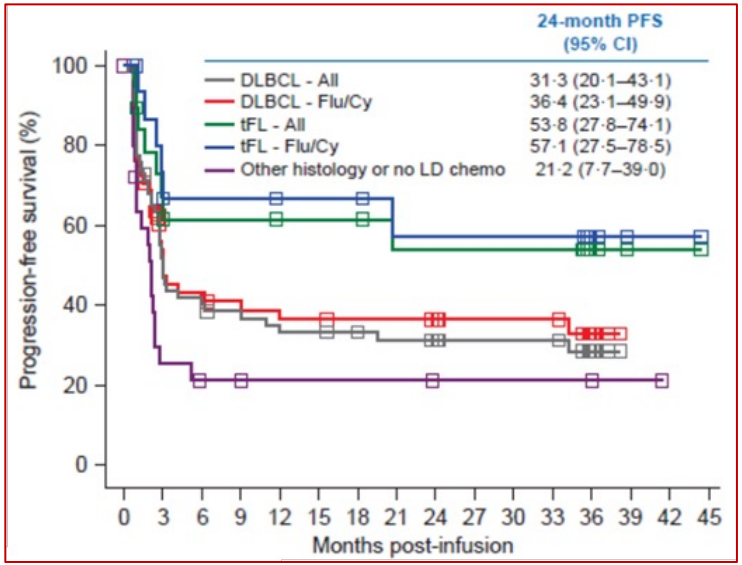
# Patient characteristics impact outcome: LBCL Subtype

- **Subtype of lymphoma impacts CAR-T response rates and progression-free survival**
  - **Data from the JULIET trial: Phase 2 trial of tisagenlecleucel in r/r LBCL**

**Overall response rates by lymphoma subtype**




**Progression-free survival by lymphoma subtype**




Schuster SJ, *et al*. Lancet Oncol. 2021;22(10):1403-141

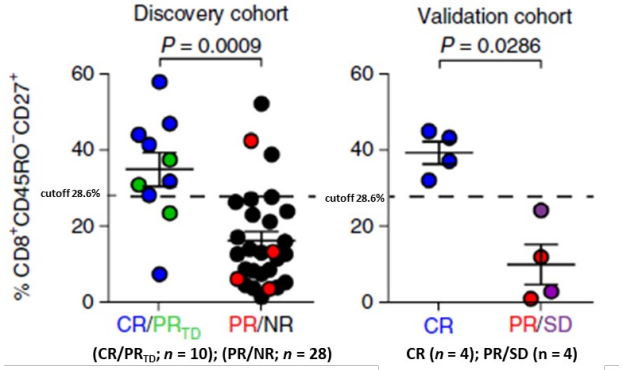
# Patient characteristics impact outcome: T cell fitness

**T cell fitness** refers to the functional capacity and metabolic vigor of T cells, reflected by their ability to effectively *recognize antigens*, *respond to co-stimulation*, *proliferate*, *produce cytokines*, *differentiate into effector cells*, *resist exhaustion*, and *provide* immunologic memory.

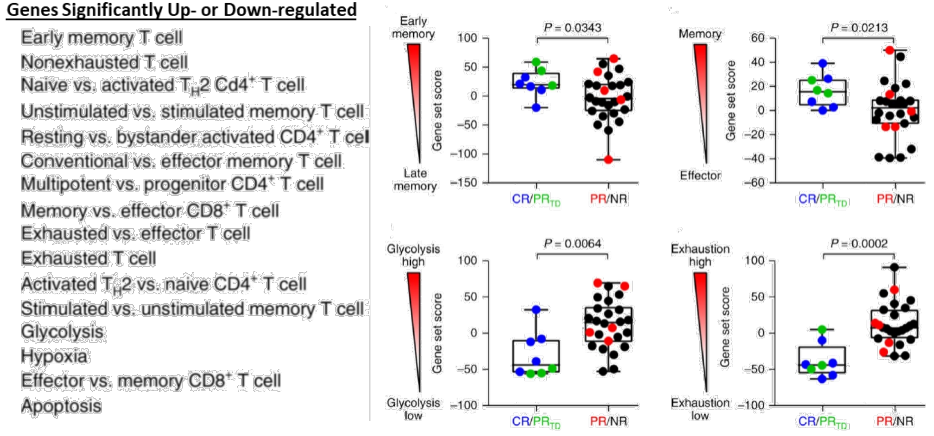
## Patient characteristics impacting T cell fitness: Considerations

- Age-related immunosenescence
- Lymphoma-related immunosuppression
- Therapy-related (iatrogenic) immunosuppression

## Naïve and memory CD8⁺ T cell content (CD45RO⁻CD27⁺ cells) in *leukapheresis material* contribute to response to CAR-T in CLL




