SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

February 25, 2019
Date of Report

MARKER THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-37939**	**45-4497941**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)
3200 Southwest Freeway Suite 2240 Houston, Texas		**77027**
(Address of principal executive offices)		(Zip Code)

(713) 400-6400
Registrant's telephone number, including area code

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On February 25, 2019, Marker Therapeutics, Inc. ("Marker" or the "Company") issued a press release announcing a clinical update from four clinical trials using the Company's multi-antigen targeted T cell (MultiTAA) therapies. The data was reviewed in oral and poster presentations at the Transplantation & Cellular Therapy ("TCT") Meetings of the American Society for Blood and Marrow Transplantation and the *Center for International Blood and Marrow Transplant Research* ("ASBMT" and "CIBMTR") The meetings took place in Houston, Texas from February 20-24, 2019.

A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

As previously announced by the Company on January 15, 2019, the Center for Cell and Gene Therapy at Baylor College of Medicine presented data from four abstracts at ASBMT and CIBMTR meetings between February 20-February 23, 2019. The presentations include: (i) an oral presentation regarding Targeting Lymphomas Using Non-Engineered, Multi-Antigen-Specific T Cells; (ii) an oral presentation regarding Administering Leukemia-Directed Donor Lymphocytes to Patients with AML or MDS to Prevent or Treat Post-Allogeneic HSCT Relapse; (iii) an oral presentation regarding Adoptive T-Cell Therapy for Acute Lymphoblastic Leukemia Targeting Multiple Tumor-Associated Antigens; and (iv) a poster presentation regarding Safety and Efficacy of Multiantigen-Targeted T Cells for Multiple Myeloma. The studies describe results achieved using multi-tumor antigen specific T cells that were developed at the Baylor College of Medicine in the laboratories of Dr. Ann Leen and Dr. Juan Vera, and exclusively licensed to Marker Therapeutics, Inc. Copies of the presentation and posters are attached hereto as Exhibits 99.2, 99.3, 99.4, and 99.5, respectively. The presentations are available on Marker Therapeutics website at www.markertherapeutics.com under the caption "Recognition."

The information furnished pursuant to Item 8.01 on this Form 8-K, including Exhibit 99.2, 99.3 and 99.4 and 99.5 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any other filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued on February 25, 2019.
99.2	2019 TCT Meeting Presentation- Targeting Lymphomas Using Non-Engineered, Multi-Antigen-Specific T Cells.*
99.3	2019 TCT Meeting Presentation- Administering Leukemia-Directed Donor Lymphocytes to Patients with AML or MDS to Prevent or Treat Post-Allogeneic HSCT Relapse. *
99.4	2019 TCT Meeting Presentation- Adoptive T-Cell Therapy for Acute Lymphoblastic Leukemia Targeting Multiple Tumor-Associated Antigens.*
99.5	2019 TCT Meeting Poster Presentation- Safety and Efficacy of Multiantigen-Targeted T Cells for Multiple Myeloma.*

*Furnished herewith.

SIGNATURES

In accordance with the requirements of the Exchange Act, the registrant caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on this 25th day of February, 2019.

MARKER THERAPEUTICS, INC.
(Registrant)

BY: /s/ Michael Loiacono
Michael Loiacono
Chief Accounting Officer

Exhibit 99.1

Marker Therapeutics Announces Clinical Update at the Transplantation & Cellular Therapy Meetings of ASBMT and CIBMTR 2019

Houston, TX – February 25, 2019 – Marker Therapeutics, Inc. (NASDAQ:MRKR), a clinical-stage immuno-oncology company specializing in the development of next-generation T cell-based immunotherapies for the treatment of hematological malignancies and solid tumor indications, today announced updated data from four clinical trials using the Company's multi-antigen targeted T cell (MultiTAA) therapies. The data was reviewed in oral and poster presentations at the Transplantation & Cellular Therapy Meetings of ASBMT and CIBMTR 2019 which took place in Houston, TX from February 20-24. Among the highlights, were results from an ongoing study including patients with acute myeloid leukemia (AML), which were reviewed in an oral presentation by Dr. Premal Lulla, M.B.B.S., Assistant Professor of Medicine, Baylor College of Medicine.

"We continue to be highly encouraged by the clinical results we've seen to date with our MultiTAA therapies. In AML, we believe we are seeing increasing evidence of meaningful therapeutic benefit for patients with limited treatment alternatives. Our MultiTAA therapy appears to be safe and well-tolerated with the potential to mediate a meaningful anti-tumor effect, in addition to demonstrating a compelling correlation between therapeutic responses, with superior *in vivo* expansion of our T cells," said Peter L. Hoang, President & CEO of Marker Therapeutics. "Similarly, the studies ongoing in acute lymphoblastic leukemia, or ALL, lymphoma and multiple myeloma continue to demonstrate positive results, and are supportive of the data we presented at ASH in December, importantly with no additional disease relapses. Overall, this data update and our update at ASH 2018 in December collectively have increased our total reported number of patients to 78 as compared to the 57 patients we had reported as of November."

AML Study Results

In Arm A of the AML study, 13 patients at Baylor College of Medicine were dosed with MultiTAA T cells as a maintenance therapy after receiving allogeneic stem cell transplant. Results demonstrated:

- 11 out of 13 patients remain alive, ranging from 6 weeks to 2.5 years post-infusion. Nine of these patients have never relapsed after MultiTAA therapy and continue to remain in complete remission (CR), durable between 6 weeks to 2.5 years;
- Two patients saw local relapse in the central nervous system, but in both cases these patients were successfully treated with local therapy alone;

- One patient saw extramedullary relapse and was subsequently treated in the active disease arm (Arm B) of the trial, generating a CR that was durable for 13 months; and
- One patient relapsed 8 months after receiving MultiTAA T cells but following a second allogeneic stem cell transplant this patient remains alive in relapse 1.5 years following his initial T cell infusion.

In Arm B of the AML study, 6 patients suffering from active disease with relapsed/refractory (r/r) AML have been treated, with 1 patient having been treated twice for active disease with MultiTAA T cells;

- 2 patients were non-responsive to MultiTAA therapy and progressed with r/r disease;
- 1 patient developed a complete response (CR), which was durable for 13 months; and
- 1 patient developed a partial response (PR) that enabled that patient to receive a second allogeneic stem cell transplant;
  - The patient who developed a partial response saw significant tumor debulking, with circulating blasts reduced from over 50% to 15%.
- 2 additional patients who did not meet partial response criteria experienced disease stabilization enabling a 2-month delay to next-line therapy
  - Of these patients with disease stability, one patient was sufficiently stabilized to enable that patient to receive a second allogeneic stem cell transplant. The second transplant eliminated the patient's MultiTAA T cells. This patient was given a second dose of MultiTAA T cells after initial disease relapse after the second transplant, but progressed to another line of therapy prior to any evaluable response assessment to the subsequent dose of MultiTAA T cells;
  - The other patient who had disease stability saw significant reduction in tumor burden, with a reduction in circulating blasts from 70% prior to infusion of MultiTAA T cells, to approximately 45% circulating blasts after MultiTAA therapy.
- For patients in Arm B, overall survival ranged from 4 to 21 months after T cell infusions.

ALL Results

In addition to data from ongoing lymphoma and multiple myeloma trials, also presented in an oral presentation at the meeting were updated results from an ongoing study in ALL. Updates from this trial included:

- Patients are now up to 28 months in CCR (Continued Complete Remission);
- The only patient who has experienced relapse was a patient who displayed mixed donor/recipient chimerism after transplant, but remained in CCR for 6 months prior to relapse;

- Patients that remain in CCR have been durable for between 4 to 28 months, with a median duration of 16 months.

“We are very excited about the results we are seeing in our early clinical trials. For patients with r/r AML, we believe that MultiTAA therapies may produce meaningful improvements in overall survival of patients who historically have had a dire prognostic outlook,” stated Mythili Koneru, Senior Vice President of Clinical Development at Marker Therapeutics. “In adjuvant settings for patients currently in remission, I believe our early clinical results suggest that we may be providing significant additional protection against relapse and disease recurrence.”

About Marker Therapeutics, Inc.
Marker Therapeutics, Inc. is a clinical-stage immuno-oncology company specializing in the development of next-generation T cell-based immunotherapies for the treatment of hematological malignancies and solid tumor indications. Marker’s cell therapy technology is based on the selective expansion of non-engineered, tumor-specific T cells that recognize tumor associated antigens (i.e. tumor targets) and kill tumor cells expressing those targets. Once infused into patients, this population of T cells attacks multiple tumor targets and acts to activate the patient’s immune system to produce broad spectrum anti-tumor activity. Because Marker does not genetically engineer its T cells, when compared to current engineered CAR-T and TCR-based approaches, its products (i) are significantly less expensive and easier to manufacture, (ii) appear to be markedly less toxic, and (iii) are associated with meaningful clinical benefit. As a result, Marker believes its portfolio of T cell therapies has a compelling therapeutic product profile, as compared to current gene-modified CAR-T and TCR-based therapies.

Marker is also advancing a number of innovative peptide- and gene-based immuno-therapeutics for the treatment of metastatic solid tumors, including the Folate Receptor Alpha program (TPIV200) for breast and ovarian cancers and the HER2/neu program (TPIV100/110) for breast cancer, currently in Phase II clinical trials. In parallel, we are developing a proprietary DNA expression technology named PolyStart™ that can enhance the ability of the immune system to recognize and destroy diseased cells.

For additional information, please call toll free at (904) 862-6490 or visit: markertherapeutics.com

To receive future press releases via email, please visit: https://markertherapeutics.com/email-alerts/

Follow us on Twitter @MRKRTherapeutic, or follow us on Facebook.

