

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

IMS meeting, Sep. 2023

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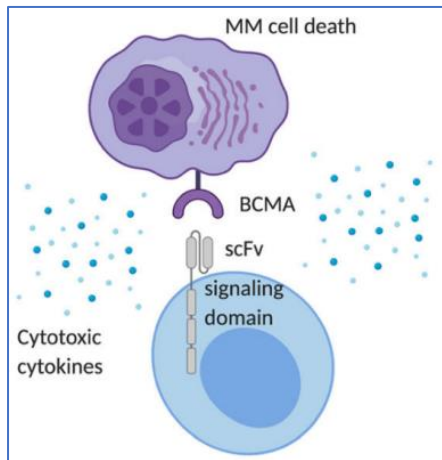
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Disclosures

Nothing to disclose

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
- In a phase Ia-b/2 study (NCT04720313), HBI0101 has demonstrated manageable safety with therapeutic efficacy in over 70 MM patients

ABSTRACT: P-026

Trianti Hall Level II Foyer,

Poster Session 1 - Wednesday, September 27

A screenshot of the haematologica journal website. The header includes the journal logo and name 'haematologica', and the text 'Open access journal of the Ferrata-Storti Foundation, a non-profit organization'. The navigation menu includes 'Home', 'Current Issue', 'Early view', 'Review Series', 'Archive', 'About Us', 'Contact', and 'Su'. The main content area shows the article title: 'Development and manufacture of novel locally produced anti-BCMA CAR T cells for the treatment of relapsed/refractory multiple myeloma: results from a phase I clinical trial'. The volume and issue information is 'Vol. 108 No. 7 (2023): July, 2023 > Development and manufacture of novel locally produced...'.

Development and manufacture of novel locally produced anti-BCMA CAR T cells for the treatment of relapsed/refractory multiple myeloma: results from a phase I clinical trial

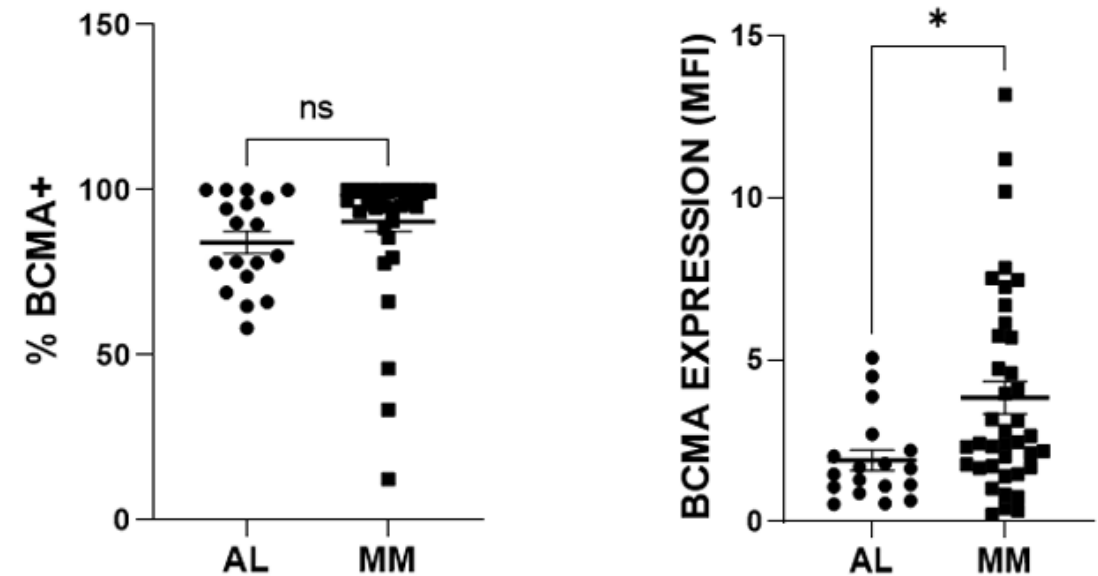
CART in AL amyloidosis

Opportunity:

- Deep responses, which are crucial in AL, were observed with CART in MM

Challenges:

- Attenuated BCMA expression on AL plasma cells compared to MM plasma cells
- Frail patients-
 - heart 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 treated with CAR-T
- We reported (Dec, 2022) on the first 4 AL patients treated with our local CAR-T

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Feasibility of a Novel Academic BCMA-CART (HBI0101) for the Treatment of Relapsed and Refractory AL Amyloidosis



