4th MEETING ON
INNOVATIVE IMMUNOTHERAPIES
FOR LYMPHOID MALIGNANCIES

Presidents
Paolo Corradini
Marco Ruella
Pier Luigi Zinzani

Società Italiana di Ematologia

CAR-T for HL: Are we catching up?

Carlos A. Ramos, MD

Baylor College of Medicine

MILANO, STARHOTELS ROSA GRAND
January 22-23, 2026

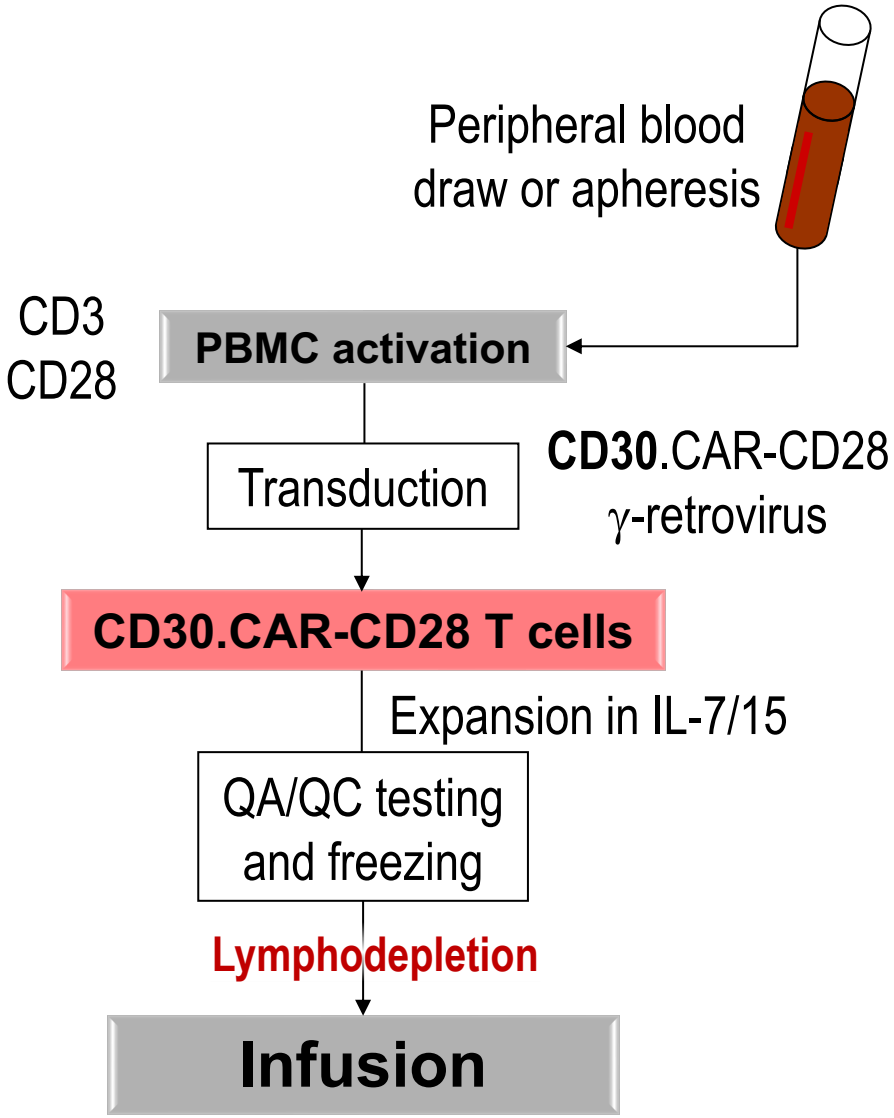
Disclosures of Carlos A. Ramos

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Tessa Therapeutics	×						
Athenex, Inc.	×						

Targeting CD30 with a CAR

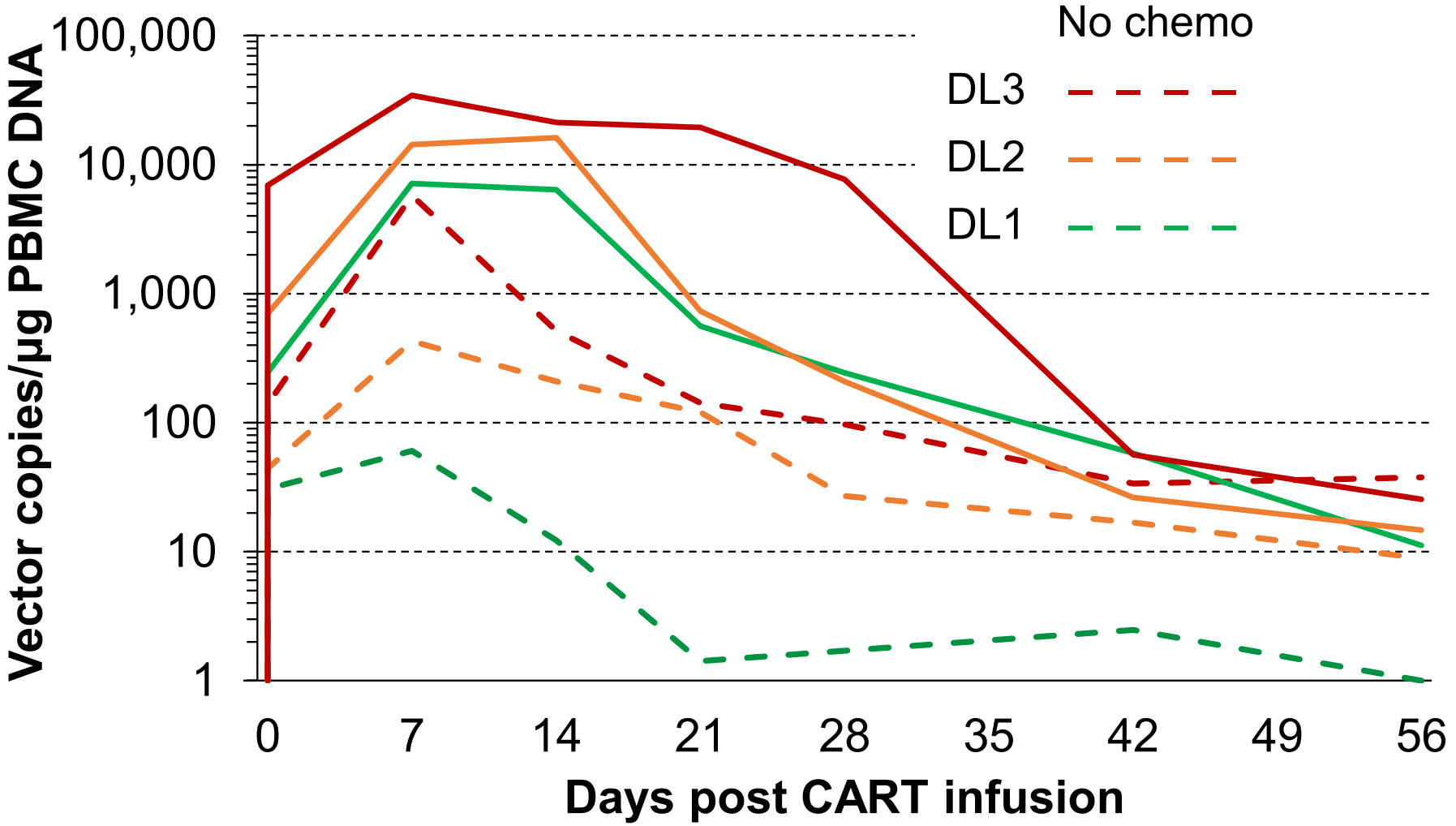
- CD19-specific (and BCMA) CAR-T cells are highly successful against B-cell NHL and ALL (and myeloma)
- Adequate targets for other disorders have been more difficult to define
- CD30 has been validated as an immune target (e.g. brentuximab vedotin)
- A CD30-specific CAR (CD30.CAR) has activity in pre-clinical models of HL (Hombach, Ca Res 1998; Savoldo, Blood 2007)

ATLAS (UNC) & RELY-30 (BCM) trials



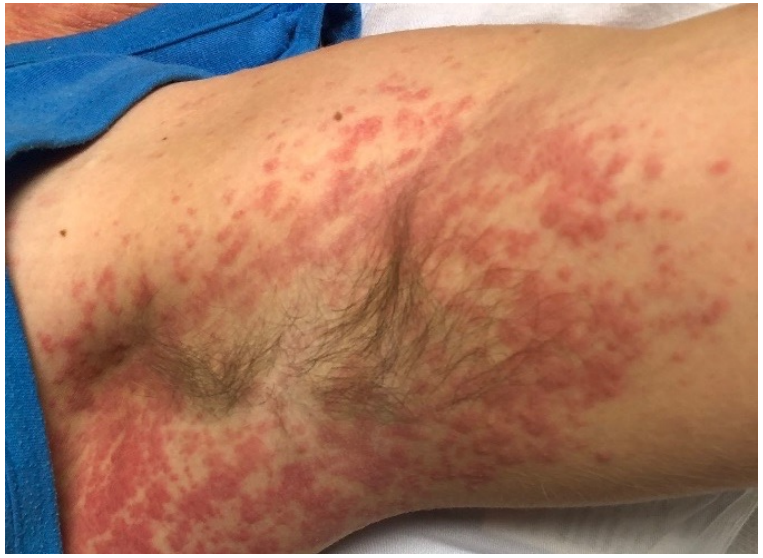
- 41 enrollments
- Gender
  - 13 F, 28 M
- Diagnoses
  - Hodgkin lymphoma (41)
    - Nodular sclerosis (32)
    - Mixed cellularity (4)
    - "NOS" (5)
- Median age 35 yrs (range 17-69)
- Median 7 prior treatments (range 2-23)
  - PD-1 inhibitor (34), brentuximab vedotin (38), HDT/ASCT (32), allo-SCT (10)

