

Feasibility of a Novel Academic Anti-BCMA Chimeric Antigen Receptor T-Cell (CART) (HBI0101) for the Treatment of Relapsed and Refractory AL Amyloidosis

ASH conference, December 10, 2023

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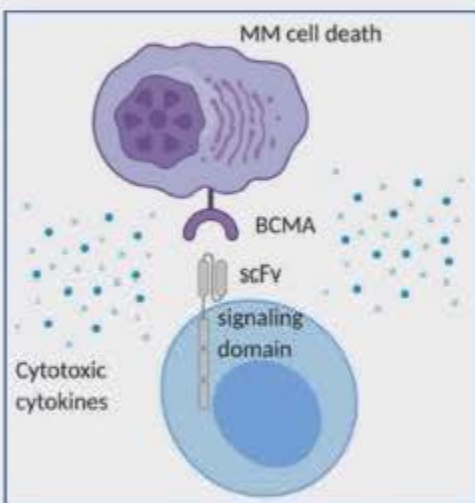
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Introduction

- Treatment for R/R AL amyloidosis is an unmet need
- Anti-BCMA CART have proven safe and efficient in MM
- HBI0101 therapy is a novel anti-BCMA CART, developed at Hadassah Medical Center for MM and amyloidosis treatment



(Asherie et al. *Haematologica*. 2022 Nov).

- In a phase Ia-b/2 study (NCT04720313), HBI0101 has demonstrated manageable safety with therapeutic efficacy. [by now over 80 MM patients]

**Abstract 4852 presented by Dr. Elias
Monday, December 11, 2023 ; 6-8 PM
San Diego Convention Center, Halls G-H**

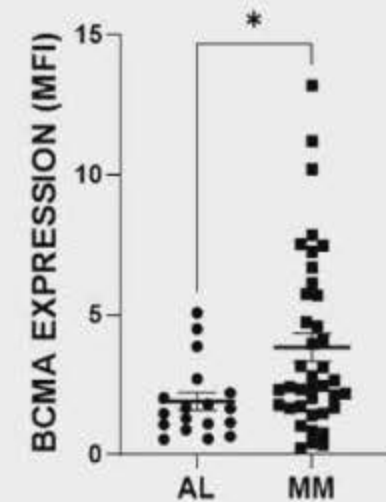
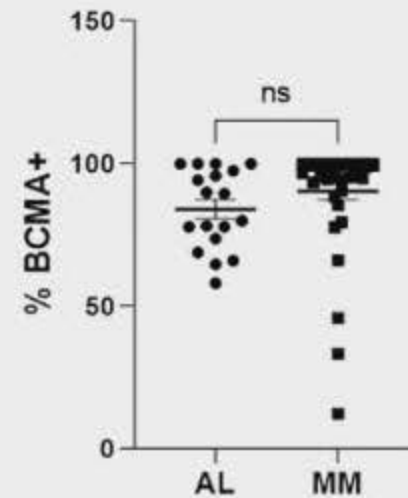
CART in AL amyloidosis

Goals:

- Deep responses are crucial in AL
- Such desired responses are observed with CART and bispecific Ab's in MM

Challenges:

- Lower BCMA expression levels are seen in AL plasma cells compared to MM plasma cells
- Frail patients-
 - Cardiac disease
 - Kidney disease
 - Multi-organ involvement



Introduction

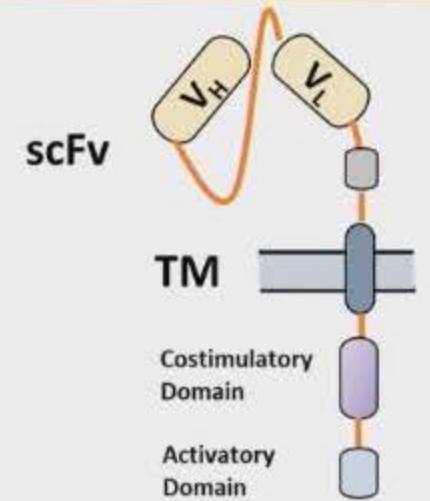
- Oliver-Caldes et al. *J Immunother Cancer*. 2021: case report of a patient with MM and renal amyloidosis involvement treated with BCMA.CART
- We reported on the first 4 AL patients treated with our local BCMA.CART