Shlomit Kfir-Erenfeld¹, Nathalie Asherie¹, Sigal Grisariu¹, Batia Avni¹, Eran Zimran^{1,2}, Miri Assayag¹, Tatyana Dubnikov Sharon¹, Marjorie Pick², Eyal Lebel², Adir Shaulov², Yael C. Cohen³, Irit Avivi³, Cyrille J. Cohen⁴, Polina Stepensky¹, and Moshe E. Gatt²

Here we aim to report of 9 AL amyloidosis
patients treated in our study

HBI0101 anti-BCMA CART



Open access journal of the Ferrata-Storti Foundation, a non-profit organization

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

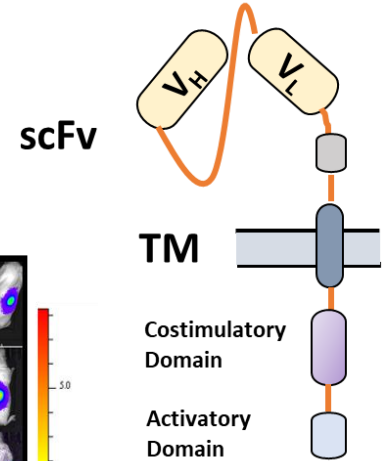
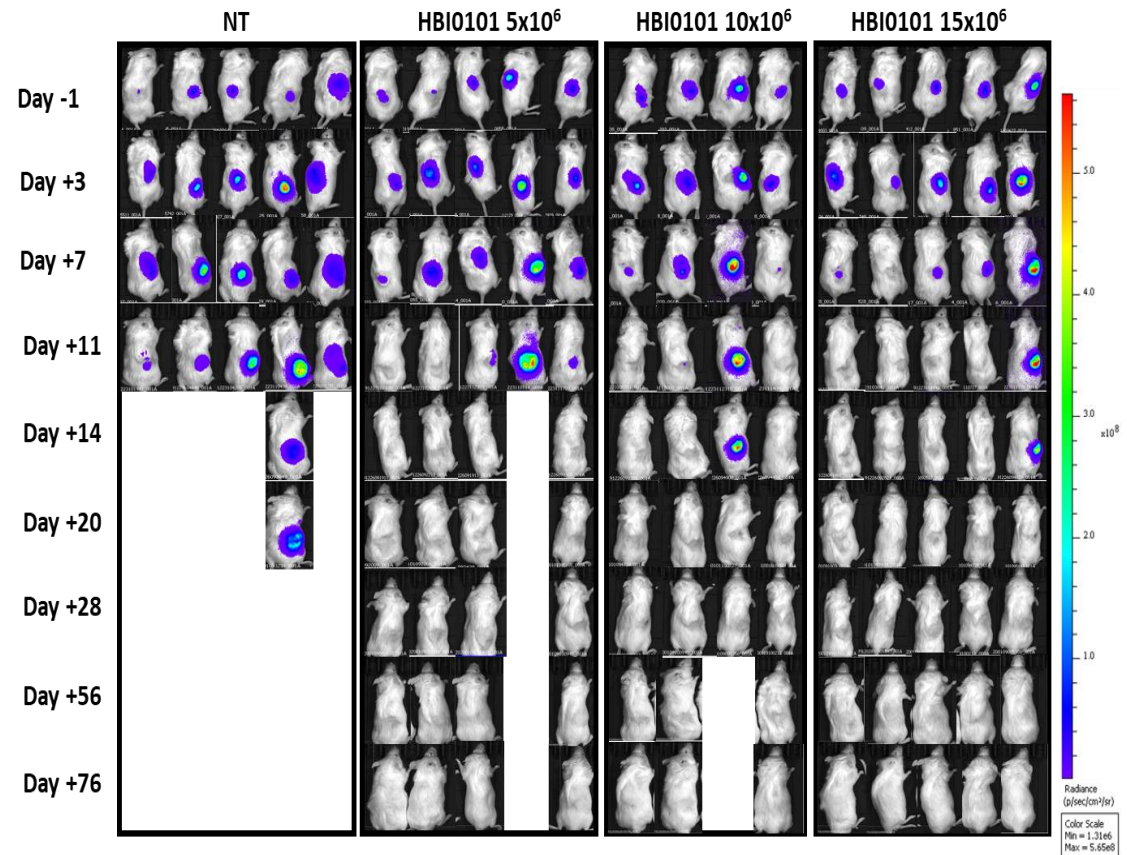
Ortal Harush, Nathalie Asherie, Shlomit Kfir-Erenfeld, Galit Adler, Tilda Barliya, Miri Assayag, Moshe E. Gatt, Polina Stepensky, Cyrille J. Cohen

Vol. 107 No. 10 (2022): October, 2022 <https://doi.org/10.3324/haematol.2021.280169>