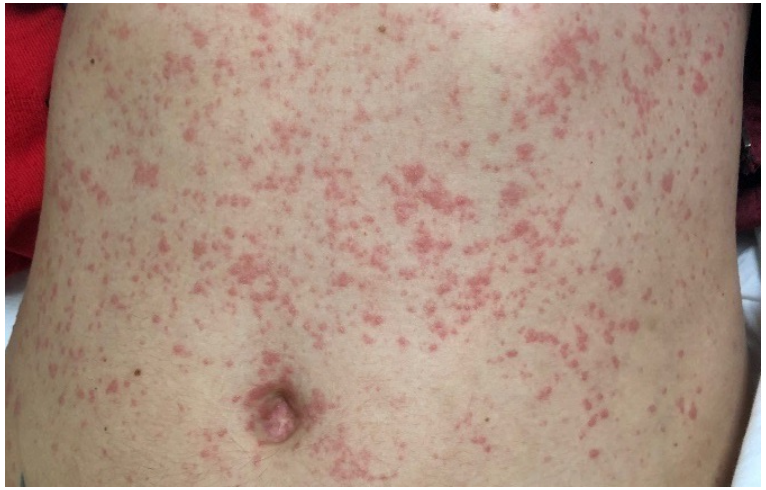
CD30.CART expansion is increased by lymphodepleting chemotherapy

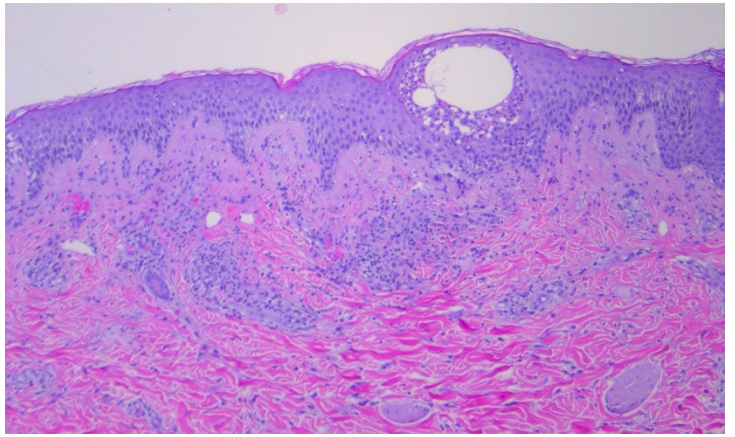


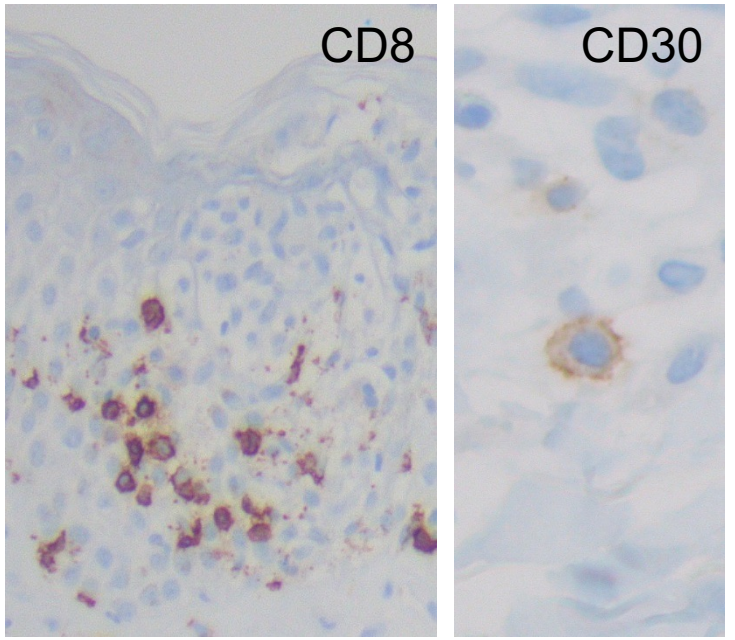
Autologous CD30.CART main toxicities

- No neurotoxicity
- CRS in 10 pts
  - all grade 1
  - all resolved spontaneously
- Rash in 20 pts
  - all resolved spontaneously
  - 3 baseline rashes









Patient B9

Grade 3 or higher toxicities

Toxicity (N= 42)	Grade 3/4 N (%)	Not resolved >28 d N (%)	Not resolved >3 mo N (%)
Lymphopenia	42 (100)	-	-
Neutropenia	20 (48)	4 (10)	0
Thrombocytopenia	11 (26)	10 (24)	4 (10)
Anemia	5 (12)	0	0
Pneumonia	1 (2)	-	-
Hypoalbuminemia	3 (7)	-	-
Hyponatremia	2 (5)	-	-

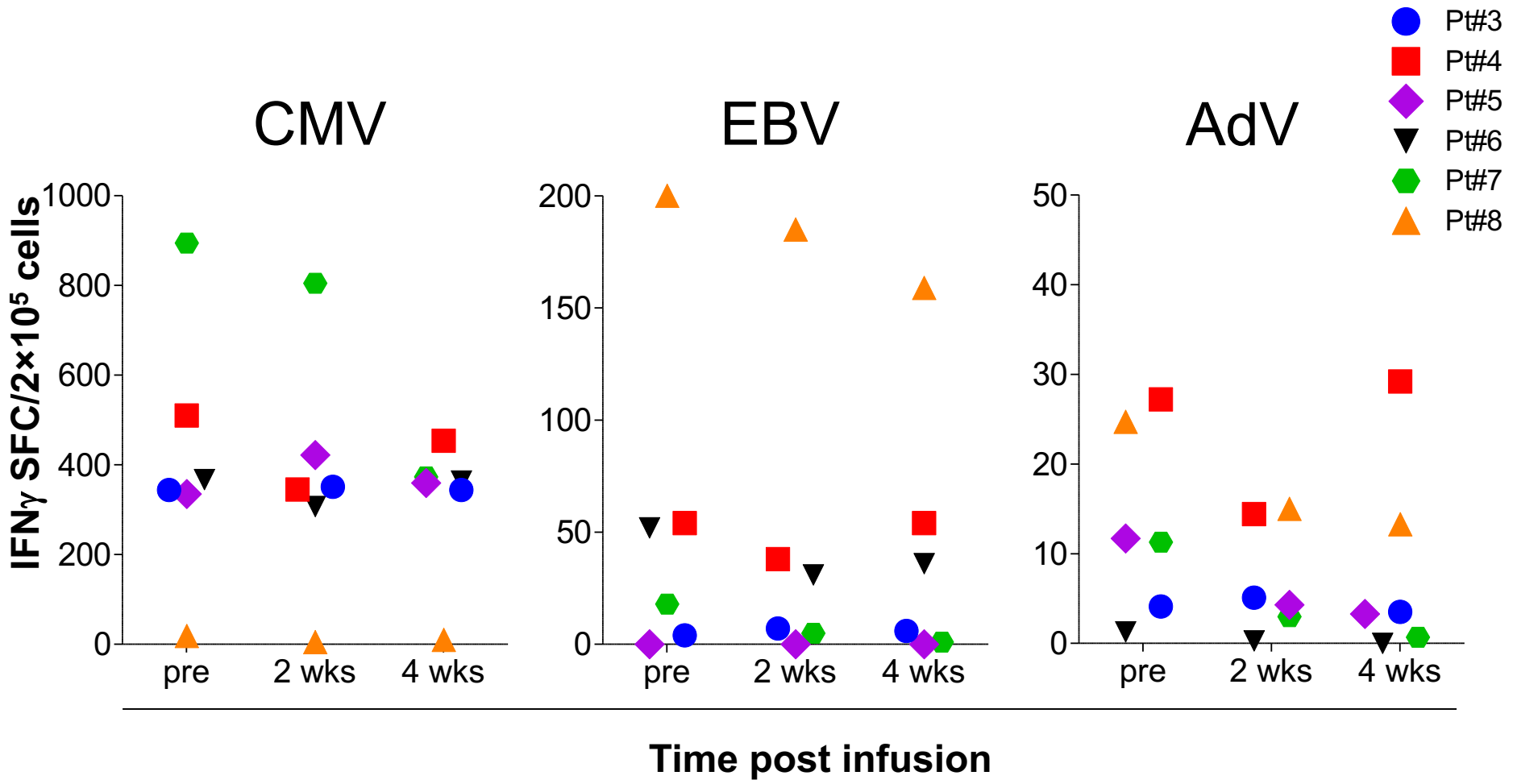
Other potential concerns related to CD30 targeting

- CD30 is preferentially and/or constitutively expressed by Th2 or Tc2 cells
- CD30 is expressed transiently by activated T cells after exposure to cognate antigen

