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

December 1, 2018
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.)

5 West Forsyth Street
Suite 200
Jacksonville, FL **32202**
(Address of principal executive offices) (Zip Code)

(904) 516-5436
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.

As previously announced by the Company, the Center for Cell and Gene Therapy at Baylor College of Medicine presented data from three abstracts at the 60th American Society of Hematology Annual Meeting between December 1-4, 2018. The Company previously issued a press release on the presentation of such dates on November 27, 2018 and the press release was filed as an exhibit to a Form 8-K on the same date. The presentations include: (i) an oral presentation regarding Safety and Efficacy of Multiantigen-Targeted T Cells for Multiple Myeloma by Premal Lulla, M.B.B.S., Assistant Professor of Medicine at the Center for Cell and Gene Therapy, Hematology-Oncology, at the Baylor College of Medicine.; (ii) a poster presentation regarding Targeting Lymphomas Using Non-Engineered, Multi-Antigen Specific T Cells; and (iii) a poster presentation regarding Adoptive T-Cell Therapy for Acute Leukemia Targeting Multiple Tumor Associated Antigens 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 99.1, 99.2 and 99.3, 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 99.1, 99.2 and 99.3 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	2018 ASH Conference Presentation- Safety and Efficacy of Multiantigen-Targeted T Cells for Multiple Myeloma.*
99.2	2018 ASH Conference Poster Presentation-Targeting Lymphomas Using Non-Engineered, Multi-Antigen Specific T Cells.*
99.3	2018 ASH Conference Poster Presentation-Adoptive T-Cell Therapy for Acute Leukemia Targeting Multiple Tumor Associated Antigens.*

*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 3rd day of December, 2018.

MARKER THERAPEUTICS, INC.
(Registrant)

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

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*

Baylor College of Medicine

Texas Children's Hospital

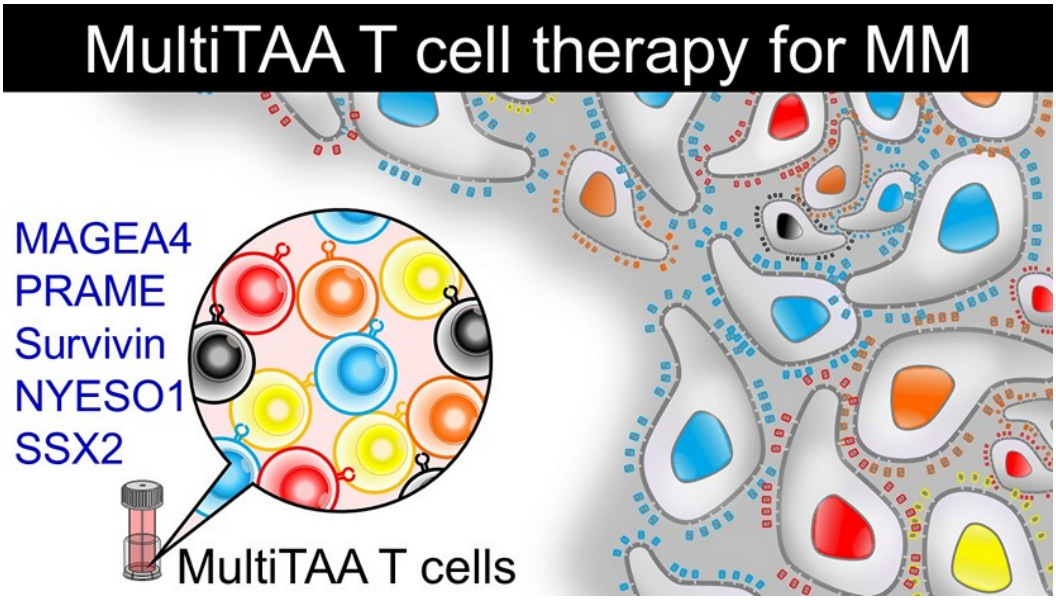
Houston Methodist

CENTER FOR CELL & GENE THERAPY

Problems with myeloma therapy

Therapy	Problems
Dexamethasone	Infections, osteoporosis
Melphalan	Immunosuppression, second cancers
Thalidomide	Neuropathy, Clots, anemia
Lenalidomide	Clots, anemia, second cancers
Bortezomib	Neuropathy, viral infections
ASCT	Immunosuppression, infections

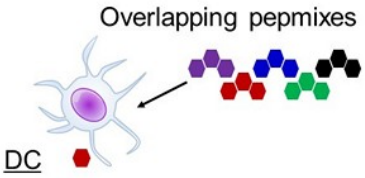
New therapies needed


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

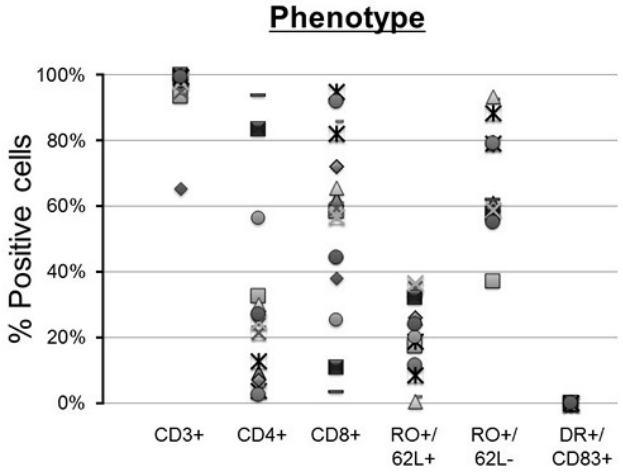
Our approach

- Simultaneously target multiple TAAs

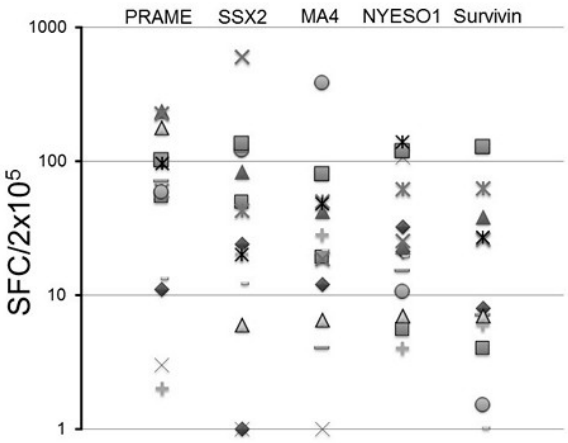
MultiTAA-T Cell Generation



Profile of MultiTAA-T cells



MultiTAA T cell specificity/polyclonality



Clinical trial design
- Dose escalation (ARM A and B)

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 - Eligibility

- Any patient ≥18 yrs with myeloma diagnosis (post completion of at least 1 treatment regimen)

