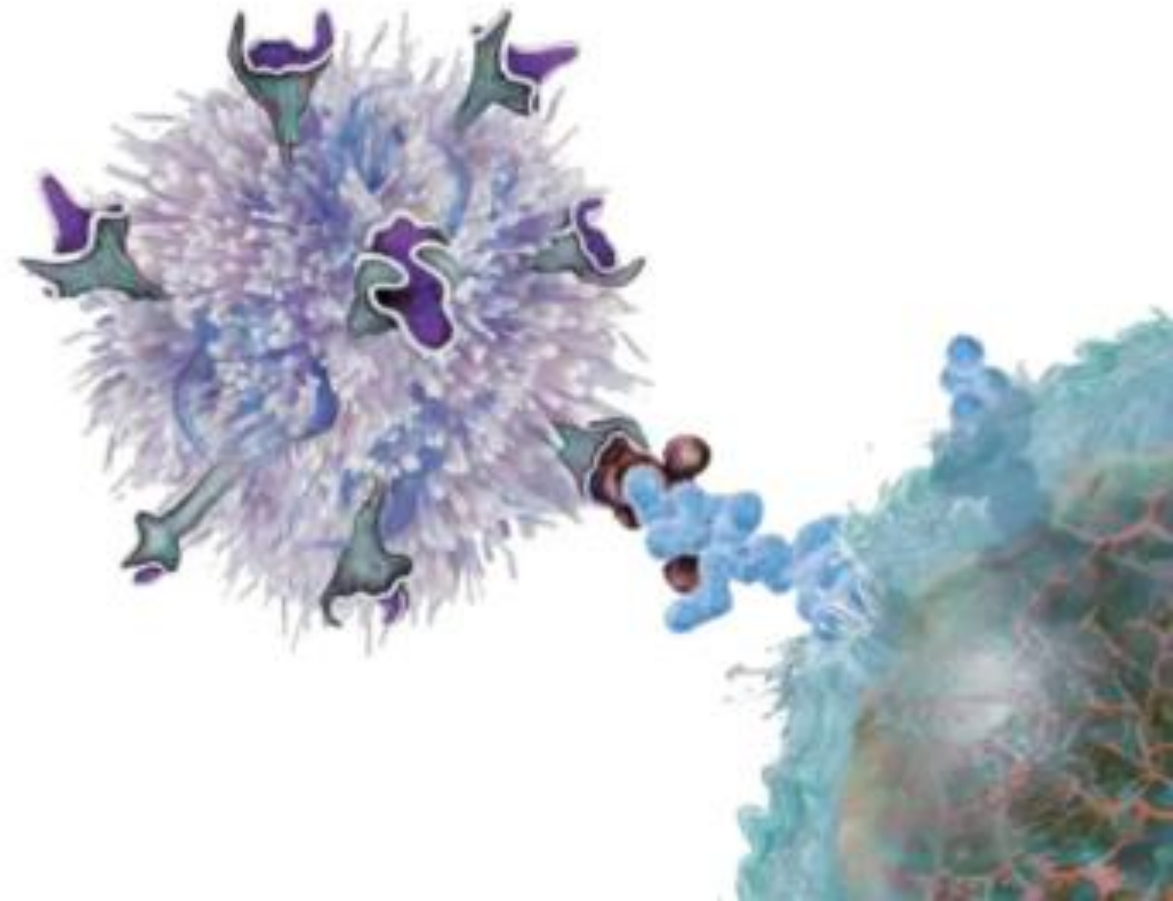


# Naïve HBI0101 CAR-T: Phase Ia/b clinical trial

Hadassah Medical Center

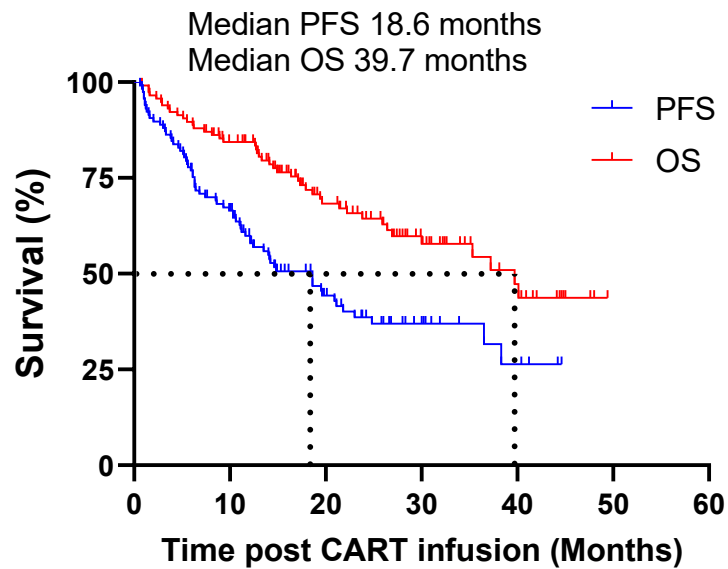
January 15th, 2026



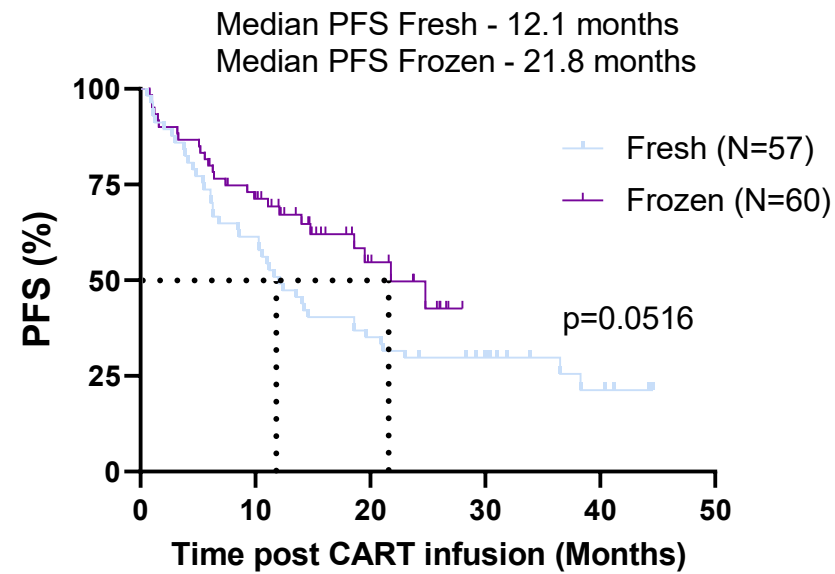


# Traditional HBI0101 Phase I summary

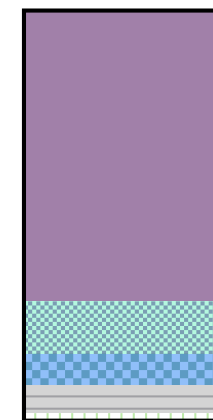
## Entire Cohort N=117



## FRESH/FROZEN



## ORR 93%



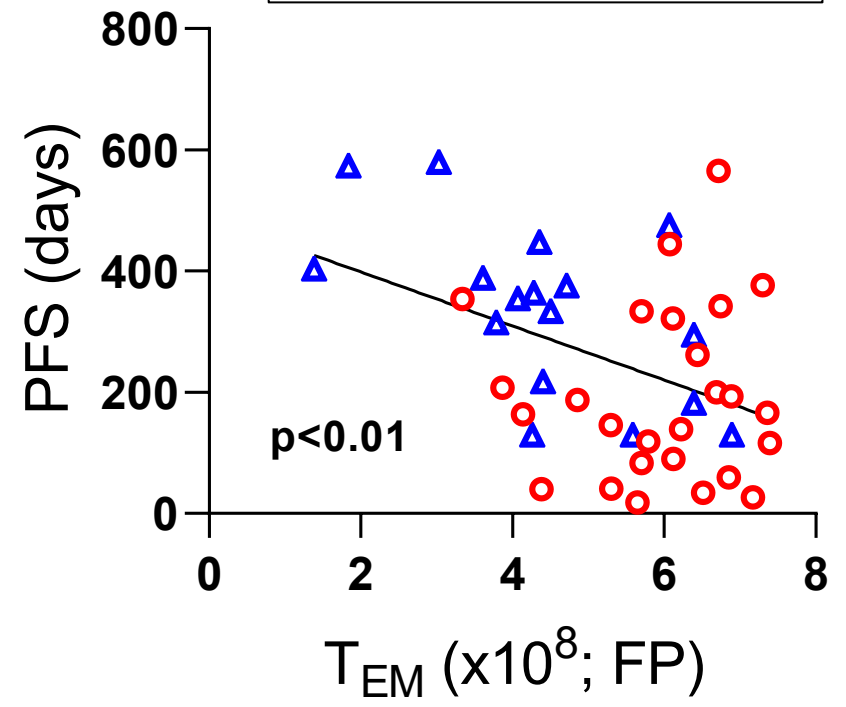
- 70.94% CR
- 12.82% VGPR
- 7.69% PR
- 6.84% PD
- 1.71% NE