(Kfir- Erenfeld et al *Clin Cancer Res* 2022;28:5156–66)

Here we aim to report on 11 AL amyloidosis patients treated in our study

HBI0101 anti-BCMA CART



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Preclinical evaluation and structural optimization of anti-BCMA CAR to target multiple myeloma

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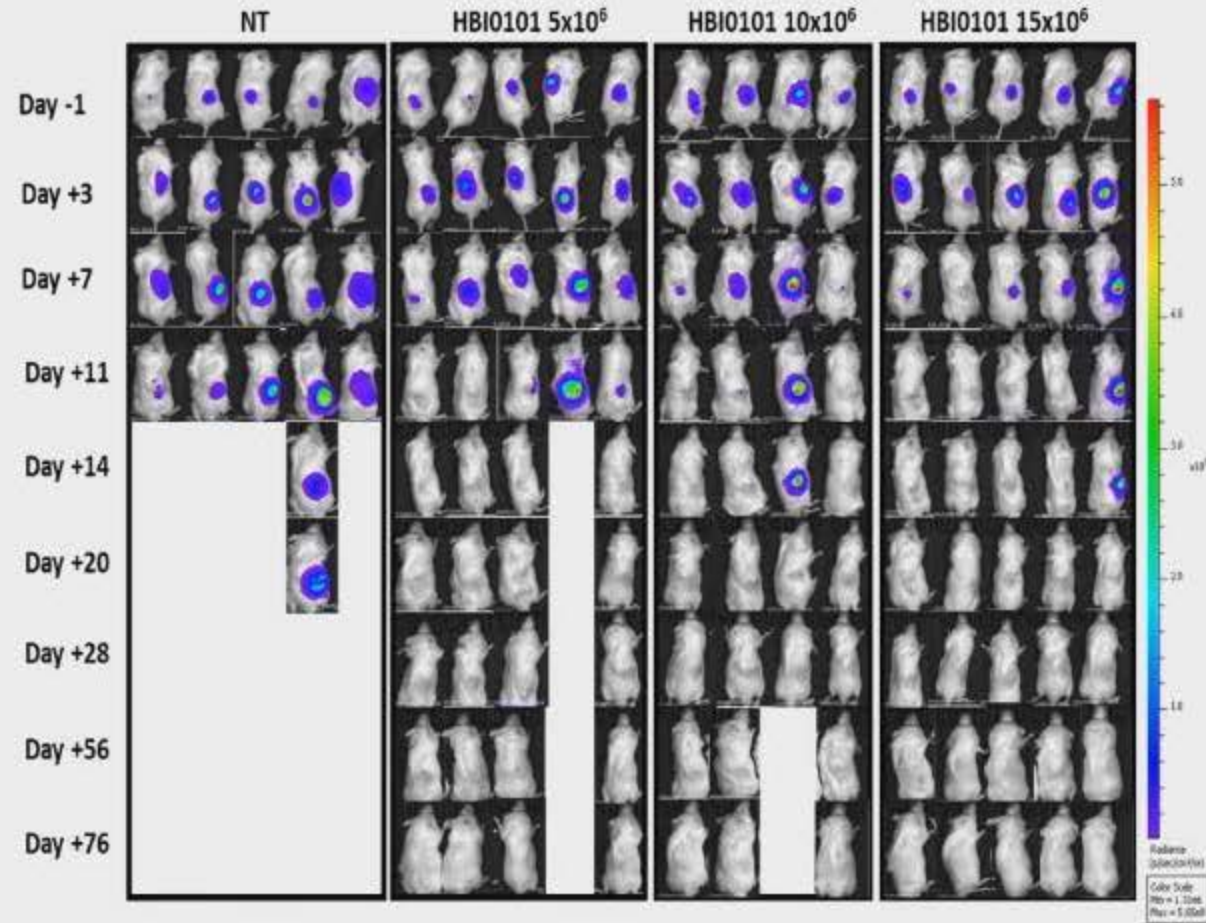
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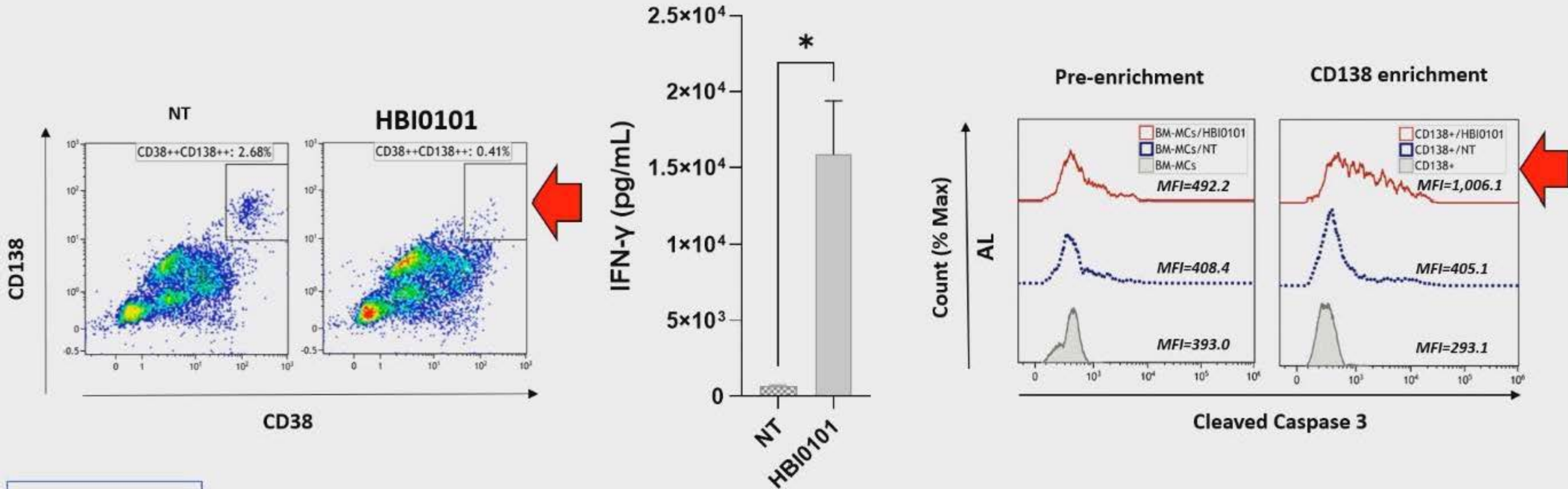