$\Rightarrow$ Need to ensure that CD30.CAR-T cells do not eliminate activated (viral) antigen-specific T cells in vivo:

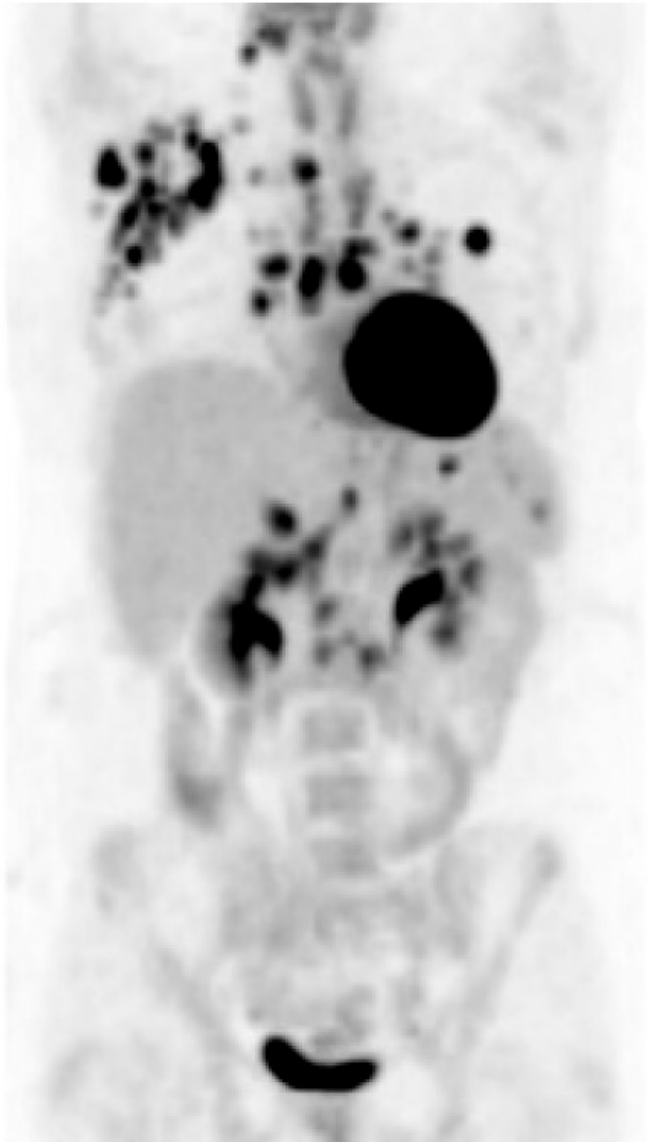
  - pre and post infusion virus-specific immune response monitoring