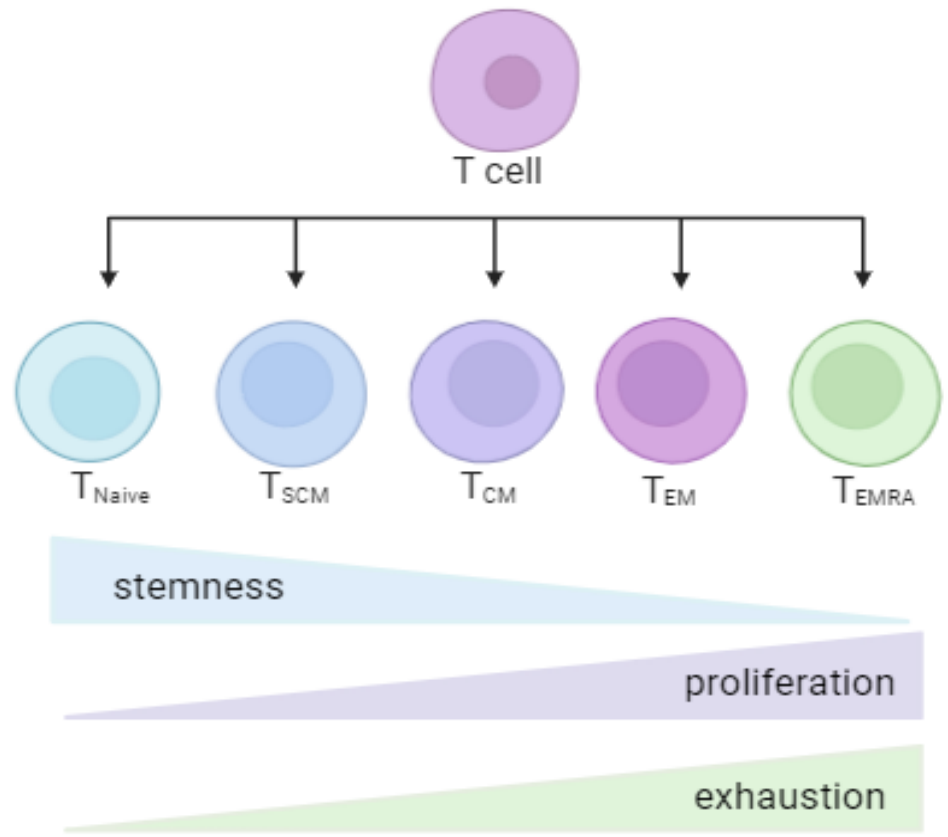
# Effector-memory CAR-T cells are associated with reduced clinical outcomes

## FRESH CAR-T PRODUCT

Median F/U: 12.3 months



Blood Adv (2024) 8 (15): 4077–4088.

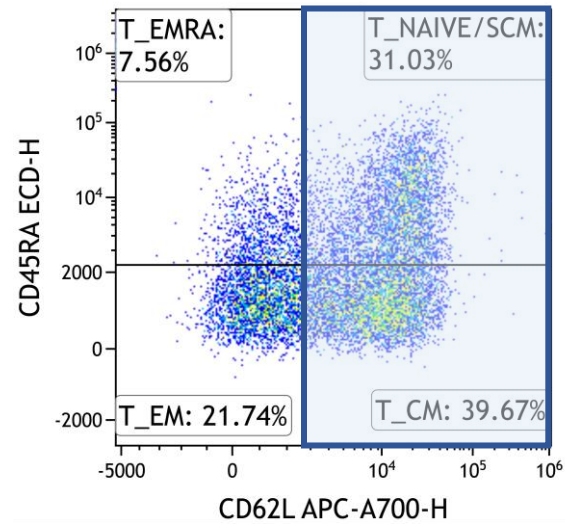




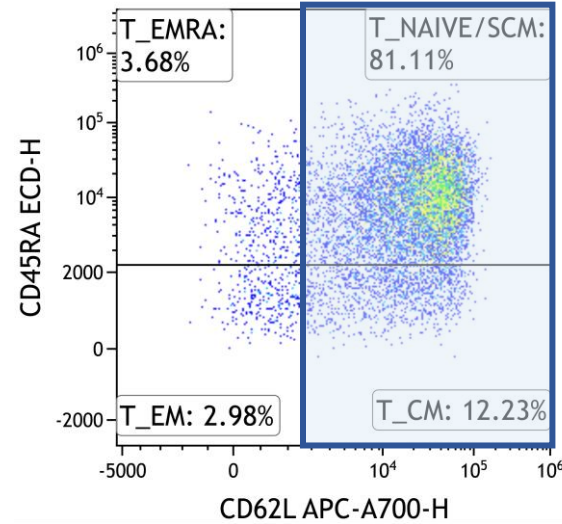
# Restoration and preservation of the early-memory compartment

Healthy donors

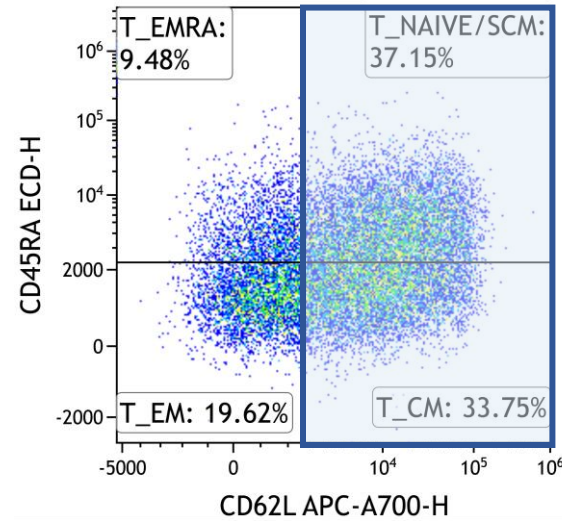
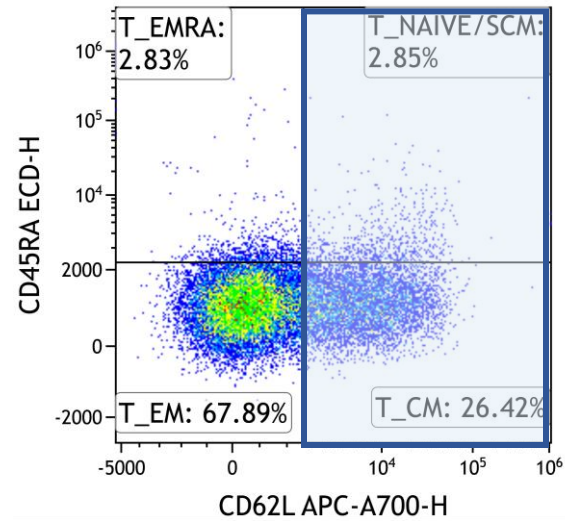
Traditional CAR-T