Group A:
>90 days post autologous or syngeneic transplant

Group B:
<90 days post autologous or syngeneic transplant

- No lymphodepletion

Patients Enrolled

Group A:

ID	Age/G	Disease	DL	Prior Treatments
1	53/M	IgG-kappa	1	Bor/Dex → ASCT
6	61/M	IgG-kappa	1	RVD → ASCT
7	44/M	IgG-kappa	1	CyBorD → ASCT
14	47/M	IgG-kappa	2	RVD → ASCT
3*	65/F	IgG-kappa	1	RVD → ASCT → CyBorD → Carf/D → ASCT
13	31/F	IgG-kappa	2	VD
10	69/F	IgG-kappa	2	VD → ASCT→ R→ Pom/Carf/D
15	70/M	IgA-kappa	3	RVD → ASCT → R-vidaza → Pom/D → ibrutinib/Carf → dinaciclib/VD → CyBorD → Daratumumab → RD-Elot → Ixa/RD
2*	40/M	Free lambda	2	RVD → ASCT → Pom/Carf/D→ASCT→mTAA T cells
18	50/F	Free Kappa	3	VD → ASCT → Dara/VD → XRT → ASCT
20	57/M	IgG-lambda	3	RVD → ASCT → R → VD → Pom/D → KPD → ASCT → Ixa → Dara/D

Patients Infused

Group A:

ID	Age/G	Disease	Marrow	Prior Treatments
1	53/M	Active	10%	Bor/Dex → ASCT
6	61/M	In remission	0%	RVD → ASCT
7	44/M	In remission	0%	CyBorD → ASCT
14	47/M	Active	0% (MRD+)	RVD → ASCT
3*	65/F	Active	90%	RVD → ASCT → CyBorD → Carf/D → ASCT
13	31/F	Active	4%	VD
10	69/F	Active	10%	VD → ASCT→ R→ Pom/Carf/D
15	70/M	Active	80%	RVD → ASCT → R-vidaza → Pom/D → ibrutinib/Carf → dinaciclib/VD → CyBorD → Daratumumab → RD-Elot → Ixa/RD
2*	40/M	Active	15%	RVD → ASCT → Pom/Carf/D→ASCT→mTAA T cells
18	50/F	In remission	0%	VD → ASCT → Dara/VD → XRT → ASCT
20	57/M	Active	5%	RVD → ASCT → R → VD → Pom/D → KPD → ASCT → Ixa → Dara/D

Patients Enrolled

Group B:

ID	Age/G	Disease	DL	Prior Treatments
2	40/M	Free lambda	1	RVD → ASCT → Pom/Carf/D → ASCT
3	65/F	IgG-kappa	1	RVD → ASCT → CyBorD → Carf/D → ASCT
5	76/M	IgG-kappa	1	CyBorD → ASCT
8	57/M	IgA-kappa	2	VTD → ASCT → Rd → Cy/Carf/D → ASCT
9	50/F	IgG-kappa	2	RVD → ASCT
11	53/M	IgG-lambda	2	VD → RVD → ASCT
12	54/M	Free lambda	2	RVD/rituximab → Rd → ASCT
17	44/F	IgG-kappa	3	VRD → KD → ASCT
19	70/M	Free kappa	3	XRT → VD → ASCT → R → VD → KPD → ASCT

Patients Infused

Group B:

ID	Age/G	Disease	Marrow	Prior Treatments
2	40/M	Active	20%	RVD → ASCT → Pom/Carf/D → ASCT
3	65/F	Active	15%	RVD → ASCT → CyBorD → Carf/D → ASCT
5	76/M	Active	20%	CyBorD → ASCT
8	57/M	In remission	0%	VTD → ASCT → Rd → Cy/Carf/D → ASCT
9	50/F	In remission	0%	RVD → ASCT
11	53/M	In remission	0%	VD → RVD → ASCT
12	54/M	In remission	0%	RVD/rituximab → Rd → ASCT
17	44/F	Active	0% (MRD+)	VRD → KD → ASCT
19	70/M	In remission	0%	XRT → VD → ASCT → R → VD → KPD → ASCT

Clinical Outcomes

Active Disease:

ID	Age/G	Disease	Marrow	Week 6	Wk 6	Mo12
1	53/M	Active	10%	Unknown	SD	PR
14	47/M	Active	0% (MRD+)	0% (MRD+)	SD	SD
3*	65/F	Active	90%	85%	SD	PD (2m)
13	31/F	Active	4%	0%	SD	SD
10	69/F	Active	10%	10%	SD	PD (7m)
15	70/M	Active	80%	80%	SD	PD (3m)
2*	40/M	Active	15%	15%	SD	SD (3m)
2*	40/M	Active	20%	0%	CR	CR
3*	65/F	Active	15%	10%	SD	PD (6m)
5	76/M	Active	20%	15%	SD	PR
17	45/F	Active	0% (0.4 g/dl)	0% (0.2 g/dl)	PR	PR (6m)
20	57/M	Active	5% (0.97 g/dl)	3% (0.53 g/dl)	SD	SD (3m)

Clinical Outcomes

In remission:

ID	Age/G	Disease	Marrow	Week 6	Wk 6	Mo12
8	57/M	In remission	0%	0%	CCR	CCR
9	50/F	In remission	0%	0%	CCR	CCR
11	53/M	In remission	0%	0%	CCR	Relapse (7m)
12	54/M	In remission	0%	0%	CCR	CCR
6	61/M	In remission	0%	0%	CCR	CCR
7	44/M	In remission	0%	0%	CCR	CCR
19	70/M	In remission	0%	0%	CCR	CCR (6m)
18	50/F	In remission	0%	0%	CCR	CCR (8m)

Only one patient has relapsed at a median f/u of 21 months

Correlating clinical benefit with infused multiTAA T cells

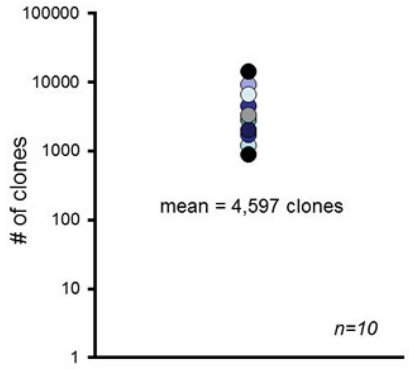
How can we track non-gene-modified multiTAA T cells in vivo?

Rationale:

- In PBMCs (pre-infusion) tumor-specific T cell frequency v. low
  - below TCR vβ deep sequencing detection threshold (1/100,000)
- Tumor-directed clones enriched in multiTAA T cells
  - Detectable by vβ deep sequencing

How many “trackable” clones are present in our multiTAA T cells?

