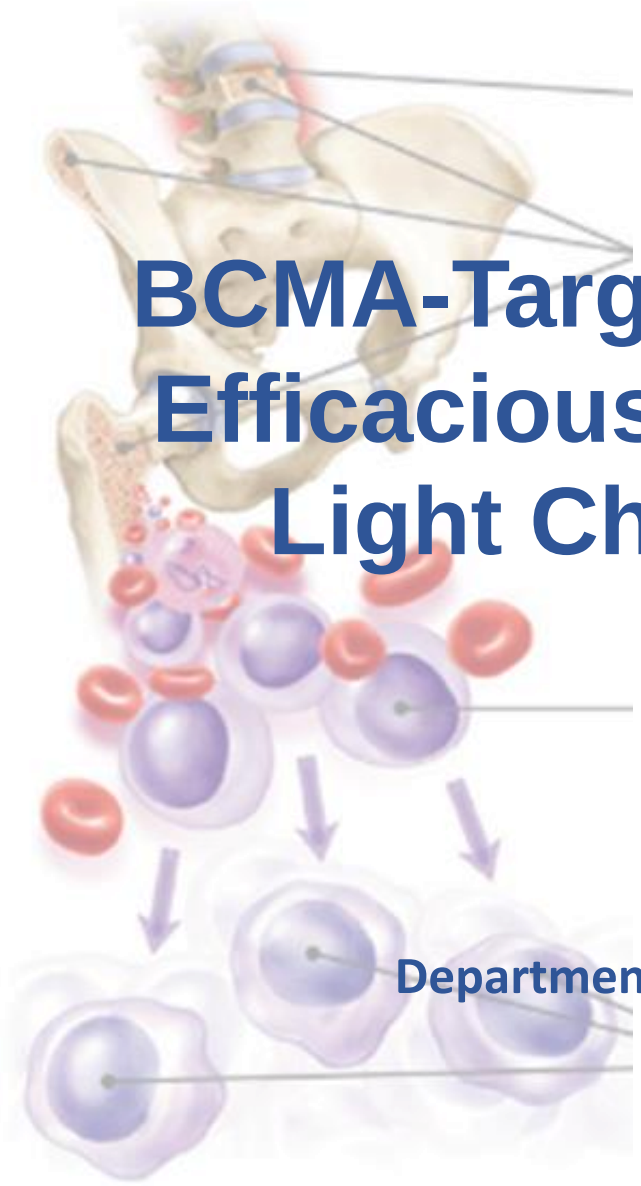


BCMA-Targeted CART (HBI0101), a Safe and Efficacious Novel Modality of Treatment for Light Chain Amyloidosis (AL) Patients

Nathalie Asherie, PhD

Department of Bone Marrow Transplantation and Cancer Immunotherapy

ASGCT, Los Angeles, CA
- May 2023-

Disclosures

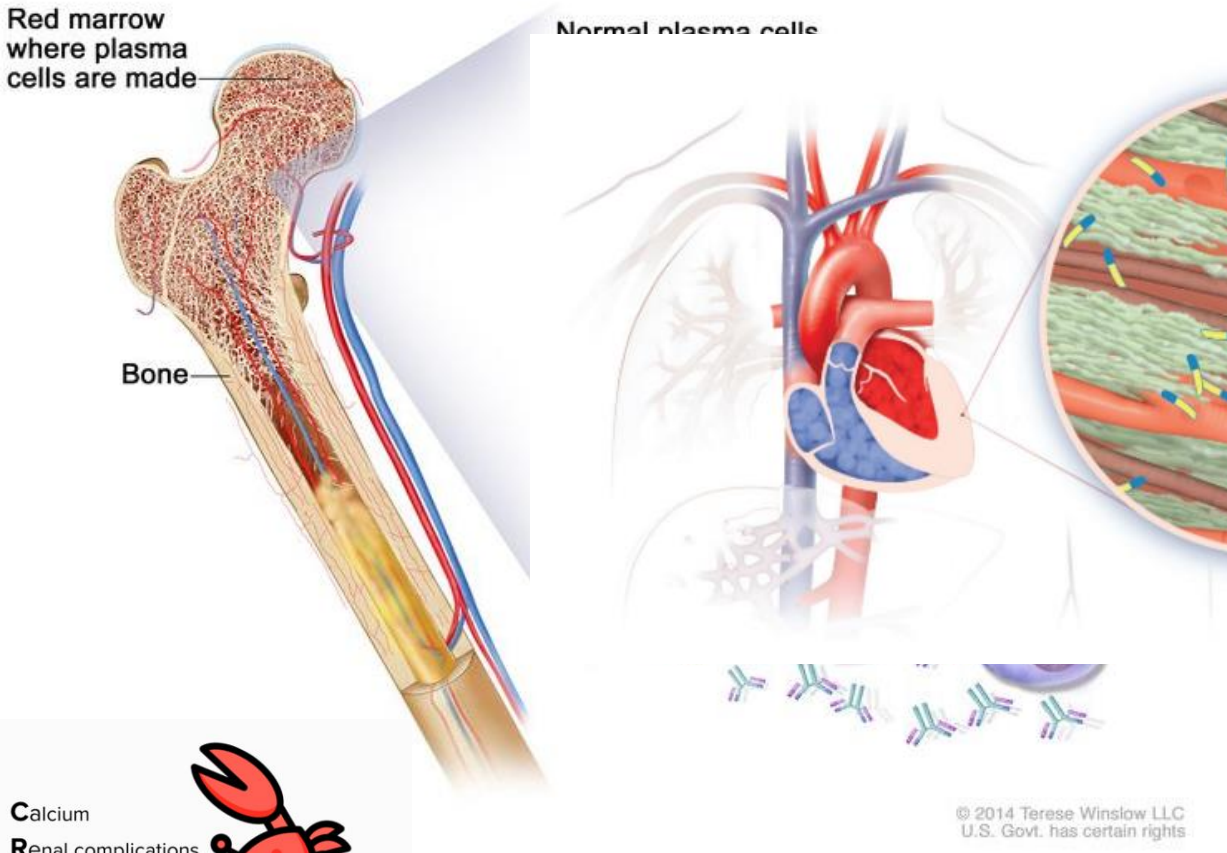
Dr Nathalie Asherie is employed by the Hadassah Medical Center.

The CART technology is protected by a worldwide patent application.

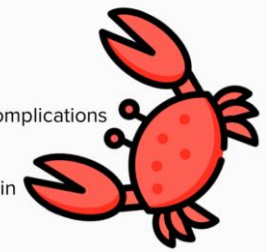
Immix Biopharma (Nasdaq: IMMX) has licensed HBI0101 CART technology (NXC-201).