CD62L-enriched CAR-T

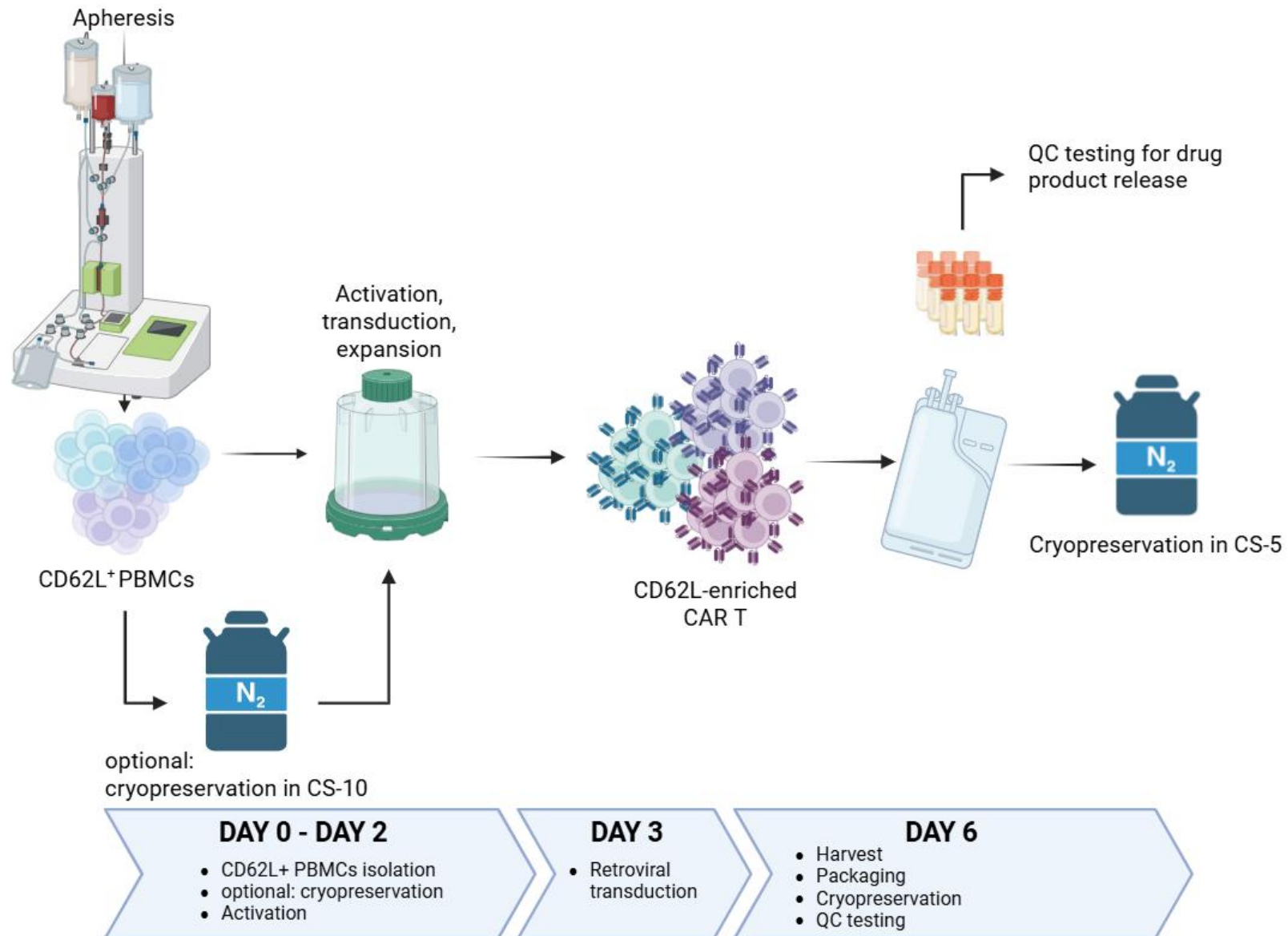


MM



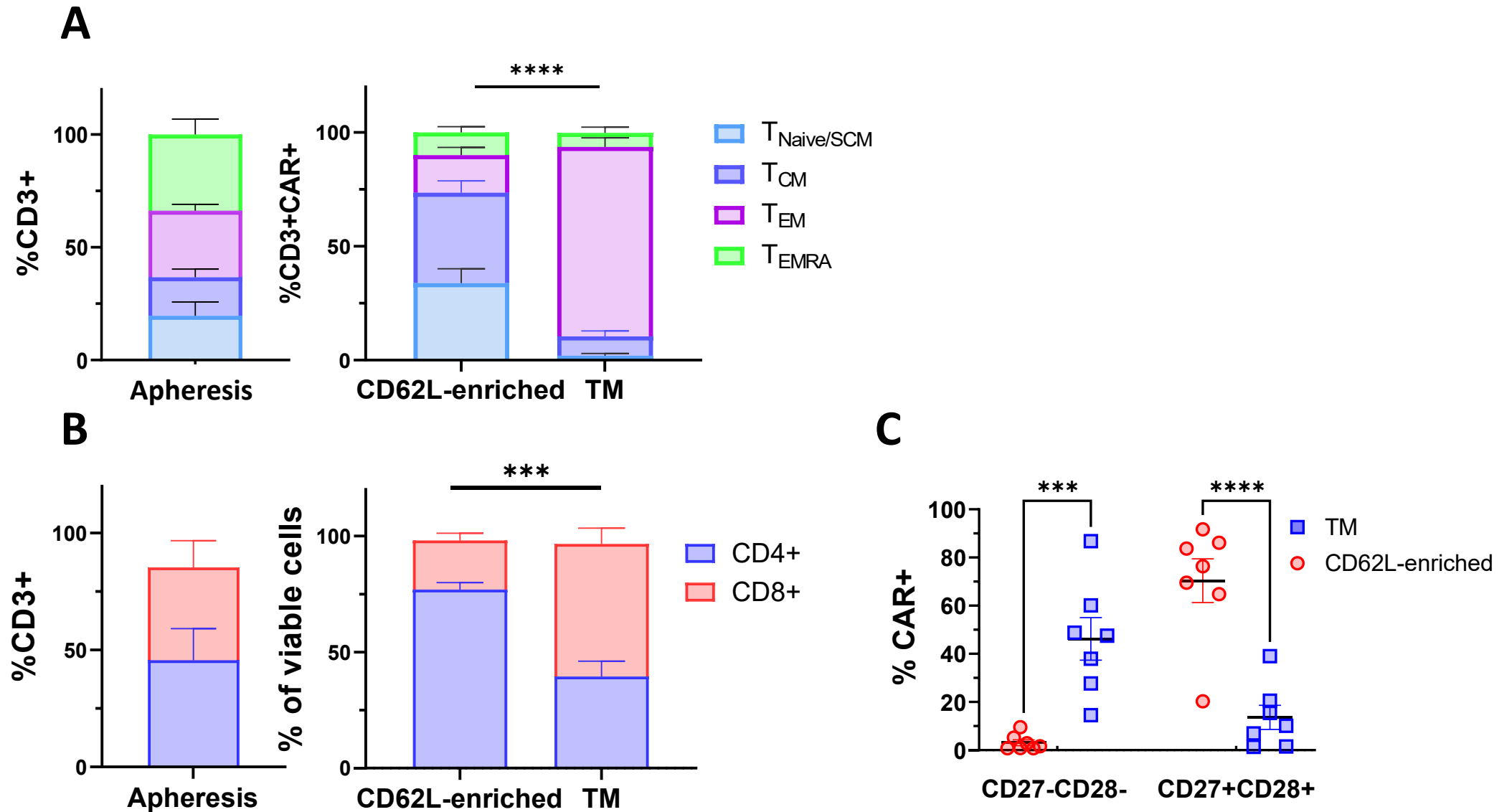


# Development of a novel manufacturing platform