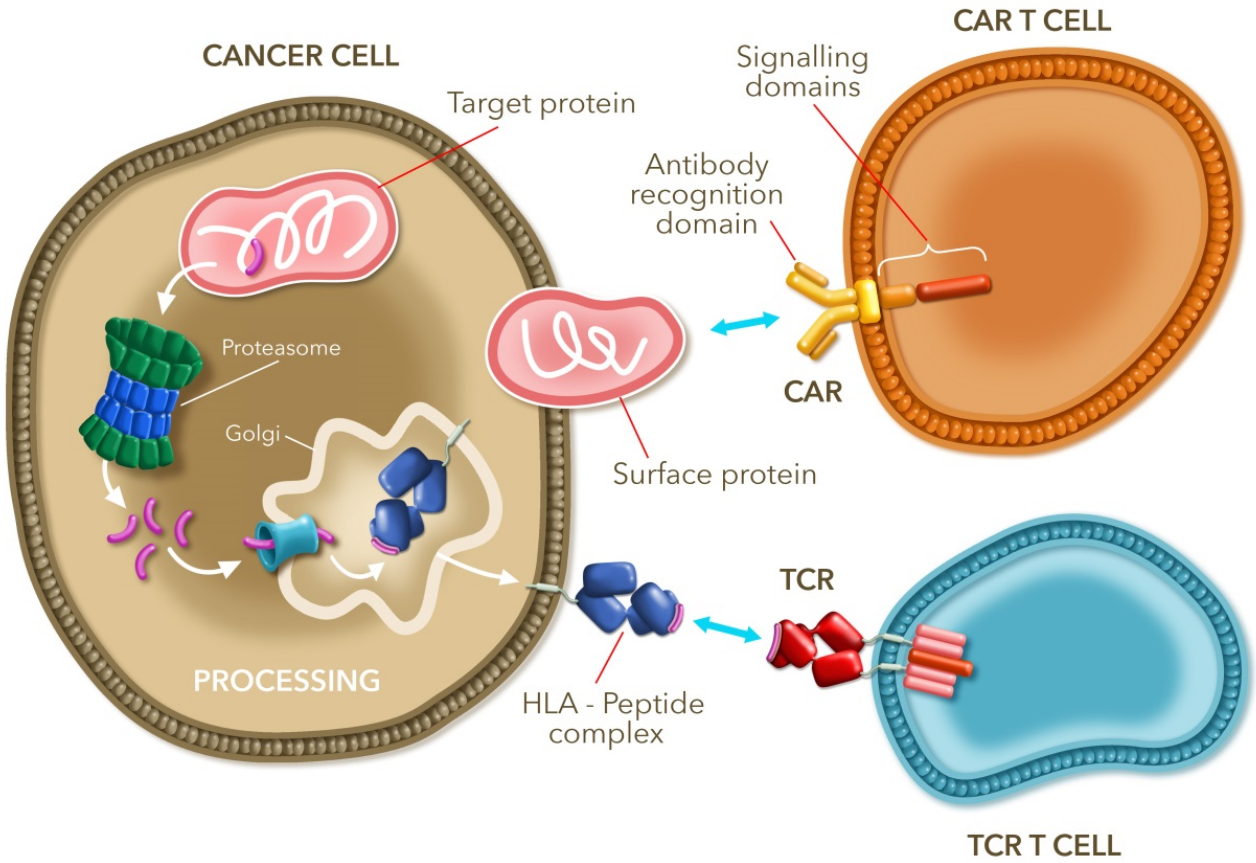
Maryland State Cancer Council Meeting -11/14/18

CAR-T Therapy for Blood Cancers

Aaron Rapoport MD
Gary Jobson Professor of Clinical Oncology
Director, Blood and Marrow Transplant Program
University of Maryland Marlene and Stewart Greenebaum
Comprehensive Cancer Center