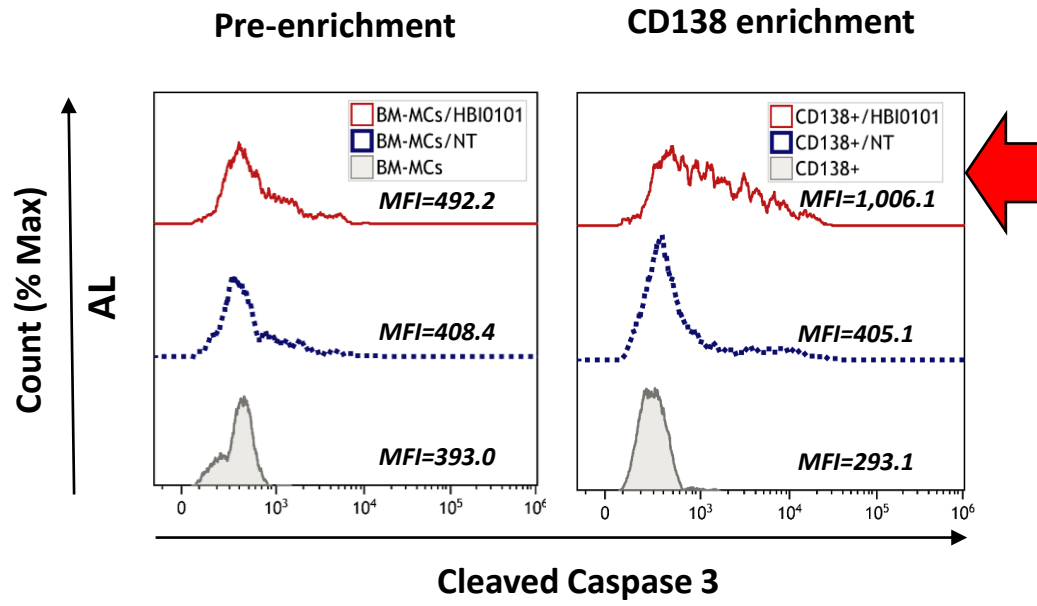
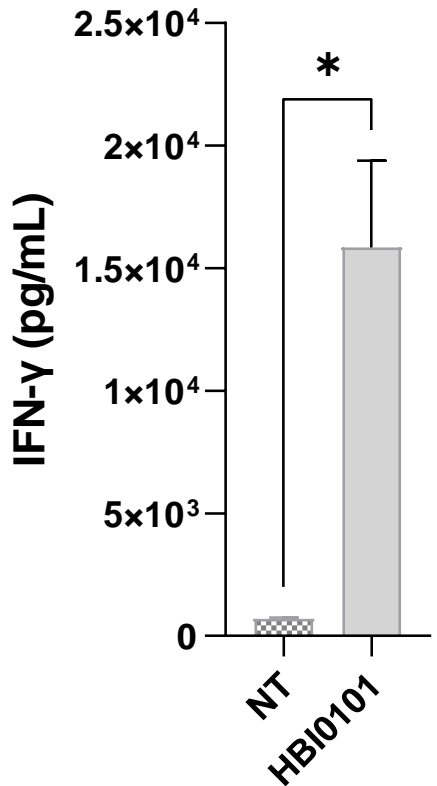
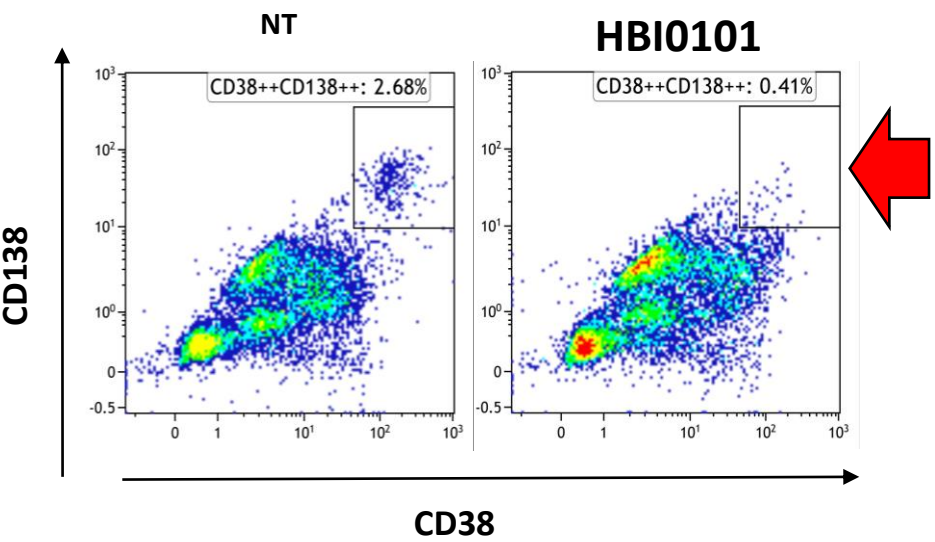
Harush et al. *Haematologica*. 2022 Mar