AL Amyloidosis - Introduction

Multiple Myeloma

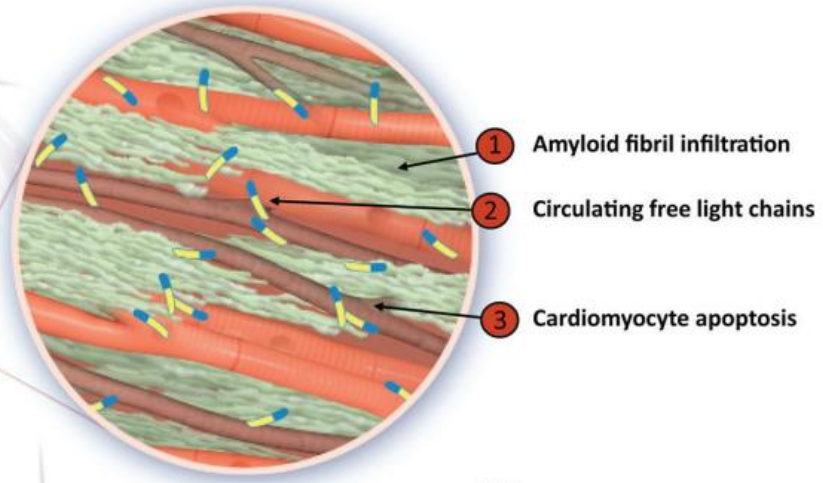


Calcium
Renal complications
Anemia
Bone pain

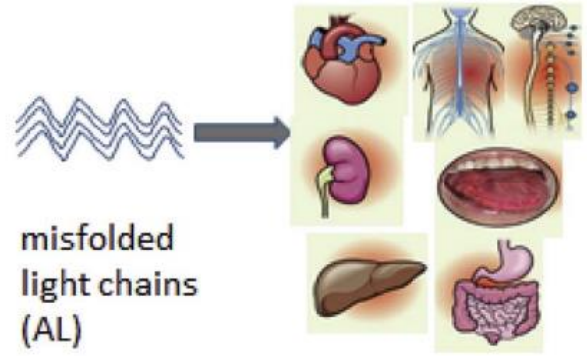


https://www.healthinsight.ca/advocacy/making-myeloma-matter/

AL amyloidosis



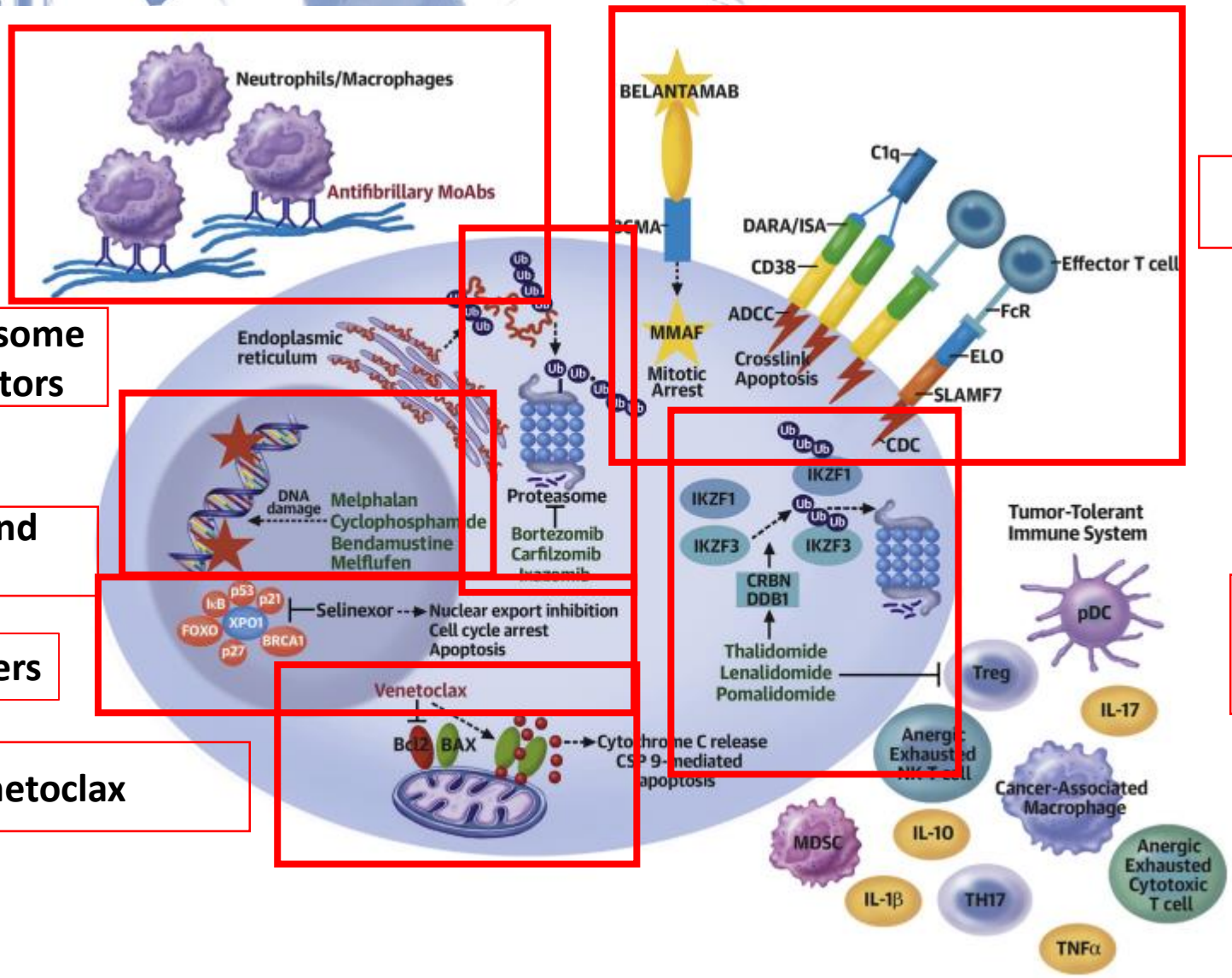
multiple myeloma



No effective treatments
Needs time for endogenous clearance
Chemotherapy adverse effects can worsen e.g. fluid retention, cardiotoxicity, neuropathy

https://doi.org/10.1016/j.conctc.2017.08.012.

Therapeutic Strategies for the treatment of AL Amyloidosis



Proteasome Inhibitors

Chemotherapy and Steroids

Others

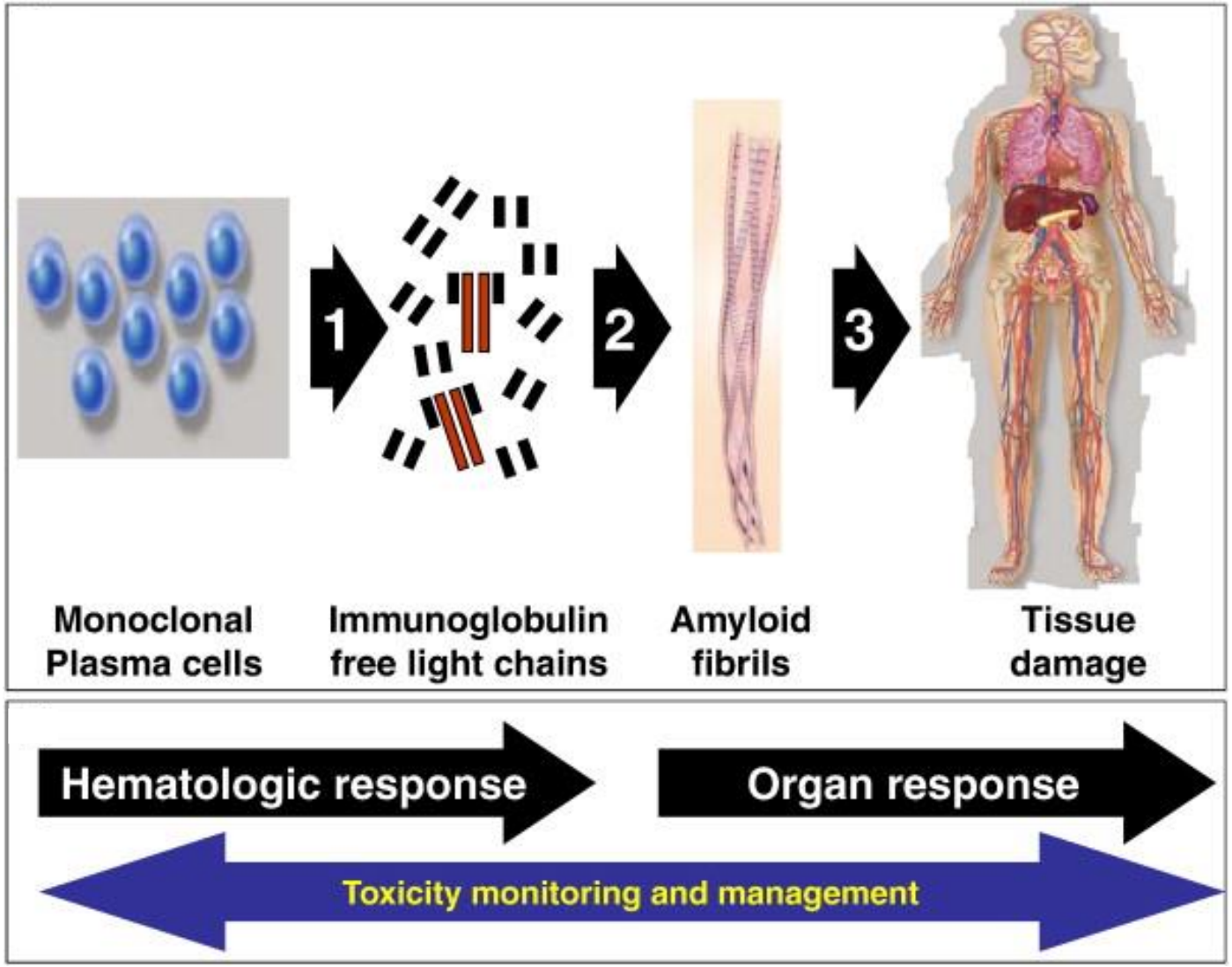
Venetoclax

Antibodies

Immune Modulators (IMiDs)