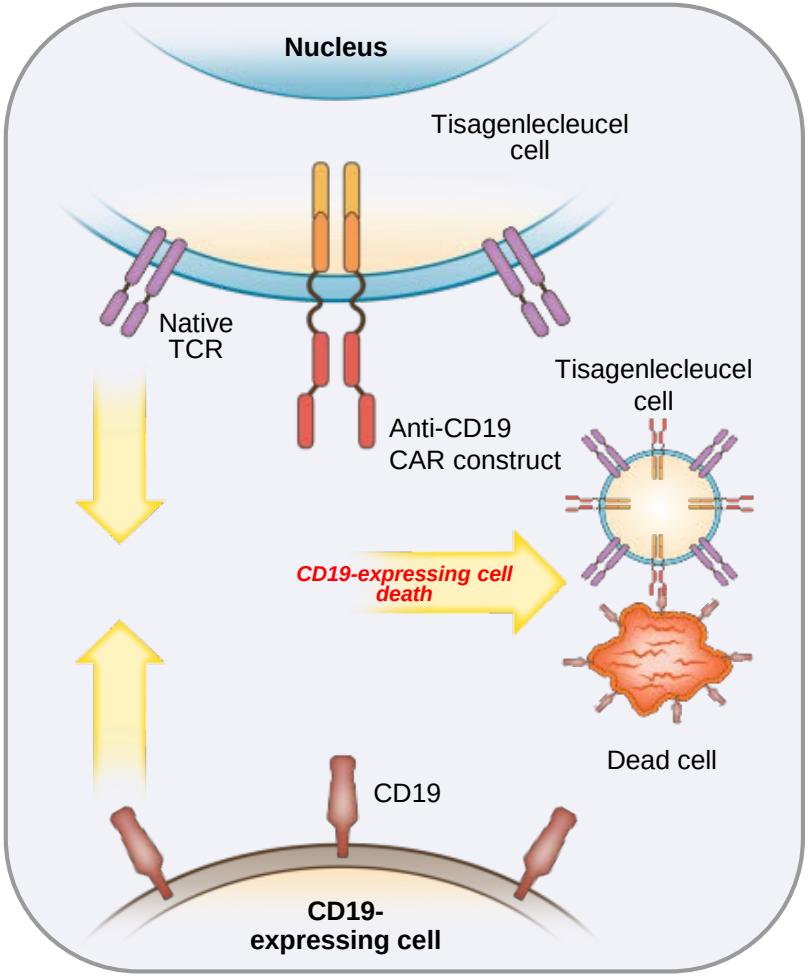
Engineered Autologous T cells: CARs vs TCR T cells



Tisagenlecleucel: Mechanism of Action

Mechanism of action

- Gene-transfer technology is used to stably express CARs on T cells, conferring novel antigen specificity[1,2]