for the generation of optimized HBI0101 CART cells



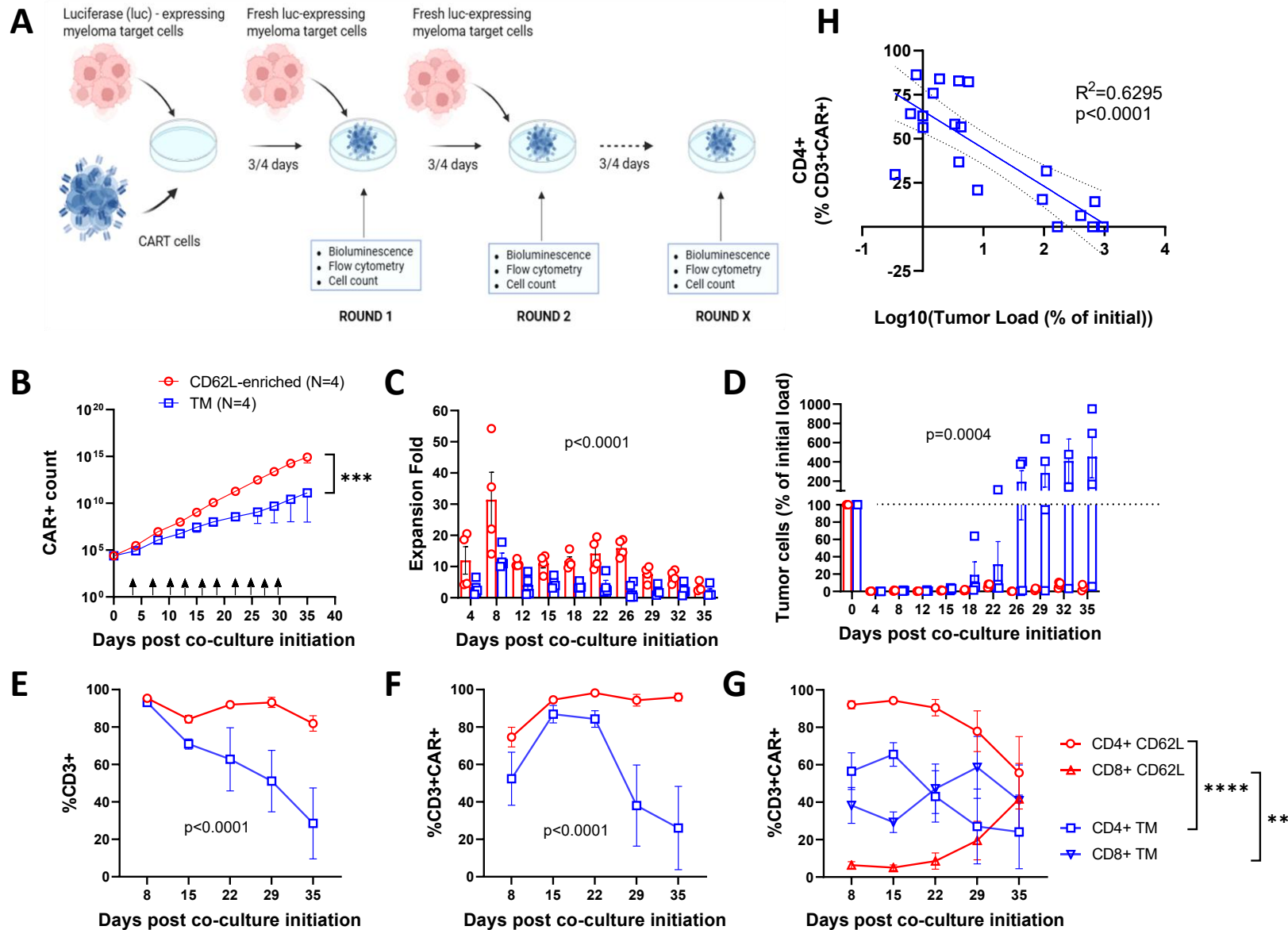


# Fitter CART products are generated via the optimized platform