Forward-Looking Statement Disclaimer

This release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this news release concerning the Company's expectations, plans, business outlook or future performance, and any other statements concerning assumptions made or expectations as to any future events, conditions, performance or other matters, are "forward-looking statements". Forward-looking statements include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: our research and development activities relating to our non-engineered multi-tumor antigen specific T cell therapies; our TPIV200 and TPIV100/110 programs and our PolyStart™ program; the effectiveness of these programs or the possible range of application and potential curative effects and safety in the treatment of diseases; and, the timing and success of our clinical trials, as well as multi-tumor antigen specific T cell clinical trials conducted by our collaborators. Forward-looking statements are by their nature subject to risks, uncertainties and other factors which could cause actual results to differ materially from those stated in such statements. Such risks, uncertainties and factors include, but are not limited to the risks set forth in the Company's most recent Form 10-K, 10-Q and other SEC filings which are available through EDGAR at www.sec.gov. The Company assumes no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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Targeting Lymphomas Using Non-Engineered, Multi-Antigen Specific T Cells

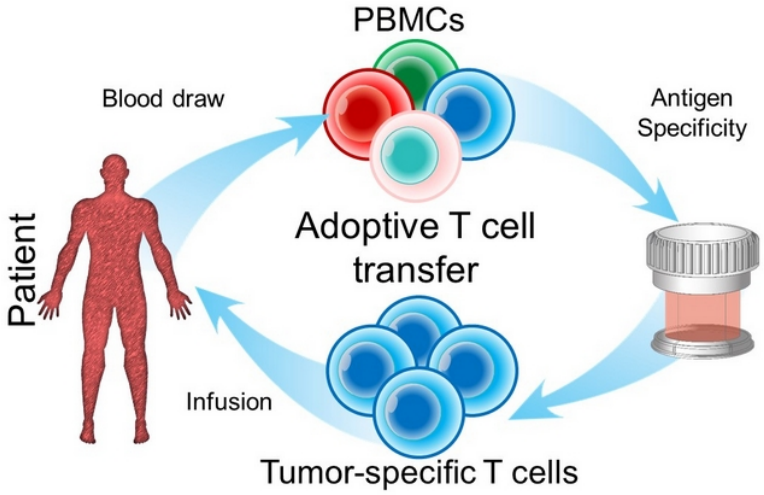
George Carrum, Premal Lulla, Ifigeneia Tzannou, Ayumi Watanabe, Manik Kuvalekar, Munu Bilgi, Tao Wang, Rammurti Kamble, Carlos A. Ramos, Rayne Rouce, Bambi J. Grilley, Adrian P. Gee, Malcolm K. Brenner, Helen E. Heslop, Cliona M. Rooney, Juan F. Vera and **Ann M. Leen**

Baylor College of Medicine

Texas Children's Hospital

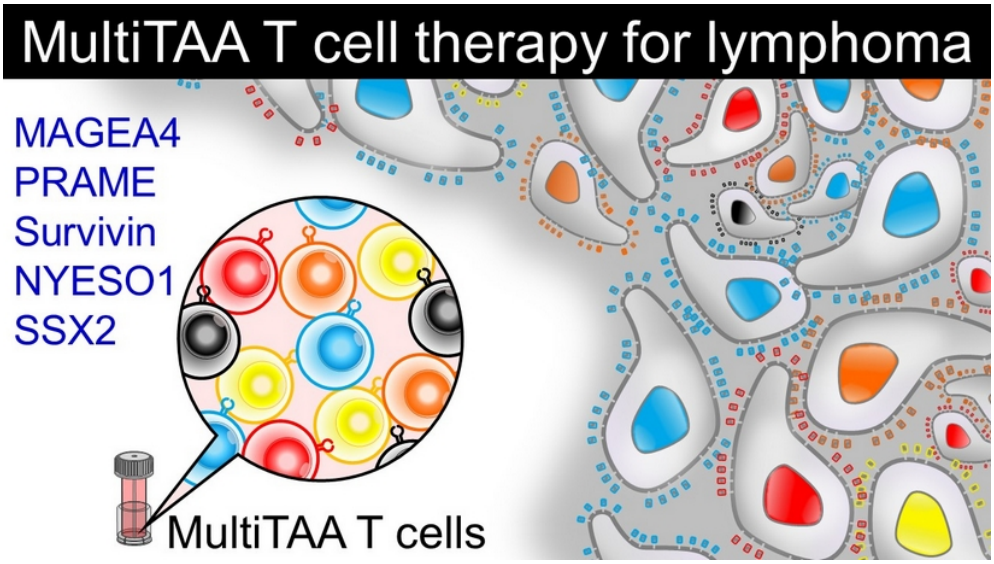
Houston Methodist

CENTER FOR CELL & GENE THERAPY

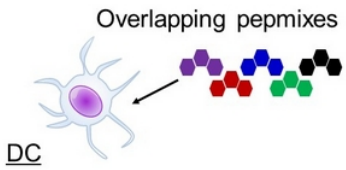

PBMCs
Blood draw
Antigen
Specificity
Patient
Adoptive T cell
transfer
Infusion
Tumor-specific T cells

Our approach

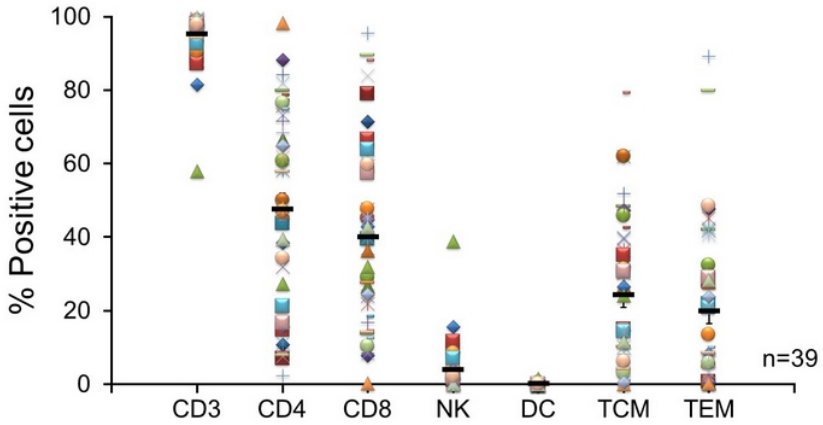
- Simultaneously target multiple TAAs


MultiTAA T cell therapy for lymphoma
MAGEA4
PRAME
Survivin
NYESO1
SSX2
MultiTAA T cells

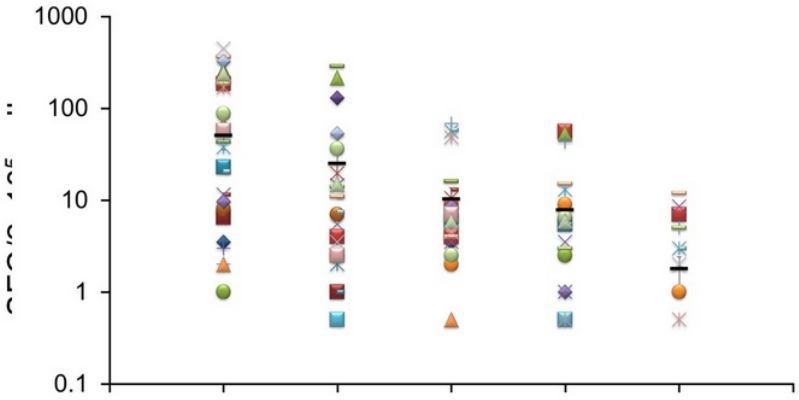
MultiTAA-T Cell manufacture



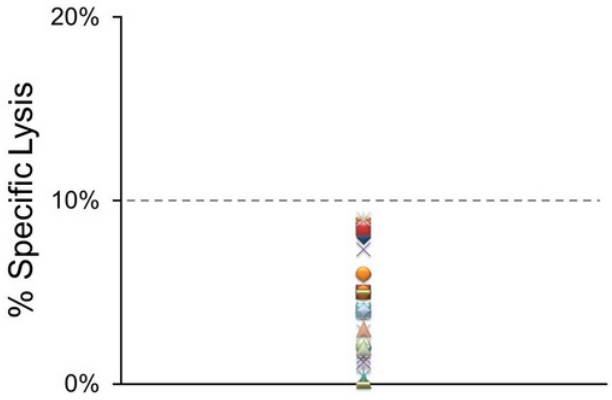
MultiTAA-T Cell Phenotype



MultiTAA-T Cell Specificity



Multi TAA-T Cell Autoreactivity



Clinical Trial: Eligibility

Any patient ≥18 yrs with HL or NHL

Active disease

- in 2nd or subsequent relapse
- in 1st relapse for indolent lymphoma after 1st line therapy for relapse
- in 1st relapse if immunosuppressive chemotherapy contraindicated
- primary refractory disease or persistent disease after 1st line therapy
- multiply relapsed patients in remission at a high risk of relapse
- lymphoma as a second malignancy e.g. Richters

After autologous or syngeneic SCT (adjuvant therapy)

Infusion of multiTAA-T cells specific for
PRAME, SSX2, MAGEA4, NYESO1, Survivin

Safety of MultiTAA T cells - Antigen escalation

Antigen Escalation Phase = fixed dose $5x10^6/m^2$ – 2 pts/stage:
Day 0: PRAME-specific T cells
Day 28: PRAME and SSX-specific T cells

Stage Two:
Day 0: PRAME and SSX-specific T cells
Day 28: PRAME/SSX/MAGE-specific T cells

Stage Three:
Day 0: PRAME/SSX/MAGE-specific T cells
Day 28: PRAME/SSX/MAGE/NYESO1-specific T cells

Stage Four:
Day 0: PRAME/SSX/MAGE/NYESO1-specific T cells
Day 28: PRAME/SSX/MAGE/NYESO1/Survivin-specific T cells

Safety of MultiTAA T cells - Dose escalation

PRAME/SSX/MAGE/NYESO1/Survivin-specific T cells:
2-4 pts at each level, 2 infusions 14 days apart