Founded by Hadassah, the Women's Zionist Organization of America

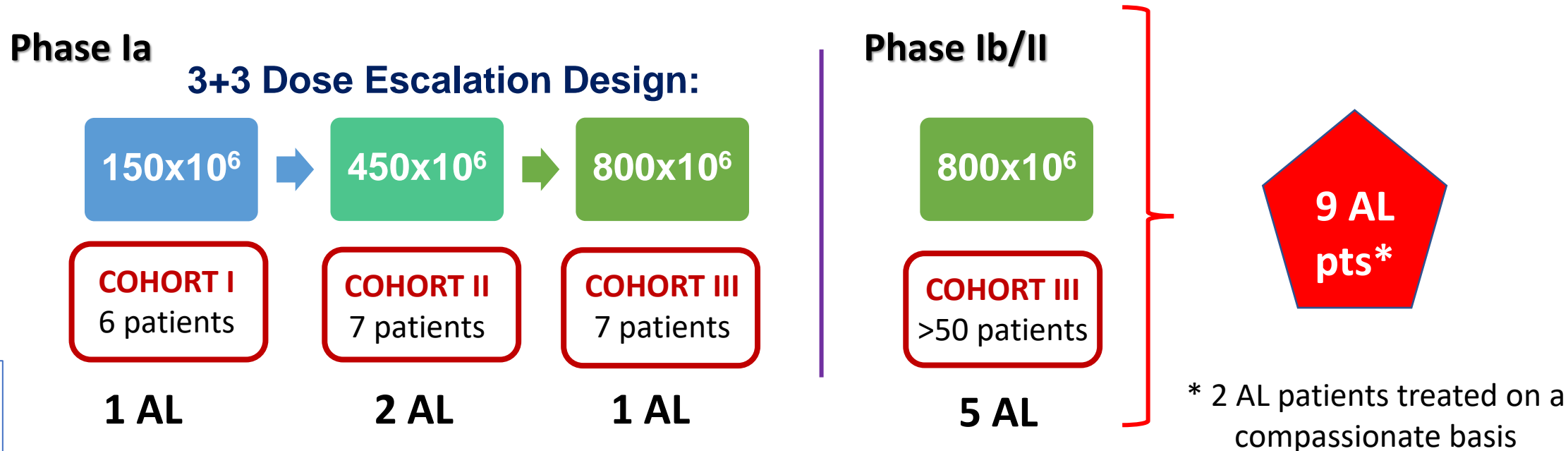


Co-cultured auto-CART with AL amyloidosis patient's plasma cells



Clinical trial of HBI0101- [NCT04720313](#)

- A Phase Ia\Ib\2 Study of HBI0101 BCMA.CART in R/R MM and AL amyloidosis
- Phase Ia was designed as a dose-escalation 3X3 protocol. 20 pts.
- Phases Ib and 2 further tested 800×10^6 cart cells, phase 2 is ongoing



Clinical trial of HBI0101- [NCT04720313](#)

Inclusion criteria:

3 prior lines including PI, IMiD, anti-CD38

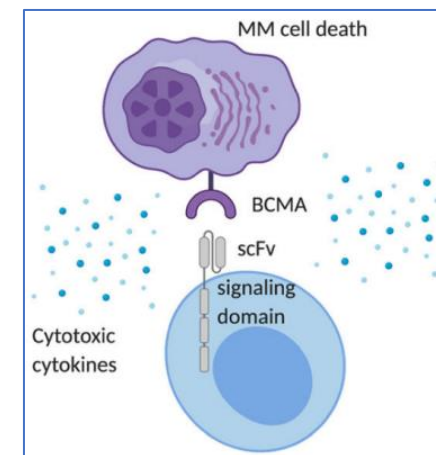
Compared to other studies-
very permissive organ function criteria:

- ✓ $PLT \geq 30 \times 10^9/L$
- ✓ $CRCL \geq 20 \text{ ml/min}$
- ✓ $EF \geq 40\%$
- ✓ $ECOG-PS \leq 2$

✓ 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

Concomitant MM

Compassionate

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

Patients' baseline characteristics

	1	2	3	4	5	6	7	8	9	Summary
Prior lines of therapy	8	6	6	10	3	4	4	7	4	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	
Previous ASCT	Yes	Yes	No	Yes	No	No	No	Yes	No	4/9
Triple-drug refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9/9
belantamab refractory	No	Yes	No	Yes	No	Yes	Yes	Yes	No	5/9
Last line refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9/9
Years since diagnosis	10.5	4	15	4.5	2	3.5	0.8	11	6	Median- 4.5