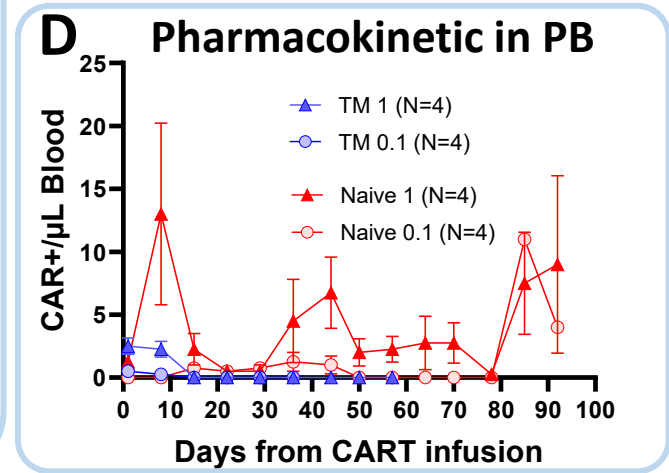
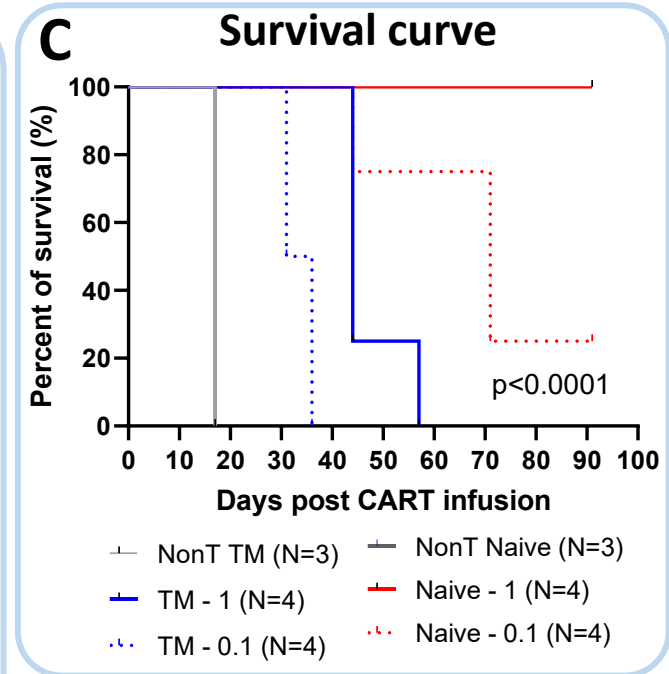
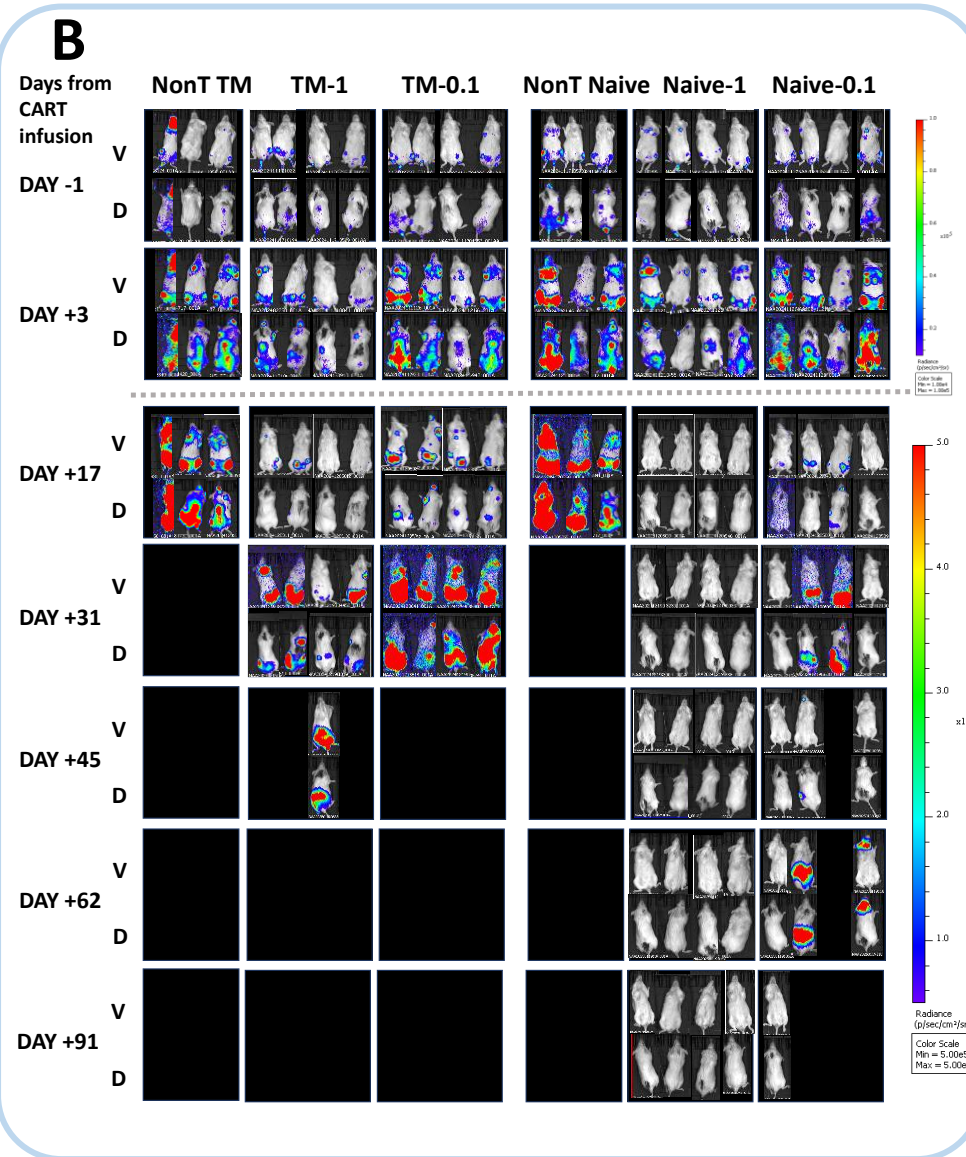
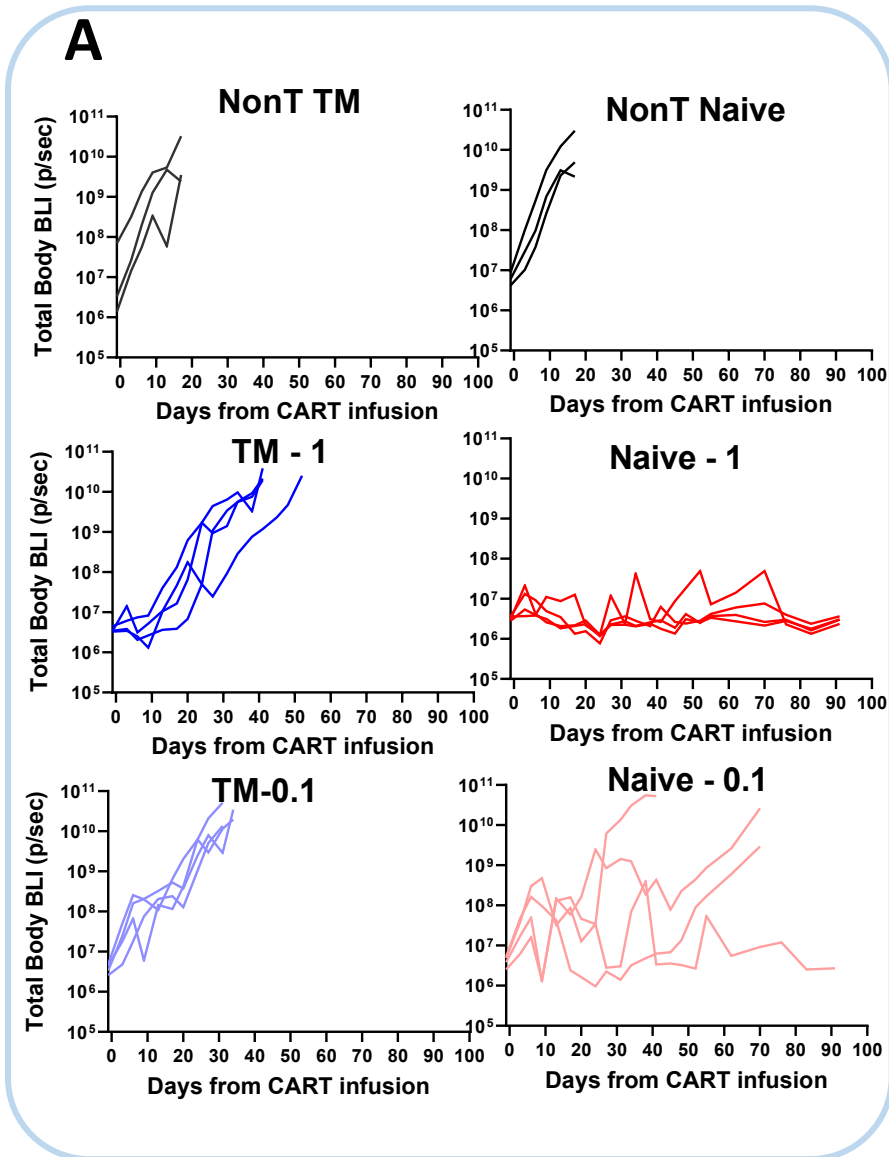