Dose Level 1:
Day 0 and 14: $5x10^6$ cells/m^2

Dose Level 2:
Day 0 and 14: $1x10^7$ cells/m^2

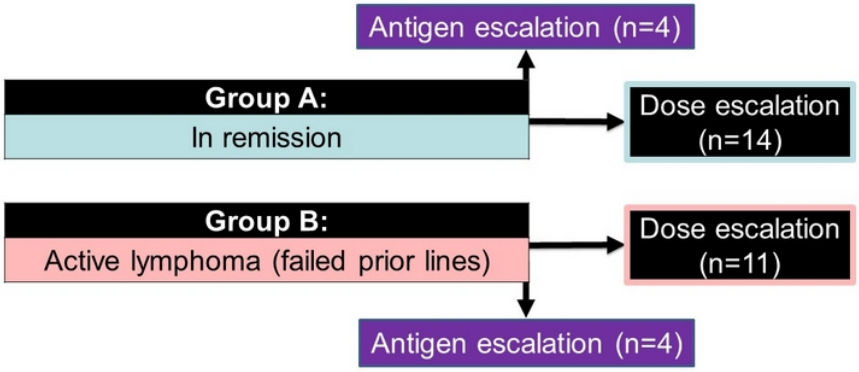
Dose Level 3:
Day 0 and 14: $2x10^7$ cells/m^2

Clinical Trial: Treatment

- 33 patients infused

Clinical Trial: Treatment

- 33 patients infused



Clinical Trial: Treatment

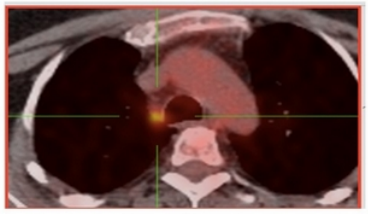
-33 patients infused (0.5-2x10^7 cells/m^2)
- 12 HL
- 19 aggressive NHL (DLBCL/mantle/peripheral T)
- 2 with composite lymphoma

- No lymphodepletion

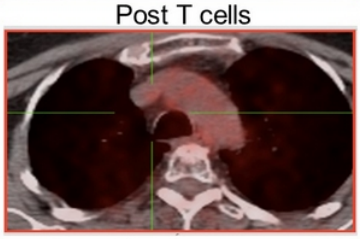
- No adverse events

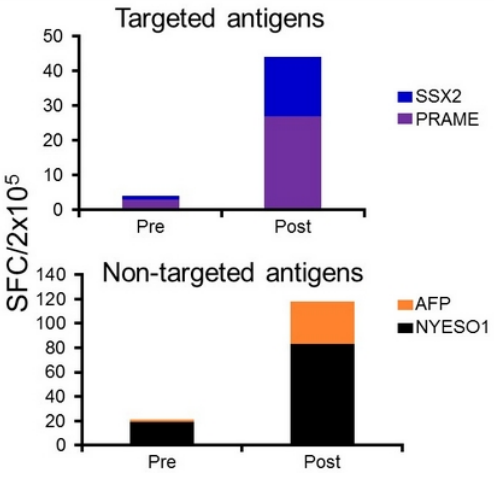
Pt1 (HL) – Clinical and Immune effects

Pre T cells

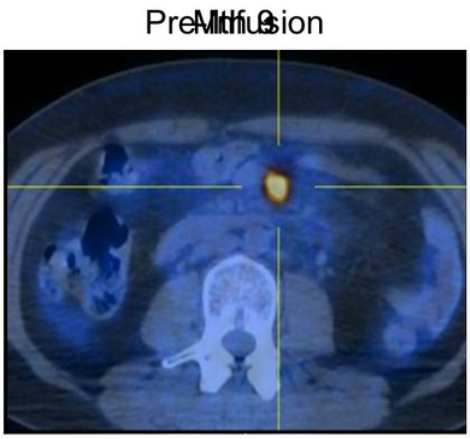


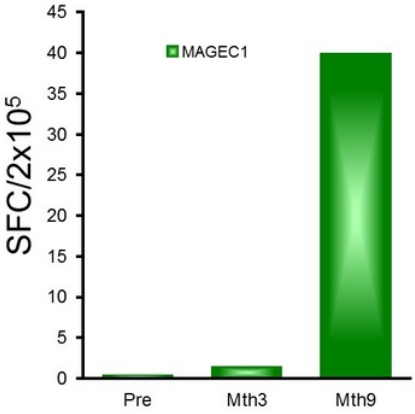
Post T cells





Pt2 (NHL) - Clinical and Immune effects





Clinical Outcomes – Adjuvant

- 18 patients infused as adjuvant
  - 15/18 in remission (median 19 months)

Clinical Outcomes – Adjuvant

ID	Age/Sex	Disease	Prior Therapies	Response to T cell therapy (duration)
1*	39/M	HL & DLBCL	ABVD → RICE → ASCT	CCR (>3 years)
2*	78/F	DLBCL	R→RCHOP	In remission (8 mo) →relapse
3*	78/F	DLBCL	R→RCHOP → multiTAA T cells → R-Bendamustine	CCR (>3 years)
4*	21/M	HL	ABVD → Brentuximab → Nav/Gem → ASCT	CCR (>4 years)
5	34/M	HL	ABVD → ICE → ASCT + XRT → Brentuximab	In remission (12 mo) → relapse
6	54/M	DLBCL	RCHOP → R-EPOCH → R-DHAP→ ASCT	In remission (19 mo) → relapse
7	61/M	DLBCL	R-EPOCH → ASCT → XRT	CCR (>2 years)
8	41/F	HL	ABVD + XRT → ICE → ASCT → XRT → Brentuximab → DHAP	CCR (>4 years)
9	62/M	T cell	CHOP + XRT → ASCT	CCR (>3 years)
10	53/M	Mantle	R-HyperCVAD → R-Bendamustine → R-Ibrutinib → ASCT + XRT	CCR (>2 years)
11	39 not 67/M	Mantle	R-Bendamustine-Ara-C → ASCT	CCR (>3 years)
12	65/F	DLBCL	R-EPOCH → ASCT	CCR (>2 years)
13	35/M	HL	ABVD → Brentuximab+Bendamustine → ASCT → XRT	CCR (> 2 years)
14	73/F	DLBCL	R-CHOP → XRT → ESHAP → RIE	CCR (>1 year)
15	50/F	DLBCL	HyperCVAD → ASCT	CCR (9 mo)
16	41/M	DLBCL	ABVD → R-ICE → ASCT	CCR (> 1 year)
17	32/F	T cell ALCL	CHOP → Brentuximab → Crizotinib → CD30 CAR T cells→Crizoinib	CCR (9 mo)
18	25/M	HL	ABVD → Brentuximab → ICE → ASCT	CCR (>1 year)

Clinical Outcomes – Active disease

- 15 patients treated for active disease
  - 6 CRs; 4 SD; 5 PD

Clinical Outcomes – Active disease

ID	Age/Sex	Disease	Prior Therapies	Response to multiTAA T cells (duration)
1*	31/F	HL	ABVD → ICE → Cis-Gem→ XRT →ASCT→ EBV T cells→Brentuximab→Yttrium90 → CART-CD30	Stable disease (5 mo) → Off study [Revilimid (5 mo) →PD1]
2*	55/F	HL/NHL	RCHOP + XRT → ICE → ASCT	CR (4 mo) Died of pneumonia
3*	38/M	HL	ABVD → XRT → IGEV → ESHAP → ASCT → GVD → XRT	CR (>2 years ongoing)
4*	44/F	HL	ABVD → ICE → ASCT → Brentuximab	CR (>5 years ongoing)
5	46/M	HL	ABVD → ICE → ASCT + XRT → Brentuximab	CR (>2 years ongoing)
6	46/F	DLBCL	RCHOP → GDC → ASCT	CR (>3 years ongoing)
7	31/F	HL	ABVD → XRT → ICE → Nav/Gem → ASCT → HDACi → Brentuximab → Bendamustine → PD1i	Stable disease (5 mo) →PD
8	69/M	NHL	EPOCH → Romidepsin → ASCT	Stable disease (>2 years)
9	54/M	DLBCL	RCHOP → R-ICE→ ASCT	Stable disease (6 mo) → PD → Started PD1i - >2 years; Alive
10	18/F	HL	ABVE-PC →XRT → IVBor →Brentuximab → PD1i	Stable disease (9 mo) → PD
11	48/M	DLBCL	EPOCH-R → R-ICE → ASCT → XRT	CR (>1 year)
12	49/M	HL	ABVD → ICE → ASCT → XRT→Brentuximab → Nivolumab → Bendamustine	PD (3 mo)
13	54/M	DLBCL	EPOCH-R → ICE-R → XRT → ASCT	SD (9 mo)
14	64/M	DLBCL	R-CHOP→Bendamustine/Rituxan→ RICE→ RIE→ ASCT	PD (9 mo)
15	68/M	DLBCL	RCHOP→GDP→ASCT	Stable disease (4 mo) → CD19-CAR-T

Summary to date

- Safe to date
- Feasible adjuvant and treatment
- In vivo expansion of T cells directed to targeted antigens
- Antigen/Epitope spreading
- Clinical benefit

Targeting Lymphomas Using Non-Engineered, Multi-Antigen Specific T Cells

George Carrum, Premal Lulla, Ifigeneia Tzannou, Ayumi Watanabe, Manik Kuvalekar, Munu Bilgi, Tao Wang, Rammurti Kamble, Carlos A. Ramos, Rayne Rouce, Bambi J. Grilley, Adrian P. Gee, Malcolm K. Brenner, Helen E. Heslop, Cliona M. Rooney, Juan F. Vera and **Ann M. Leen**