Clonal diversity in multiTAA T cells

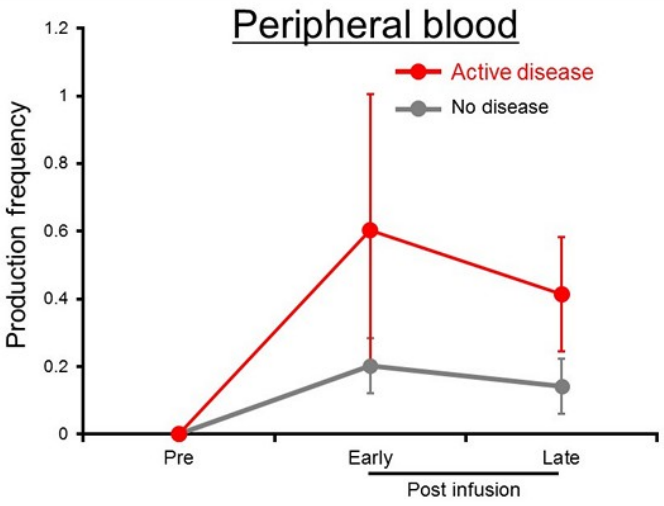


What drives in vivo multiTAA expansion?

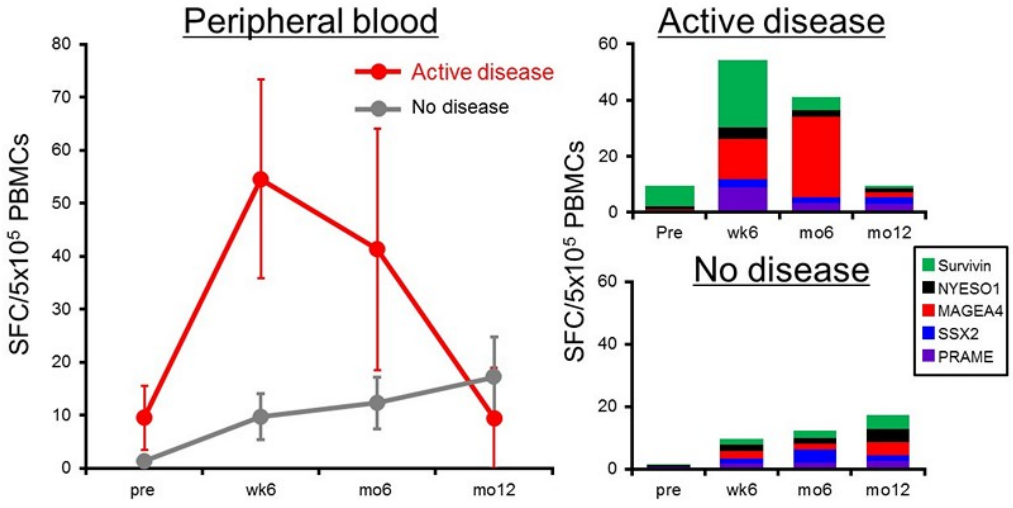
- Patients enrolled on different arms depending on proximity to transplant [> (Grp A) or < (Grp B) 90 days]
  - Does post-transplant lymphodepletion impact expansion?

- Patients with and without disease enrolled on study
  - Does presence of antigen influence in vivo expansion?