Viral immunity is not compromised

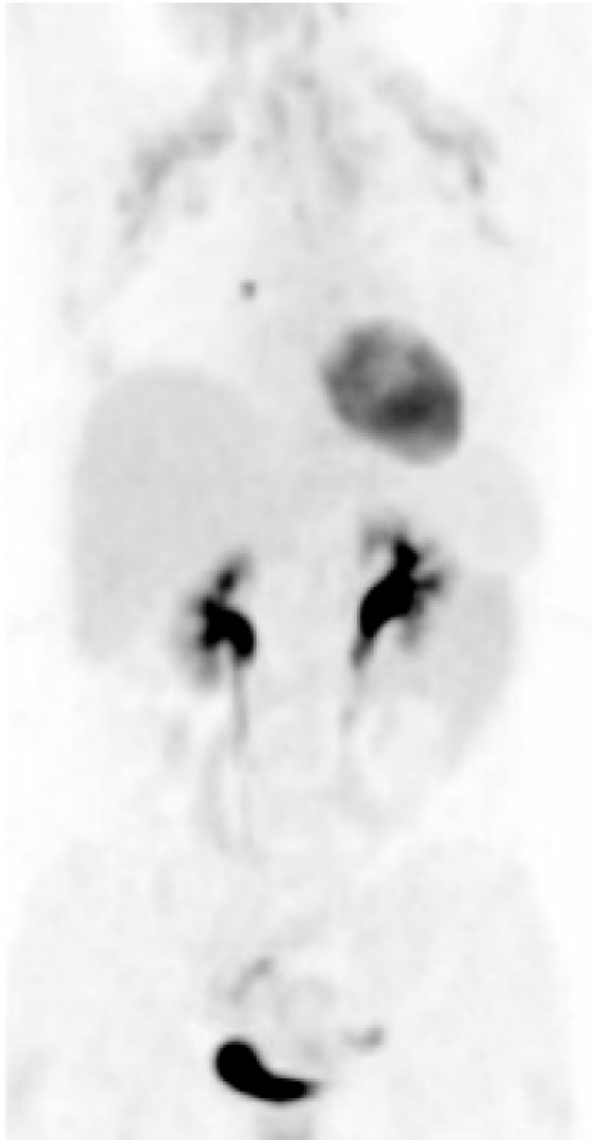


Response to autologous CD30.CART

Pre-infusion

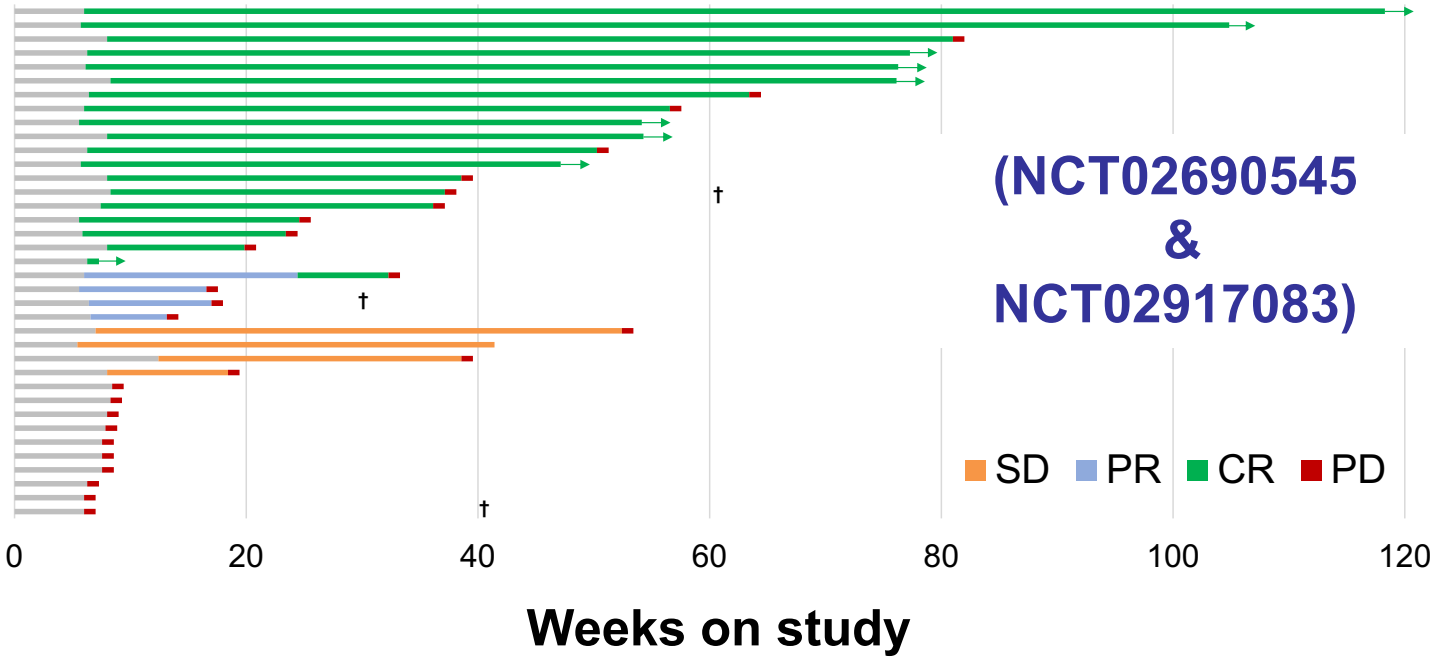


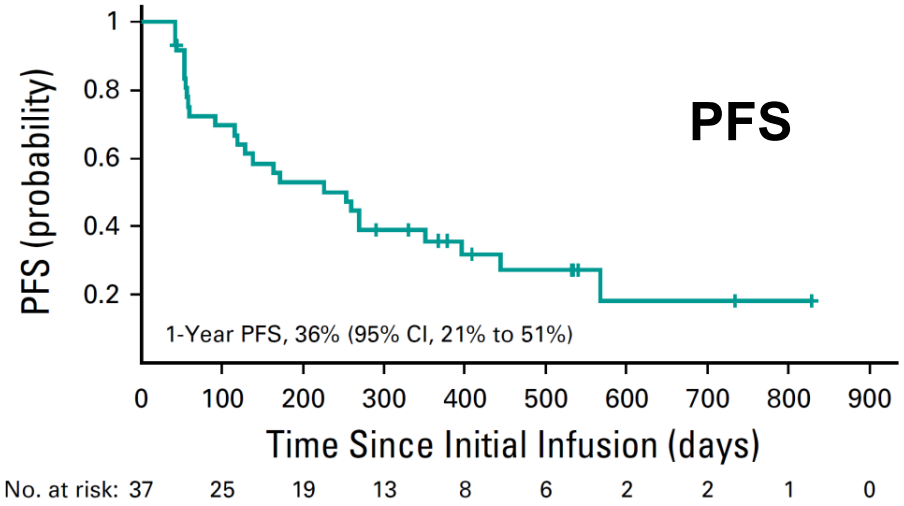
6 wks post-infusion

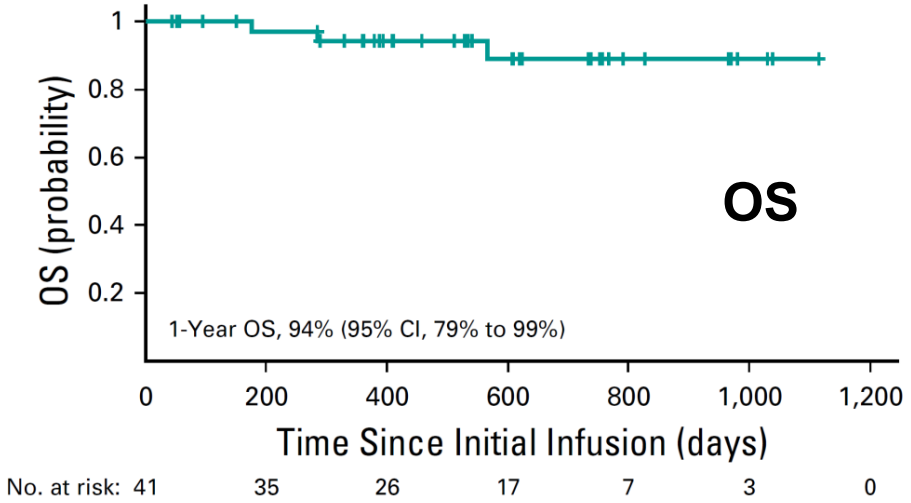


Autologous CD30.CAR-T cells in HL (BCM/UNC)

- With optimal lymphodepletion:
  - 72% overall response rate
  - 59% complete responses







(Ramos, Grover *et al.*, J Clin Oncol 2020)

CHARIOT (NCT04268706) trial

Study Population

Patients with R/R cHL:

- 12-75 years old
- Failed ≥3 lines of therapy including:
  - Chemotherapy
  - Brentuximab vedotin,@ and
  - PD-1 inhibitor@

May have received an autologous or allogeneic stem cell transplant

Study Treatment

(Pilot: n = >12, Pivotal: n = 82)

LD (3 days)*

- Fludarabine 30 mg/m^2/day
- Bendamustine 70 mg/m^2/day

CD30.CAR-T#

Allowable dose range: 2.0-2.7 x 10^8 cells/m^2

Endpoints

Primary

- Pilot: Safety
- Pivotal: ORR

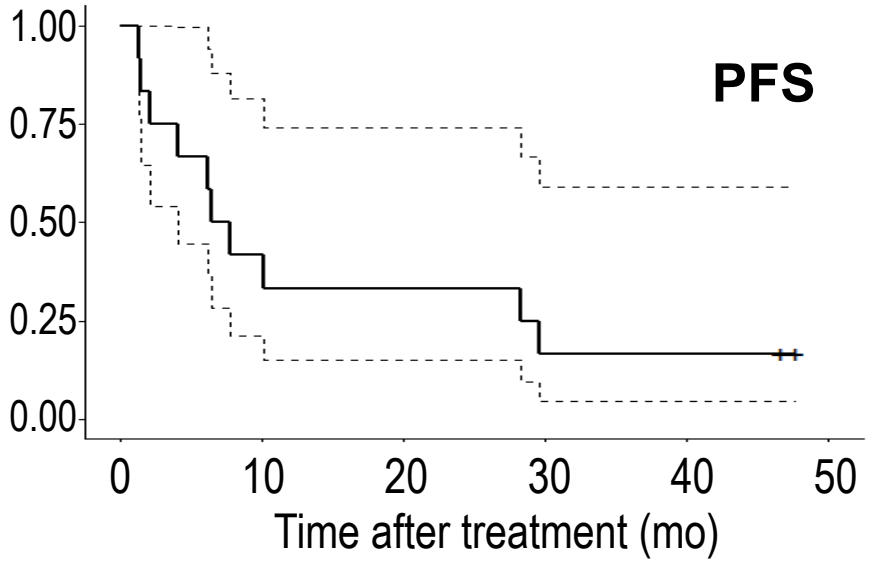
Secondary

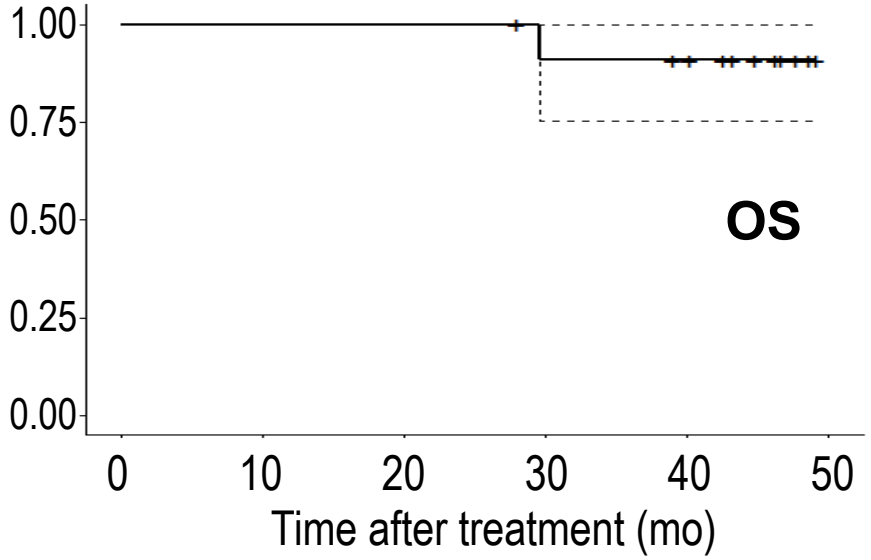
- Pilot: ORR, DOR, PFS, OS, HRQoL
- Pivotal: Safety, DOR, PFS, OS, HRQoL

Long term follow-up of CHARIOT trial

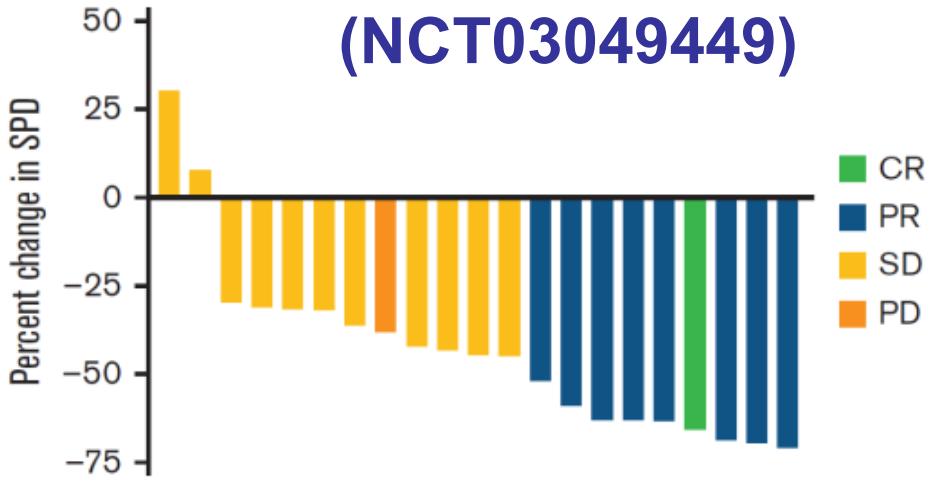
Response (data available for 12 pt)	N (%)
Objective response rate (ORR)	9 (75%)
Complete remission (CR)	6 (50%)
Partial response (PR)	3 (25%)
Median duration of response (range)	8.8 months (2.7–45.3 months)

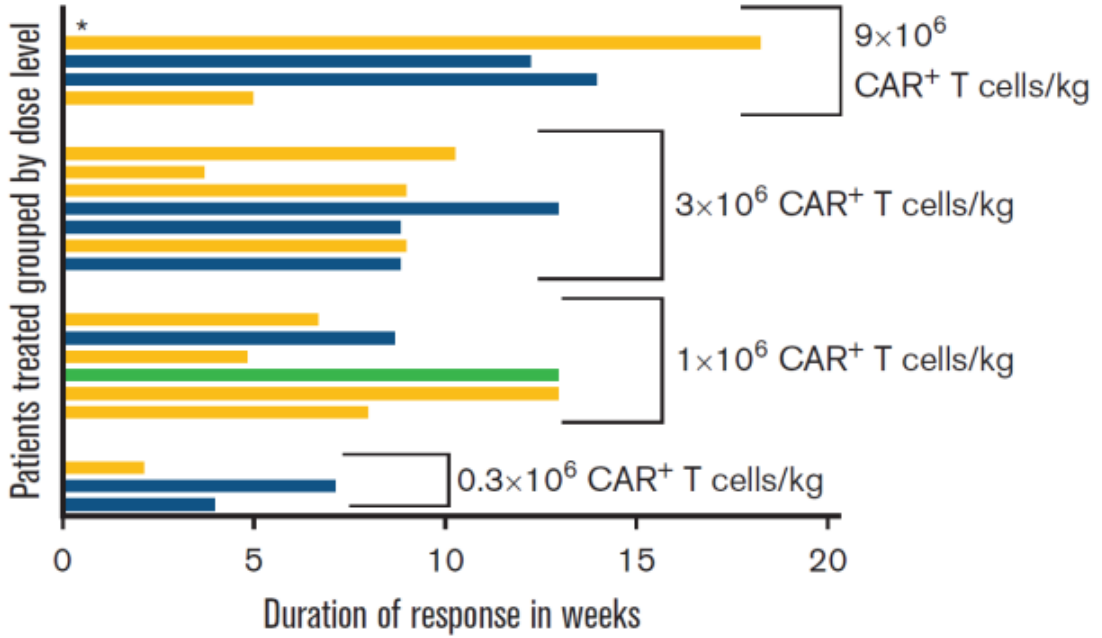
(Ahmed *et al.*, ASH 2025)