- Tisagenlecleucel cells can thus be directed against any cell that expresses the CD19 surface antigen
- Tisagenlecleucel has demonstrated cytolytic activity against CD19-expressing cells in an antigen-dependent manner[1,3]



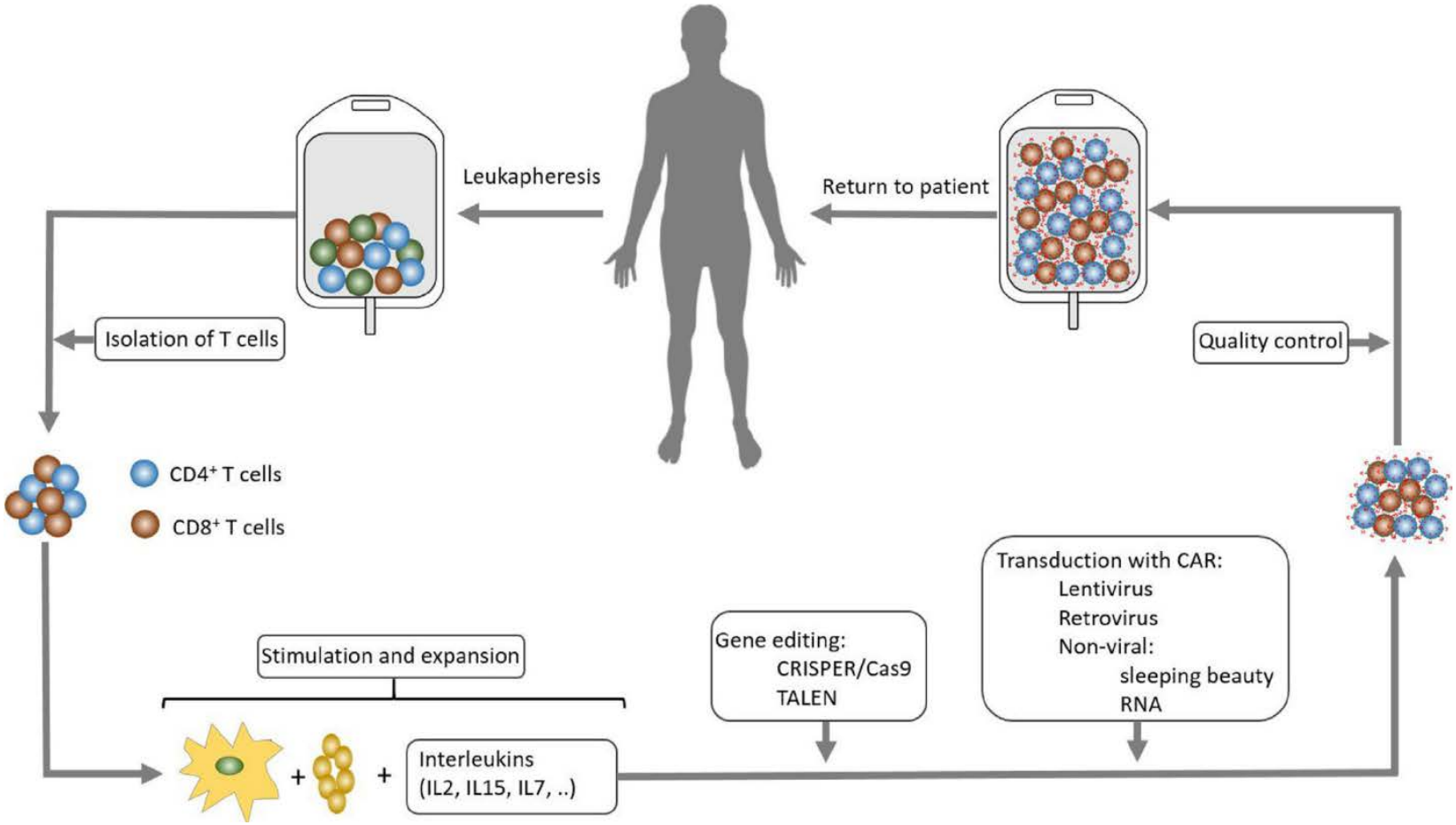
TCR, T cell receptor.