## Genomic evaluation of CLL patient-derived *CAR-T cell products* and response to CAR-T cells

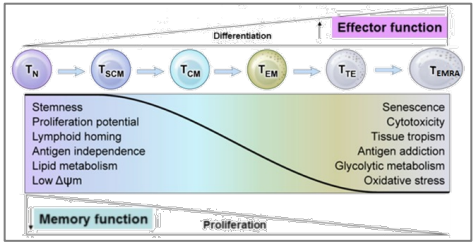


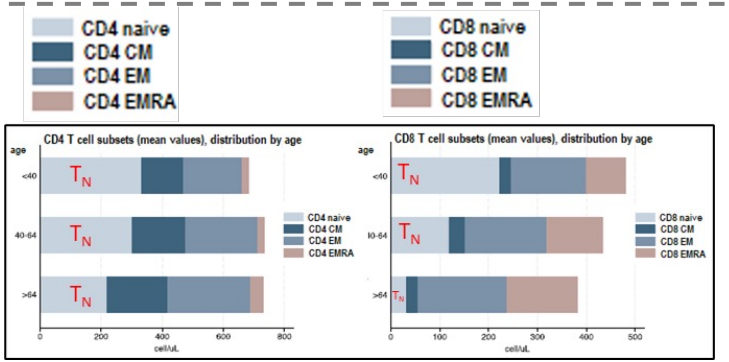

CR, complete remission; $PR_{TD}$, partial remission with late relapse of transformed disease; PR, partial response; NR, no response

Fraietta, *et al*. Nat Med 2018; 24:563–571.

# Impact of *Age-Related* Immunosenescence on Naïve and Memory T Cells

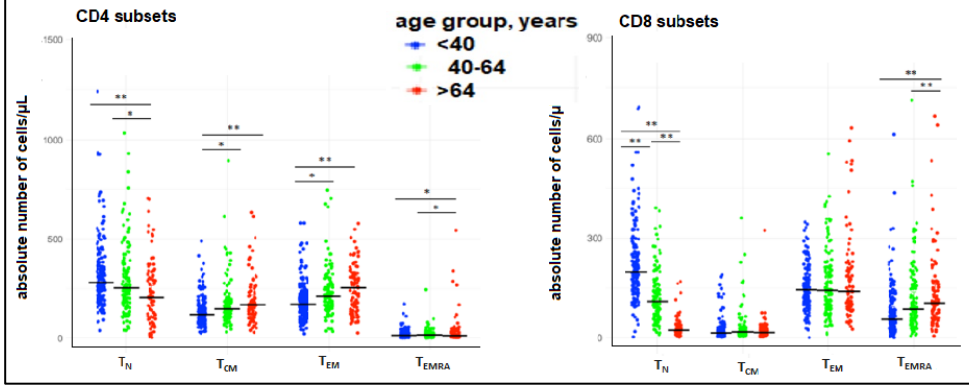
- **Study of healthy adults (n = 363) established *age-specific, immune cell reference ranges*;**
  **A systematic review and meta-analysis validated these findings (n = 7,425)[1]**




Demographics and immune cell subsets distribution of study population ($n = 363$) by three age groups

| | <40 years old ($n = 158$) | 40–64 years old ($n = 127$) | >64 years old ($n = 78$) |
|---|---|---|---|
| Age, median (Q1, Q3) | 29 (27, 34) | 47 (43, 55) | 70.5 (67, 76) |
| Gender; Male, *n* (%) | 72 (45.6%) | 56 (44.1%) | 29 (37.2%) |