Baylor College of Medicine

Texas Children's Hospital

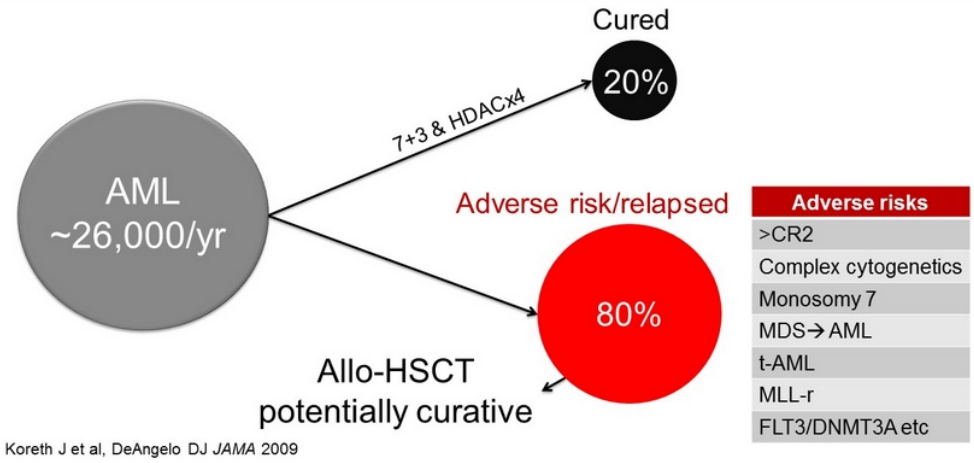
Houston Methodist

CENTER FOR CELL & GENE THERAPY

Administering AML-directed DLIs to patients with AML or MDS Post-Allogeneic HSCT Relapse

Premal Lulla, Swati Naik, Ifigeneia Tzannou, Shivani Mukhi, Manik Kuvalekar, Catherine Robertson, Carlos A Ramos, George Carrum, Rammurti Kamble, Jasleen Randhawa, Adrian P Gee, Bambi Grilley Malcolm K Brenner, Helen E Heslop, Juan F Vera and Ann M Leen

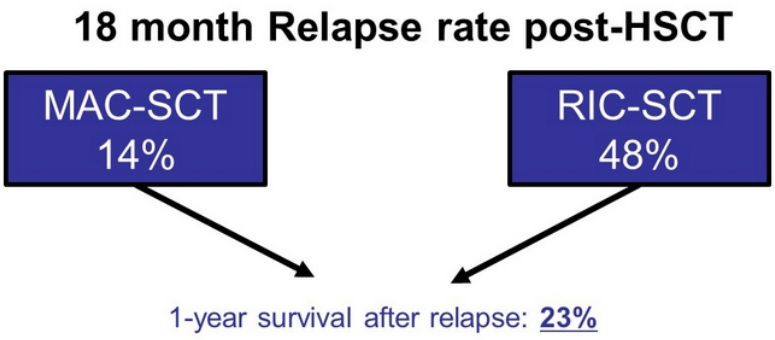
Acute Myeloid Leukemia



Adverse risks
>CR2
Complex cytogenetics
Monosomy 7
MDS→ AML
t-AML
MLL-r
FLT3/DNMT3A etc

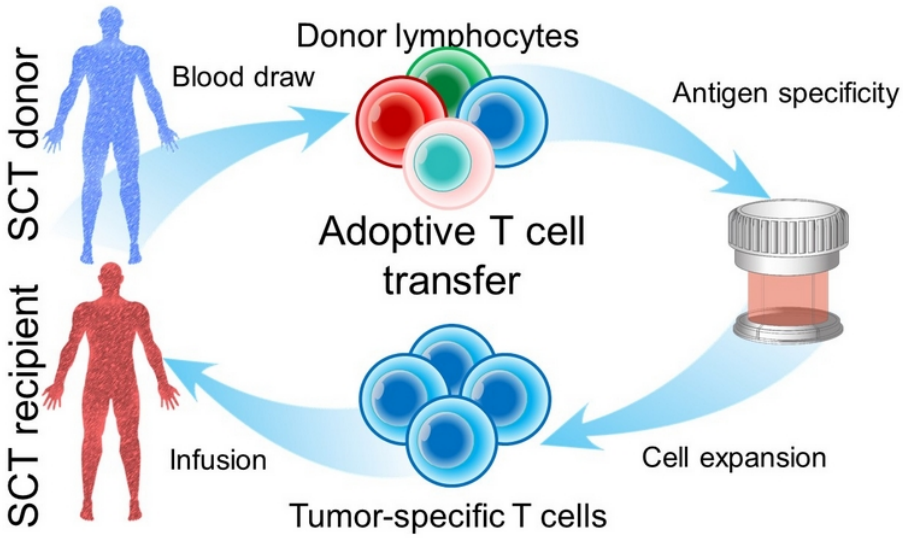
Koreth J et al, DeAngelo DJ *JAMA* 2009

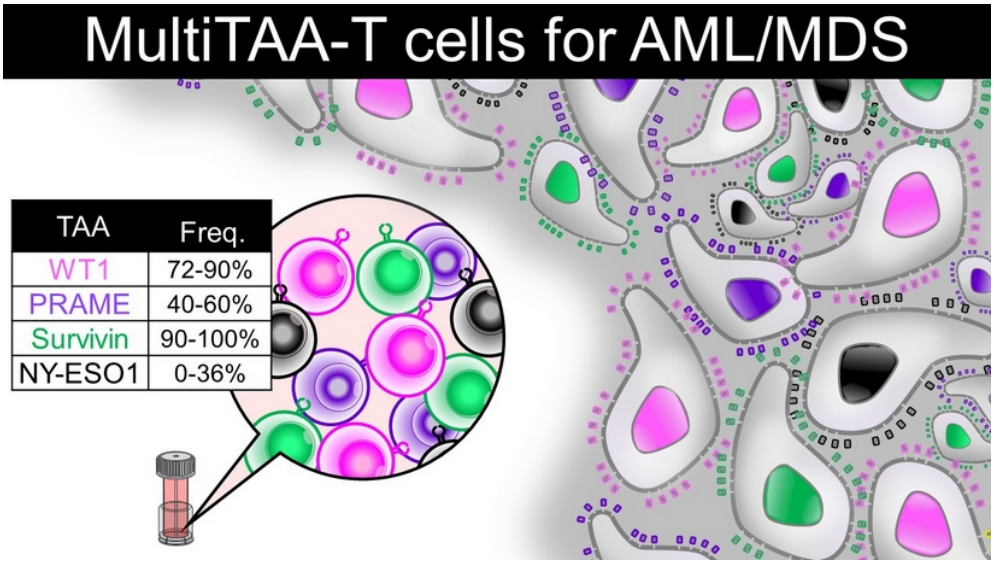
Outcomes of AML patients post-alloHSCT



BMT-CTN 0901. Scott et al *J Clin Oncol.* 2017

Bejanyan et al *BBMT* 2015

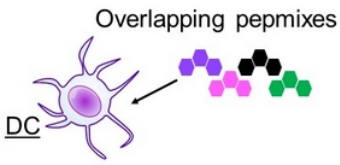

SCT donor
SCT recipient
Blood draw
Donor lymphocytes
Antigen specificity
Adoptive T cell transfer
Infusion
Cell expansion
Tumor-specific T cells


MultiTAA-T cells for AML/MDS
TAA
Freq.
WT1
72-90%
PRAME
40-60%
Survivin
90-100%
NY-ESO1
0-36%

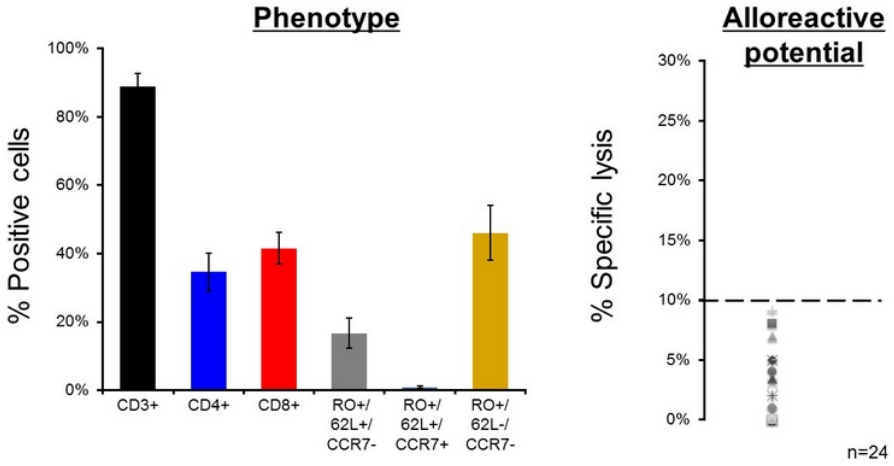
Our approach

- Simultaneously target multiple TAAs

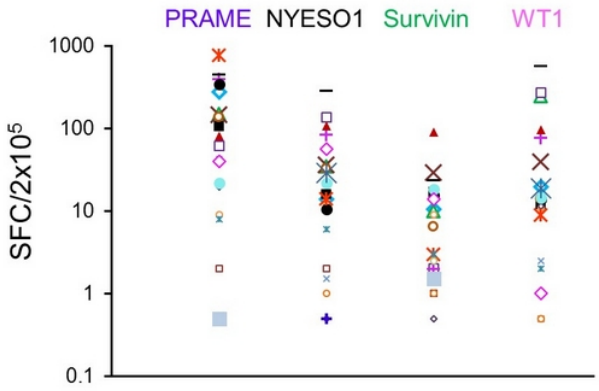
MultiTAA Manufacture



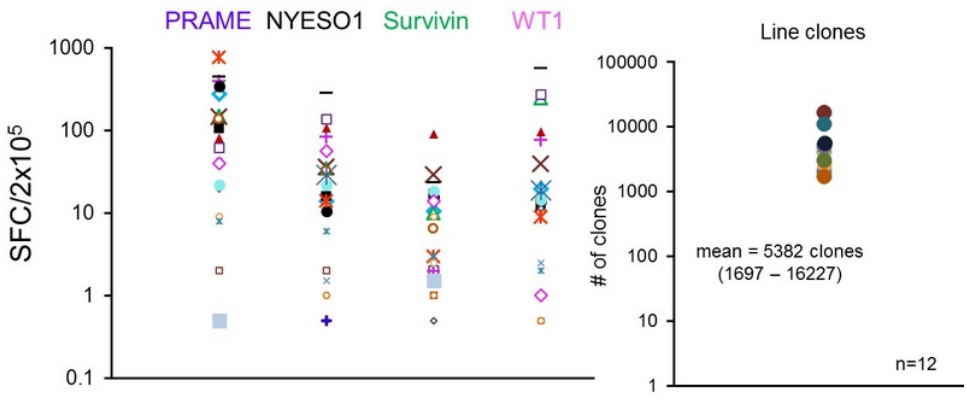
Profile of MultiTAA-T cells



MultiTAA T cell specificity



MultiTAA T cell specificity



Phase I trial - ADSPAM

Any patient with AML/MDS post allo-HSCT

Donor-derived multiTAA T cells

GROUP A - Adjuvant

AML/MDS patients
≥30 days post allo-HSCT

GROUP B – Active disease

AML/MDS patients
≥30 days post allo-HSCT

Dose Escalation

DL1	$5x10^6$ cells/m^2
DL2	$1x10^7$ cells/m^2
DL3	$2x10^7$ cells/m^2

Clinical trial: Current status

Patients Enrolled:

27 patients (24 AML and 3 MDS)

Patients Treated:

20 patients (0.5-2x10^7 cells/m^2)

Grade II or lesser	Grade III
3 (all grade I elevation in LFTs	***1 grade III LFT elevation (resolved with 0.5 mg/kg prednisone)***

Patients infused – ARM A

ID	Age/ G	Disease	Prior Treatments
1*	57/F	FLT3-ITD	CIA → Sorafenib → CIAx2 → RIC-SCT
2	18/F	FLT3-ITD	Bortezomib/Dauno EC → sorafenib → MAC-SCT
5	55/F	MLL-*r*	7+3 → HiDAC → MAC-SCT
6	70/F	AML CR3	7+3 → HiDAC → CIA → RIC-SCT-***Relapse*** → 7+3
7	53/F	DNMT3a	7+3 → HiDAC → MAC-SCT
10	65/M	MLL-*r*	7+3x2 → 5-Azax11 → RIC-SCT
11	55/M	t-AML	Mitoxantrone/Ara-C → RIC-SCT → ***Relapse*** → 7+3
12	45/M	*Ph*+AML	7+3+imatinib→ MAC-SCT
13	51/F	AML CR2	7+3 → HiDAC → ***Relapse*** → FLA → HiDAC → MAC-SCT
14	54/F	Complex-rIPSS: Int-2	5-azax11 → Transf-dep → RIC-SCT
15	58/M	RAEB-1 rIPSS: Int-2	Decitabine → RIC-SCT→ ***Relapse with RAEB*** → CIA → ***relapse as MDS***→ DLIx4
16	53/F	CR2 (MRD+)	7+3 → HiDAC → ***Relapse*** → FLA → ***MRD+*** → MAC-SCT
18	18/F	FLT3-ITD/MRD+	AAML1031 → ***Relapse*** --. CPX-351 → FLAG → Ara-C/Peg/Midostaurin → ***refractory*** → Venetoclax/Decitabine→ Residual disease→MAC-SCT

Outcomes – ARM A

ID	Disease	Wk 4 Marrow (% blasts)	Relapse?	Status at last f/up
1*	FLT3-ITD	0	No, but **bone relapse**	Treated on ARM B (9 mo's post-infusion)
2	FLT3-ITD	0	No	Alive in **CR** (2.5 years)
5	MLL-*r*	0	No, **CNS relapse,** Local Rx alone	Alive in **CR** (2 years)
6	AML CR3	0	No, **CNS relapse** Local Rx alone	Alive in **CR** (1.5 years)
7	DNMT3a	0	No	Alive in **CR** (1.5 years)
10	MLL-*r*	0	No	Alive in **CR** (6 mo)
11	t-AML	0	No	Alive in **CR** (6 mo)
12	*Ph*+AML	0	No	Alive in **CR** (9 mo)
13	AML CR2	0	No	Alive in **CR** (9 mo)
14	MDS	0	No	Died in **CR** (1 year)
15	MDS	0	**Yes (8 months)**	2nd transplant, alive in **relapse** (1.5 years)
16	CR2 MRD+	0	No	Alive in **CR** (6 mo)
18	FLT3-ITD/MRD+	0	No	Alive in **CR** (week 6)

Patients infused – ARM B

GROUP B: *Active AML:* 7 patients treated for active AML

ID	Age/G	Disease	Prior Treatments
3	70/M	IDH1*mut*	7+3 → decitabine → IDH inhib → cutis relapse → CIA → RIC-SCT→ ***Relapse***
4	16/M	MDS→ AML	Double cord SCT → AML ***Relapse*** → C → haplo-SCTx2 → ***Relapse***
1*	57/F	FLT3-ITD	CIA → Sorafenib → CIAx2 → RIC-SCT → mTAA-T cells → steroids → ***Relapse***
8	55/M	Induc. failure	7+3 →HiDAC x4 →RIC-SCT →***Relapse*** → DLIx4 → MEC → 5-aza → ***Relapse***
9	23/M	Del 17p	CIAx3 → haplo-SCT → ***Relapse*** → CIA-decitabine → haplo-SCT → 5-aza → Nivolumab → CD123 BiTE →MEC-decitabine → midostaurin → ***Relapse***
9*	23/M	Del 17p	CIAx3 → haplo-SCT#1 → ***Relapse*** → CIA-decitabine → haplo-SCT#2 → 5-aza → Nivolumab → CD123 BiTE →MEC-decitabine → midostaurin → ***Relapse*** → ***mTAA T cells*** → haplo-SCT#3 → ***Relapse***
17	20/F	FLT3-ITD	7+3 → HiDAC→ MAC-SCT → ***Relapse*** → CIA → ***Relapse***

Outcomes – ARM B

ID	Disease	Day 0	Week 4	Response
3	IDH1*mut*	Skin relapse	Stable skin lesion	NR
4	MDS→ AML	30% blasts	30%	NR
1*	FLT3-ITD	4 bone lesions	All resolved	**CR**
8	Induc. failure	50% blasts	15%	**PR**
9	Del 17p	30% blasts	30%	NR
9*	Del 17p	30% blasts	N/E	N/E
17	FLT3-ITD	70% blasts	45%	NR

Outcomes – ARM B

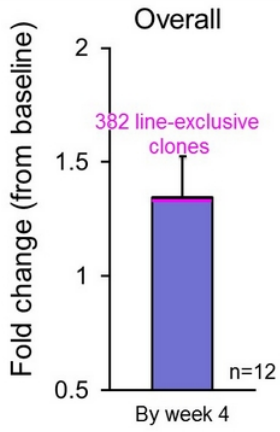
ID	Disease	Day 0	Week 4	Response	Status at last f/up
3	IDH1*mut*	Skin relapse	Stable skin lesion	NR	**PD (3 mo)** → HiDAC chemo
4	MDS→ AML	30% blasts	30%	NR	**PD (4 wks)** → Hospice
1*	FLT3-ITD	4 bone lesions	All resolved	**CR**	**CR (13 mo)** →Relapse → 7+3 chemo
8	Induc. failure	50% blasts	15%	**PR**	**PR (4 mo)** → 2nd alloHSCT
9	Del 17p	30% blasts	30%	NR	**SD (2 mo)** → Chemo/venetoclax → 4th alloHSCT
9*	Del 17p	30% blasts	N/E	N/E	**PD (3 wks)** → Ara-C chemo
17	FLT3-ITD	70% blasts	45%	NR	**SD (2 mo)** → Chemo/venetoclax

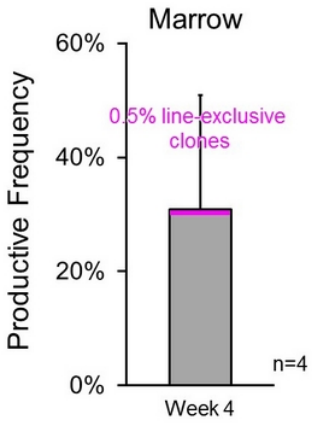
Tracking infused clones *in vivo*

Rationale:

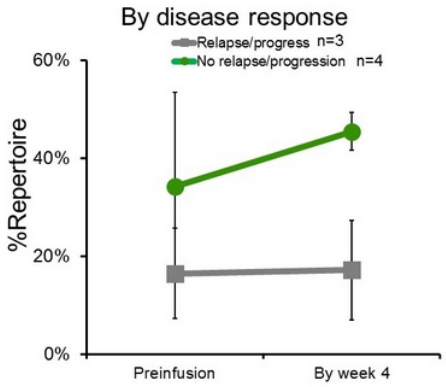
- Infused lymphocytes are not gene modified
- Leukemia specific T cell clones enriched in infused line

In vivo expansion of line clones



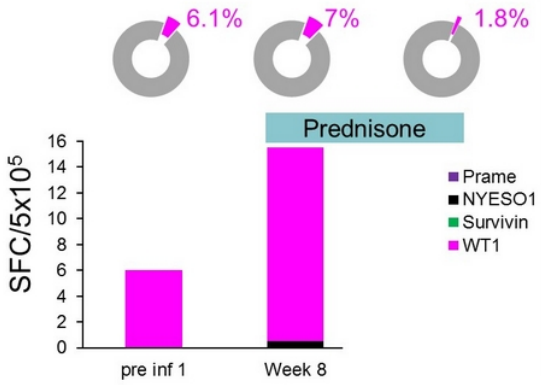


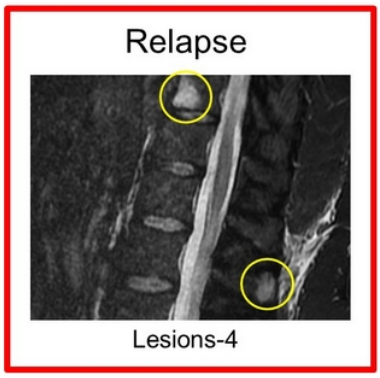
Responders vs Non-responders



Clinical course – Pt#1

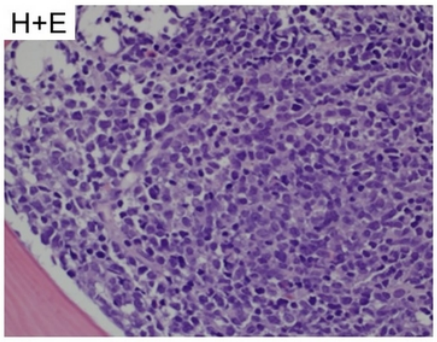
FLT3mut AML received T cells as adjuvant (120 days post HSCT)