Antigen drives multiTAA expansion – TCR tracking

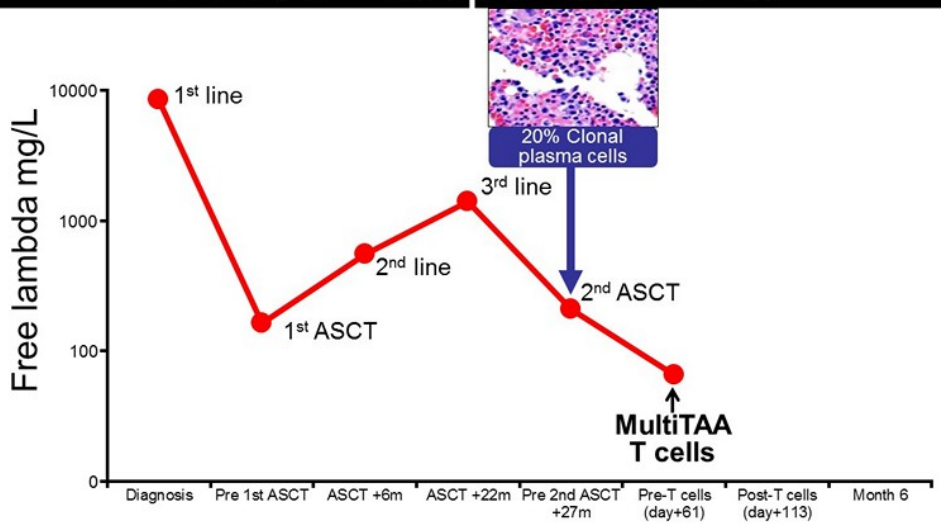


Antigen drives multiTAA expansion – ELIspot

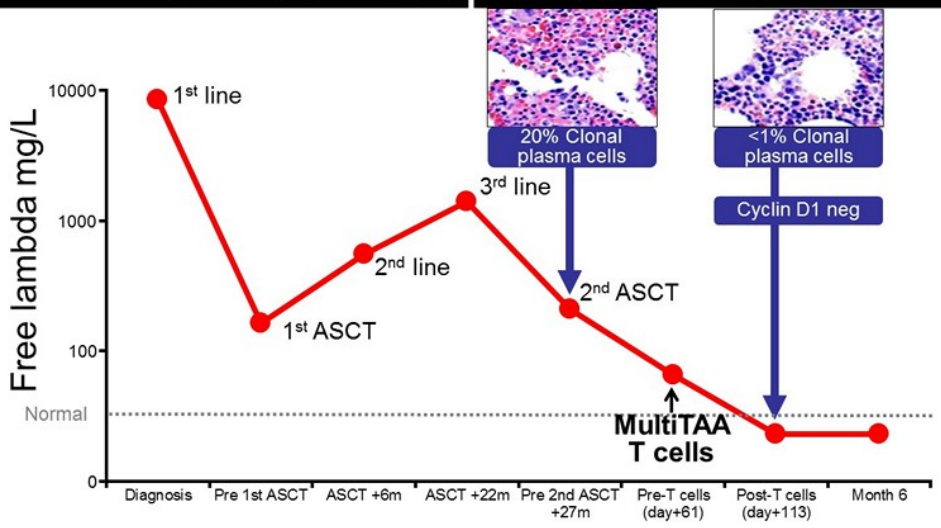


T cell kinetics in responders

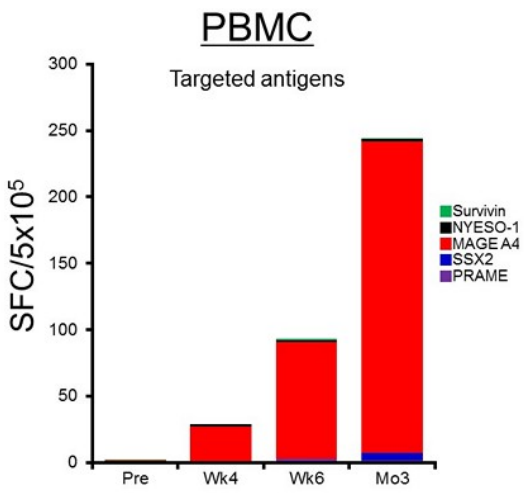
Clinical Response – Pt#2



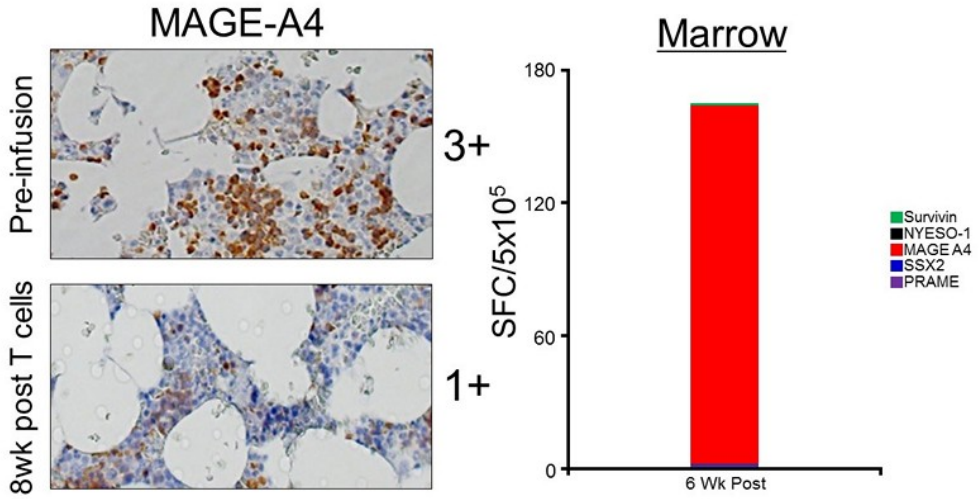
Clinical Response – Pt#2



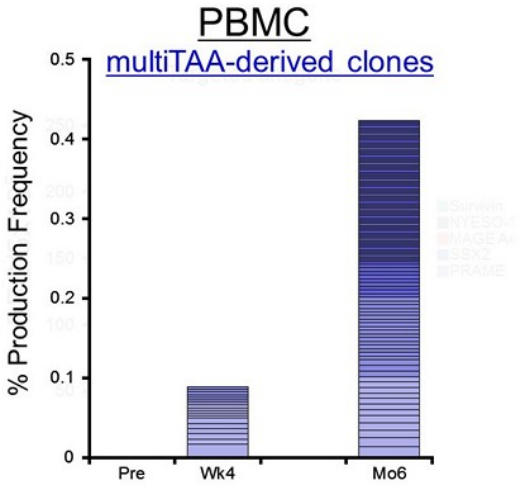
Clinical Response – Pt#2

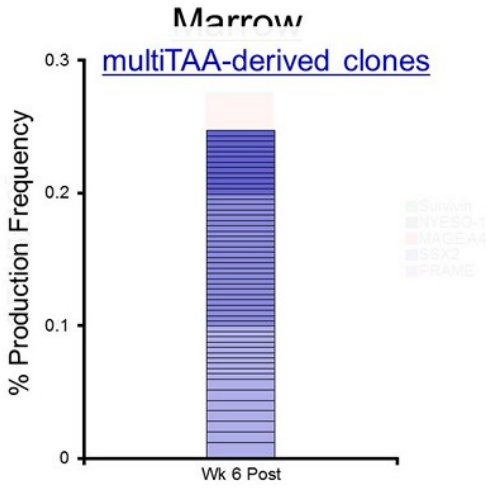


Clinical Response – Pt#2



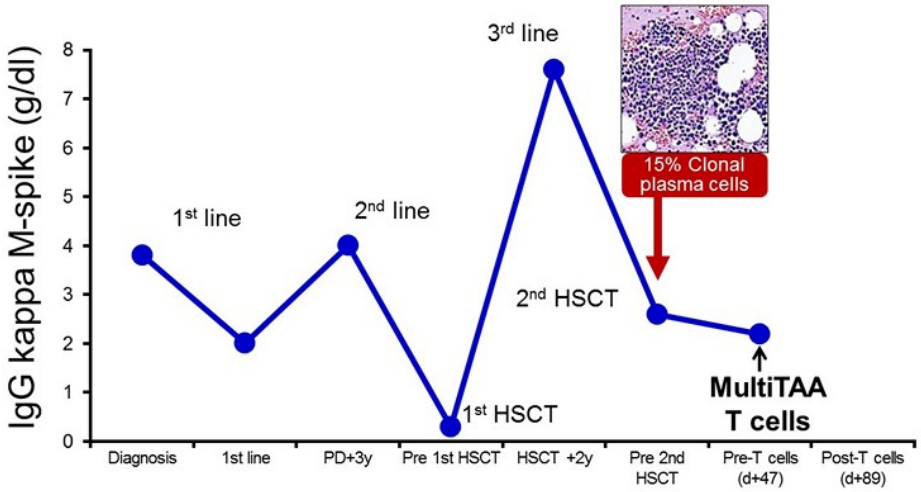