(Harush et al. *Haematologica*. 2022 Mar).



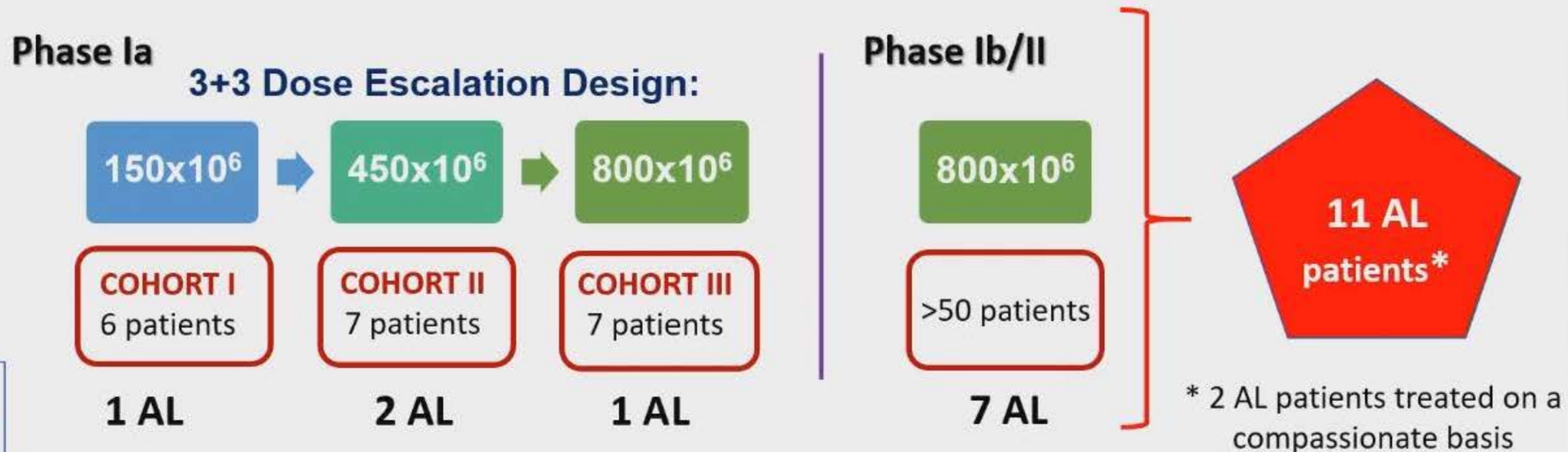
Founded by Hadassah, the Western Zionist Organization of America