Results: Safety- CRS and ICANS

Patients	1	2	3	4	5	6	7	8	9	Summary
CART cells infused (x10 ⁶)	150	450	800	450	800	800	800	800	800	
CRS	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	7/9
CRS grade	N/A	2	3	3	1	N/A	1	2	2	
Time to onset (days)	N/A	2	3	1	2	N/A	2	2	1	Median- 2d
CRS duration (days)	N/A	2	4	1	1	N/A	1	1	3	Median- 1d
Tocilizumab use (number of doses)	N/A	1	3	1	1	N/A	0	1	3	6/7 with CRS
Steroids use	N/A	No	Yes	No	No	N/A	No	No	Yes	2/7 with CRS
Vasopressor use	N/A	No	Yes	No	No	N/A	No	No	No	1/7 with CRS
High-flow oxygen use	N/A	No	Yes	Yes	No	N/A	No	No	No	2/7 with CRS
ICANS	No	No	No	No	No	No	No	No	No	0/7

Safety- Other Adverse Events

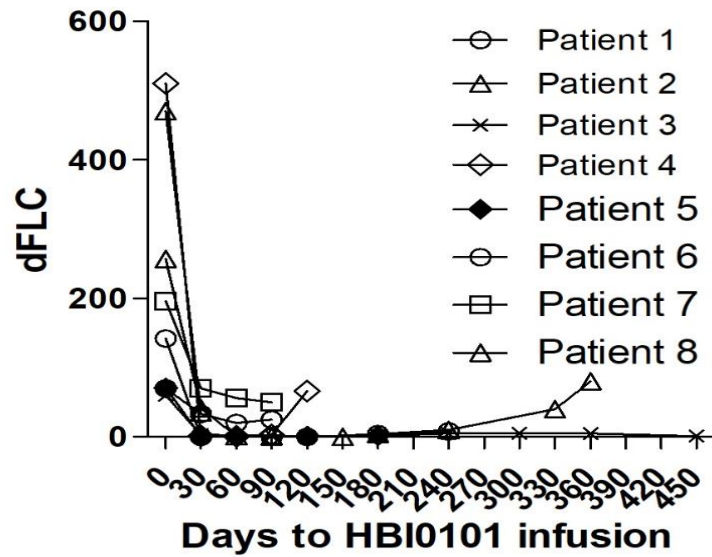
	1	2	3	4	5	6	7	8	9
CART cells infused (x10⁶)	150	450	800	450	800	800	800	800	800
Neutropenia- grade	1	3	3	4	3	0	2	4	0
Anemia- grade	0	1	2	3	1	0	0	0	3
Thrombocytopenia-- grade	0	2	1	4*	1	0	0	0	0
Duration of Hematologic AE	<1 week	<1 week	<1 week	>2 months (predated the CART, MDS)	>2 months	NA	<1 week	<1 week	<1 week
CHF exacerbation	No	Yes	No	Yes	No	Yes (prior to CART)	No	No	No
Acute renal failure	No	No	No	No	No	Yes	No	No	Yes
Hepatic dysfunction	No	Yes. G3	No	No	No	No	No	No	No
Fatigue- grade	1	2	3	1	1	1	0	2	2
GI- grade	0	0	2	0	0	0	0	0	0
Febrile Neutropenia- grade	0	0	3	3	0	0	0	3	3
Infections- grade	0	3	3	3	1	0	2	3	3
Hypogammaglobulinemia	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