In vivo T cell tracking – Pt#2



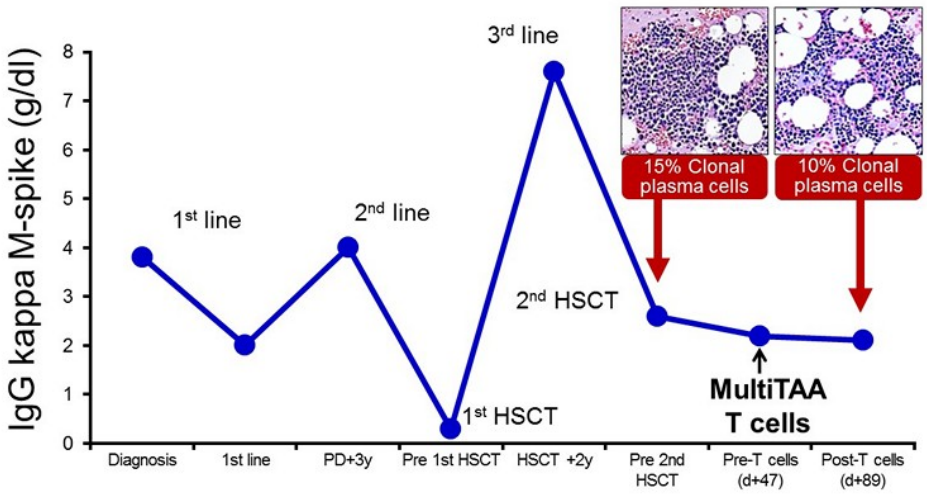


Immune escape post multiTAA T cells

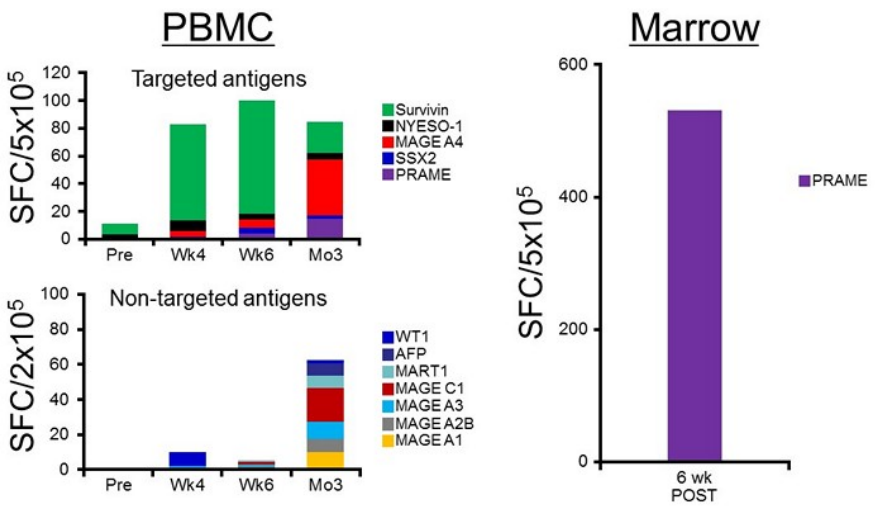
Clinical Course - Pt#3



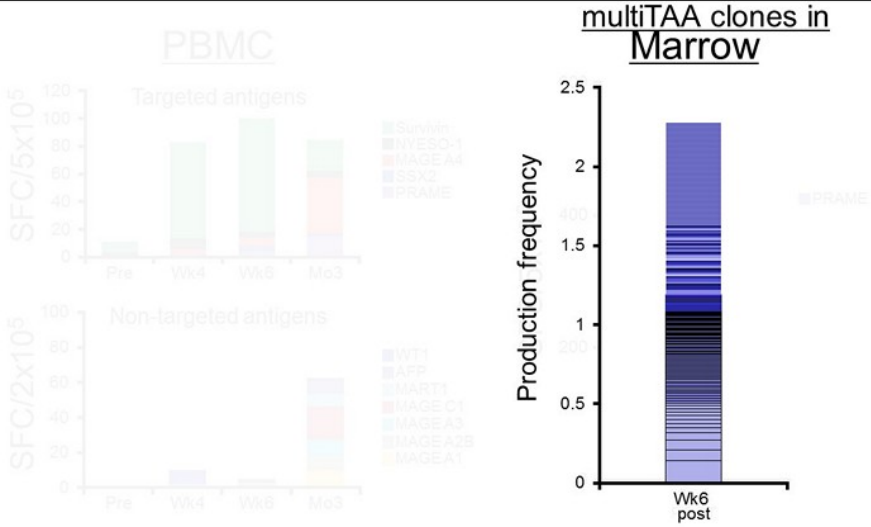
Clinical Course - Pt#3



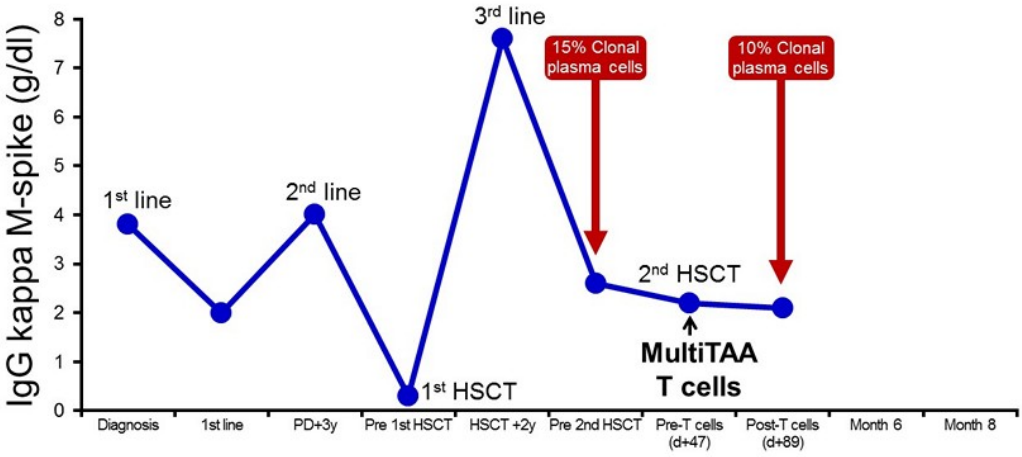
Clinical Course - Pt#3 - ELIspot



Clinical Course - Pt#3



Clinical Course - Pt#3



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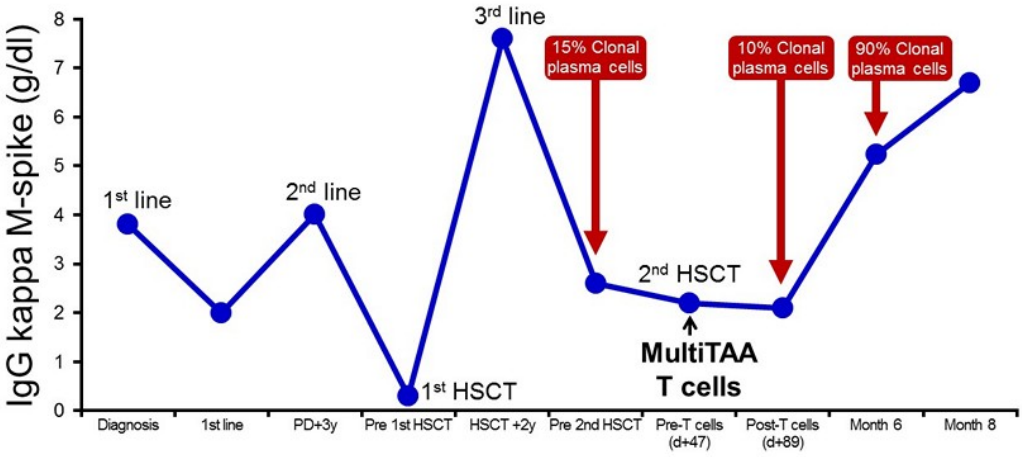
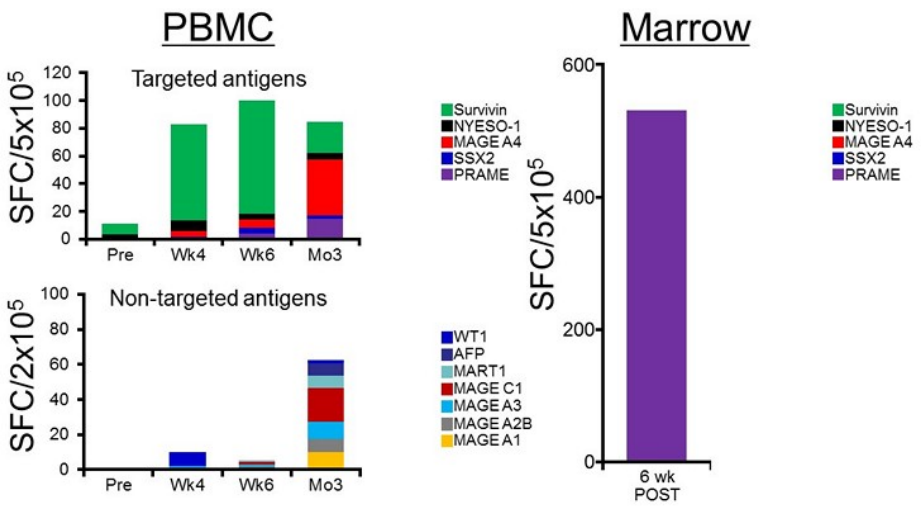
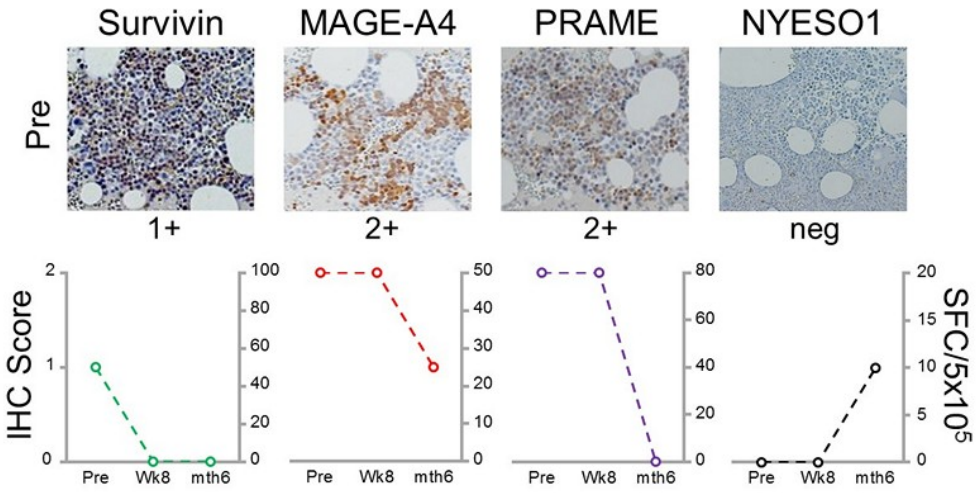