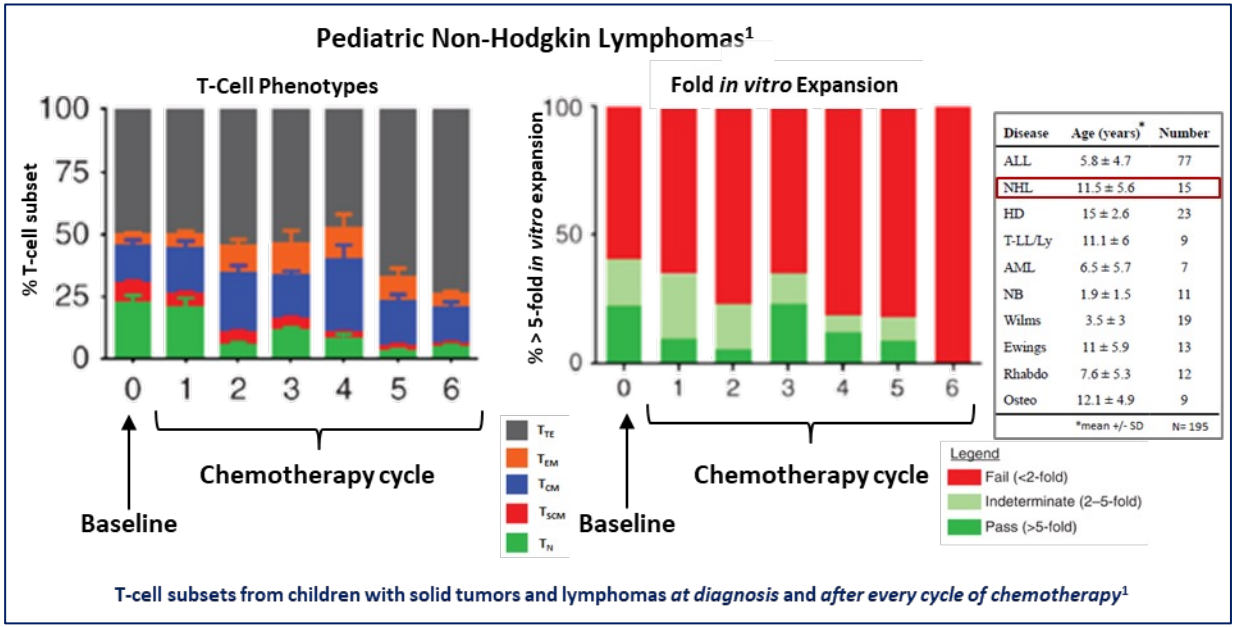



$T_N$, naive T cells; $T_{SCM}$, T stem cell memory cells; $T_{CM}$, T central memory cells; $T_{EM}$, T effector memory cells; $T_{TE}$, T effector cells; $T_{EMRA}$, CD45RA$^+$ terminal effector memory T cells

[1]Chang, *et al*. Immunity & Ageing.2024; 21:75

# Pre-Existing *Lymphoma- and Therapy-Related* Immunodeficiency

- **Naïve T-cell deficits *at diagnosis* and *after chemotherapy* may impair cell therapy potential**




| Disease | Age (years)* | Number |
|---|---|---|
| ALL | 5.8 ± 4.7 | 77 |
| NHL | 11.5 ± 5.6 | 15 |
| HD | 15 ± 2.6 | 23 |
| T-LL/Ly | 11.1 ± 6 | 9 |
| AML | 6.5 ± 5.7 | 7 |
| NB | 1.9 ± 1.5 | 11 |
| Wilms | 3.5 ± 3 | 19 |
| Ewings | 11 ± 5.9 | 13 |
| Rhabdo | 7.6 ± 5.3 | 12 |
| Osteo | 12.1 ± 4.9 | 9 |
| | *mean +/- SD | N= 195 |

**T-cell subsets from children with solid tumors and lymphomas *at diagnosis* and *after every cycle of chemotherapy*[1]**

**% $T_N$ in blood of healthy children: Distribution by age**
**CD4, n = 805; CD8, n = 807 [2]**

| Subset | 0-3 mo | 2-6 y |
|---|---|---|
| CD 4+ /45RA + /62L+ | 89 (61-94) | 70 (50-85) |
| CD 8+ /45RA + /62L + | 79 (56-88) | 64 (42-81) |
| | **3-6 mo** | **6-12 y** |
| CD 4+ /45RA + /62L+ | 88 (64-92) | 58 (42-74) |
| CD 8+ /45RA + /62L + | 77 (53-88) | 58 (39-73) |
| | **6-12 mo** | **12-18 y** |
| CD 4+ /45RA + /62L+ | 83 (58-91) | 51 (31-65) |
| CD 8+ /45RA + /62L + | 72 (47-87) | 56 (42-73) |
| | **1-2 y** | |
| CD 4+ /45RA + /62L+ | 79 (62-90) | |
| CD 8+ /45RA + /62L + | 71 (46-85) | |

**$T_N$**, naive T cells; **$T_{SCM}$**, T stem cell memory cells; **$T_{CM}$**, T central memory cells; **$T_{EM}$**, T effector memory cells; **$T_{TE}$**, T effector cells; **$T_{EMRA}$**, $CD45RA^+$ terminal effector memory T cells

[1]Das, *et al.* Cancer Discov. 2019; 9(4):492-499.
[2]Shearer, *et al.* J Allergy Clin Immunol. 2003; 112(5):973-980.

# So, how can we more accurately predict CAR-T outcome?


Image adapted from: https://fineartamerica.com/featured/hands-on-crystal-ball-allan-swart.html

# Deep Learning-Based Image Analysis: Radiomics

***"Images are more than pictures, they are data."*** Gillies RJ, *et al.* Radiology (2016) 278 (2): 563-77.

**Hypothesis**:

- Radiologic images contain *image-agnostic features* beyond that used to reconstruct humanly recognizable anatomic and functional pictures

**Objectives**:

1) extract *image-agnostic features* (data) from PET/CT images that correlate with clinical outcome using machine learning

2) develop a computerized decision support system (program) by retraining a pre-trained neural network (AlexNet[1])

3) prospectively validate this program for predicting CAR-T outcome

**Validation**:

- Analyze *pre-treatment* PET/CT images using the retrained neural network to test prediction of CAR-T outcome with *investigators blinded to patients' outcomes*

**Lesion Level Model**

**Training Set: Predicting Lesion-level Response from Pre-Treatment Imaging**

Diagnostic performance of **lesion-Level** treatment response predictions for LBCL cohort:

- Data shown for 3 imaging modalities using 3 whole-slice per lesion input and transfer learning approach
- Median time from imaging to CAR-T infusion: diagnostic CT scan, 15 days (range 4-62 days)
  low-dose CT + PET, 30 days (range 5-46 days)

**Diagnostic CT scan**

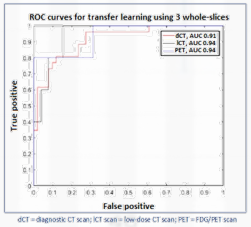
| Input | Accuracy | Sensitivity | Specificity | AUC |
|---|---|---|---|---|
| 3-whole slices | 0.84 ± 0.05 | 0.90 ± 0.04 | 0.76 ± 0.12 | 0.90 ± 0.05 |

**Low-dose CT scan**

| Input | Accuracy | Sensitivity | Specificity | AUC |
|---|---|---|---|---|
| 3-whole slices | 0.90 ± 0.05 | 0.95 ± 0.04 | 0.74 ± 0.02 | 0.94 ± 0.07 |

**PET scan**

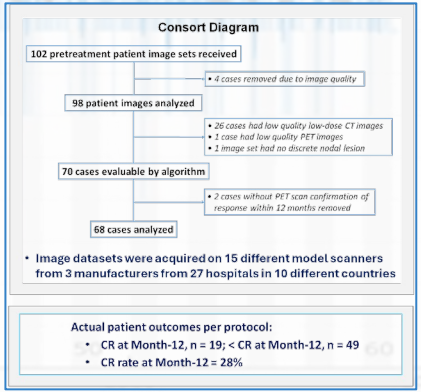
| Input | Accuracy | Sensitivity | Specificity | AUC |
|---|---|---|---|---|
| 3-whole slices | 0.90 ± 0.07 | 0.95 ± 0.05 | 0.81 ± 0.19 | 0.95 ± 0.06 |

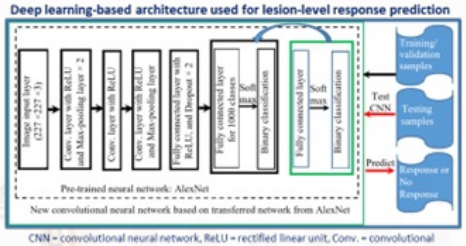



dCT = diagnostic CT scan; ICT scan = low dose CT scan; PET = FDG/PET scan

*Sensitivity = correctly identifies lesions in complete remission at 12-months after CAR-T (*true positive rate*)

*Specificity = correctly identifies lesions not in remission at 12 months or at last follow-up if < 12 months (*true negative rate*)




Binary response output:
CR or non-CR at 12 months post CAR-T

**Results**

**Predicting Outcome from Pretreatment Image Analysis + Pretreatment LDH**

- JULIET Cohort: Cumulative Sensitivity and Cumulative Specificity

| Pretreatment Serum LDH > 2 x Upper Limit of Normal Predicts Failure (no CR by Month-12) | | | | | |
|---|---|---|---|---|---|
| Input: LDH > 2 x ULN n = 67 (cohort evaluated by image analysis) | Sensitivity | Specificity | Balanced Accuracy* | Positive Predictive Value | Negative Predictive Value |
| | 15% | 100% | 63% | 100% | 75% |

| Deep Learning-Based Image Analysis Predicts Failure (no CR at Month-12) from Pretreatment PET/CT, ≥ 60% Rule | | | | | |
|---|---|---|---|---|---|
| Input: PET + LD-CT, 3 slices each per lesion n = 68 | Sensitivity | Specificity | Balanced Accuracy* | Positive Predictive Value | Negative Predictive Value |
| | 49% | 77% | 63% | 85% | 37% |

| Parallel Analysis of Pretreatment DL-Image Analysis + Pretreatment LDH to Predict CAR-T Failure (no CR at Month-12) Cumulative Sensitivity and Cumulative Specificity | | | | | |
|---|---|---|---|---|---|
| Input: DL-Image Analysis + LDH > 2 x ULN | Sensitivity_cumulative | Specificity_cumulative | Balanced Accuracy* | PPV_cumulative | NPV_cumulative |
| | 57% | 77% | 67% | 86% | 41% |

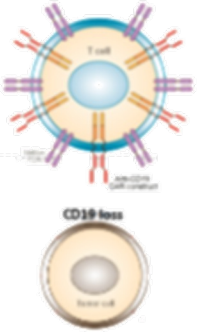
CR, complete response; LD-CT, low-dose CT; NPV, negative predictive value; PPV, Positive predictive value

*Balanced Accuracy = (sensitivity + specificity) / 2. Balanced accuracy reported because of imbalance between number of responders and non-responders in test group

[1]Tong Y, et al. PLoS ONE 2023;18(7):e0282573.
[2]Schuster S J, et al. ASH 2025 (poster)