1. Milone MC et al. *Mol Ther.* 2009;17:1453-1464. 2. Hollyman D et al. *J Immunother.* 2009;32:169-180. 3. Kalos M et al. *Sci Transl Med.* 2011;3:95ra73.

Advantages of CAR-T Immunotherapy

- Kills “resistant” tumors (e.g. 17p – P53 del)
- Penetrates “sanctuary” sites (e.g. CNS)
- Through expansion and serial killing can eradicate “large” tumors
- Can generate long-lived “memory” responses to protect against recurrence
- High degree of specificity, avoids second malignancies and immunodepletion

Manufacturing



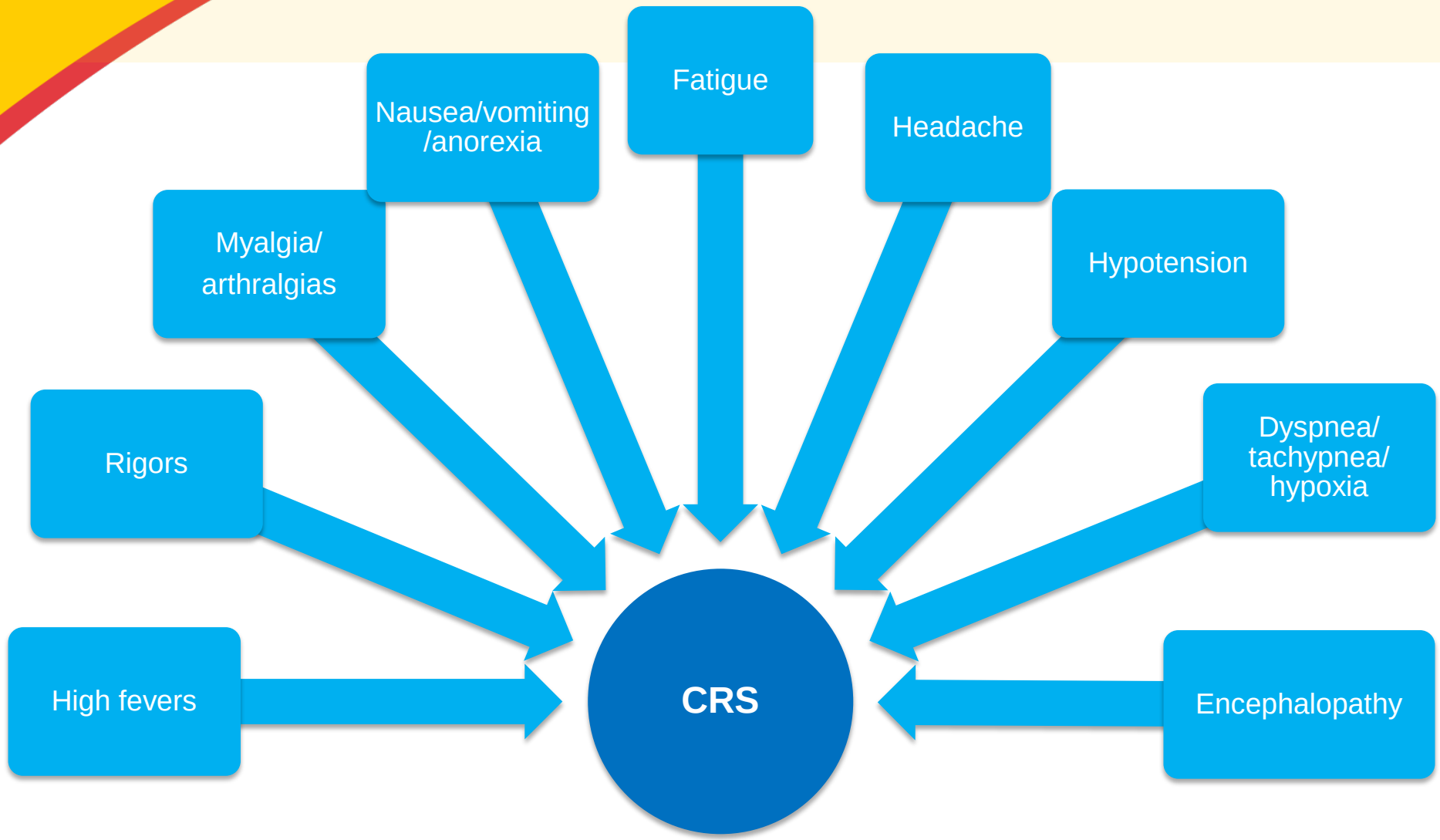
Manufacturing Time ~ 3 weeks

Efficacy Comparison

	Yescarta	Kymriah
Best ORR – 6 months	82% (101)	53% (81)
ORR per FDA label	**72% (101)**	**50% (68)**
Best CR	54% (101)	40% (81)
CR per FDA label	**51% (101)**	**32% (68)**
Long term	52 % (15.4 months, ASCO18)	n/a