Experience at NIH, Bethesda



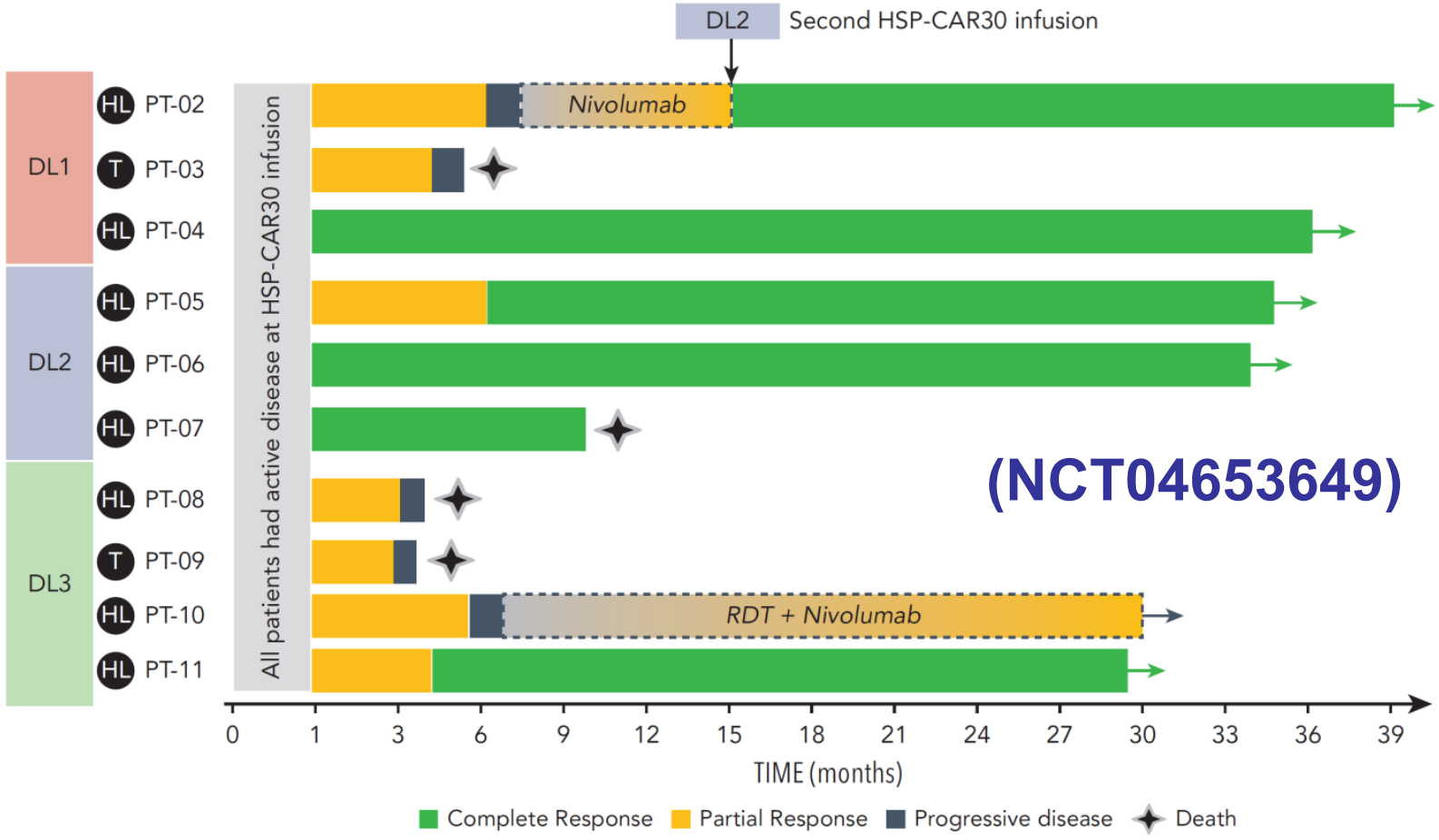


- 20 HL patients treated in phase 1 trial
- More toxicities, 2 dose-limiting:
  - 9 patients had rash, but 2 required prolonged steroid course
  - 5 had grade 3-4 cytopenias, with 2 complicated by life-threatening sepsis
- ORR 43%,CRR 5%, median DOR ~9 wks
- Further development was discontinued

(Brudno *et al.*, Blood Adv 2024)

Experience at H. Sant Pau, Barcelona

- 8 HL patients
  - Fresh product
  - Less “differentiated” CARTs (IL-21 in culture)
  - More bendamustine
- Limited toxicity
- ORR 100%, CRR 63%
- All complete responses ongoing after a mean follow-up of 34 months

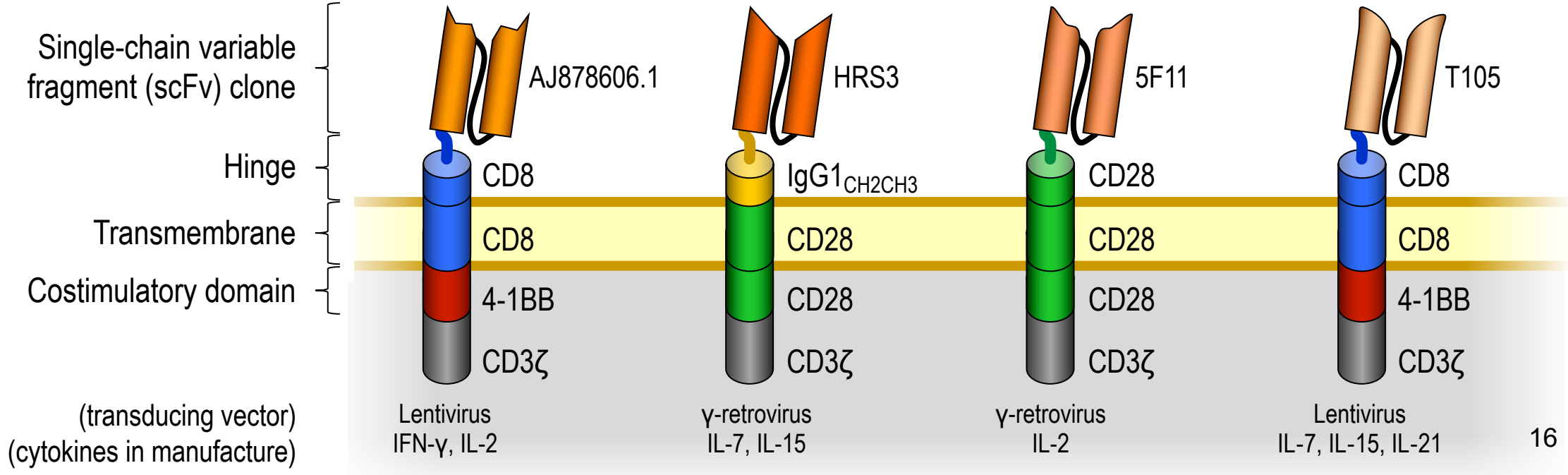


(NCT04653649)

(Caballero *et al.*, Blood 2025)

Autologous CD30.CART studies in cHL

Study (year)	Wang *et al.* (2017)	Ramos *et al.* (2021)	Brudno *et al.* (2024)	Caballero *et al.* (2025)
Number of HL patients	17	42	20	8
Median age (range)	31 (13-55)	35 (17-69)	33 (18-64)	46 (21-63)
ORR | CR (%)	35 | 0	72 | 59	43 | 5	100 | 63
G3+ CRS | ICANS (%)	0 | 0	0 | 0	1 | 0	0 | 0
Other toxicities	Transient cytopenias	Transient rash Cytopenias	Rash requiring therapy Longer cytopenias	Transient rash Cytopenias, Infections