Co-cultured auto-CART with AL amyloidosis patients' plasma cells



Clinical trial of HBI0101- [NCT04720313](#)

- A Phase Ia\Ib\II Study of HBI0101 anti-BCMA CART in R/R MM and AL amyloidosis
- Phase Ia was designed as a dose-escalation 3X3 protocol. 20 pts.
- Phases Ib and II further tested 800×10^6 cart cells, phase II is ongoing



Clinical trial of HBI0101- [NCT04720313](#)

Inclusion criteria:

3 prior lines including PI, IMiD, anti-CD38

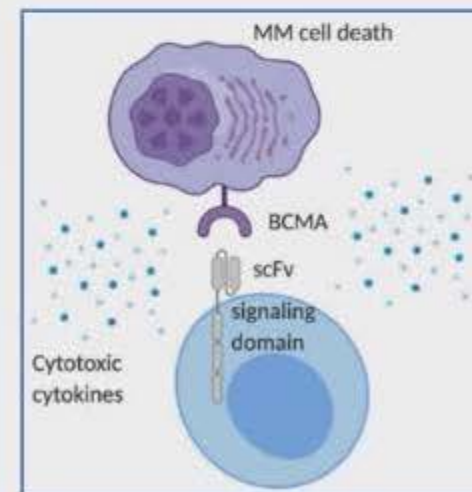
Compared to other studies-
very permissive organ function criteria:

- ✓ $PLT \geq 30 \times 10^9/L$
- ✓ $CRCL \geq 20 \text{ ml/min}$
- ✓ $EF \geq 40\%$. **NO upper proBNP limit**
- ✓ $ECOG-PS \leq 2$

✓ 10 days manufacturing time

✓ Lymphodepletion:

- fludarabine $25\text{mg}/\text{m}^2$ and cyclophosphamide $250\text{mg}/\text{m}^2$ on days -5 to -3
- For patients with creatinine clearance $<30\text{ml}/\text{min}$: bendamustine $90\text{mg}/\text{m}^2$ on days -4 and -3