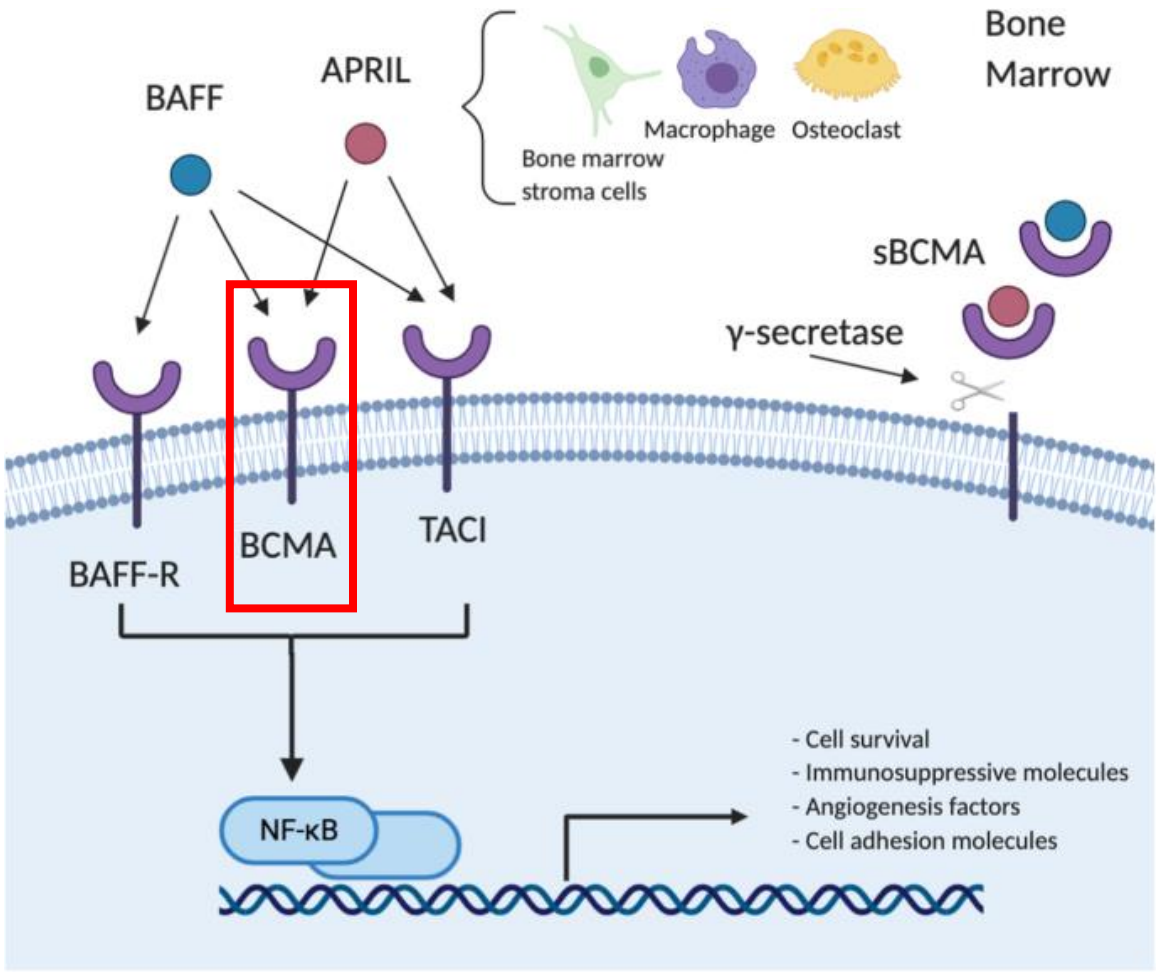
https://doi.org/10.1016/j.jaccao.2021.09.003

Organ response is the ultimate goal in the treatment of AL amyloidosis

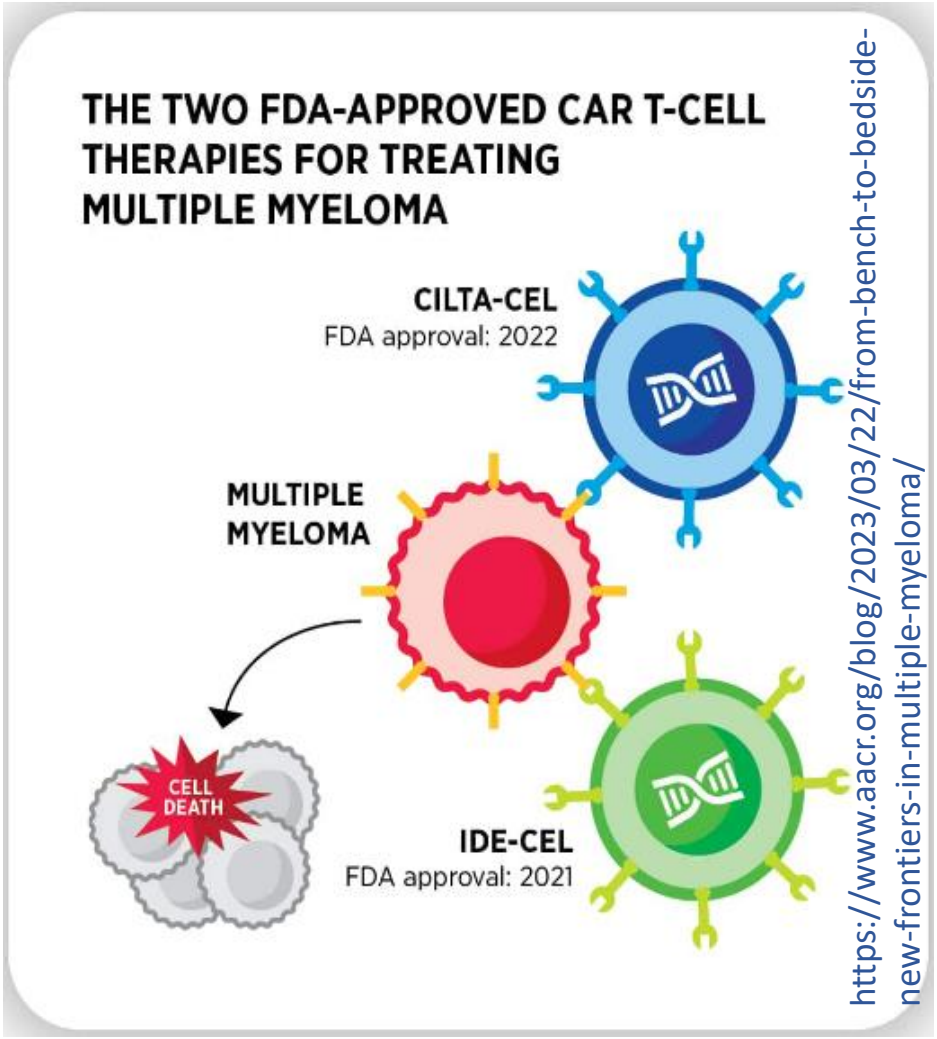


https://doi.org/10.1016/j.blre.2012.03.001

Anti-BCMA CART therapy has proven safe and efficient for the treatment of multiple myeloma



Journal of Hematology & Oncology.13:125. 2020.

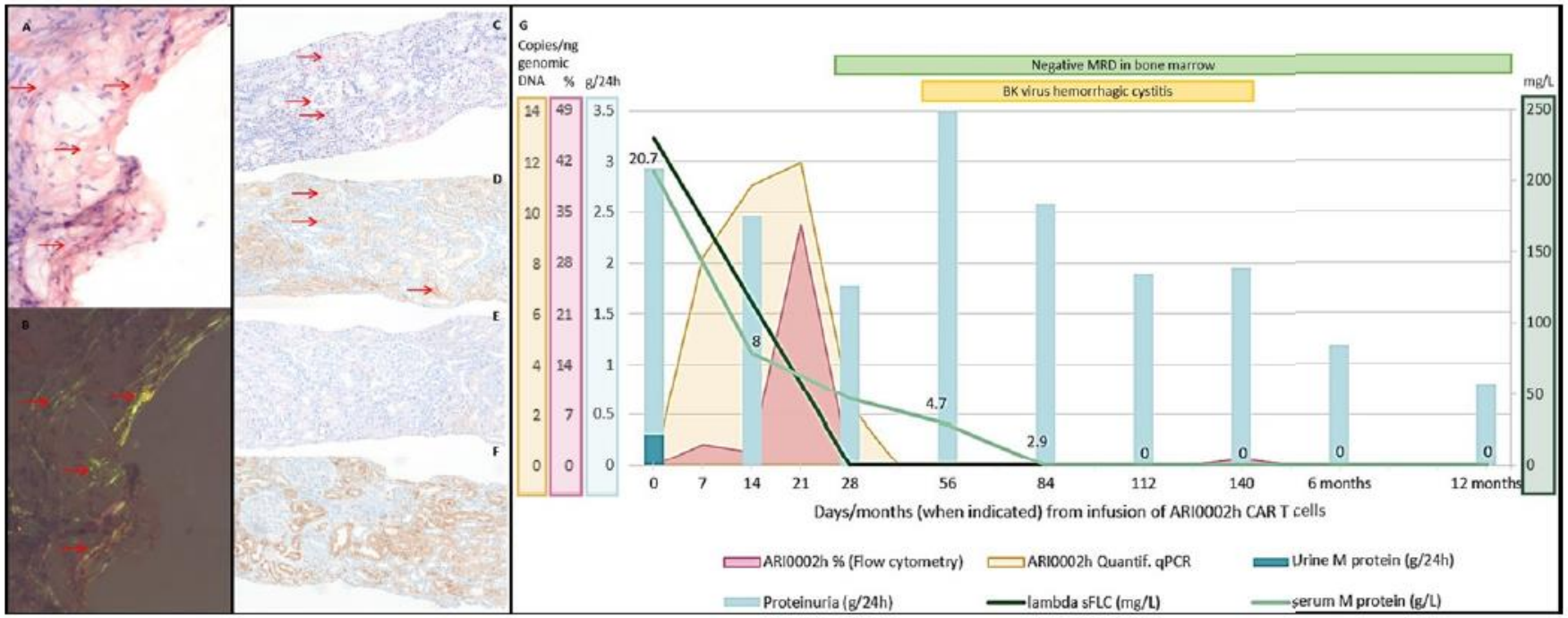


Limitations of CART therapy approach in AL patients

Open access Case report

Journal for ImmunoTherapy of Cancer

First report of CART treatment in AL amyloidosis and relapsed/refractory multiple myeloma