Efficacy- responses

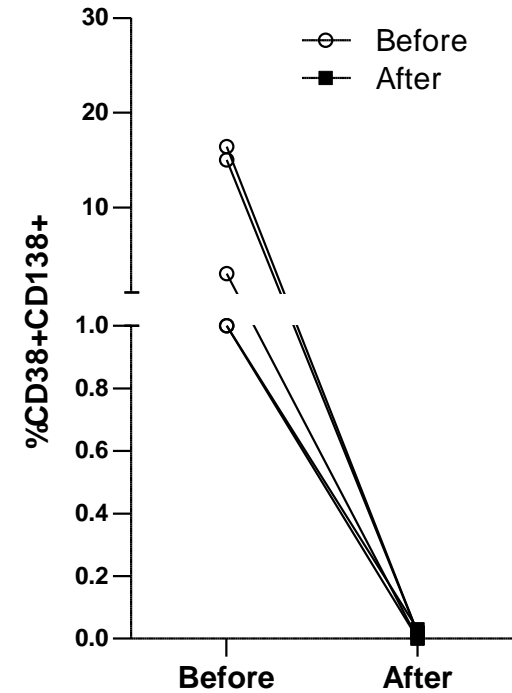
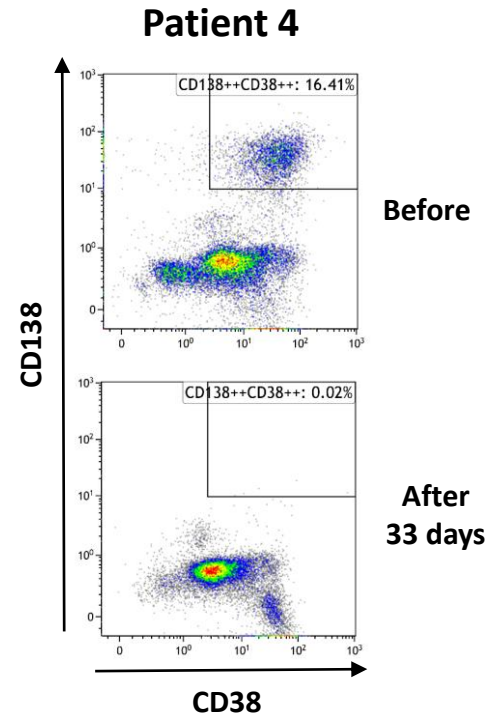
	1	2	3	4	5	6	7	8	9
CAR+ cells infused (x10 ⁶)	150	450	800	450	800	800	800	800	800
Best hematologic response	CR	CR	CR	CR	CR	VGPR	PR	VGPR	CR
iFLC at best response (mg/L)	0.6	0.9	1	7	0.4	0	56	36	0.1
dFLC at best response (mg/L)	0	0	0	1.4	0.2	20	50	30	0
MRD (10 ⁻⁵) negativity									
Day 30	Yes	Yes	Yes	Yes	Yes	No	N/A	No	Yes
Day 180	Yes	Yes	Yes		Yes				
Time to best hematologic response (days)	27	57	17	17	30	25	34	45	14
Follow-up (months)	10.1	12.2	22.7	7.3	13.7	3.3	6.5	5.2	1.8
Duration Of Response (months)	9.2	8.7	19.2-ongoing	1.5	12.9-ongoing	2.2	2.5	4.1	0.5-ongoing