Patients' baseline characteristics

Compassionate

Concomitant
MM

	1	2	3	4	5	6	7	8	9	10	11
Age	64	58	82	63	64	72	55	68	78	59	64
Gender	Male	Female	Male	Male	Male	Female	Female	Male	Male	Male	Female
dFLC (mg/L)	143	177	50	550	51	103	196	408	41	108	64
BMPCs (%)	3	15	1	15	1	1	1	10	15	1	1
FISH cytogenetics	t(11:14)	t(14:16) 10+	14Q-	t(11:14)	t(11:14)	t(11:14) 10+	14Q-	17p-	normal	17p-	t(4:14) 10+
Organ involvement	Cardiac, Renal, Autonomic	Cardiac, Renal, Hepatic	Renal, GI	Cardiac, Hepatic, Lung, Soft tissue, Autonomic	Cardiac, Soft tissue PNS	Cardiac, Renal, Liver	Cardiac, Soft tissue	Cardiac, Renal, Soft tissue	Renal	Cardiac, Renal, Autonomic	Cardiac, Renal, GI, liver, Soft tissue, Autonomic
NYHA stage	3	4	1	3	2	4	4	2	1	2	2
ProBNP (pg/ml)	7500	2008	119	2773	731	28000	6600	220	930	669	211
Trop T (ng/L)	60	40	8	78	18.3	110	30	12	9	8	20
Creatinine (mmol/L)	80	72	110	100	82	108	83	69	220	227	79
Albuminuria (g/24h)	0.3	0.3	2.4	0.1	0.1	1.0	0	0	0.3	1.5	0
ALKP (u/L)	45	218	84	140	84	186	166	106	160	59	160
MAYO stage	3a	3a	1	3a	2	3b	2	1	1	2	2
ECOG PS	0	2	0	0	1	2	4	0	1	1	1

Patients' baseline characteristics

	1	2	3	4	5	6	7	8	9	10	11	Summary
Prior lines of therapy	8	6	6	10	3	4	4	7	4	7	3	Median- 6
Best previous response/ which line	VGPR/ 3rd	VGPR/ 2nd	CR/ 1st	CR/ 1st , 4th	VGPR/ 2nd	VGPR/ 2nd	VGPR/ 3rd	VGPR/ 1st , 2nd	CR/ 4th	VGPR/ 3rd	CR	
Previous ASCT	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	No	5/11
Triple-drug refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	10/11
belantamab refractory	No	Yes	No	Yes	No	Yes	Yes	Yes	No	Yes	No	6/11
Last line refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11/11
Years since diagnosis	10.5	4	15	4.5	2	3.5	0.8	11	6	11	0.9	Median- 4.5

Results: Safety- CRS and ICANS

Patients	1	2	3	4	5	6	7	8	9	10	11	Summary
CART cells infused (x10⁶)	150	450	800	450	800	800	800	800	800	800	800	
CRS	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	9/11
CRS grade	N/A	2	3	3	1	N/A	1	2	2	2	1	
Time to onset (days)	N/A	2	3	1	2	N/A	2	2	1	1	1	Median-1.5d
CRS duration (days)	N/A	2	4	1	1	N/A	1	1	3	1	3	Median-1d
Tocilizumab use (number of doses)	N/A	1	3	1	1	N/A	0	1	3	1	0	7/9 with CRS
Steroids use	N/A	No	Yes	No	No	N/A	No	No	Yes	No	No	2/9 with CRS
Vasopressor use	N/A	No	Yes	No	No	N/A	No	No	No	No	No	1/7 with CRS
High-flow oxygen use	N/A	No	Yes	Yes	No	N/A	No	No	No	No	No	2/7 with CRS
ICANs	No	No	No	No	No	No	No	No	No	No	No	0/11