Oliver-Caldes et al. *J Immunother Cancer*. 2021

HBI0101, self-developed anti-BCMA CAR

NXC-201 (Formerly HBI0101) Multiple Myeloma

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04720313

Recruitment Status : Recruiting

First Posted : January 22, 2021

Last Update Posted : March 27, 2023

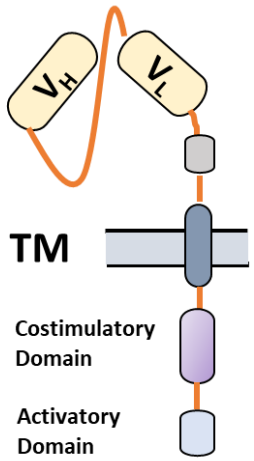
See **Contacts and Locations**

View this study on Beta.ClinicalTrials.gov

HBI0101 preclinical and clinical evaluation

α-BCMA scFv	Hinge CD8α	TM CD8α	4-1BB	CD3zeta

HBI0101 CAR



haematologica
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

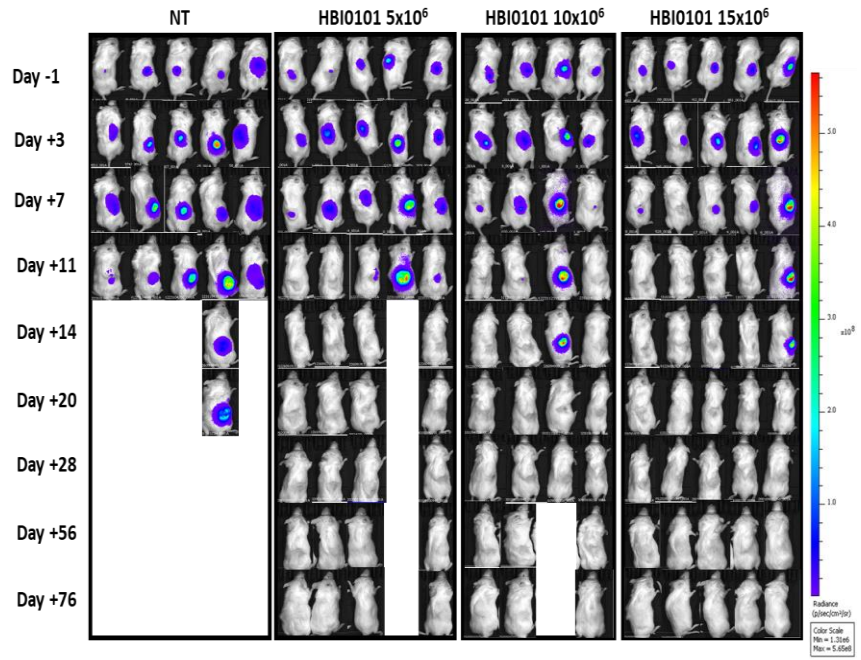
Ortal Harush, Nathalie Asherie, Shlomit Kfir-Erenfeld, Galit Adler, Tilda Barliya, Miri Assayag, Moshe E. Gatt, Polina Stepensky, Cyrille J. Cohen

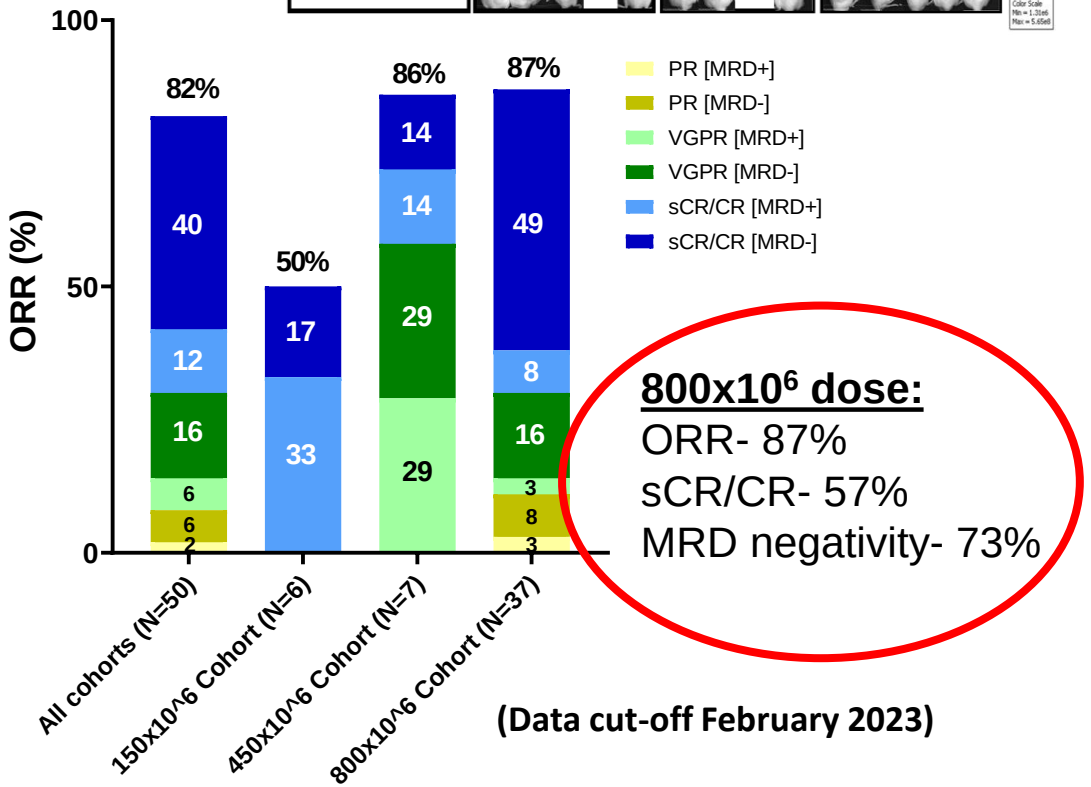
Vol. 107 No. 10 (2022): October, 2022 https://doi.org/10.3324/haematol.2021.280169

Development and manufacturing of novel locally produced anti-BCMA CART cells for the treatment of relapsed/refractory multiple myeloma: phase I clinical results

Nathalie Asherie, Shlomit Kfir-Erenfeld, Batia Avni, Miri Assayag, Tatyana Dubnikov, Nomi Zalcman, Eyal Lebel, Eran Zimran, Adir Shaulov, Marjorie Pick, Yael Cohen, Irit Avivi, Cyrille Cohen, Moshe E. Gatt, Sigal Grisariu, Polina Stepensky

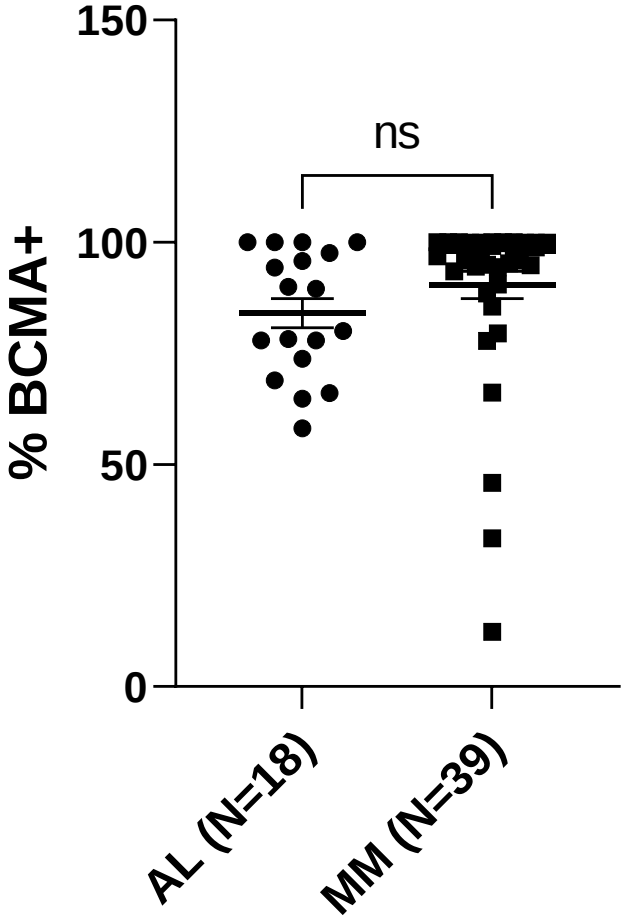
Haematologica Early view Oct 6, 2022 https://doi.org/10.3324/haematol.2022.281628