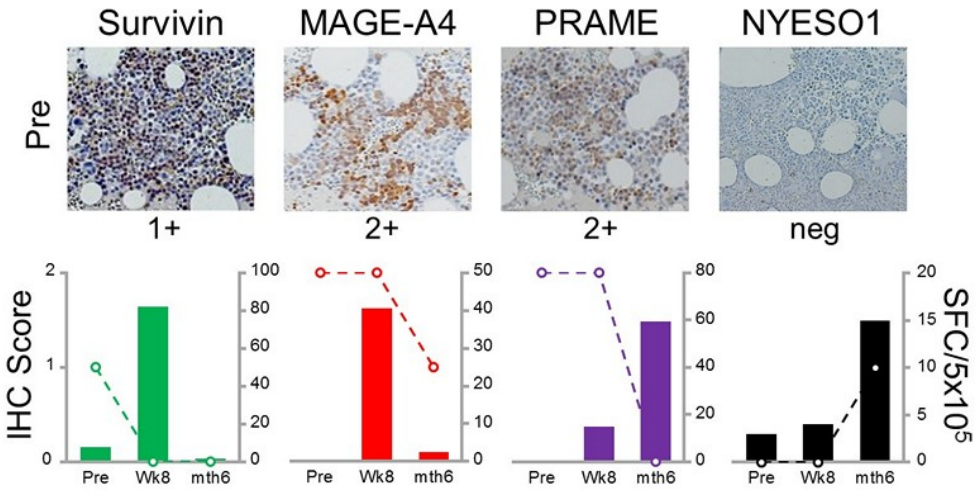
Clinical Course - Pt#3



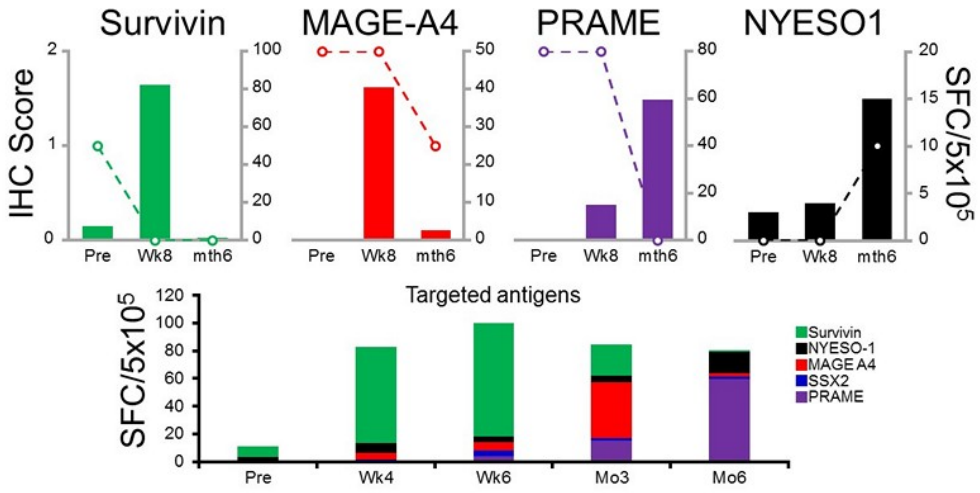
Mechanism of Escape



Mechanism of Escape

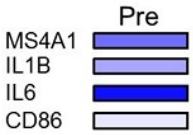


Mechanism of Escape



Mechanism of Escape

Immune activating genes



Immune inhibitory genes

Linghua Wang, David Wheeler HGSC-BCM

MultiTAA T cells for myeloma

- Safe to date (DL3 – Arm A & B)
- Feasible
- In vivo expansion of tumor-specific T cells directed to target antigens
- Antigen spreading
- Clinical benefit