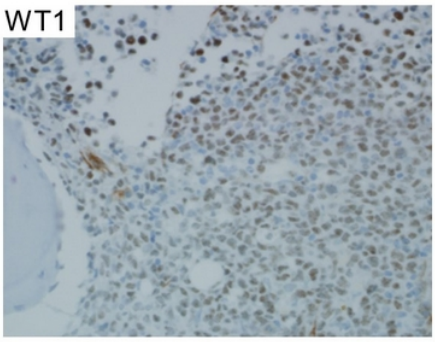




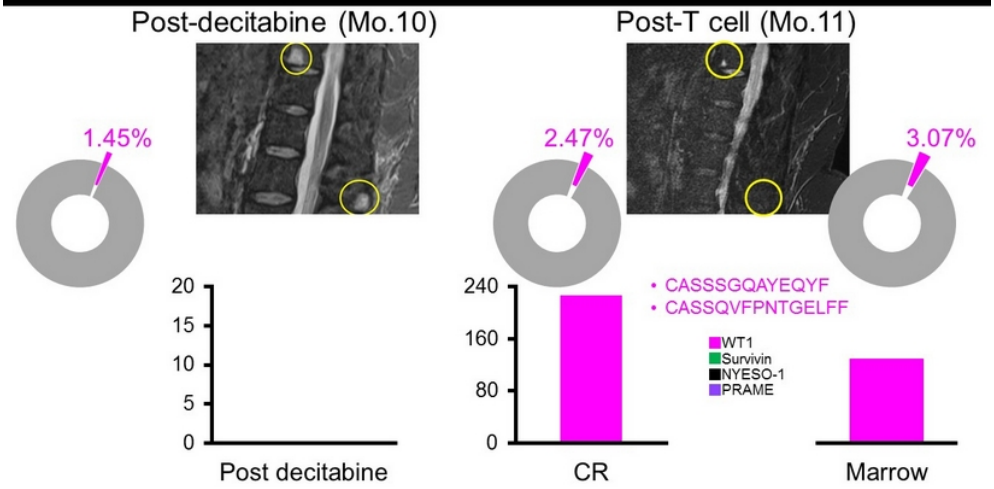
Clinical course – Pt#1

Tumor – antigen expression





Clinical course – Pt#1



Clinical course – Pt#8

TAA expression	% cells	Intensity
PRAME	50-75%	2+
Survivin	<10%	2+
NYESO1	<10%	1+
WT1	<10%	1+

Summary

- Leukemia-directed donor T cell infusions are safe
- Mediate anti-tumor effects
- In vivo expansion superior in responders
- Antigen spreading studies ongoing
- Investigation of immune escape mechanisms

Administering AML-directed DLIs to patients with AML or MDS Post-Allogeneic HSCT Relapse

Premal Lulla, Swati Naik, Ifigeneia Tzannou, Shivani Mukhi, Manik Kuvalekar, Catherine Robertson, Carlos A Ramos, George Carrum, Rammurti Kamble, Jasleen Randhawa, Adrian P Gee, Bambi Grilley Malcolm K Brenner, Helen E Heslop, Juan F Vera and Ann M Leen

Funding:

Evans MDS discovery research grant, Leukemia Texas, Leukemia and Lymphoma SCOR, Lymphoma SPORE, ASBMT New Investigator Award, ASH Scholar Award, BCM Junior Faculty Seed Funding Award, EPCRS-DLDCC, LLS/Rising Tide, ARC-Coalition


Adoptive T cell therapy for ALL targeting multiple tumor associated antigens
Swati Naik, Premal Lulla, Ifigeneia Tzannou, Shivani Mukhi, Manik Kuvalekar, Catherine Robertson, George Carrum, Rammurti Kamble, Adrian P Gee, Bambi Grilley, Robert Krance, Malcolm K Brenner, Helen E Heslop, Juan F Vera, Stephen Gottschalk and Ann M Leen
BCM
Baylor College of Medicine
Texas Children's Hospital
Methodist
CAGT
CENTER FOR CELL AND GENE THERAPY

ALL Relapse after HSCT

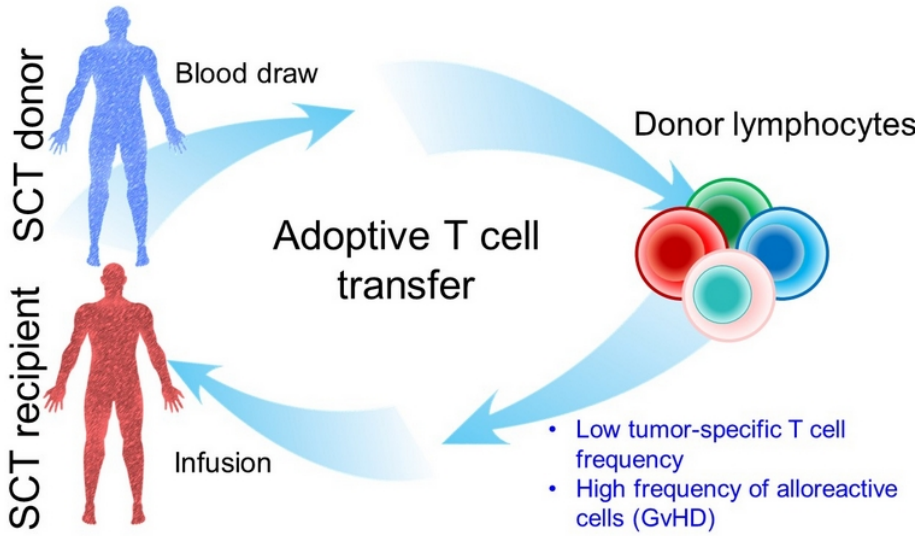
- Leukemic relapse is major cause of treatment failure after HSCT
  - Incidence of relapse: 24-35%
- Poor prognosis for pts who relapse
  - Particularly those who relapse early post-HSCT
  - Overall survival: 7- 32%

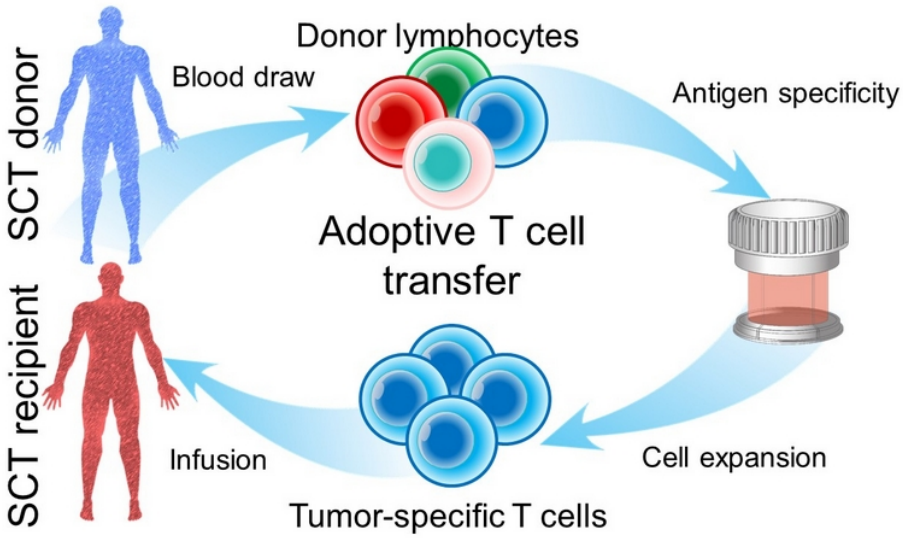
Fagioli Hematologica 2013
Porter et al , BBMT 2011
Arellano, BBMT 2006

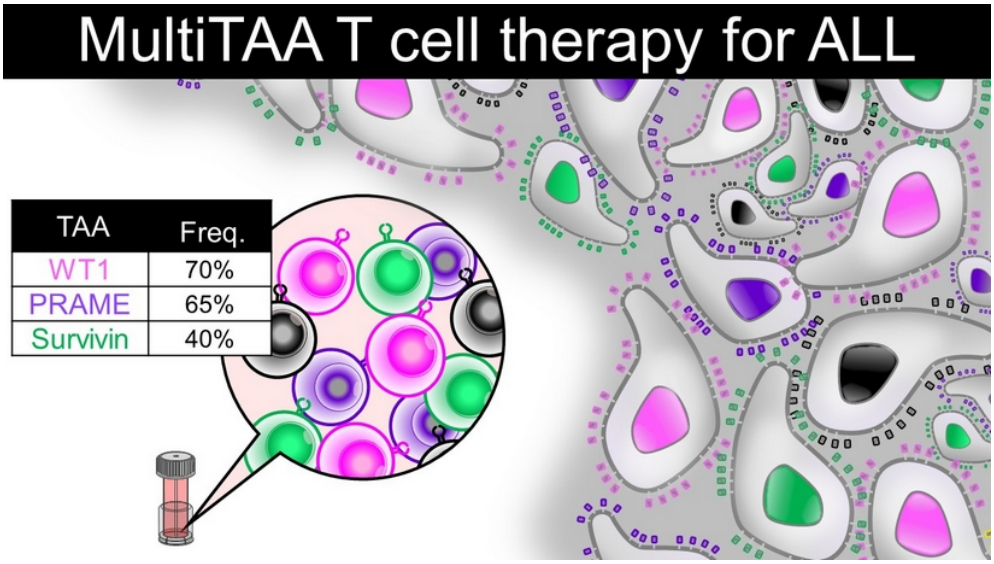
Prevention of ALL relapse

- Strategies to prevent relapse
  - Prophylactic use of targeted agents (e.g. TKIs)
  - Modulation of immune suppression
    - Promote immune reconstitution resulting in GvL effect
  - Immunotherapeutic intervention with DLIs
    - Enhance GvL effect