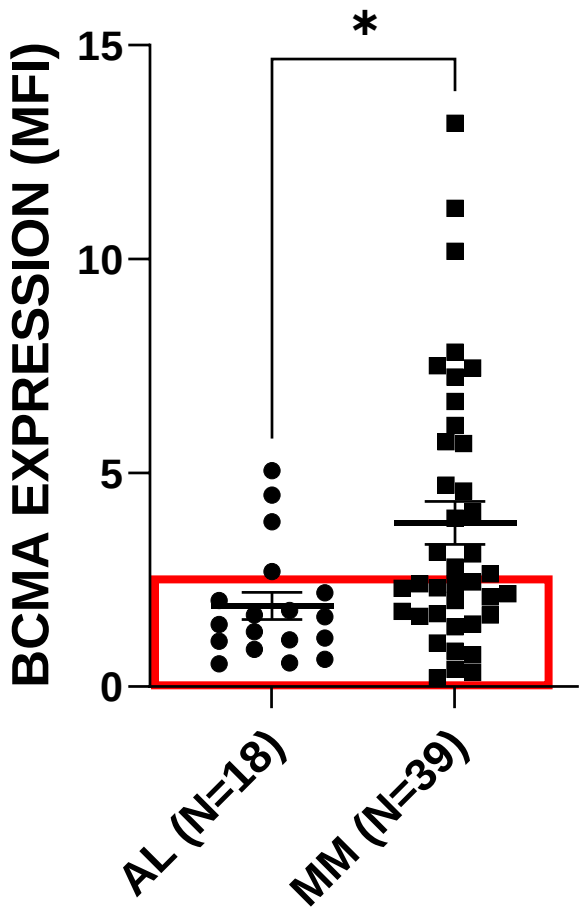




800x10⁶ dose:
ORR- 87%
sCR/CR- 57%
MRD negativity- 73%

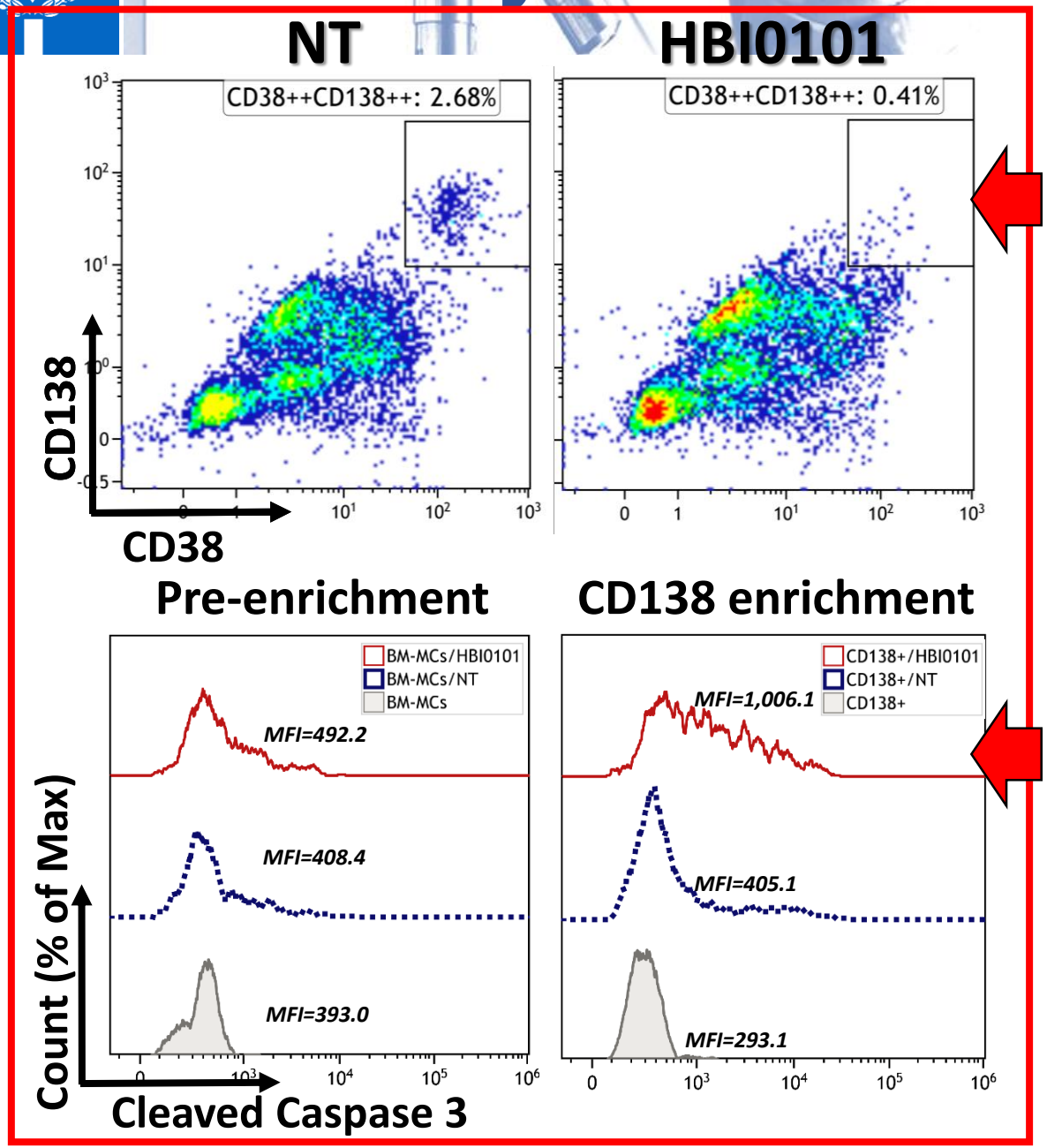
BCMA targeting in the context of AL amyloidosis





Kfir-Erenfeld, S. et al. *Clin. Cancer Res.* 2022.