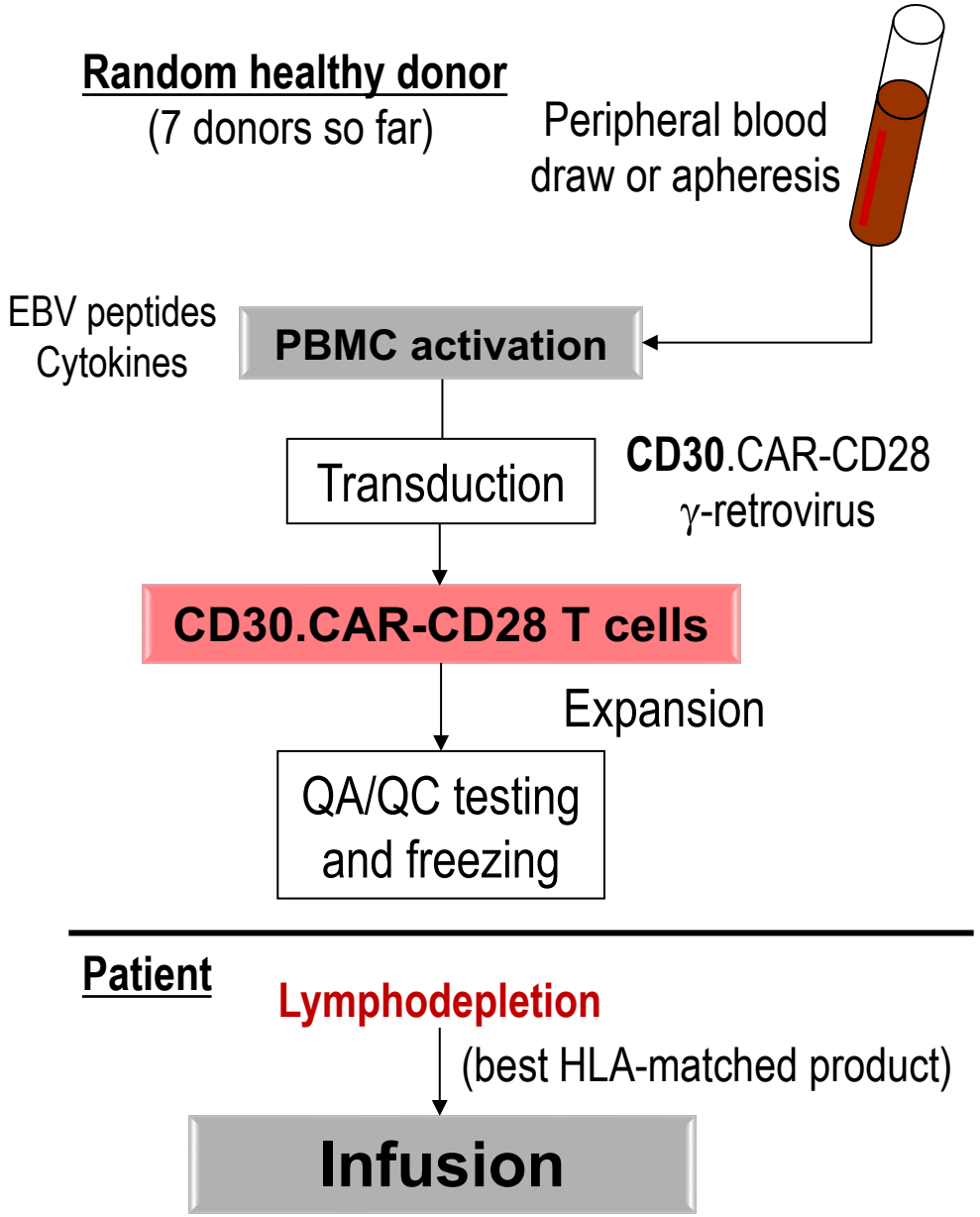
Limitations of autologous CAR-T Cells

- Manufacture of individual patient-derived CAR T-cells
  - too time consuming to benefit acutely ill patients
  - prior chemotherapy exposure may result in suboptimal product
  - difficult to scale for large numbers of patients, expensive
- "Off-the-shelf" immune effector products that are banked from healthy donors would improve accessibility, allow rapid treatment, and reduce costs
  - need to avoid consequences of alloreactivity
    - Graft-versus-host disease (GVHD) and CAR-T cell rejection

Why allogeneic CD30.CAR-EBVSTs?

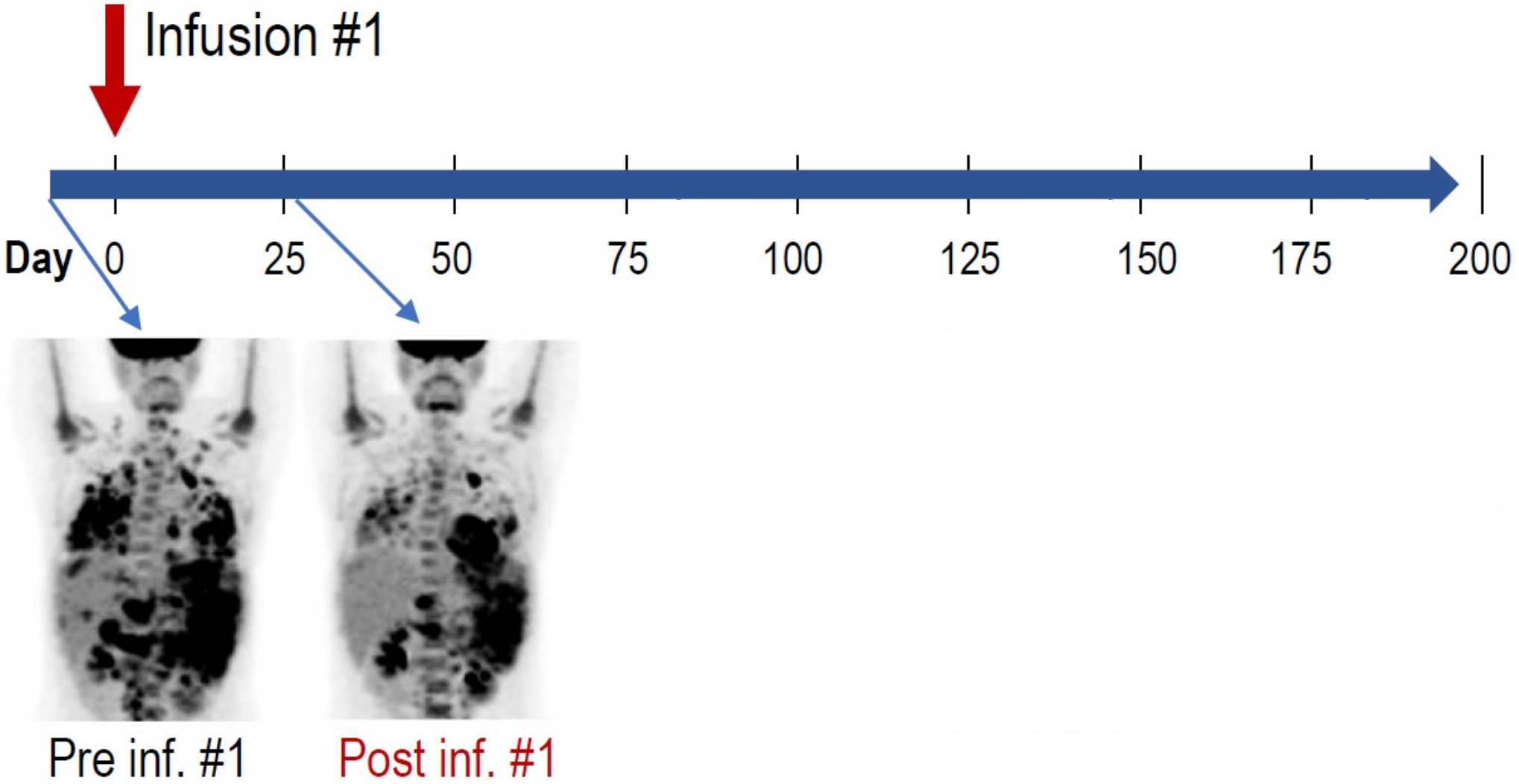
- Allogeneic EBV-specific T cells (EBVSTs) are safe in SCT and non-SCT recipients (Heslop, Sharma, Rooney, JCO 2021)
  - Manufactured from healthy individuals
  - Many patients treated in several trials without GVHD
  - Can localize to lymphoid tissues and sites of inflammation, proliferate in vivo and have potential to persist
- Activated T cells express CD30
  - Recipient T cells reacting against donor CAR-T cells may be killed by CD30.CAR-T cells
- May avoid GVHD and be protected from rejection

BESTA clinical trial (NCT04288726)



- 26 enrollments (23 patients)
- Gender
  - 10 F, 13 M
- Diagnoses
  - Hodgkin lymphoma (21)
    - Nodular sclerosis (19)
    - Mixed cellularity (2)
  - Composite/gray zone lymphoma (2)
- Median age 35 yrs (range 22-62)
- Median 5 prior treatments (range 3-8)
  - PD-1 inhibitor (21), brentuximab vedotin (23), HDT/ASCT (12), allo-SCT (2), CD30.CAR-EBVST (3)