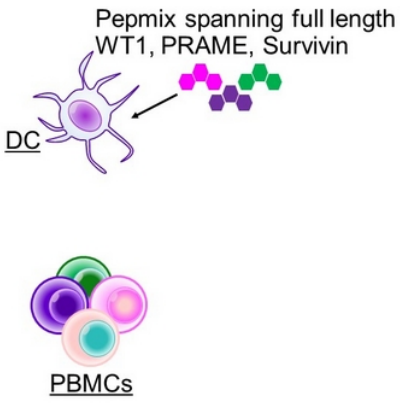
Wayne, Hematology 2017
De Lima,BBMT 2013
Alyea et al, BBMT, 2010


SCT donor
Blood draw
Donor lymphocytes
Adoptive T cell transfer
SCT recipient
Infusion
• Low tumor-specific T cell frequency
• High frequency of alloreactive cells (GvHD)

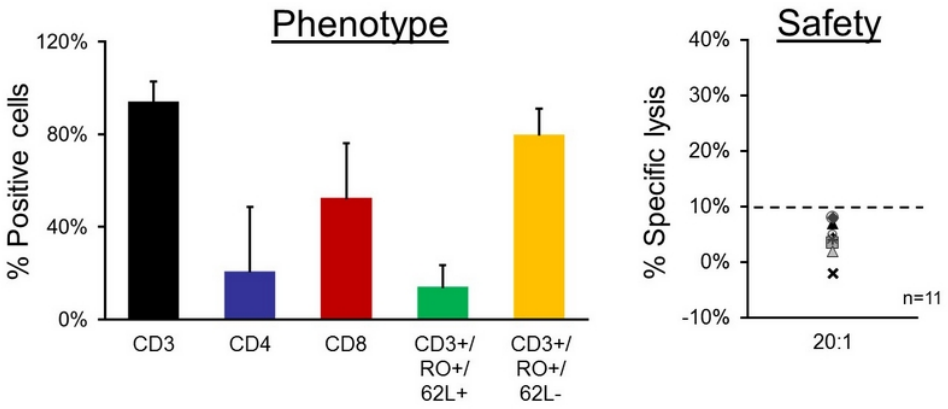

SCT donor
SCT recipient
Blood draw
Donor lymphocytes
Antigen specificity
Adoptive T cell transfer
Infusion
Cell expansion
Tumor-specific T cells


MultiTAA T cell therapy for ALL
TAA
Freq.
WT1
70%
PRAME
65%
Survivin
40%

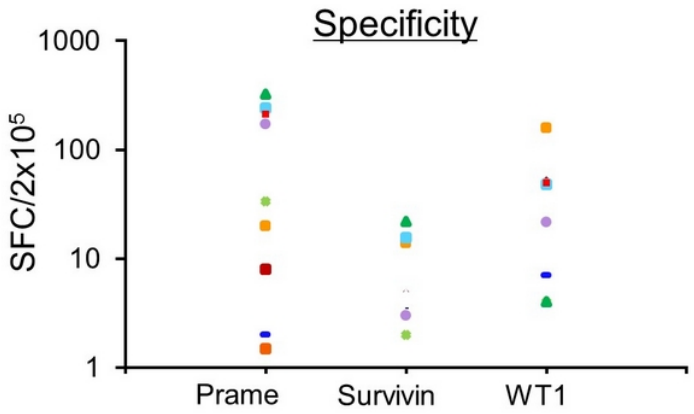
MultiTAA-T Cell manufacture



MultiTAA T cell profile



MultiTAA T cell profile



Study design (STELLA)

Any patient with ALL who received an allogeneic SCT from a family donor

DL1	$5x10^6$ cells/m^2
DL2	$1x10^7$ cells/m^2
DL3	$2x10^7$ cells/m^2

Given after day +30 post-transplant

Patients infused – STELLA

ID	Age/G	Disease	Prior Treatments	Dose level
1	5/F	Ph+ ALL	Induction chemo → Primary induction failure → MRD SCT	1
2	18/F	HR- ALL	Completed therapy for HR- ALL → Relapse → MRD SCT	1
3	18/F	Ph+ ALL	Completed therapy for HR- ALL → Relapse → MRDSCT→ Relapse → Chemo→ CD34+ top -off	1
4	41/M	HR- ALL	HyperCVAD + Ofatumumab x 5 cycles →MRD SCT	1
5	8/M	Ph+ ALL	Completed therapy for HR- ALL → Relapse → MRD SCT	1
6	48/F	HR- ALL	Induction chemo → Primary induction failure → MRD SCT	2
9	12/F	T-cell ALL	Completed therapy for T- ALL → Relapse → MRD SCT	2
10	18/M	HR-ALL	Induction chemo → Primary induction failure → MRD SCT	2
11	12/F	MPAL	Induction chemotherapy → MRD SCT	3
12	16/M	Ph+ ALL	Relapsed on therapy for HR- ALL → MRD SCT	3

n=10

Safety

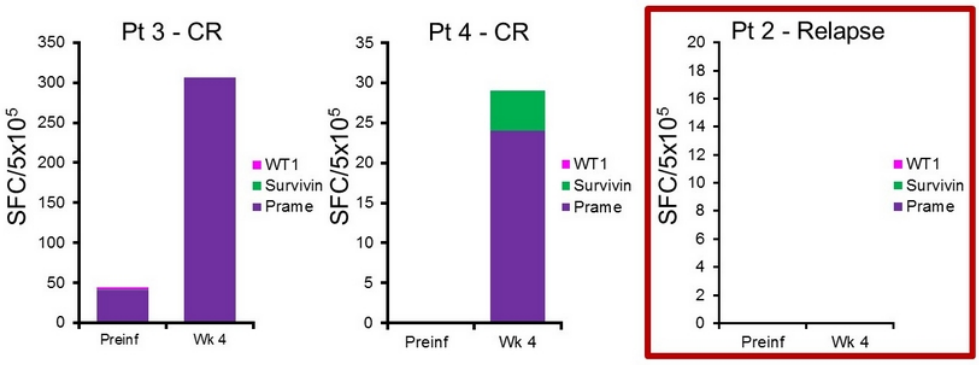
- No Dose Limiting Toxicities (DLTs)
- No GVHD
- No CRS/neurotoxicity or other adverse events

Clinical outcomes

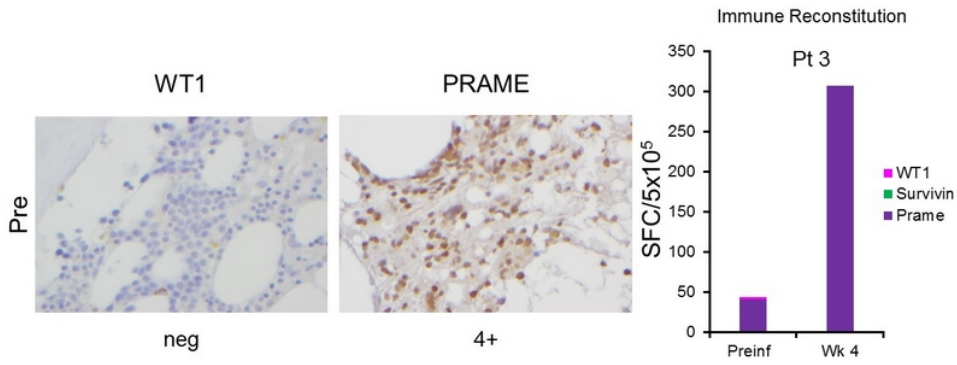
ID	Age/G	Disease	Dose level	Clinical course
2	18/F	HR- ALL	1	CR with mixed chimerism for 6 months→ Relapse
3	18/F	Ph+ ALL	1	Alive in CR (22 months post-infusion)
4	41/M	HR- ALL	1	Alive in CR (28 months post-infusion)
5	8/M	Ph+ ALL	1	Died in CR (9 months post-infusion)
9	12/F	T-cell ALL	2	Alive in CR (17 months post-infusion)
10	18/M	HR-ALL	2	Alive in CR (15 months post -infusion)
11	12/F	MPAL	3	Alive in CR (4 months post-infusion)

Median follow-up 16 months (range 4-28 months)

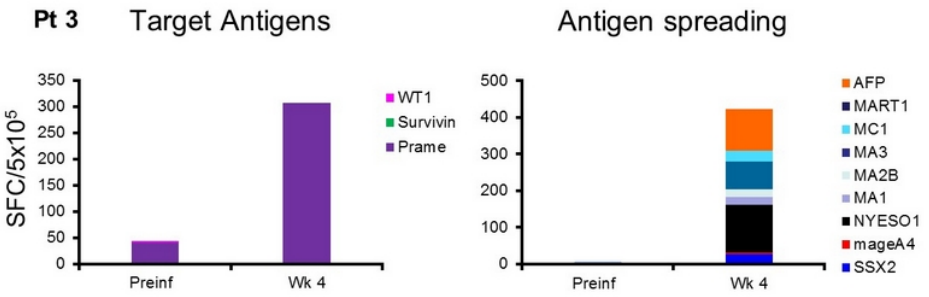
Immune Reconstitution



Tumor antigen expression and T cell expansion



Antigen Spreading



Summary

- Feasible for both B-cell and T-cell ALL
- Safe to date, well-tolerated
- In vivo expansion of tumor-antigen associated T-cells directed to target antigens
- Evidence of antigen spreading which may contribute to relapse prevention
- May present a safe and effective strategy to prevent leukemic relapse post-HSCT

Safety and efficacy of multi-TAA-T cells for Myeloma

Premal Lulla, Ifigeneia Tzannou, George Carrum, Carlos A. Ramos, Rammurti Kamble, Mrinalini Bilgi, Adrian P. Gee Shivani Mukhi, Betty Chung, Ayumi Watanabe, Manik Kuvalekar, Bambi Grilley, Malcolm K. Brenner, Helen E. Heslop, Juan F. Vera and Ann M. Leen

Center for Cell and Gene Therapy, Baylor College of Medicine, Houston Methodist Hospital, and Texas Children's Hospital, Houston, Texas, USA

Introduction

Despite an array of approved agents for the treatment of multiple myeloma (MM), most patients eventually relapse after conventional treatments. The adoptive transfer of tumor-targeted T cells has demonstrated efficacy in the treatment of patients with chemo-refractory hematological malignancies including MM. While the majority of T cell-based therapies in the clinic explore genetically modified T cells that target a single tumor-expressed antigen, we have developed a strategy to generate non-engineered T cell lines that simultaneously target a number of MM-expressed antigens, thereby reducing the risk of tumor immune evasion. We manufacture multiTAA-specific T cells targeting the tumor antigens PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin (**Table 1**) by culturing patient-derived PBMCs with DCs loaded with pepmixes spanning all 5 target antigens in the presence of a Th1-polarizing/pro-proliferative cytokine cocktail (**Figure 2**).