# *Disease-specific* determinants of CAR-T success or failure

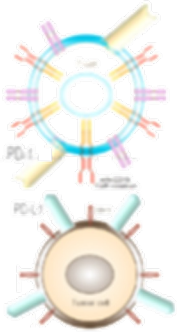
## Some Mechanisms of Tumor Resistance to CAR-T Cells Targeting CD19 in B-Cell Lymphomas




### CD19 antigen loss

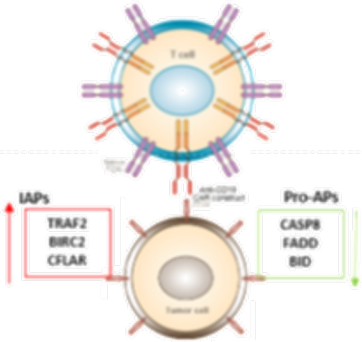
- acquired mutations and alternative splicing of CD19

(Sotillo et al. Cancer Disc. 2015)




### T-cell exhaustion/hypofunction

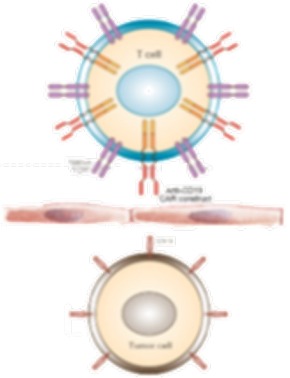
- mediated by inhibitory ligands on tumor cells and cells in the TME
- peripheral self-tolerance (B cell recovery? late relapses?)
- TME-induced T cell hypofunction (reversible)




### Intrinsic tumor resistance

- loss of death receptor signaling molecules causes resistance to CAR T in vitro + in vivo
- failed CAR-T assoc./w lower death receptor-assoc. gene expression by tumor cells

(Singh, et al. Cancer Disc. 2020)




### Insufficient T-cell infiltration

- T cells paralysis
- physiologic factors (high interstitial fluid pressure, hypoxia, pH)

# Recently completed, active, and upcoming *investigator-initiated* clinical trials at UPenn addressing tumor-specific mechanisms of resistance

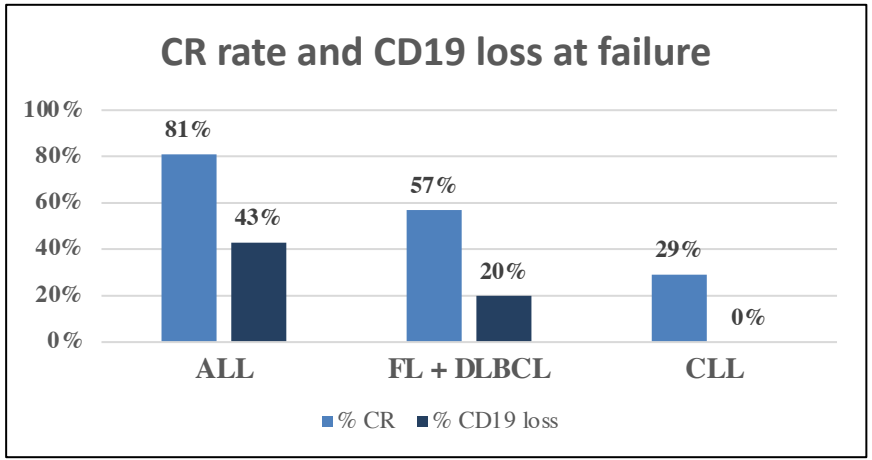
| CD19 antigen loss | T-cell exhaustion/hypofunction | Intrinsic tumor resistance | Insufficient T-cell infiltration |
|---|---|---|---|
| **Phase II study of dual targeting of CD19 and CD20 antigens using CD19-CAR T cells and CD20-BsAb**<br>PI: E. Chong<br>NCT04889716<br>• *active* • *recruiting* | **Interleukin-18 secreting anti-CD19 CAR T cells [huCART19-IL18 cells]**<br>PI: J. Svoboda<br>NCT04684563<br>• *fully accrued*<br>**KIR-CAR/Dap12–modified T cells**<br>Pre-clinical completed*<br>*Wang, et al. Cancer Imm Res 2015;3:815<br>PI: S. Schuster<br>NCT06544265<br>• *active* • *recruiting*<br>**CD5 knockout CAR-T cells**<br>Pre-clinical completed*<br>*Patel, et al. Sci Imm 2024;19:9(97):eadn6509<br>PI: S. Barta<br>NCT06420089<br>• *active (for T-cell)* • *recruiting* | **Venetoclax-resistant CAR T overexpressing mutated BCL-2(F104L) [BCL-2(F104L)-CART19]**<br>Pre-clinical completed*<br>* Lee, et al. Cancer Discov 2022;12:2372<br>PI: M. Ruella<br>• *clinical trial planned* | *Under non-disclosure agreement* |