Acknowledgements

TRL Lab PIs
Helen Heslop
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Natasha Lapteva
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April Durett
Suzanne Poole
Zhuyong Mei
Crystal Silva-Lentz

GMP Laboratory
Huimin Zhang
Birju Mehta

TRL Laboratory
Ifigeneia Tzannou
Shivani Mukhi
Aster Workineh
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Bridget Medina
Hao Liu
Munu Bilgi
Catherine Robertson
Elicia Casteneda

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Baylor College of Medicine | Texas Children's Hospital | Houston Methodist

CENTER FOR CELL & GENE THERAPY

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, 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

Immunotherapy is emerging as a potent therapy for a range of hematologic malignancies including lymphomas. Indeed adoptive transfer of T cells genetically engineered to express the CD19 chimeric antigen receptor (CAR) has now received FDA approval for the treatment of patients with refractory diffuse large B cell lymphomas (DLBCL). We have developed a non-engineered T cell-based therapy to treat patients with all types of lymphomas: Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL). The approach uses single T cell lines that simultaneously target a range of tumor-associated antigens (TAAs) that are frequently expressed by these tumors, including PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin (**Table 1**). The use of whole antigen should remove the HLA restriction imposed by the use of transgenic TCRs specific for single peptides, while targeting multiple antigens simultaneously would reduce the risk of tumor immune evasion.

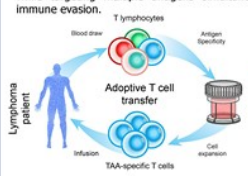

Figure 1

Table 1: Expression of TAAs on lymphoma cells

Antigen	Expression in lymphomas
PRAME	28-33%
SSX2	22-58%
MAGEA4	11-28%
NYESO1	12-37%
Survivin	18-88%

Characteristics of mTAA-T cells

We have generated 42 clinical-grade multiTAA-specific T cell lines (**Figure 2**), comprising CD3+ T cells (mean 98±1.1%) with a mixture of CD4+ (mean 48±4.3%) and CD8+ (mean 37±4%) T cells, which expressed central and effector memory markers (CD45RO+/CD62L+/CCR7+ -- mean 14±3%; CD45RO+/CD62L+/CCR7- -- 10±2.2%; CD45RO+/CD62L-/CCR7- -- 28.3±3.6%) (n=42, **Figure 3**). The expanded lines recognized the targeted antigens PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin (range 0-463, 0-496, 0-330, 0-379 and 0-304 spot forming units (SFU)/2x10^5 input cells, respectively in IFNγ ELIspot, n=34). None of the lines reacted against non-malignant autologous recipient cells (3±3.8% specific lysis; E:T 20:1 **Figure 5**).

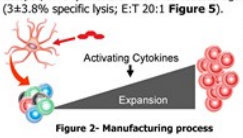

Figure 2- Manufacturing process

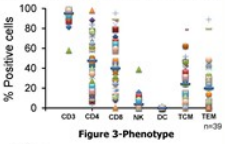

Figure 3-Phenotype

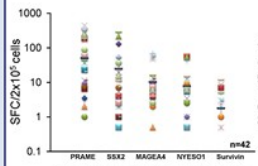

Figure 4-Specificity in an ELISPOT Assay

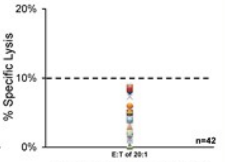

Figure 5 Lack of self-reactivity

We have implemented a phase I/II clinical trial to explore the safety and efficacy of the administration of mTAA-directed T cells to patients with lymphomas who have failed at least one line of prior therapy. The schema for enrollment is shown in **Figure 6**. We have treated 33 patients (Group A: 18, Group B: 15) so far: 13 with HL, 17 with aggressive NHL (diffuse large B-cell, mantle cell, or T cell lymphomas) and 3 with indolent NHLs (FL and marginal zone lymphoma) at doses of 0.5-2x10^7 multiTAA-T cells/m^2 in 2 infusions 2 weeks apart **without prior lymphodepletion** chemotherapy.

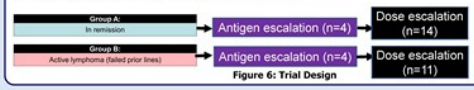

Figure 6: Trial Design

Clinical Outcomes

We first treated patients on the antigen escalation scheme (4 in each arm). None of the infused patients experienced infusion related toxicities, so we then proceeded with the dose escalation phase of the study. Of 18 patients who were infused as adjuvant therapy all but 2 remain in remission (range 3-42 months post-infusion).

Table 2: Clinical outcomes of patients treated on group A (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)

*Antigen escalation cohort

Fifteen patients have received multiTAA-specific T cells to treat active disease, all of whom had failed a median of 4 lines of prior therapy. Of these, 5 had transient disease stabilization followed by disease progression, 4 have ongoing stable disease, 3-18 months post-multiTAA-specific T cells while the remaining 6 (3 with HL and 3 with DLBCL) have all had complete and durable responses (4 to 41 months), as assessed by PET imaging (**Table 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 (active)

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 → HDAC) →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

*Antigen escalation cohort

Responding patients

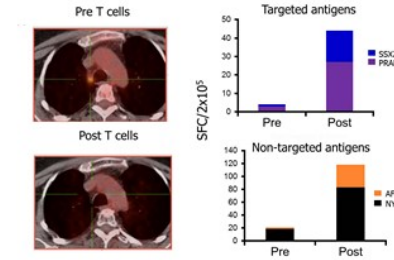

Figure 7: Complete responses in a patient with Hodgkin lymphoma correlates with expansion of infused mTAA-T cells along with antigen spreading

Six of 15 patients entered a durable CR, which correlated the in vivo expansion of mTAA-directed T cells. Shown in Figure 7 is an example of a patient with **Hodgkin lymphoma** with residual mediastinal disease despite undergoing an autologous hematopoietic stem cell transplant (ASCT). Eight weeks post-infusion, this patient enters a CR concomitant with an increase in the circulating frequency of targeted as well as non-targeted tumor antigen-specific T cells (**Figure 7**).