RESULTS- Efficacy

dFLC decrease post CART



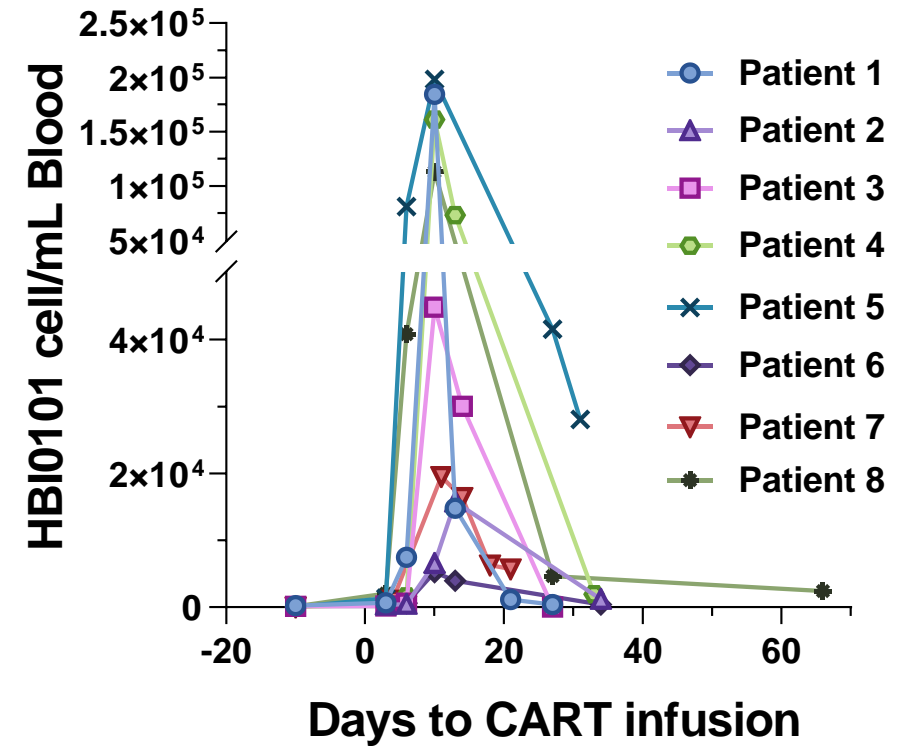
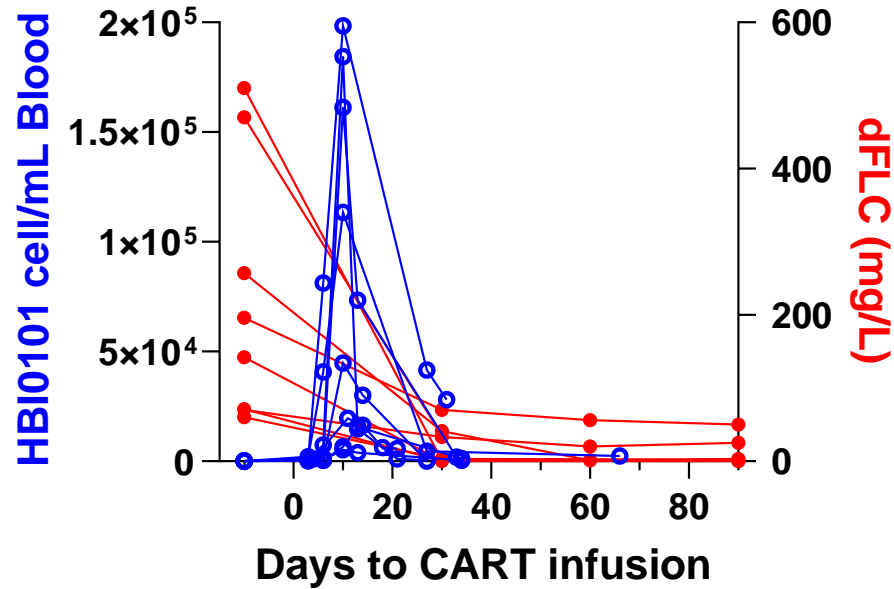
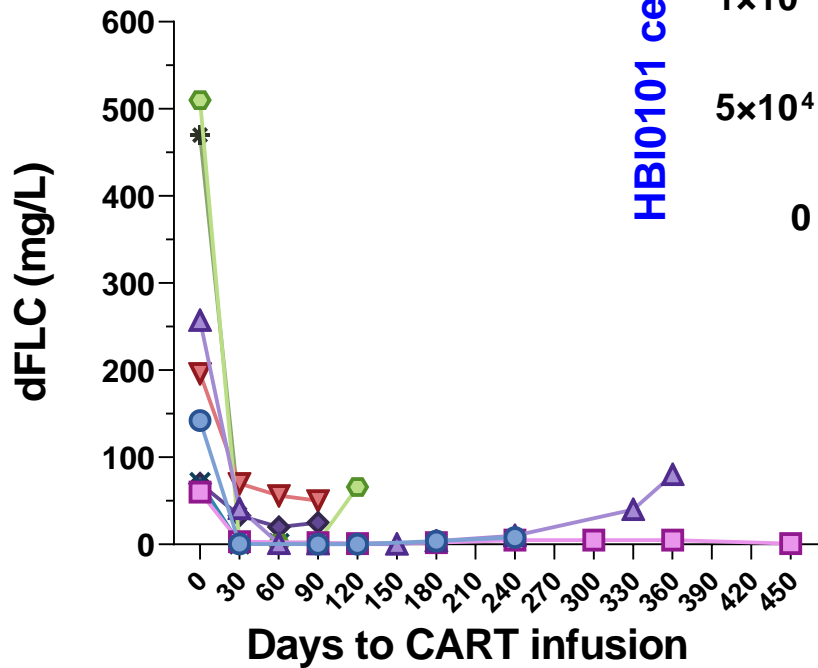
BM-PC decrease post CART