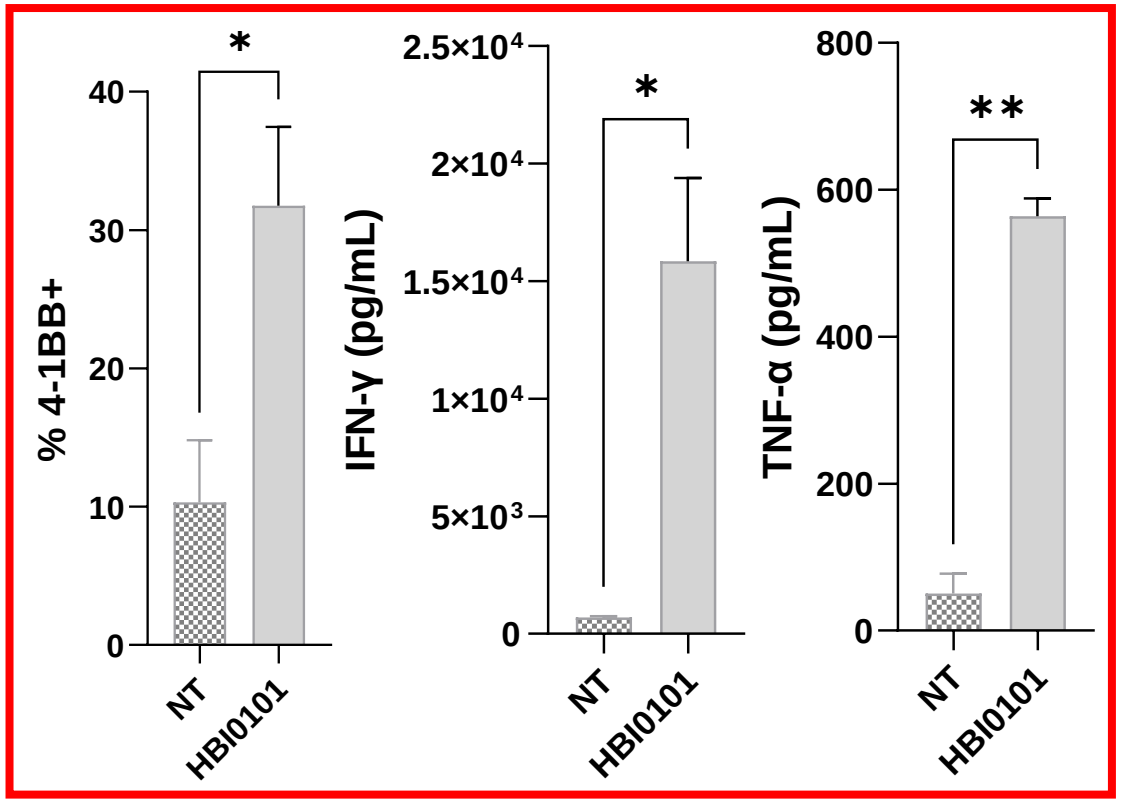
Anti-amyloidosis function of HBI0101



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

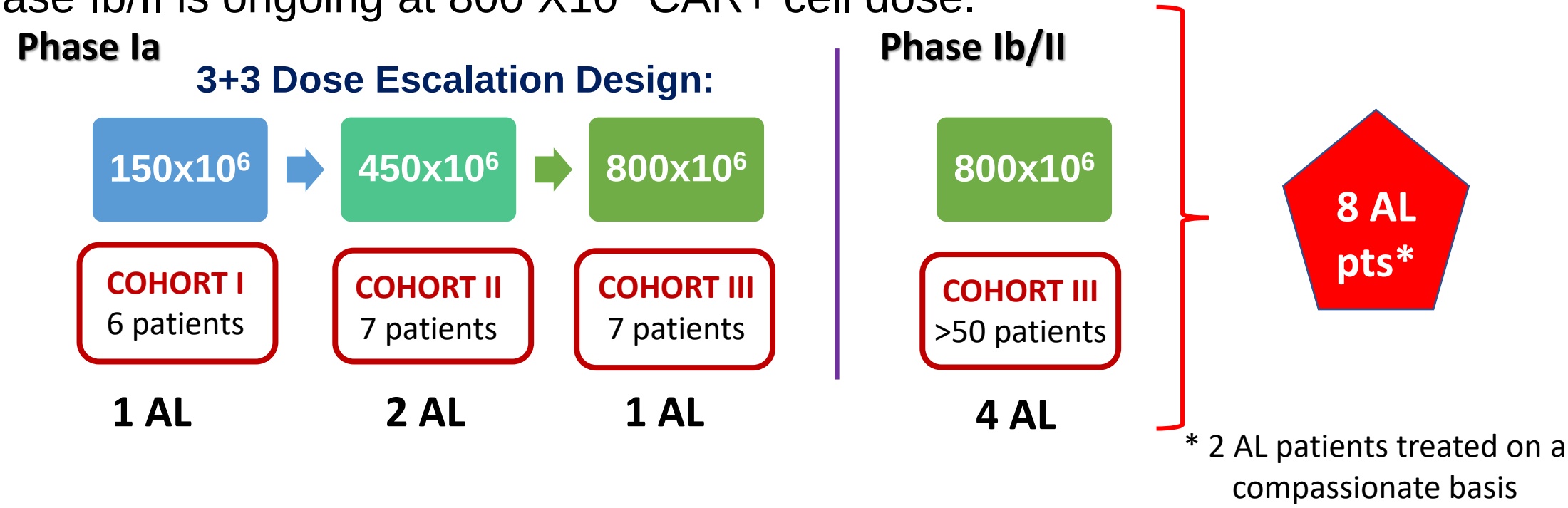
Shlomit Kfir-Erenfeld[1], Nathalie Asherie[1], Sigal Grisariu[1], Batia Avni[1], Eran Zimran[1,2], Miri Assayag[1], Tatyana Dubnikov Sharon[1], Marjorie Pick[2], Eyal Lebel[2], Adir Shaulov[2], Yael C. Cohen[3], Irit Avivi[3], Cyrille J. Cohen[4], Polina Stepensky[1], and Moshe E. Gatt[2]



Kfir-Erenfeld, S. et al. *Clin. Cancer Res.* 2022.

Clinical Study of HBI0101 in myeloma AND AL amyloidosis patients

- A Phase Ia/Ib Dose Escalation and Safety Study of HBI0101 BCMA.CART in Relapsed Refractory Multiple Myeloma and AL amyloidosis Patients (NCT04720313).
- The Phase Ia was designed as a dose-escalation 3+3 protocol (20 patients).
- The Phase Ib/II is ongoing at 800 $X10^6$ CAR+ cell dose.



Patients' baseline characteristics

	Pt 1*	Pt 2	Pt 3	Pt 4**	Pt 5*	Pt 6	Pt 7**	Pt 8*
Involved FLC (mg/L)	155	183	87	560	71	113	198	410
dFLC (mg/L)	143	177	50	550	51	103	196	408
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
NYHA stage	3	4	1	3	2	4	4	2
ProBNP (pg/ml)	**7500**	2008	119	2773	731	**28000**	**6600**	220
MAYO stage	3a	3a	1	3a	2	3B	2	1
ECOG PS	0	2	0	0	1	2	4	0
MAYO stage	3a	3a	1	3a	2	3B	2	1
ECOG PS	0	2	0	0	1	2	4	0

*Concomitant MM
** Compassionate

Patients' baseline characteristics

	Pt 1*	Pt 2	Pt 3	Pt 4**	Pt 5 *	Pt 6	Pt 7**	Pt 8*
Prior lines of therapy	8	6	6	10 and MDS	3	4	4	7
Best response/ which line	VGPR/ 3rd	VGPR/ 2nd	CR/ 1st	CR/ 1st + 4th	VGPR/ 2nd	VGPR/ 2nd	VGPR/ 3rd	VGPR/ 1st + 2nd
Previous ASCT	Yes	Yes	No	Yes (as salvage)	No	No	No	Yes
Triple-drug refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Penta-drug refractory	Yes	Yes	No	Yes	No	Yes	Yes	Yes
Belantamab refractory	No	Yes	No	Yes	No	Yes	Yes	Yes
Last line refractory	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Years since diagnosis	10.5	4	15	4.5	2	3.5	0.8	11

Safety Results

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8
CAR+ cells infused ($x10^6$)	150	450	800	450	800	800	800	800
Adverse events of interest								
CRS	No	Yes	Yes	Yes	Yes	No	Yes	Yes
CRS grade		2	3	3	1		1	2
Time to onset (days)		2	3	1	2		2	2
CRS duration (days)		2	4	1	1		1	1
Tocilizumab doses	0	1	3	1	1	0	0	1
Steroids use	No	No	Yes	No	No	No	No	No
Vasopressor use	No	No	Yes	No	No	No	No	No
High flow oxygen use	No	No	Yes	Yes	No	No	No	No
ICANs	No	No	No	No	No	No	No	No

Safety Results

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8
CAR+ cells infused ($x10^6$)	150	450	800	450	800	800	800	800
Hematologic AEs (grades)								
Neutropenia	1	3	3	4	3	0	2	4
Anemia	0	1	2	3	1	0	0	0
Thrombocytopenia	0	2	1	4*	1	0	0	0
Duration of Hematologic AE (days)**	4	3	5	Ongoing >31	2	0	2	6
AL Organ deterioration	No	Yes	No	Yes	No	No	No	No
CHF exacerbation	No	Yes	No	Yes	No	Yes (prior to CART)	No	No
Acute renal failure	No	No	No	No	No	Yes (prior to CART)	No	No
Hepatic dysfunction	No	Yes. Grade 3	No	No	No	No	No	No

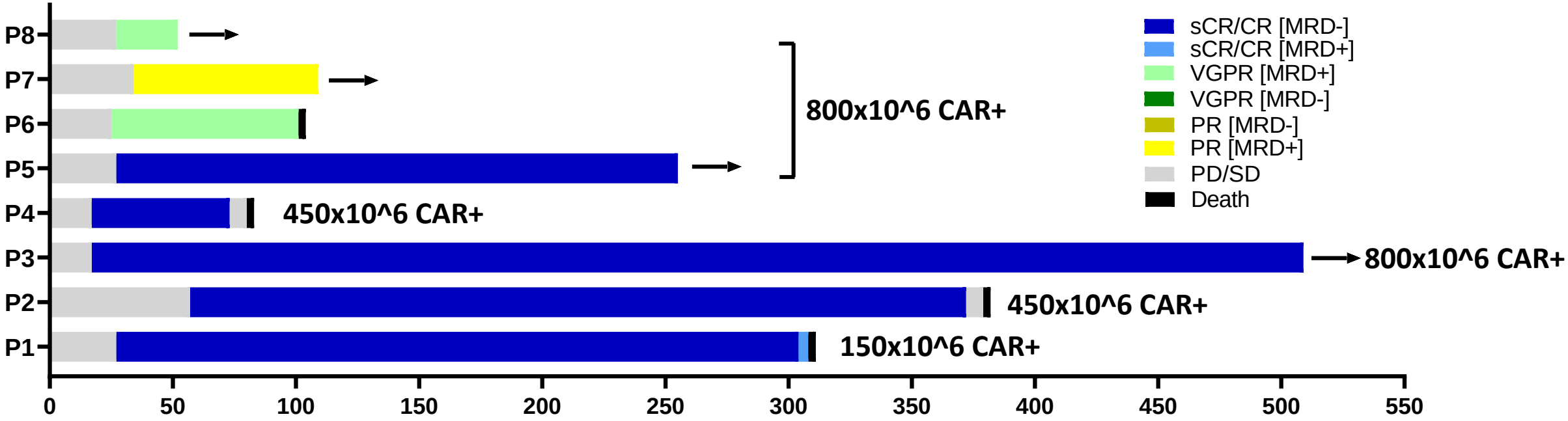
HBI0101 induces fast, deep and durable responses