Safety- Other Adverse Events

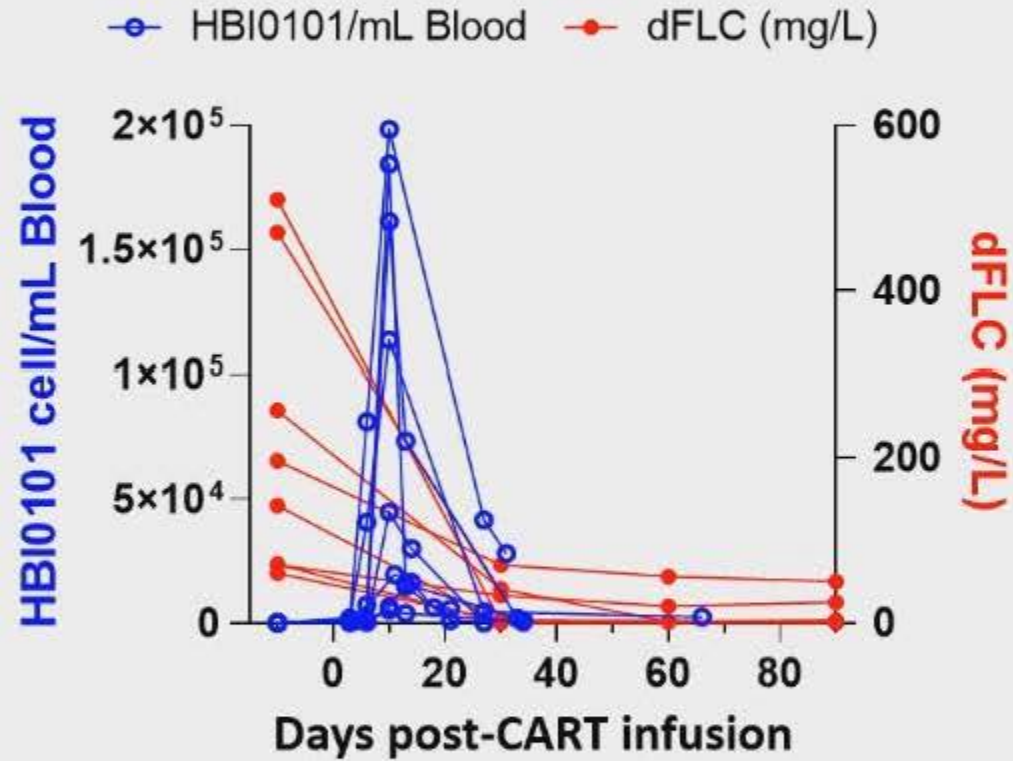
	1	2	3	4	5	6	7	8	9	10	11
CART cells infused (x10⁶)	150	450	800	450	800	800	800	800	800	800	800
Neutropenia- grade	1	3	3	4	3	0	2	4	0	0	3
Anemia- grade	0	1	2	3	1	0	0	0	3	2	2
Thrombocytopenia-- grade	0	2	1	4	1	0	0	0	0	0	2
Duration of Hematologic AE	<1 week	<1 week	<1 week	>2 months (predated the CART- MDS)	>2 months	N/A	<1 week	<1 week	<1 week	<1 week	<1 week
CHF exacerbation	No	Yes	No	Yes	No	Yes (prior infusion)	No	No	No	No	No
Acute renal failure	No	No	No	No	No	Yes	No	No	Yes	Yes	No
Hepatic dysfunction	No	Yes. G3	No	No	No	No	No	No	No	No	No
Fatigue- grade	1	2	3	1	1	1	0	2	2	1	1
GI- grade	0	0	2	0	0	0	0	0	0	0	0
Febrile Neutropenia- grade	0	0	3	3	0	0	0	3	3	0	0
Early Infections- grade	0	3	3	3	1	0	2	3	3	0	0
Hypogammaglobulinemia	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Infections during f/U (pna= pneumonia)	Day 248 pna	Day 33 OM	No	No	Day 62 pna and FN	No	Day 120 pna	No	No	No	No