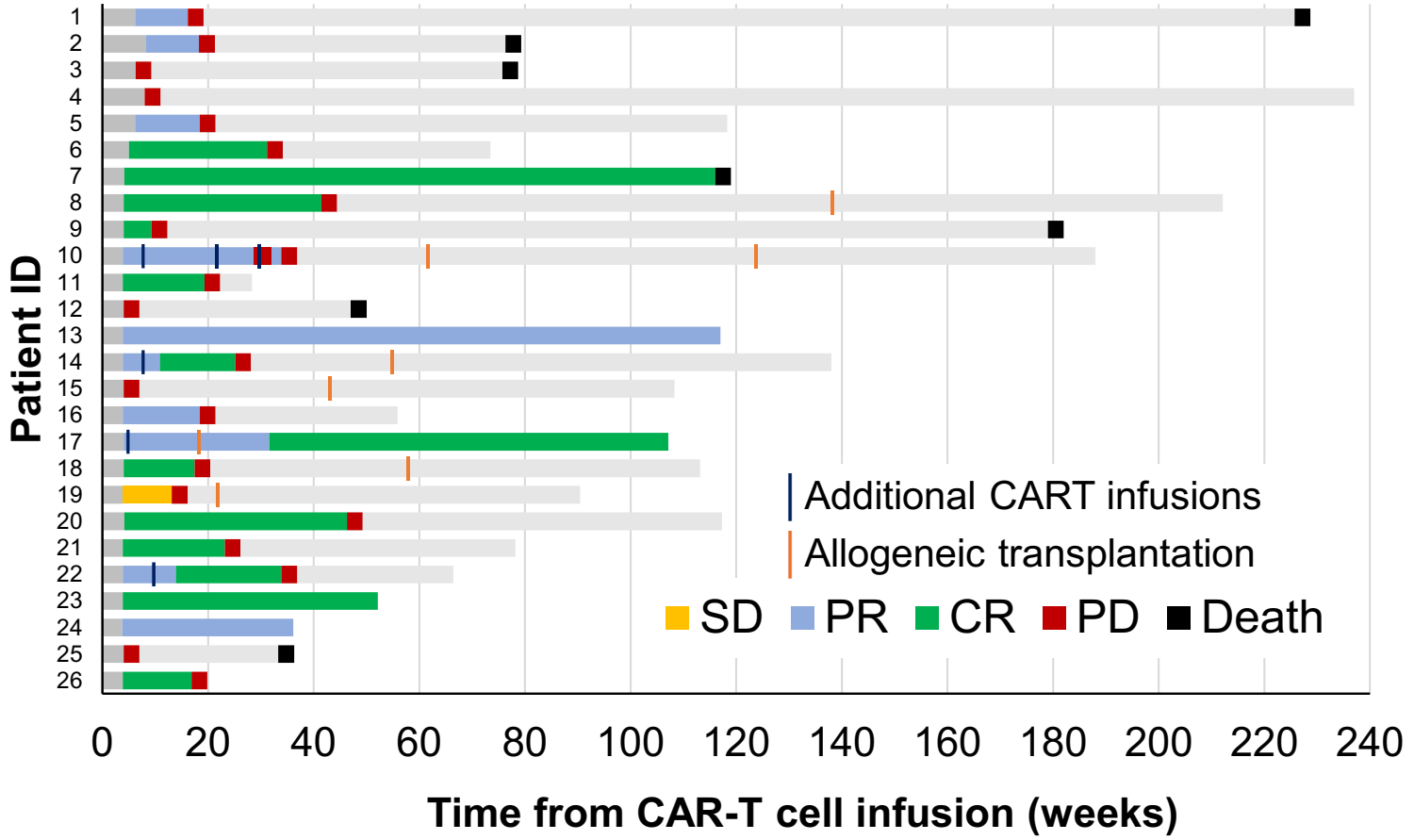
Response to allogeneic CD30.CARTs



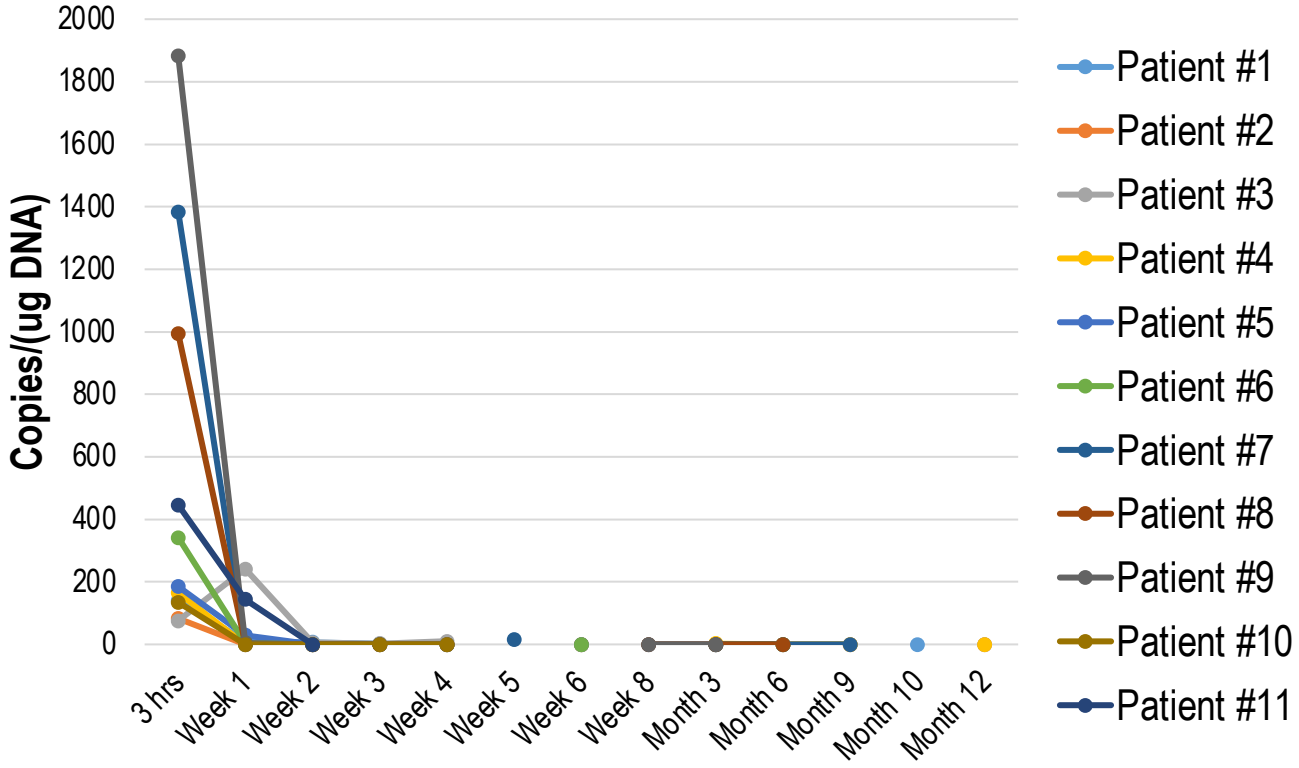
Allo CD30.CAR-EBVST safety & response data

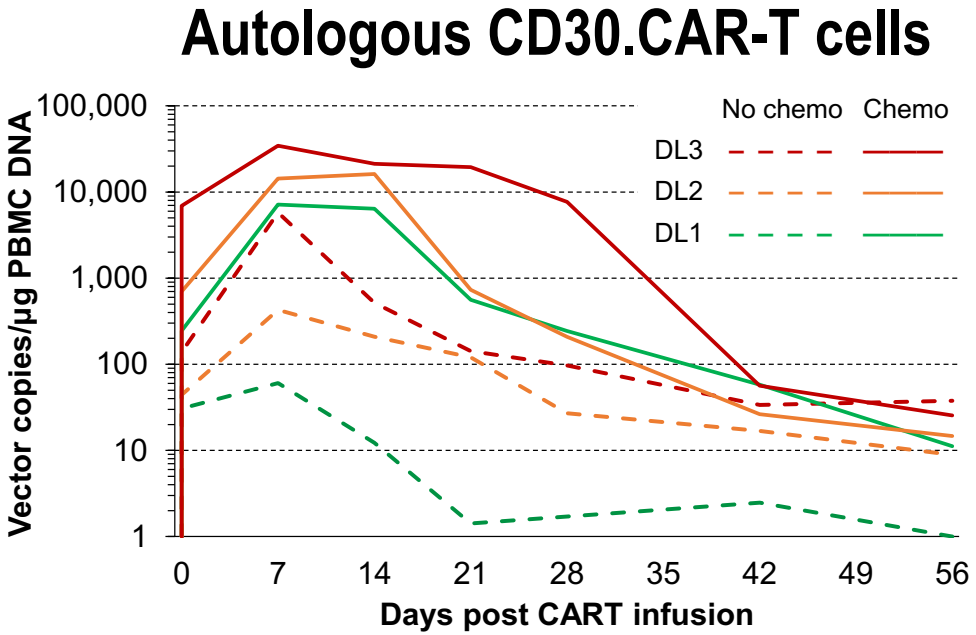
- No GVHD
  - Median 2 HLA matches
  - Range 1-7
- 9 episodes of CRS
  - All grade 1
- No ICANS
- Other AEs:
  - Mostly cytopenia due to chemo
    - 2 prolonged thrombocytopenias

77% ORR (20/26), 46% CR (12/26)