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8
CAR+ cells infused ($x10^6$)	150	450	800	450	800	800	800	800
Best hematologic response	**CR**	**CR**	**CR**	**CR**	**CR**	**VGPR**	**PR**	**VGPR**
iFLC at best response (mg/L)	0.6	0.9	1	7	0.4	0	56	36
dFLC at best response (mg/L)	0	0	0	1.4	0.2	20	50	30
MRD (10^{-5}) negativity at Day 30 Day 180	Yes Yes	Yes Yes	Yes Yes	Yes	Yes	No	N/A	No
Time to best confirmed response (days)	27	57	17	17	30	25	34	45
Follow up (months)	10.5	14	17	7	9	3	5	3
DOR (months)	9.5	12	16.5	3	8	3	4	2.5

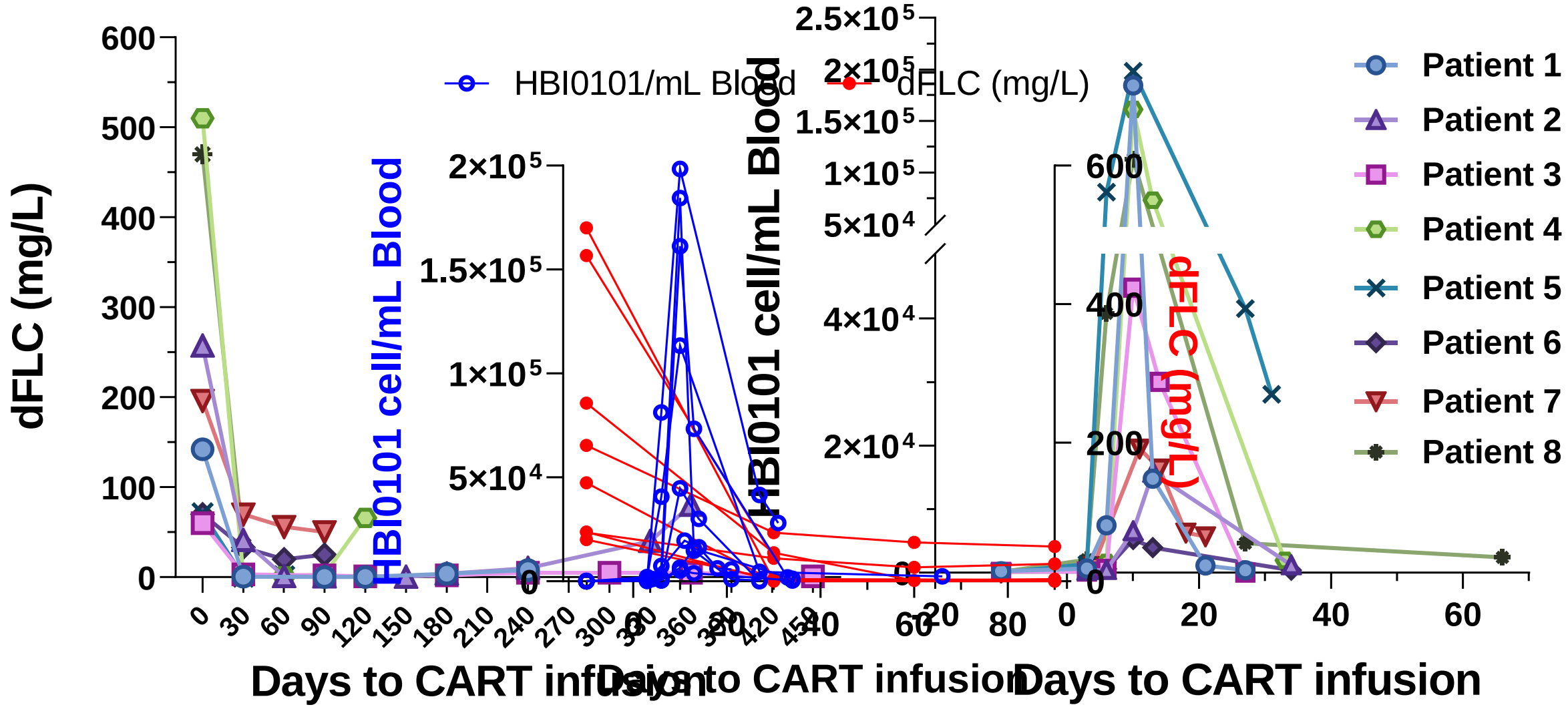
HBI0101 induces organ responses

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8
CAR+ cells infused ($x10^6$)	150	450	800	450	800	800	800	800
Best hematologic response	**CR**	**CR**	**CR**	**CR**	**CR**	**VGPR**	**PR**	**VGPR**
Organ response	**Yes**	**Yes**	**Yes complete**	**Yes**	**No**	**No**	**Yes**	**Yes**
Delta proBNP response (% reduction) (pg/ml)	-4800 (-64%)	-1295 (-64%)	NA	-1872 (-68%)	0	-4700 (-20%)	-3800 (- 57%)	NA
Albuminuria (g/d)	NA	NA	**-3 (-100%)**	NA	NA	0	NA	
NYHA change	III to II	IV to II	NA	III to II	II	IV to III	IV to III	NA
Additional organ responses Alk Phos (u/l)	NA	Hepatic: 280 to 150	NA	NA	NA	No	NA	NA
Survival (mth)/ Cause of death	**10.5 Covid**	**14 Disease**	17	**7 Disease**	9	**3.5 Disease**	5	3