# Improved anti-myeloma efficacy upon chronic exposure to target cells



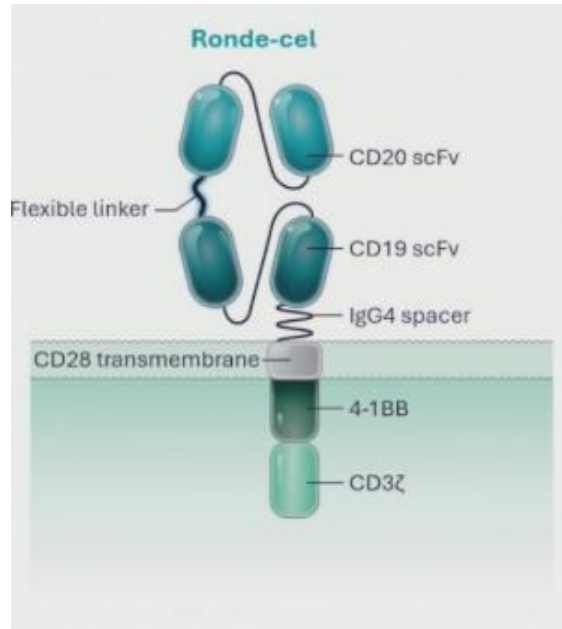


# Improved anti-myeloma efficacy in vivo at suboptimal dosage





# CD62L-enriched CD19/CD20 dual CAR for LBCCL - ASH 2025



Oral

628. Aggressive Lymphomas: Cellular Therapies

Rondecabtagene autoleucel, an autologous, dual-targeting CD19/CD20 CAR T-cell candidate manufactured from CD62L+ enriched T cells, achieves durable responses in patients with large B-cell lymphoma

- ORR 87-90%, CR 70-70%
- No grade  $\geq 3$  CRS
- 8/60 with grade  $\geq 3$  ICANS but only 1/15 with DEX prophylaxis (with same efficacy)



# Naïve HBI0101 CART – Clinical context

- Continuation of the HMC anti-BCMA CART program
  - Same CAR construct and clinical infrastructure
  - First study using naïve / early-memory–enriched HBI0101 CART
  - Goal: safe introduction and preliminary efficacy assessment



# Naïve HBI0101 CART – Clinical Study Overview

- **Primary objectives:**

- Determine MTD and recommended dose (Part 1a)
- Evaluate safety (Parts 1a and 1b)

- **Key endpoints:**

- DLTs in first 21 days
- SAEs and AEs of special interest (to Month 24)
- Secondary: ORR, MRD negativity, PFS, OS
- Exploratory: CART kinetics



# Study design

- **Phase 1a/1b, single-center, open-label**
  - Up to 60 patients total
  - Part 1a: dose escalation
  - Part 1b: expansion
  - Mandatory hospitalization  $\geq 14$  days post-infusion
  - Follow-up through Month 24