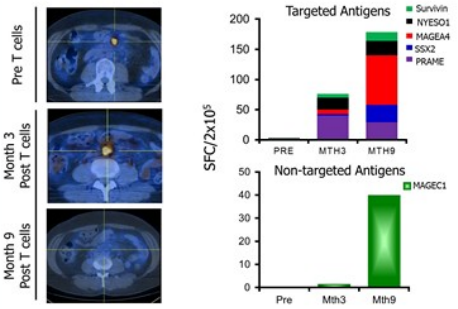

Figure 8: Durable CR in a patient with DLBCL of the mesentery that was refractory to high dose chemo/ASCT correlates with in vivo expansion of mTAA-T cells and antigen spreading

Three of the six CR patients had treatment refractory diffuse large B cell lymphoma. In one of these cases the patient initially developed a "tumor flare", 3 months post-infusion which coincided with increasing levels of TAA-directed T cell in the circulation. Without additional therapies, the patient entered a complete response, 9 months post-infusion at which time-point not only was there a robust increase in target TAA-specific T cells, but also non-targeted MAGEC1-specific T cells indicating antigen spreading.

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

ADOPTIVE T-CELL THERAPY FOR ACUTE LEUKEMIA TARGETING MULTIPLE TUMOR ASSOCIATED ANTIGENS

Naik S, Lulla P, Tzannou I, Velasquez M, Vera JF, Gee AG, Liu H, Krance R, Brenner MK, Rooney CM, Heslop HE, Gottschalk S, Leen AM.
Center for Cell and Gene Therapy, Texas Children's Hospital, Baylor College of Medicine, Houston, Texas.

BACKGROUND

•Leukemic relapse remains the major cause of treatment failure in hematopoietic stem cell transplant (HSCT) recipients

•Donor lymphocyte infusions (DLIs) are not always effective and are associated with the risk of life-threatening graft-versus-host disease (GVHD)

•The adoptive transfer of T cells, genetically modified to express CD19-specific chimeric antigen receptors (CARs), has shown potent anti-leukemia activity in HSCT recipients with recurrent disease.

•However, CD19-CAR T cells carry the inherent risk of immune escape since a single antigen is targeted, and is limited to malignancies of B-cell lineage

•To overcome these limitations, we now propose to target multiple tumor associated antigens (multiTAAs) expressed in B- and T-cell ALL with donor-derived, multiTAA-specific T cells.

DESIGN AND METHODS

Choosing optimal TAA

•We choose the following tumor associated antigens that are over expressed on the surface of leukemic cells

TAA	Function	Expression in leukemia
WT1	Zn finger transcription factor	ALL : 70-90%
Survivin	Inhibitor of apoptosis	ALL : 65-70%
PRAME	Repressor of retinoic acid receptor function	ALL : 40-45%

Generating multi TAA specific T-cells

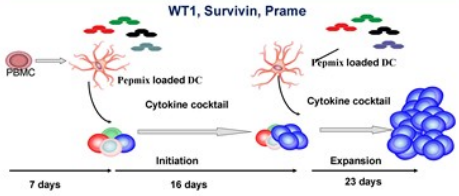

Fig 1. Dendritic cells loaded with pepmixes are used as APCs. In the presence of a Th1-polarizing/pro-proliferative cytokine cocktail T-cells are repeatedly stimulated to activate multi TAA specific T-cells.

CLINICAL TRANSLATION

Study outline

•Designed a Phase 1 study for patients with high-risk ALL who undergo allogeneic HSCT.

•Donor-derived mTAA specific T-cells are infused after day +30 following allogeneic HSCT in 3 escalating dose levels : 1) DL1 : $5x10^6$ cells/m^2 2) DL2 : $1x10^7$ cells/m^2 3) DL3 : $2x10^7$ cells/m^2

•Eligible patients can receive up to 6 mTAA specific T-cell infusions, 4-6 weeks apart

•There are 2 groups on study : 1) Group A : As Adjuvant therapy for patients in remission and 2) Group B : Patients with relapsed disease after transplant

Preliminary data

To date, we have enrolled 14 patients and infused 10 patients with ALL with multiTAA specific T-cell lines on Group A

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

Characterization of Multi TAA specific T-cells

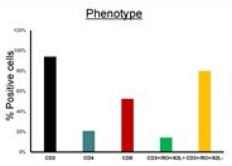

Fig 2. Donor-derived multi TAA specific T cell lines are predominantly comprised of T-cells and have polyclonal repertoire as assessed by Flow Cytometry

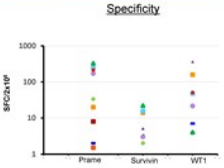

Fig 3 Donor-derived multi TAA specific T cell lines (n= 11) show antigen specificity as assessed by Elispot assay,

Clinical outcome

- All infusions were well tolerated without any adverse events
- To date, infused patients have not experienced any Dose Limiting Toxicities, Graft-versus-Host disease or CRS

ID	Age/G	Disease	Dose level	Outcome
1	5/F	Ph+ ALL	1	*Not evaluable**
2	18/F	HR- ALL	1	CR with mixed chimerism for 6 months→ Relapse
3	18/F	Ph+ ALL	1	Remains in CR (16 months)
4	41/M	HR- ALL	1	Remains in CR (22.4 months)
5	8/M	Ph+ ALL	1	Remains in CR (9 months)
6	48/F	HR- ALL	2	*Not evaluable**
9	12/F	T-cell ALL	2	Remains in CR (11 month)
10	18/M	HR-ALL	2	Remains in CR (9 months)
11	12/F	MPAL	3	Remains in CR - recent infusion
12	16/M	Ph+ ALL	3	Remains in CR – recent infusion

*Two patients not evaluable per protocol as they received > 0.5mg/kg of steroids within 4 weeks of infusion and were replaced for dose escalation : 1) Pt 1 : Stress dose steroids for sepsis 2) Pt 6 : Steroids for transaminitis (GVHD ruled out later)

Correlative studies

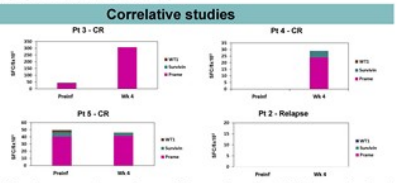

Fig 4. Elispot assays show evidence of expansion of multi-TAA specific T-cell expansion by week 4 post-infusion in all patients that remained in CR. The one patient who relapse had no evidence of multiTAA expansion, despite 3 additional infusions

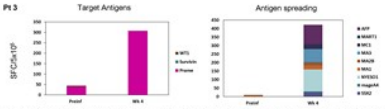

Fig 5. In-vivo antigen cascade. Elispot assays show evidence of antigen spreading, probably contributing to tumor control.

CONCLUSIONS

- Safe to date and feasible for both B-cell and T-cell ALL
- In-vivo expansion of tumor-antigen associated T-cells directed to target antigens and evidence of antigen spreading which may contribute to disease control.
- Adoptive transfer of multi TAA-specific T cells may present a promising addition to current immunotherapeutic approaches for prophylaxis for leukemic relapse in HSCT recipients.