Patients' responses over time



Efficacy Results: Pharmacokinetics

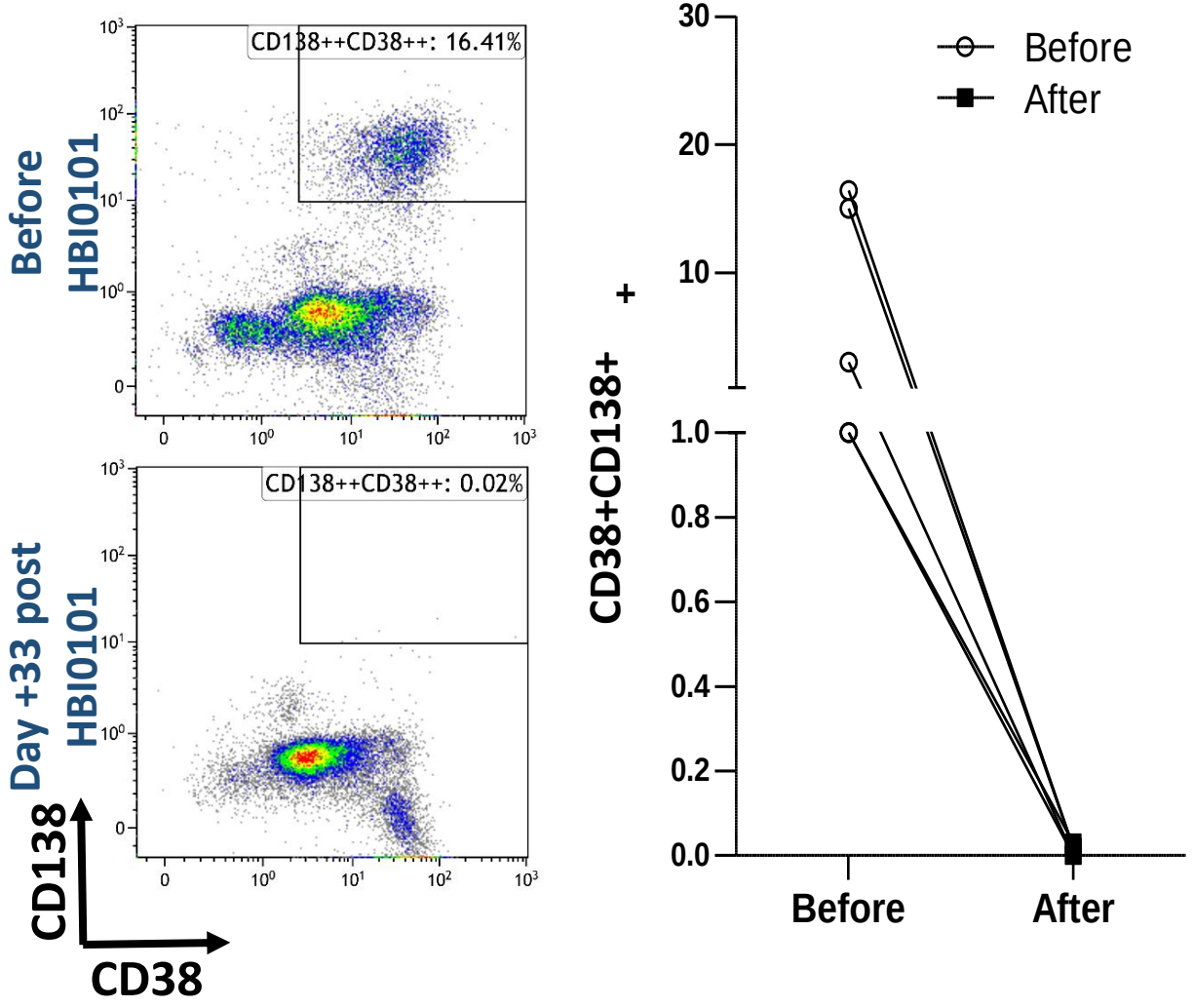


*dFLC (=involved FLC-uninvolved FLC)

Efficacy Results

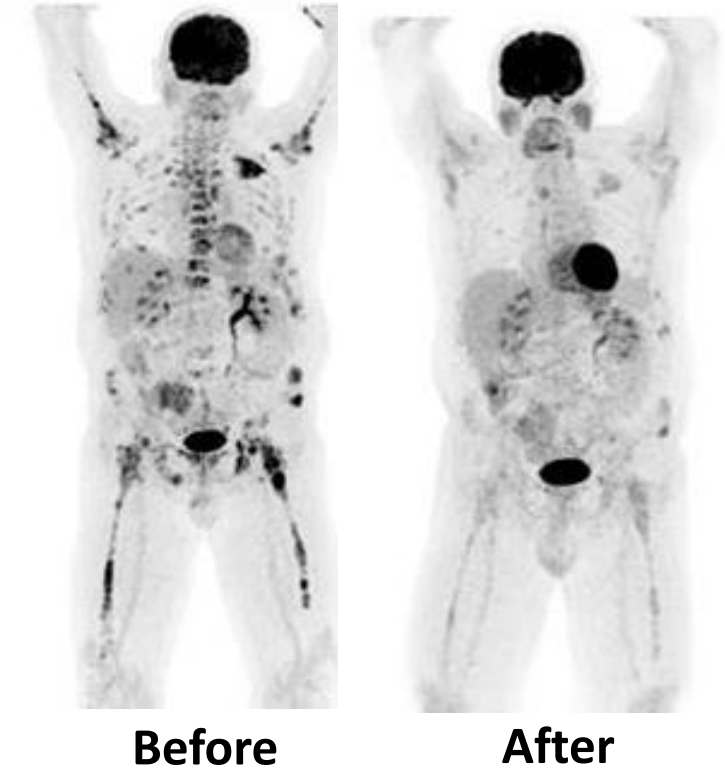
Bone Marrow plasma cells elimination

Patient 4



FDG-PET avidity

Patient 1

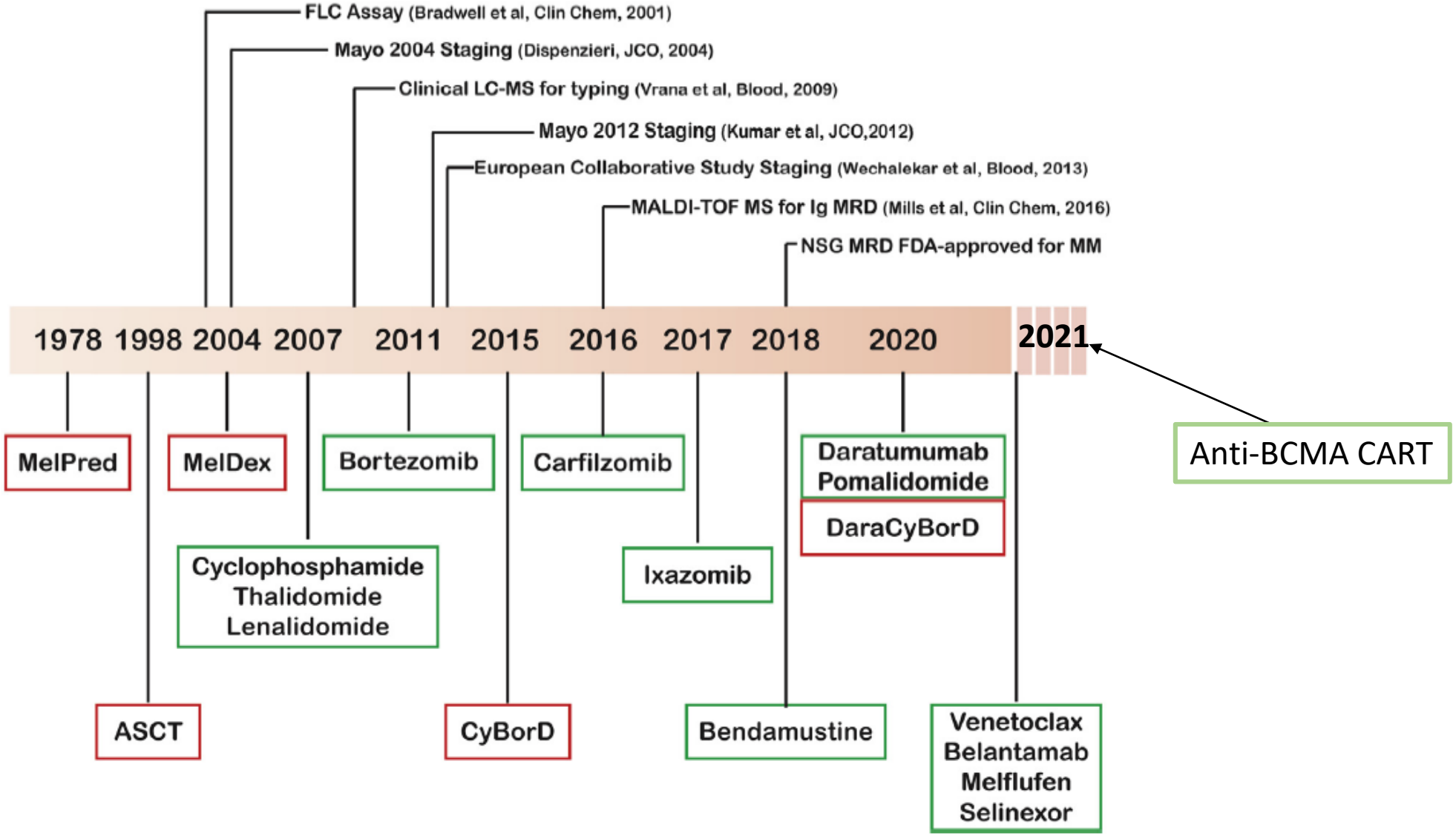


Kfir-Erenfeld, S. et al. *Clin. Cancer Res.* 2022.

Anti-BCMA CART is a clinically tested novel modality of treatment for relapsed and refractory AL patients

- BCMA expression on AL amyloidosis plasma cell is sufficient for *in-vitro* and clinical targeting by CART.
- Largest cohort of AL amyloidosis patients (8 pts) treated with BCMA CART therapy described so far in the literature.
- The 8 patients described were able to endure CART therapy with relative **safety**.
- Rapid organ response is achieved owing to the fast reduction of free light chain toxicity.
- HBI0101 therapy provides a first proof-*of*-concept that BCMA CART therapy is safe enough and highly efficacious for the treatment of advanced, RR AL amyloidosis patients.

Evolution of Treatment in AL Amyloidosis



Adapted from Bianchi, G. et al. *JACC: CardioOncology*. 2021.

Expanding access to HBI0101 therapy

IMMIX BIOPHARMA

NEXCELLA

Acknowledgements

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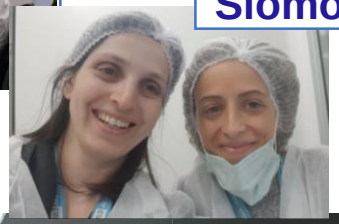
Rivka Alexander Shani, MSc

Alaa Sheaddeh, MSc

Aseel Ashtai

Shlomit Her, MSc

Avigail Avraham



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Prof. Yael Cohen

Prof. Irit Avivi

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