Efficacy- Responses

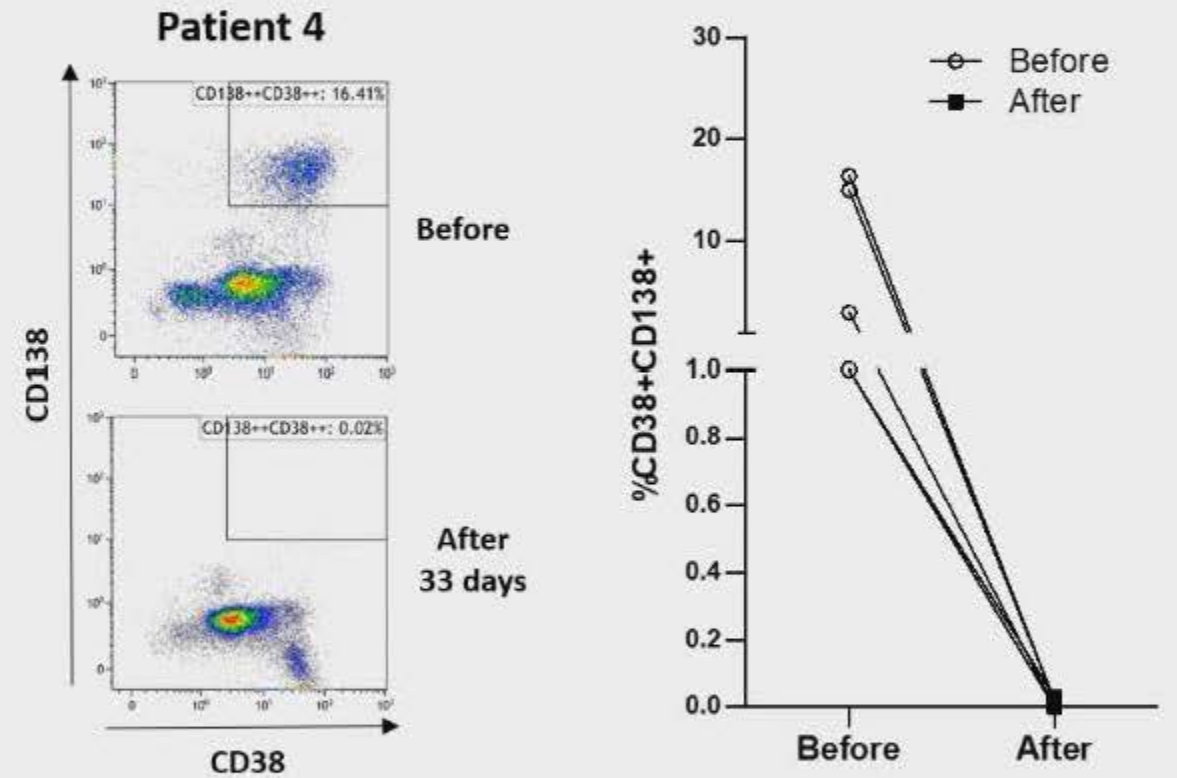
	1	2	3	4	5	6	7	8	9	10	11
CART cells infused (x10 ⁶)	150	450	800	450	800	800	800	800	800	800	800
Best hematologic response	CR	CR	CR	CR	CR	VGPR	PR	VGPR	CR	CR	N/A
iFLC at best response (mg/L)	0.6	0.9	1	7	0.4	0	56	36	0.1	2	N/A
dFLC at best response (mg/L)	0	0	0	1.4	0.2	20	50	30	0	2	N/A
MRD (10 ⁻⁵) negativity											
Day 30	Yes	Yes	Yes	Yes	Yes	No	N/A	No	Yes	No	N/A
Day 180	Yes	Yes	Yes		Yes						
Time to best hematologic response (days)	27	57	17	17	30	25	34	45	14	26	N/A
Follow-up (months)	10.1	12.2	24.7	7.3	18.7	3.3	6.5	5.2	4.8	3	0.5
Duration Of Response (months)	9.2	8.7	23.7, ongoing	1.5	18.4, ongoing	2.2	2.5	4.1	4, ongoing	2, ongoing	N/A