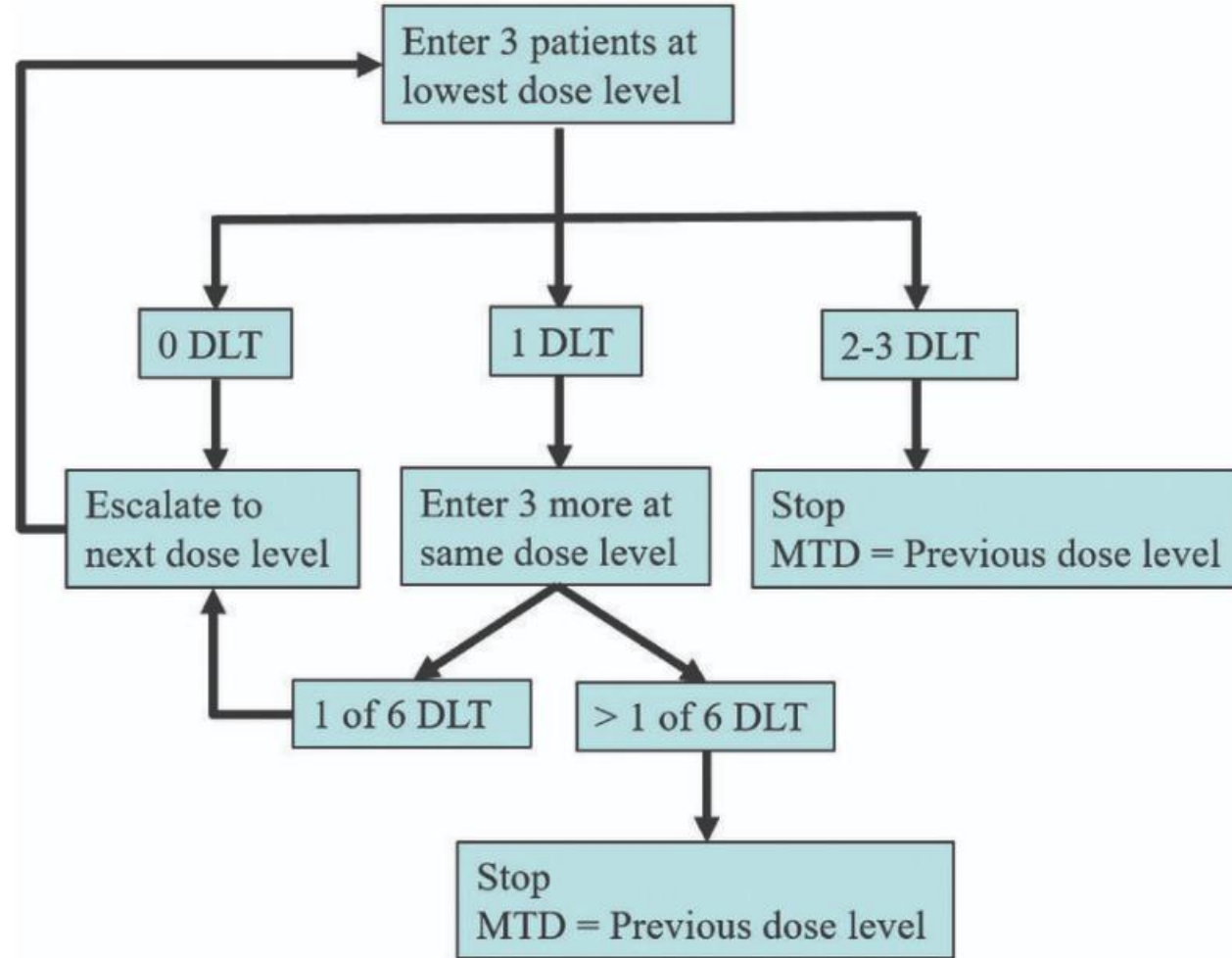
# Study Design- phase 1a- 3+3

Dose 1:  $80 \times 10^6$  CAR+  $\pm$  30%

Dose 2:  $160 \times 10^6$  CAR+  $\pm$  25%

Dose 3:  $240 \times 10^6$  CAR+  $\pm$  20%

*Optional Dose-1: TBD*



DLT = Dose Limiting Toxicity

MTD = Maximum Tolerable Dose



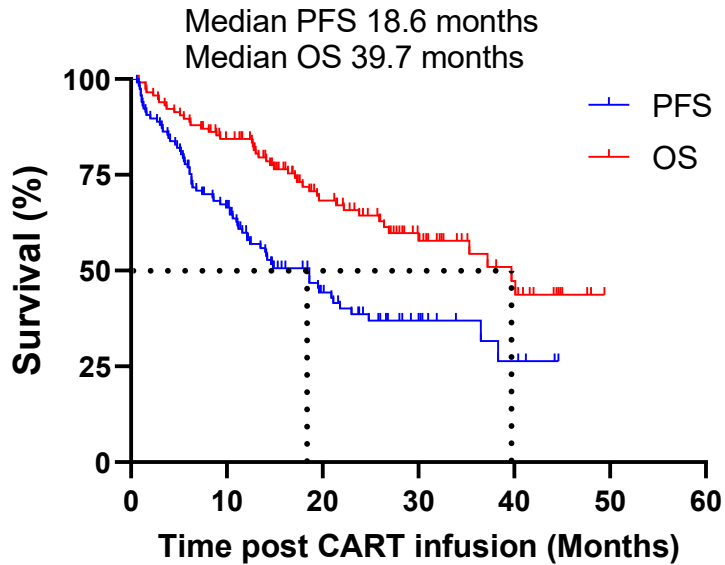
# Inclusion criteria

- **Adults  $\geq 18$  years with R/R multiple myeloma**
  - $\geq 3$  prior lines: PI, IMiD, anti-CD38
  - ECOG 0–2
  - Measurable disease, at least one of the following:
    - Serum M-protein  $\geq 0.5$  g/dL
    - Urine M-protein  $\geq 200$  mg/24h
    - Serum free light chain (FLC) assay: involved FLC level greater or equal to 3 mg/dL (**30 mg/L**) provided serum FLC ratio is abnormal.
    - **Bone marrow plasma cells  $>10\%$**
    - **Biopsy-proven plasmacytoma**
    - **PET/CT or marrow-based disease allowed (non-secretory)**

מבחינת מחלה מדידה,  
למעשה כל חולה עם  
מיאלומה בהתקדמות יכול  
להכנס למחקר...



# We've faced a dilemma in the study design...



- Naïve HBI0101 **maybe** better but HBI0101 already proved safety and efficacy

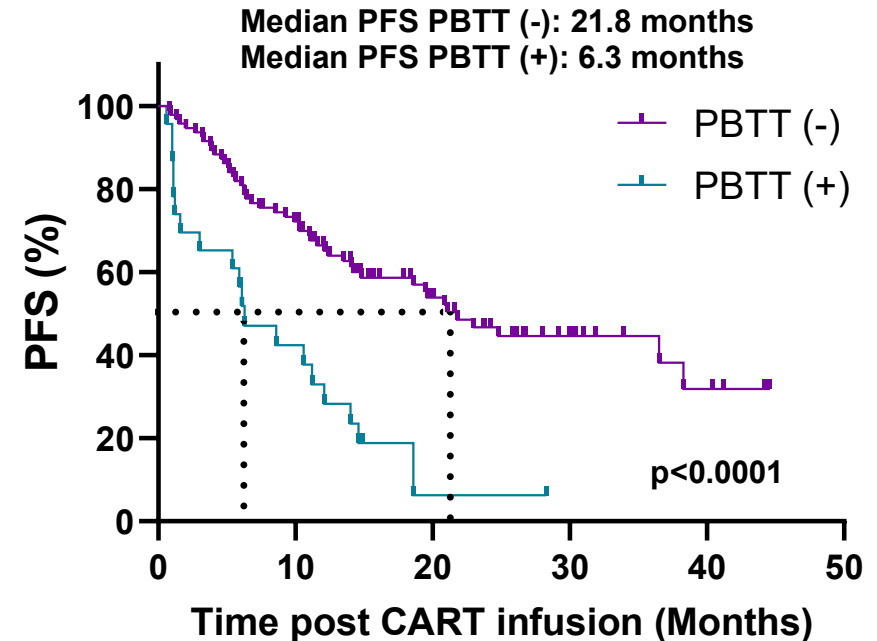
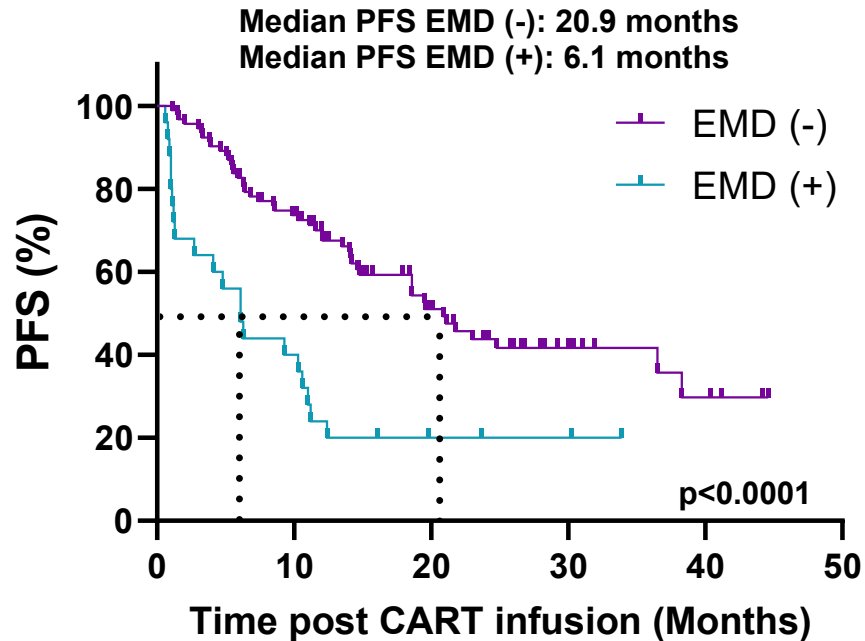


- Starting material characteristics which predict worse outcomes? No convincing findings

- Clinical characteristics which predict worse outcomes?  
**EMD** and **prior BCMA-targeted therapy**