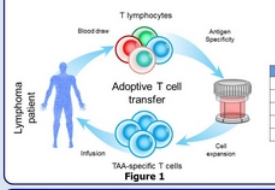


Figure 1

Table 1: Expression of TAAs on lymphoma cells

Antigen	Expression in lymphomas
Survivin	90-100%
SSX2	35-61%
PRAME	36-48%
NY-ESO-1	25-31%
MAGE-A4	17-30%

Characteristics of mTAA-T cells

We have successfully generated multi-antigen-targeted lines for 19 patients, comprising a polyclonal mixture of CD4+ (28.9±7.2%) and CD8+ (56.6±7.2%) T cells (**Figure 3**) reactive against 2 to 5 of the target antigens (**Figure 4**), with no activity against non-malignant autologous targets (2±3% specific lysis; E:T 20:1). We assessed the clonal diversity using TCR vβ deep sequencing analysis and found that the majority (mean 79%; range: 59 to 95%; **Figure 5**) represented rare T cell clones that were unique to the *ex vivo* expanded cell line, thereby enabling *in vivo* tracking studies.

Figure 2- Manufacturing process

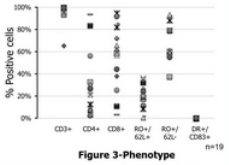


Figure 3-Phenotype

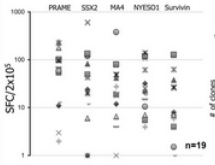


Figure 4-Specificity in an ELISPOT Assay

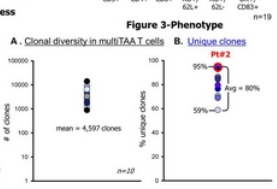


Figure 5 TCR clonality

We have initiated a phase I/II clinical trial to explore the safety and efficacy of mTAA-directed T cells administered to patients with myeloma who have failed at least one line of prior therapy. The schema for enrollment is shown in **Figure 6**. We have treated 20 patients (Group A: 11, Group B: 9) so far: 12 with active myeloma and 8 with myeloma in at doses of 0.5-2x10^7 multiTAA-T cells/m^2 in 2 infusions 2 weeks apart **without prior lymphodepleting** chemotherapy.

Group A:	**Group B:**
>90 days post autologous transplant or no transplant	<90 days post autologous transplant

Clinical Outcomes

To date we have infused 20 patients who had received a median of 4 lines of prior therapy at cell doses ranging from 0.5-2x10^7/m^2. 12 patients were refractory to their latest therapy and had active MM, while 8 were in remission at the time of infusion. Of the 8 patients in CR at the time of T cell infusion, all remained in CCR at the week 6 disease assessment and of the 6 evaluable patients who are >1 year post T cells, only 1 has relapsed.

Table 2: Clinical outcomes of patients treated on group A

ID	Age/G	Prior Treatments	Marrow	Week 6	Response	Mo 12
1	53/M	Bor/Dex → ASCT	10%	Unknown	SD	PR
6	61/M	RVD → ASCT	0%	0%	CCR	CCR
7	44/M	CyBorD → ASCT	0%	0%	CCR	CCR
14	47/M	RVD → ASCT	0% (MRD+)	0% (MRD+)	SD	SD
3*	65/F	RVD → ASCT → CyBorD → Carf/D → ASCT	90%	85%	SD	PD (2m)
13	31/F	VD	4%	0%	SD	SD
10	69/F	VD → ASCT→ R→ Pom/Carf/D	10%	10%	SD	PD (7m)
15	70/M	RVD → ASCT → R-vidaza → Pom/D → ibrutinib/Carf → dinaciclib/VD → CyBorD → Daratumumab → RD-Elot → Ixa/RD	80%	80%	SD	PD (3m)
2*	40/M	RVD → ASCT → Pom/Carf/D→ASCT→mTAA T cells	15%	15%	SD	SD (3m)
18	50/F	VD → ASCT → Dara/VD → XRT → ASCT	0%	0%	CCR	CCR (8m)
20	57/M	RVD → ASCT → R → VD → Pom/D → KPD → ASCT → Ixa → Dara/D	5% (0.97 g/dl)	3% (0.53 g/dl)	SD	SD (3m)

Ten patients were refractory to their latest therapy and had active MM, while 8 were in remission at the time of infusion. At the 6 week assessment, of the 10 patients infused to treat active disease, 1 had a CR, 1 had a PR and 8 had SD. Seven of these 10 patients were infused >1 year ago. Although 2 of the 7 subsequently had disease progression, the remaining 5 continue to respond, with sustained CR (1), PR (2) or SD (2). **(Tables 2, 3). None of the treated patients developed cytokine release syndrome, neurotoxicity or any other infusion related adverse events.**

Table 3: Clinical outcomes of patients treated on group B

ID	Age/G	Prior Treatments	Marrow	Week 6	Response	Mo 12
2	40/M	RVD → ASCT → Pom/Carf/D → ASCT	20%	0%	CR	CR
3	65/F	RVD → ASCT → CyBorD → Carf/D → ASCT	15%	10%	SD	PD (6m)
5	76/M	CyBorD → ASCT	20%	15%	SD	PR
8	57/M	VTD → ASCT → Rd → Cy/Carf/D → ASCT	0%	0%	CCR	CCR
9	50/F	RVD → ASCT	0%	0%	CCR	CCR
11	53/M	VD → RVD → ASCT	0%	0%	CCR	Relapse (7m)
12	54/M	RVD/rituximab → Rd → ASCT	0%	0%	CCR	CCR
17	44/F	VRD → KD → ASCT	0% (0.4 g/dl	0% (0.2 g/dl)	PR	PR (6m)
19	70/M	XRT → VD → ASCT → R → VD → KPD → ASCT	0%	0%	CCR	CCR (6m)

Clinical responses correlated with the emergence and persistence (>6mths) of "line-exclusive" tumor-reactive T cells in patient peripheral blood (**Figure 6A**) and marrow (**6B**), as assessed by TCR deep sequencing. The expansion of product-derived clones was higher among patients with active MM than those in remission (**6A**). This matched the pattern of expansion of TAA-directed T cells as measured by an IFN-Y ELISPOT assay (**6C & D**)

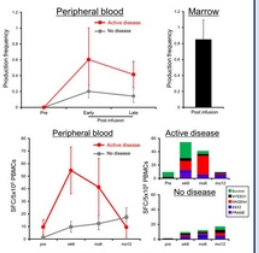


Figure 6 T cell expansion/persistence

Responses in patients

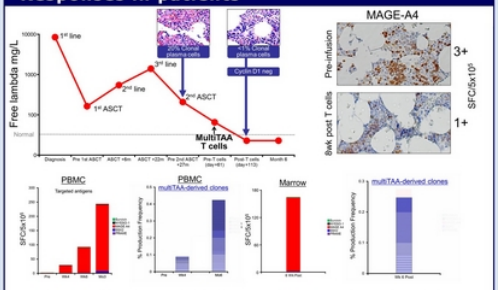


Figure 7: Complete responses in a patient (ID:#2) with lambda light chain myeloma correlates with expansion of infused mTAA-T cells

Shown in **Figure 7** is an example of a patient with **lambda light chain myeloma** with residual marrow disease despite undergoing several lines of prior therapies. Six weeks post-infusion, this patient entered a CR as measured by paraprotein levels as well as by marrow findings concomitant with an increase in the circulating frequency of TAA-(MAGE-A4)-specific T cells in both the blood as well as the bone marrow. The same pattern of expansion was observed when monitoring for the T cell clones present in the infused T cell line but absent in the patient prior to infusion (**Figure 7**).

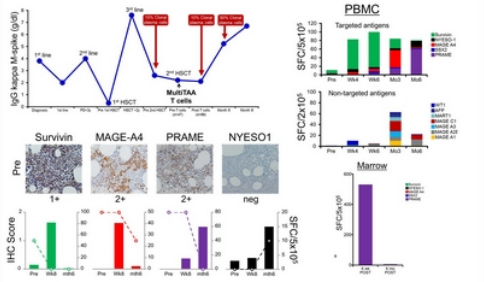


Figure 8: Immune escape in a patient (ID#3) with treatment refractory multiple myeloma

Patient #3 had active multiple myeloma despite recently undergoing an autologous HSCT. At baseline the patients tumor cells expressed Survivin, MAGE-A4 and PRAME as assessed by immunohistochemistry analysis (**Figure 8**). Within 3 months of T cell infusion, there was an increase in the circulating frequency of T cells specific for the targeted TAAs as well as non-targeted TAAs (antigen spreading) in the blood and the bone marrow. However by month 6 the patient developed progressive disease along with loss of TAA-specific T cells within the marrow. Coincident with relapse the patients tumor lost expression of Survivin, MAGEA4 and PRAME in the presence of circulating Survivin, PRAME and MAGE-A4 specific T cells (Fig 8). Furthermore, mRNA sequencing demonstrated an increase in immune inhibitory markers (CTLA4 and LAG3) and an upregulation of >400 cell cycle promoters.

Conclusions

Thus, infusion of autologous multiTAA-targeted T cells directed to PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin has been safe and provided durable clinical benefit to patients with lymphomas. Responses in all six patients who entered a CR were durable and associated with an expansion of infused T cells as well as the induction of antigen spreading.

AL, JFV, MKB and HH are co-founders of Marker Therapeutics that aspires to commercialize the described approach to cell therapy