# *Disease-specific* determinants of CAR-T success or failure

## CD19 antigen loss or downregulation

### Early (prehistoric) CTL019 efficacy data from Penn and CHOP

| Disease | N | CD19 loss at PD |
|---|---|---|
| ALL[1] | 30 | 3/7 |
| FL + DLBCL[2] | 28 | 1/5 |
| CLL[3] | 14 | 0/10 |




- More responsive diseases seem more likely to fail due to CD19 loss
- Less responsive diseases, like CLL, require alternative explanations

[1]Maude S, *et al*. NEJM. 2014; 371(16): 1507-1517; [2]Schuster SJ, *et al*. N Engl J Med. 2017;377(26):2545-2554; [3]Porter DL, *personal communication 2018 Mar 12.*

# *Disease-specific* determinants of CAR-T success or failure

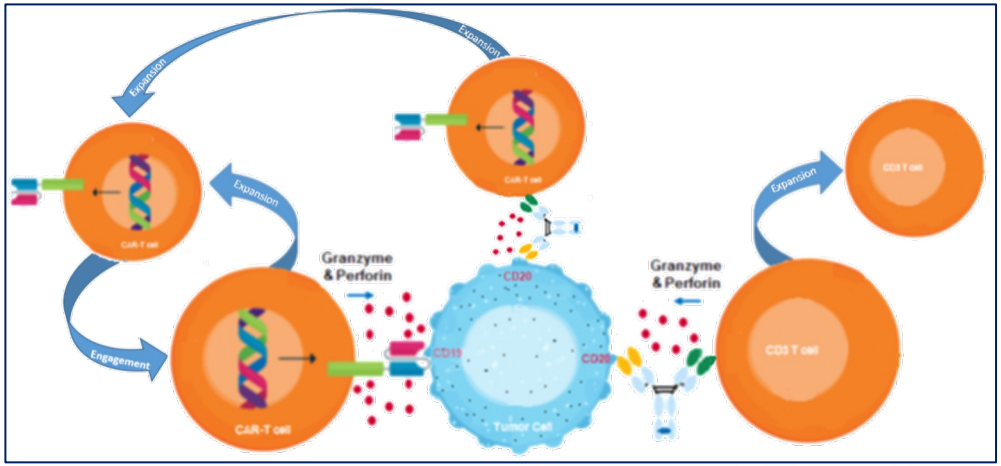
- **Recruiting UPenn clinical trial addressing CD19 antigen loss or downregulation**

**Phase II Study of Dual Targeting of CD19 and CD20 Antigens Using Sequential CD19-directed 4-1BB-CD3ζ CAR-T Cells Followed by Mosunetuzumab or Glofitamab in Relapsed or Refractory DLBCL or Transformed FL**

**Rationale:**

**Early administration of CD20:CD3 bispecific antibodies (mosunetuzumab or glofitamab) after CD19-directed CAR-T cell therapy may enhance tumor cytotoxicity by:**

- **synergistic or additive B cell cytotoxicity via simultaneously targeting two different B cell (tumor) antigens, *i.e.*, CD19 and CD20**
- **reducing CD19-negative tumor cell escape by targeting a second B cell antigen**
- **enhancing *in vivo* expansion of CAR T cells, as observed for T cells in general, after bispecific T cell engaging antibody exposure**




ClinicalTrials.gov Identifier: NCT04889716

Recruitment Status : Recruiting
First Posted : May 17, 2021

| | |
|---|---|
| Study Type : | Interventional (Clinical Trial) |
| Estimated Enrollment : | 42 participants |
| Allocation: | Non-Randomized |
| Intervention Model: | Sequential Assignment |
| Actual Study Start Date : | November 5, 2021 |
| Estimated Primary Completion Date : | December 31, 2023 |
| Estimated Study Completion Date : | December 31, 2025 |

**PI: E. Chong**

# *Disease-specific* determinants of CAR-T success or failure

## • UPenn clinical trial addressing T cell exhaustion

### Phase I Trial of huCART19-IL18 Cells in Patients With Relapsed or Refractory CD19+ Cancers

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enhanced CAR T-Cell Therapy for Lymphoma after Previous Failure

Jakub Svoboda, M.D.,[1] et al.

N Engl J Med 2025;392:1824-35.
DOI: 10.1056/NEJMoa2408771


**Rationale**

**to utilize IL-18 as a pro-inflammatory cytokine to:**

- **enhance CAR T cell proliferation**
- **recruit additional immune cells into the TME to mediate antitumor effects toward CAR-T resistant tumor cells**
- **mitigate the potential impact of CAR T cell exhaustion**