# EMD & prior BCMA targeted therapy are the strongest predictors of lower efficacy with HBI0101

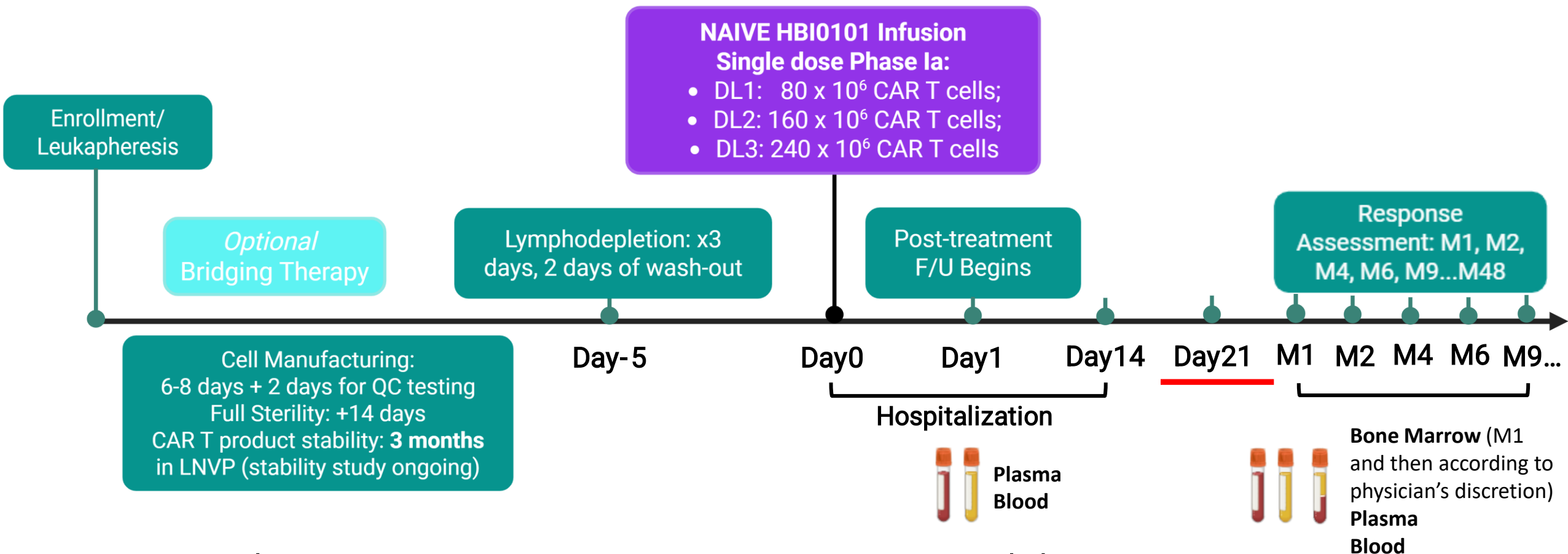


- Phase 1a will enroll only patients with EMD / PBTT
- “Back-up” salvage with HBI0101 “regular” CART



# Key exclusion criteria

- **Bulky** CNS myeloma
- AL amyloidosis
- Creatinine clearance  $<20$  ml/min
- AST/ALT  $>2.5 \times$  ULN
- ANC  $< 1000$  / PLT  $< 30,000$  / hemoglobin  $< 8$
- ALC  $< 300$  may be excluded per investigator judgement
- LVEF  $<40\%$
- Active infection
- Any limiting serious comorbidity
- Other non-skin cancer with active treatment in the last 2 years



### Patient Population

- Phase Ia:  
MM patients with EMD or after prior BCMA-targeted therapy(ies)
- Phase Ib:  
All MM patients

### Trial Objectives

- Safety and tolerability
- Overall response rate, complete response rate
- Duration of response
- Selection of Phase Ib dose
- Cell expansion pharmacokinetics

Inclusion/exclusion criteria: **similar to traditional HBI0101**

Post-CAR T F/U: similar to traditional HBI0101, except for 21-day additional F/U visit

Expected enrolled patients ~60



# Washout times before apheresis & LD

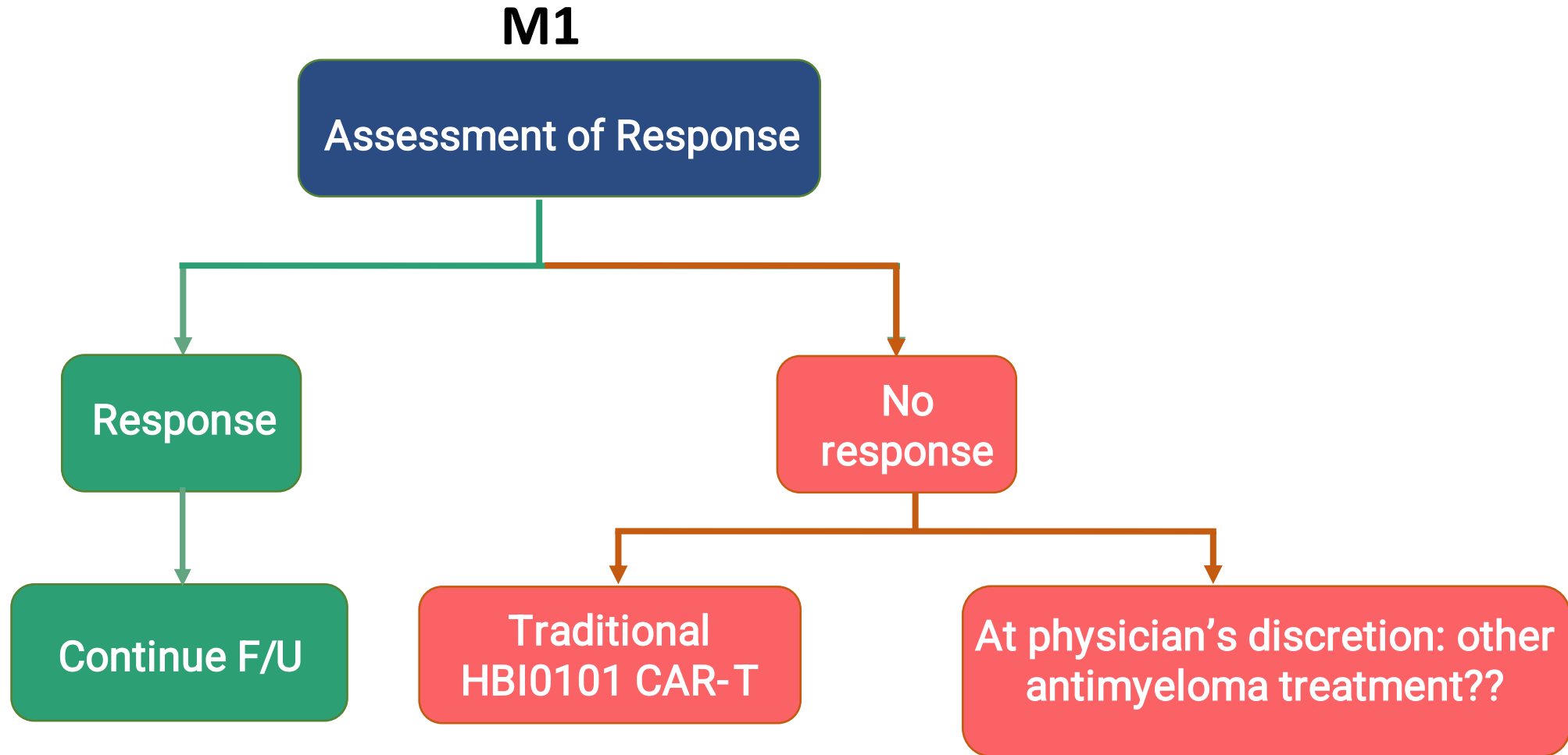
Generally- No prior systemic therapy for MM within **14 days prior**

## Exceptions:

- a) IMiDs- 7 days
- b) Venetoclax- 7 days
- c) Radiation therapy- 3 days
- d) Short-acting growth factors- 3 days (long-acting- 14 days)
- e) Therapeutic doses of steroids- 3 days
- f) CNS radiotherapy- 8 weeks prior to LD
- g) Other CART - 8 weeks prior to LD



# Response Evaluation and Rescue Plan





# Reminder-

# Phase 2 study with traditional HBI0101 is ongoing!

- **R/R multiple myeloma**

≥2 prior lines: PI, IMiD, anti-CD38

OR

Functional high-risk (defined as relapse  $\leq$  18m from treatment initiation)

Non-secretory allowed

- **AL amyloidosis**

≥1 prior line: PI, anti-CD38 (IMiD not required)

OR

Insufficient response to frontline therapy (which included PI, anti-CD38)



# Coming soon:

- Phase 1a/1b study with **locally produced anti-GPRC5D CART**
- MM and AL amyloidosis
- Very permissive inclusion criteria, prior anti-BCMA CART and prior Talquetamab- allowed



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- Batia Avni
- Shlomo Elias
- Eran Zimran
- Alexander Lvovich
- Adly Jabari



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- Nasreen Husein
- Shira Azrad

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- Ortal Harush, MSc
- Yael Cohen, MD
- Irit Avivi, MD

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IMMIX  
biopharma

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# נשמח מאד להפניית מטופלים