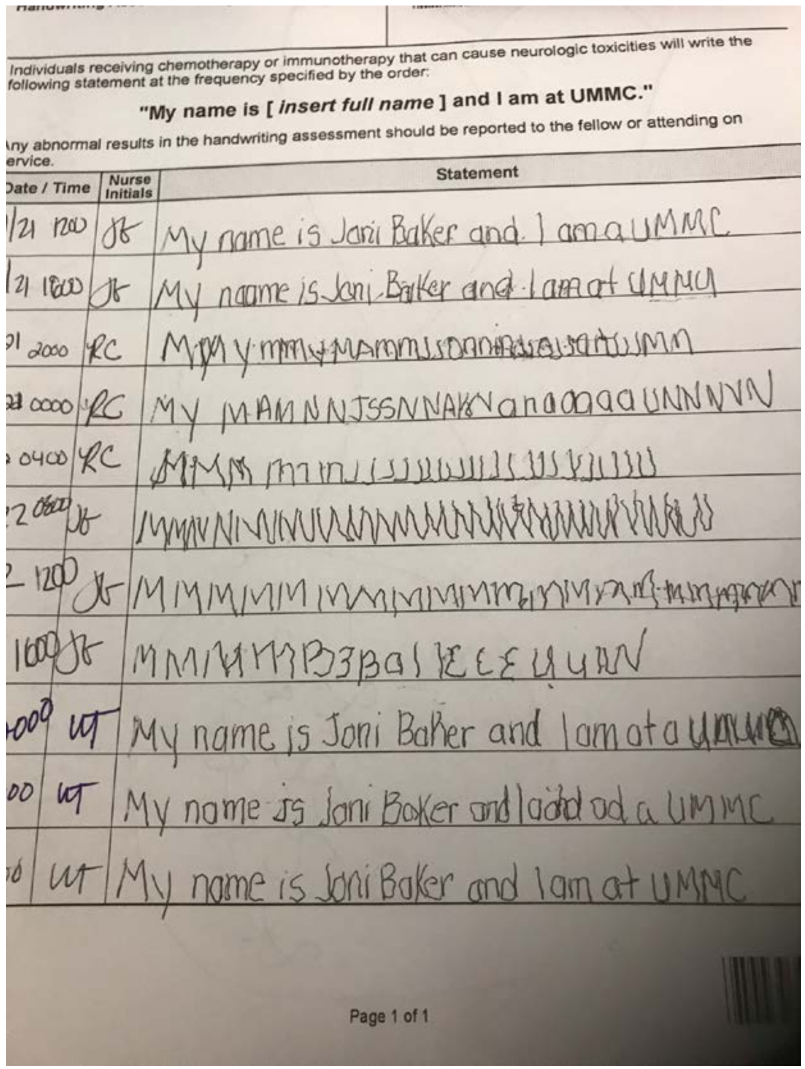
Scholar 1: ORR 26% and CR 8%

CRS- Cytokine Release Syndrome



Diagnosis based on <u>clinical</u> symptoms and events

Writing Sample in patient with Neurotoxicity



Individuals receiving chemotherapy or immunotherapy that can cause neurologic toxicities will write the following statement at the frequency specified by the order:

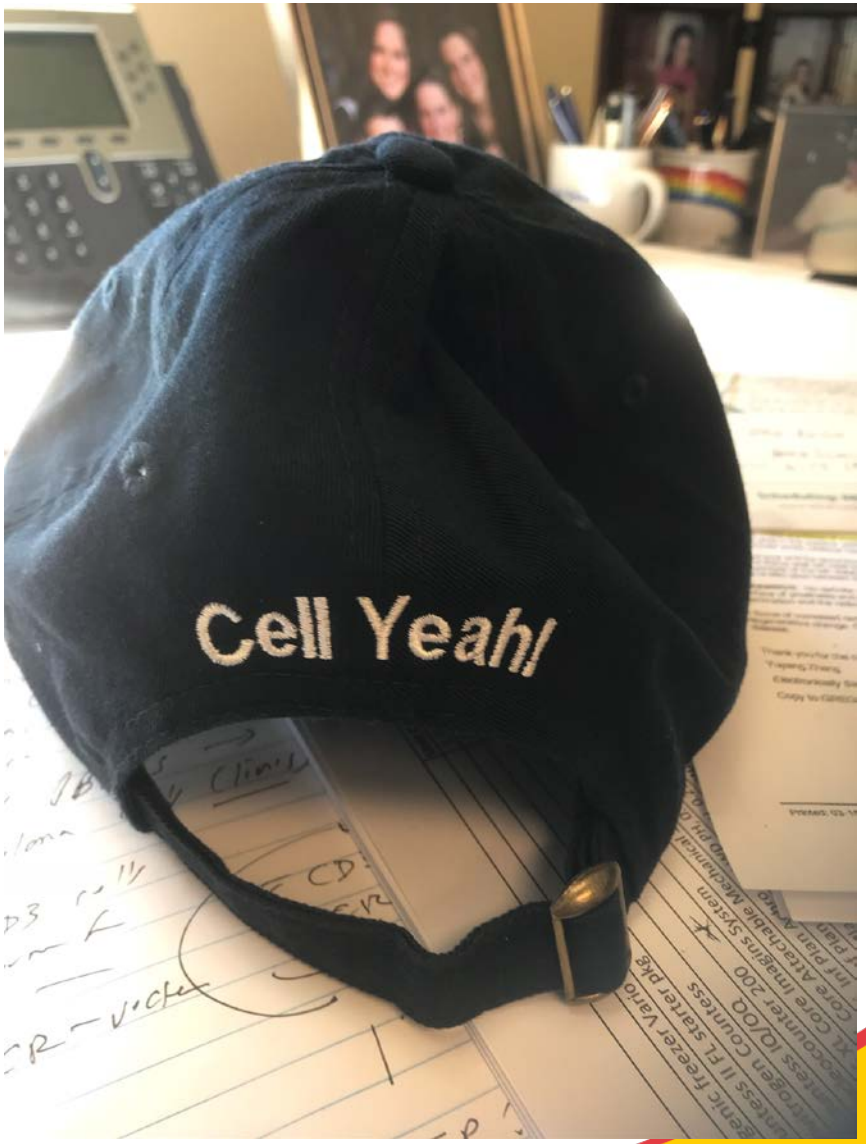
"My name is [*insert full name*] and I am at UMMC."

Any abnormal results in the handwriting assessment should be reported to the fellow or attending on service.