**Results**

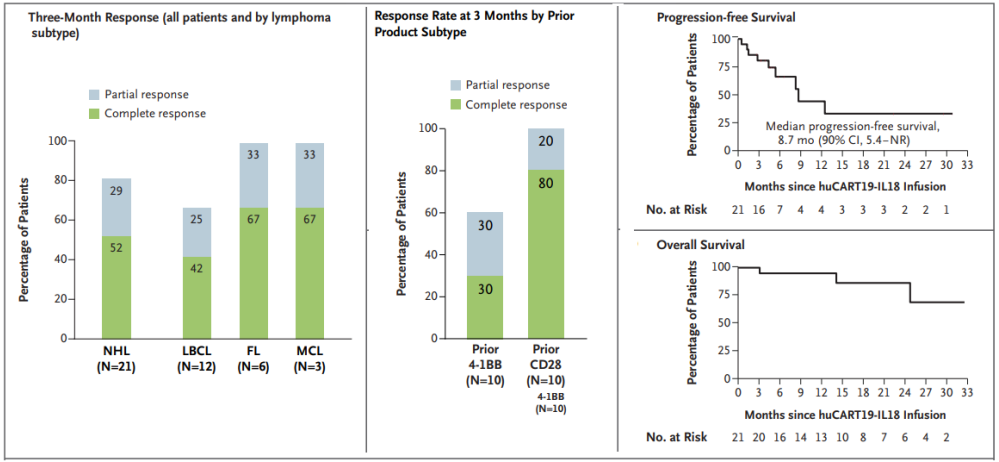
**N = 21 received huCART19-IL18**

**Median follow-up: 17.5 months (range 3 - 34)**

- **3-months ORR: 81% (90%CI, 62-93)**
- **3-months CRR: 52% (90% CI, 33-71)**
- **Median DOR: 9.6 months (90% CI, 5.5-NR)**

**Table 1. Characteristics of the Patients at Baseline.***

| Characteristic | Patients (N=21) |
|---|---|
| Median age (range) — yr | 64 (47–74) |
| Male sex — no. (%) | 16 (76) |
| ECOG performance-status score — no. (%)† | |
| 0 | 2 (10) |
| 1 | 19 (90) |
| Lymphoma subtype — no. (%) | |
| Large B-cell lymphoma | 12 (57) |
| Diffuse large B-cell lymphoma, not otherwise specified | 8 (38) |
| Transformed follicular lymphoma | 2 (10) |
| High-grade B-cell lymphoma | 1 (5) |
| T-cell histiocyte-rich large B-cell lymphoma | 1 (5) |
| Follicular lymphoma | 6 (29) |
| Mantle-cell lymphoma | 3 (14) |
| Previous CAR therapy — no./total no. (%) | |
| CD28-based product | 10/20 (50) |
| Axicabtagene ciloleucel | 8/20 (40) |
| Brexucabtagene autoleucel | 2/20 (10) |
| 4-1BB–based product | 10/20 (50) |
| Tisagenlecleucel | 8/20 (40) |
| Lisocabtagene maraleucel | 2/20 (10) |
| Response to previous therapy | |
| Progressive disease — no./total no. (%) | 7/20 (35) |
| Median progression-free survival — mo (90% CI) | 6.7 (3.1–10.2) |



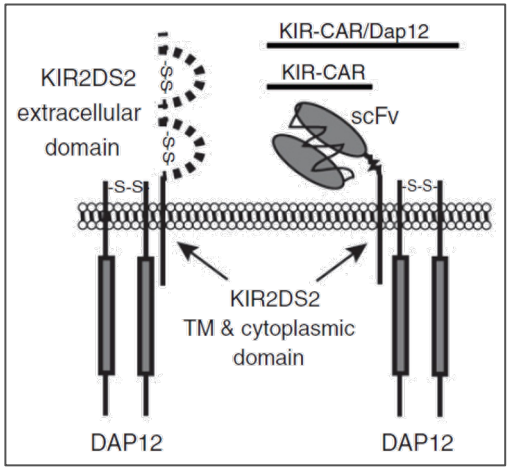

**PI: J. Svoboda**

# *Disease-specific* determinants of CAR-T success or failure

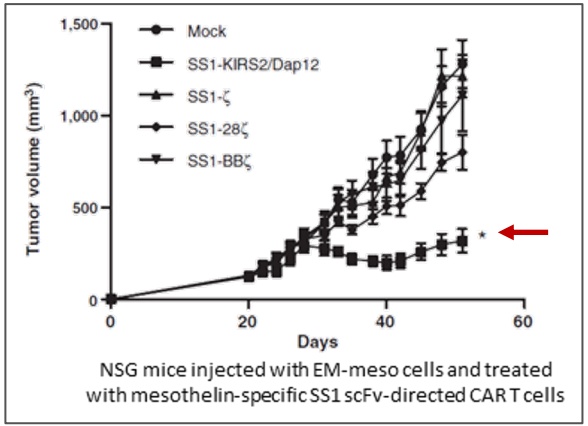
- **Recruiting UPenn clinical trial addressing T cell exhaustion or hypofunction**

## CD19-directed KIR-CAR/DAP12-modified cells for CD19+ lymphomas

**Rationale**: **KIR-CAR/Dap12 expressing CAR T cells have potent *in vivo* antitumor activity that is resistant to the tumor- and/or TME-induced T-cell hypofunction observed with CD3ζ-based CAR T cells. This potent activity *may* be of benefit in LBCLs with bulky disease.**