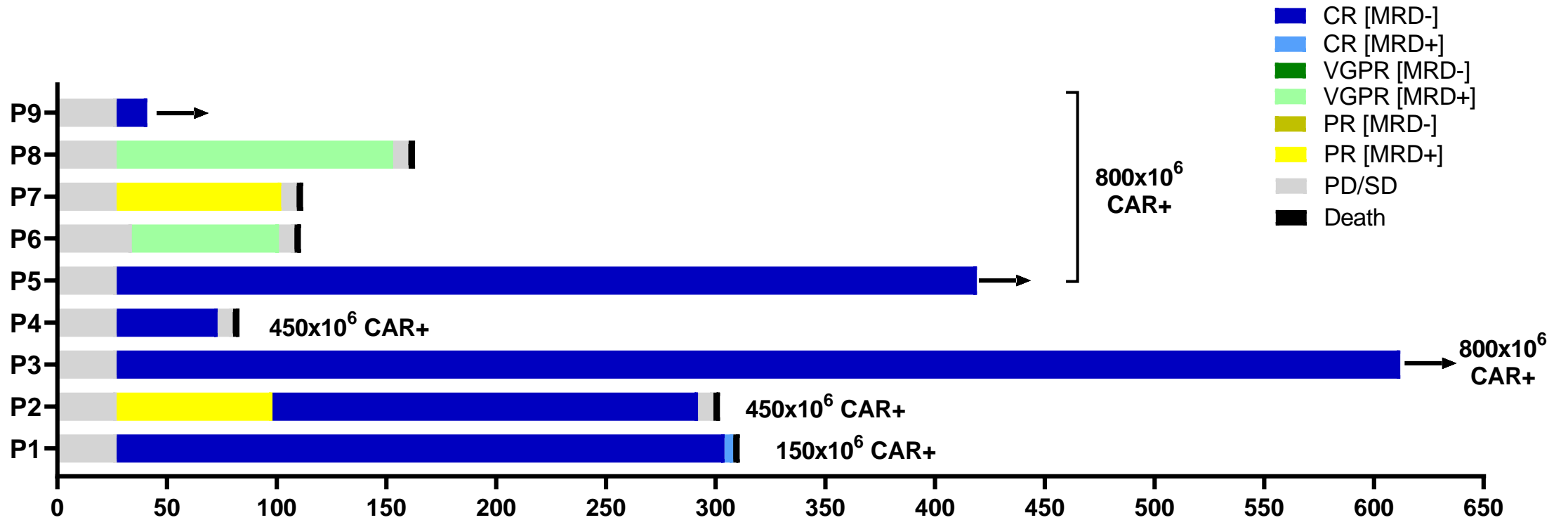
Efficacy Results: Pharmacokinetics

○ HBI0101/mL Blood ● dFLC (mg/L)



*dFLC (=involved FLC-uninvolved FLC)

RESULTS- AL amyloidosis: Efficacy

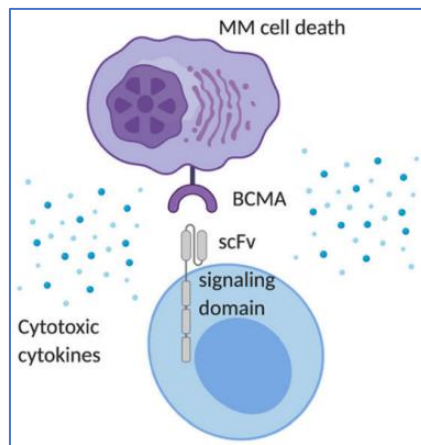


Efficacy- Organ Responses, Survival

	1	2	3	4	5	6	7	8	9
CAR+ cells infused (x10⁶)	150	450	800	450	800	800	800	800	800
Best heme. response	CR	CR	CR	CR	CR	VGPR	PR	VGPR	CR
Organ response	Yes	Yes	Yes	Yes	No	No	Yes	No	No
Reduction in biomarkers	proBNP- -64%	proBNP- -64%	Albuminuria -100%	proBNP- -68%	No	proBNP- -20%	proBNP- -57%	No	N/A
NYHA change	III to II	IV to II	N/A	III to II	No change	IV to III	IV to III	No change	N/A
Survival (Months)	10.1	12.2	22.7	7.3	13.7	3.3	6.5	5.2	1.8
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

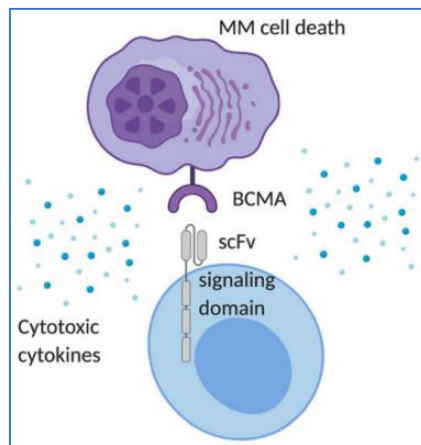
Conclusions

- ✓ AL amyloidosis PC express BCMA sufficiently for in-vitro and eventually clinical targeting
- ✓ CART can be given safely in AL amyloidosis, including in frail patients
- ✓ Due to the deep and quick reduction of light chain toxicity, organ response is observed quickly



Conclusions

- ✓ HBI0101 anti-BCMA-CART therapy provide a first proof-of-concept that this therapy is safe enough and highly efficacious for the treatment of AL amyloidosis
- ✓ In these advanced cardiac amyloidosis patients there was no early mortality, however deaths due to cardiac disease in the first year was frequent
- ✓ Usage earlier in the disease may provide better organ responses and survival



THANK YOU!



Prof. Polina Stepensky, PI



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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: IMMIX) has licensed HBI0101 CART technology (NXC-201)