RESULTS- Efficacy

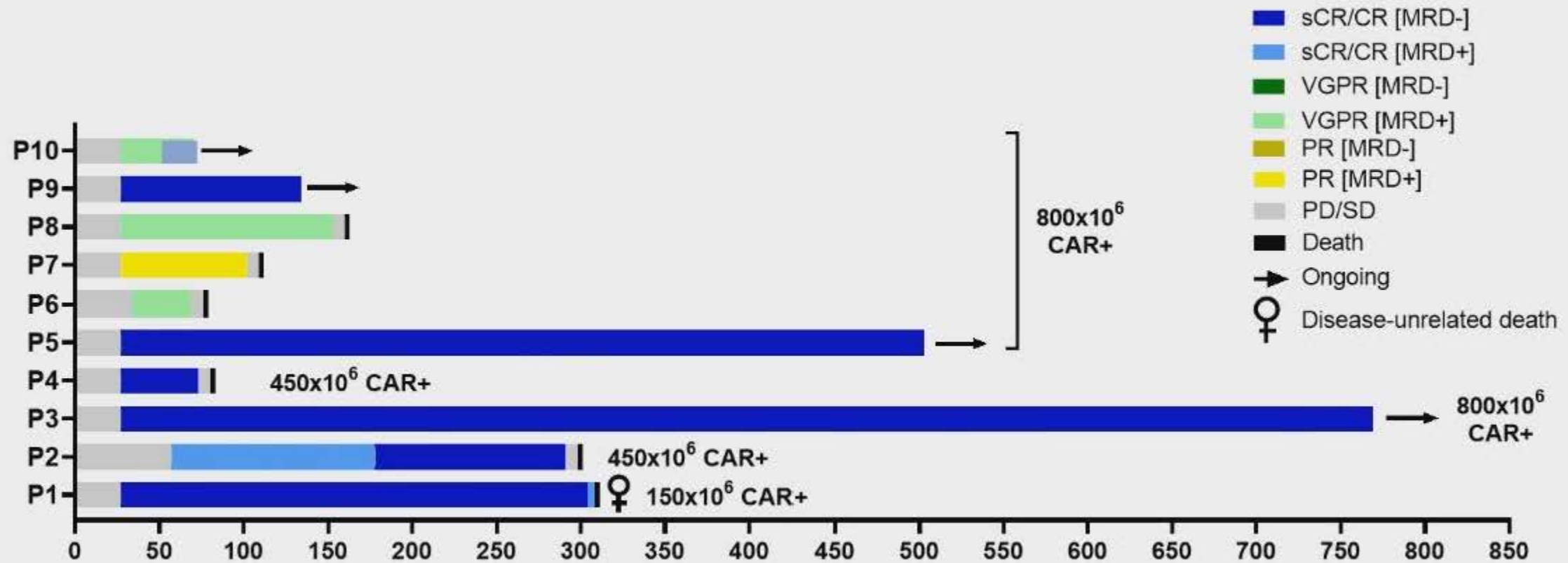
dFLC decrease post-CART expansion peak



BM-PC clearance post-CART



RESULTS- AL amyloidosis: Efficacy



	1	2	3	4	5	6	7	8	9	10	11
CART cells infused (x10⁶)	150	450	800	450	800	800	800	800	800	800	800
Best heme. response	CR	CR	CR	CR	CR	VGPR	PR	VGPR	CR	CR	N/A
Organ response	Yes	Yes	Yes	Yes	No	No	Yes	No	No	Yes	N/A
Reduction in biomarkers	proBNP- -64%	proBNP- -64%	Albumin- uria -100%	proBNP- -68%	No	proBNP- -20%	proBNP- -57%	No	N/A	Orthostati sm resolved Albumin- uria -35%	N/A
NYHA change	III to II	IV to I	N/A	III to II	No change	IV to III	IV to III	No change	N/A	N/A	N/A
Survival (Months)	10.1	12.2	25.2	7.3	16.2	3.3	6.5	5.2	4.3	3	0.5
Cause of death	Died COVID, in CR	Died Cardiac, PD	alive	Died Cardiac, PD	alive	Died Cardiac, in VGPR	Died Cardiac, in PR	Died Cardiac, PD	Alive	Alive	Alive

Conclusions- based on these 11 patients cohort

- ✓ HBI0101 anti-BCMA.CART provides a proof-of-concept that this therapy is safe enough , including in frail cardiac patients. Organ Deconditioning was manageable.
- ✓ It is a highly efficacious therapy for the treatment of AL amyloidosis.
- ✓ Due to the deep and quick reduction of light chain toxicity, *organ response is observed quickly*
- ✓ In these advanced cardiac amyloidosis patients no early mortality was observed. However cardiac related death in the first year was frequent, arguing for earlier usage in the course of disease, which may provide better organ responses and survival

THANK YOU!



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Hadassah Hebrew University Medical Center Directors and management board



Israeli Amyloidosis patient association

Generous donation from Manfred Steinfeld and Cuniff family

PATIENTS and FAMILIES!!!

Immix Biopharma (Nasdaq: IMMX) has licensed HBI0101 CART technology (NXC-201)