Allogeneic CD30.CAR-EBVSTs have limited persistence in peripheral blood

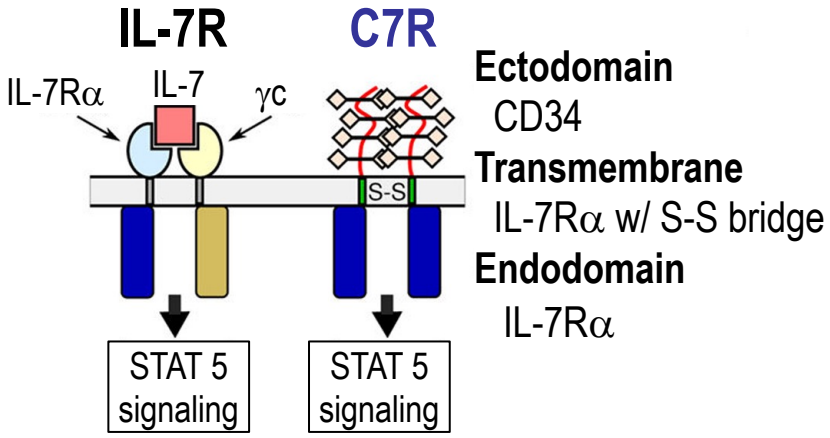




Ramos CA, *et al.* JCI (2017) & JCO (2020)

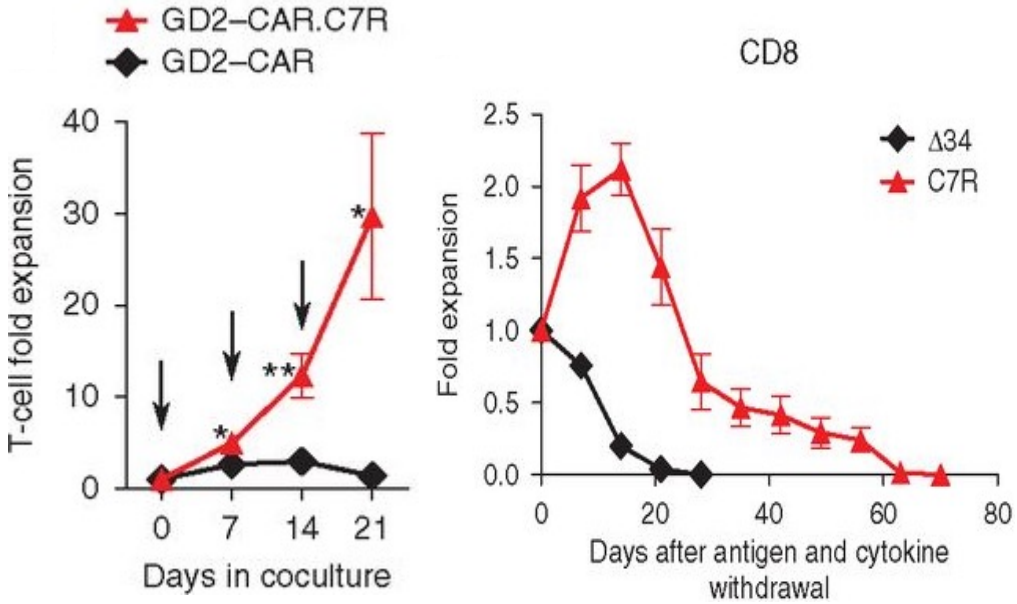
- Most patients show rapid loss of CD30.CAR EBVSTs in blood compared to autologous CD30.CAR-T cells with median DOR of ~24 vs 44 weeks
- Strategies to improve persistence are being developed:
  - E.g., constitutively active IL7 receptor expression in EBVSTs

Constitutive IL-7R in CD30.CAR-EBVSTs



Ectodomain
CD34
Transmembrane
IL-7Rα w/ S-S bridge
Endodomain
IL-7Rα

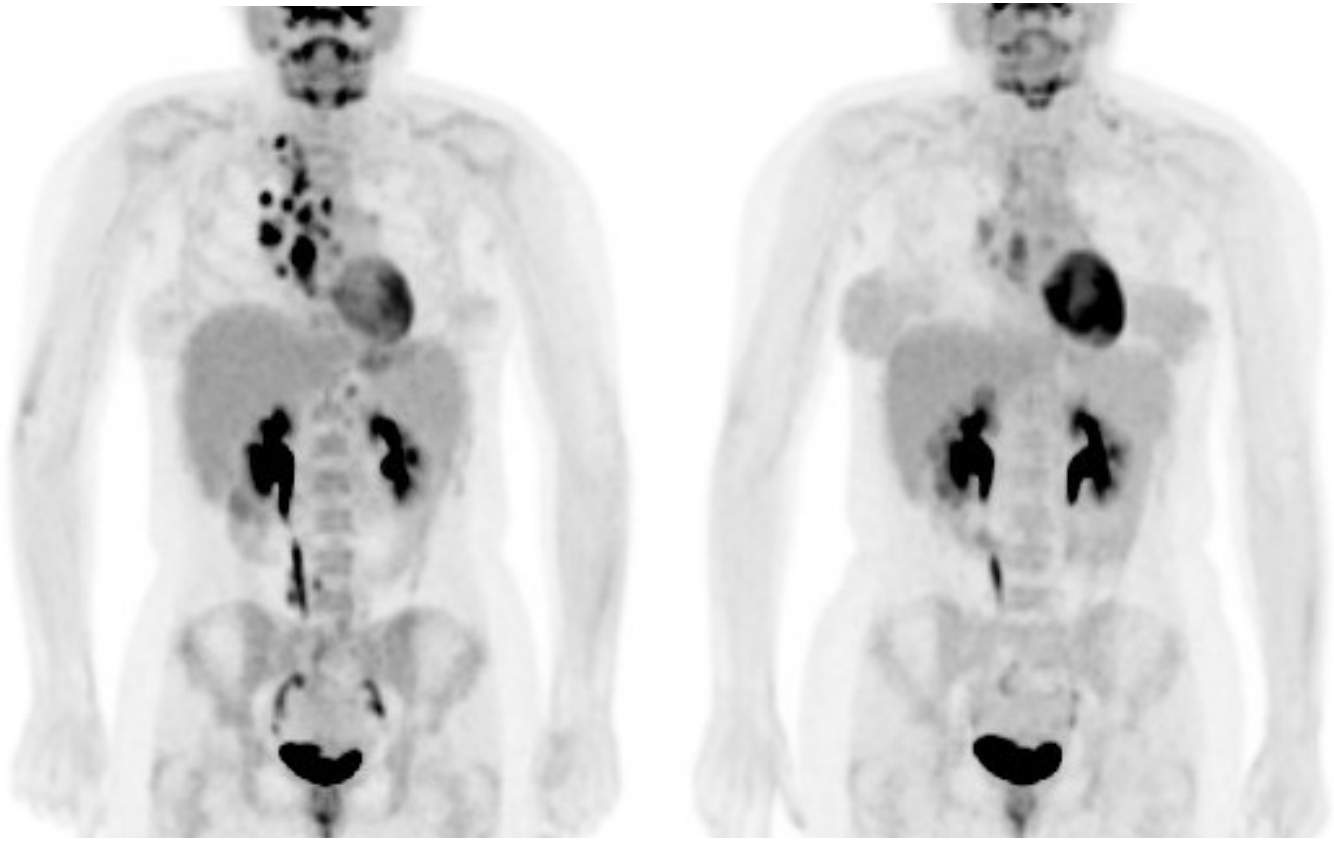
(wild type)



(Shum *et al.*, Cancer Discov 2017)

CABAL2 trial (NCT06176690)

Pre-infusion **6 wks post-infusion**



Conclusions

- Adoptive transfer of autologous and allogeneic CD30.CARTs is feasible, safe, and potentially clinically effective
  - CRS and ICANS limited; maculopapular rash is seen often
- However, overall results are worse than those seen with autologous CD19.CART in NHL
  - But some products may be associated with better activity
- Allogeneic CD30.CAR EBVSTs lack persistence in patient blood
  - But immediate rejection does not seem be a major limitation
- Additional strategies are being explored to improve these results
  - But more patients and longer follow-up will be needed for validation
- But are we catching up? Unclear…
  - Cellular immune therapy seems to work for HL but…
  - Industry? Academia? Hybrid model?

Grazie!

Cliona Rooney
Malcolm Brenner
Helen Heslop

David Quach
Haran Ganesh
Yolanda Briones
Nazila Nouraee
Sandhya Sharma
Luis Dominguez
Yezan Hadidi
Emily Hsieh

Sairah Ahmed
Jinwen Cao
Matthew Mei
Amer Beitinjaneh
Maryam Alasfour
Mohamed Maideen
Adam Braun
Peter Riedell

UNC
Barbara Savoldo
Gianpietro Dotti
Natalie Grover

Clinical Research
Premal Lulla
LaQuisa Hill
Rayne Rouce
George Carrum
Rammurti Kamble
Vicky Torrano
Anaid Reyes
Bambi Grilley

Statistics
Tao Wang
Jessie Wu

GMP Laboratories
Adrian Gee
Huimin Zhang
Birju Mehta
Silvana Perconti
Sreerekha Venu
Ka Liu

GLP Laboratories
Sachin Thakkar
Maria Isabel
Ana Elizondo

QA
Natasha Lapteva
Sara Richman

QC
Debbie Lyon

All patients and donors

Funding: NIH Lymphoma SPORE (Heslop)
Leukemia and Lymphoma Society SCOR (Heslop)
Tessa Therapeutics (Rooney/Ramos)
NIH Cancer Center Grant (Heslop/Reddy)
National Gene Vector Repository (Indiana University) for RCR