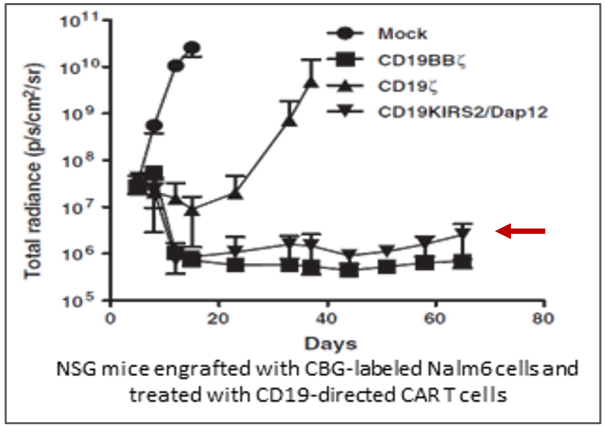



### Solid tumor model




NSG mice injected with EM-meso cells and treated with mesothelin-specific SS1 scFv-directed CAR T cells

### B-cell tumor model

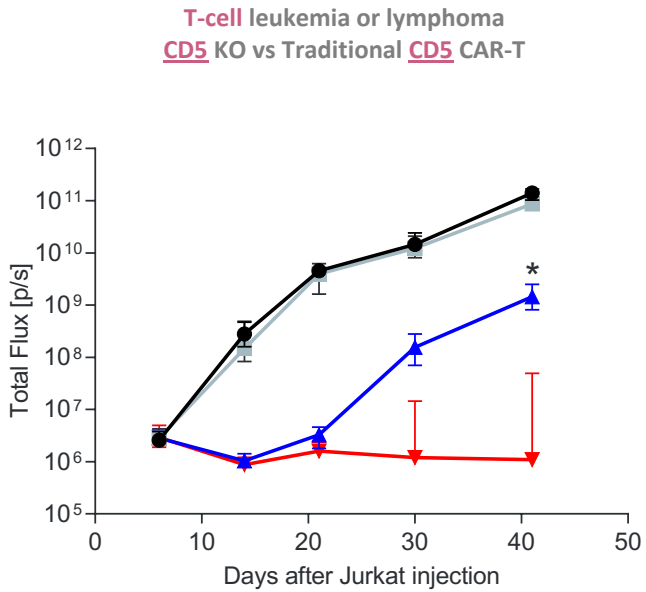



NSG mice engrafted with CBG-labeled Nalm6 cells and treated with CD19-directed CAR T cells

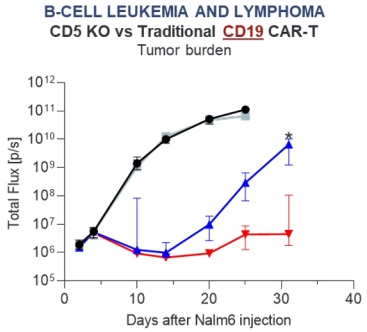
[1]Moon, et al. Clin Cancer Res 2014;20:4262–73.
[2]Wang, et al. Cancer Imm Res 2015;3:815-826. (*data show on the right*)

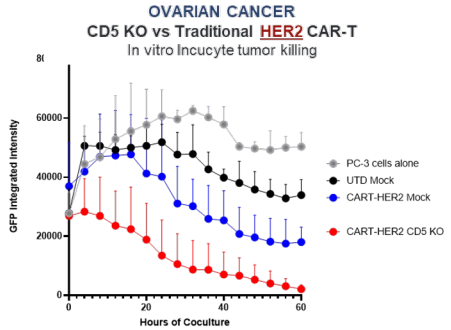
# *Disease-specific* determinants of CAR-T success or failure

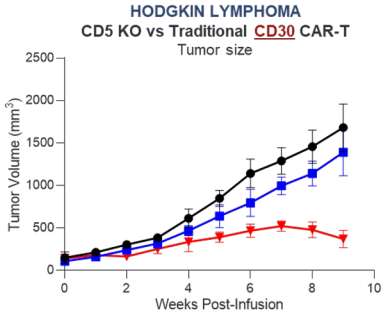
## CD5 KO CAR T cells can enhance efficacy in multiple liquid + solid tumor models

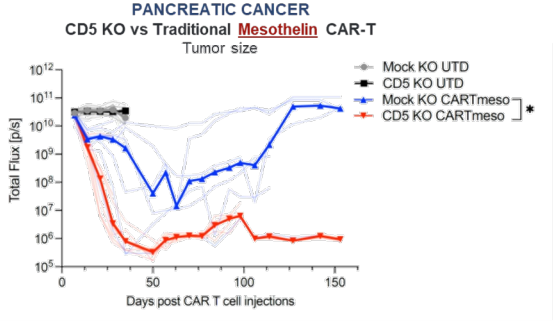



**Ruella lab data**
Patel RP, ASH, 2022 #662



# Grazie / Thank You!