Date / Time	Nurse Initials	Statement
1/21 1200	JB	My name is Joni Baker and I am a UMMC
1/21 1800	JB	My name is Joni Baker and I am at UMMC
21 2000	RC	[illegible]
21 0000	RC	MY MAMNNJSSNNAKVanaaaaaUNNNVN
0400	RC	[illegible]
22 0800	JB	[illegible]
2 1200	JB	[illegible]
1600	JB	[illegible]
2000	WT	My name is Joni Baher and I am at a [illegible]
00	WT	My name is Joni Boker and I [illegible] a UMMC
00	WT	My name is Joni Baker and I am at UMMC

Page 1 of 1

UMGCCC was 20th Center in the USA to be qualified to Administer Yescarta (KITE CD19) CART Therapy for DLBCL



University of Maryland Experience

- Certified to administer Yescarta in February 2018.
- 20th Center in the US to be qualified to administer Yescarta
- ~500 have undergone REMS training (Cancer center, ICU, Neuro, General medicine, Residents and Fellows)
- 1st patient in March 2018.
- Total **23 patients** have been treated for lymphoma indication (including 21 on commercial platform and 2 on research trials).
- Additional **3 patients** treated for ALL

University of Maryland Greenebaum Comprehensive Cancer Center Now Among Select Institutions Certified to Administer CAR T-cell Therapy for Lymphoma

For Immediate Release March 20, 2018

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UMGCCC Treating Blood Cancer Patients with New Genetically Engineered Immunotherapy

Baltimore – The University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC) is now certified to offer a groundbreaking treatment for non-Hodgkin lymphoma, in which a patient's own immune cells are genetically engineered to recognize and attack the cancer.

Last October, the U.S. Food and Drug Administration (FDA) approved Yescarta, a chimeric antigen receptor (CAR) T-cell therapy, to treat adults with certain types of large B-cell lymphoma, a cancer of white blood cells. It was the FDA's second approval of a gene therapy to treat cancer since August 2017.

"We are very excited to offer this customized gene therapy to non-Hodgkin lymphoma patients who have not been helped by other treatments, such as chemotherapy or bone marrow transplants," says Aaron P. Rapoport, MD, the Gary Jobson Professor in Medical Oncology at the University of Maryland School of Medicine (UMSOM). "Having the ability to reprogram a patient's immune cells to attack their cancer is a powerful new tool, which will help many patients who have few treatment options."

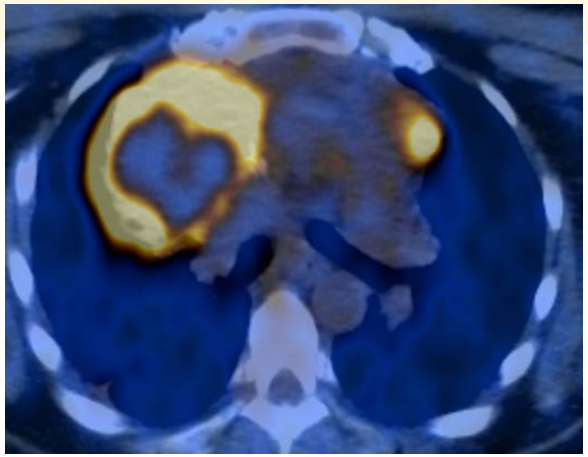
Fifty-four percent of large B-cell lymphoma patients who participated in a multi-center clinical study showed no evidence of cancer after treatment, even though they had received two or more previous therapies that had failed.

University of Maryland Experience

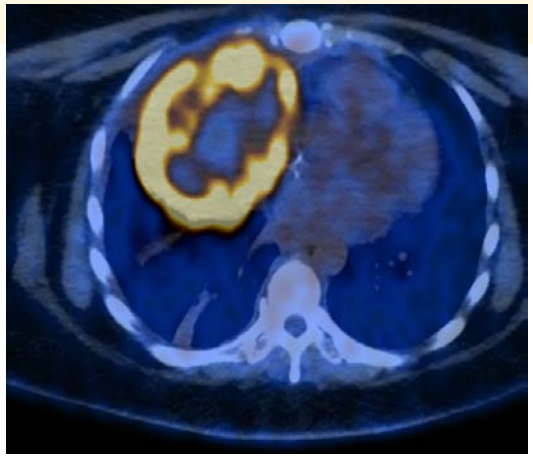
- 14/21 (67%) evaluable patients in CR (13) or PR(1).
- 2 patients treated and not yet evaluable
- 7/21 (33%) had progression of disease; 3 patients alive on additional therapies, 4 patients died.
- No CRS nor Neurotoxicity related deaths.
- Close collaboration with critical care, consultation (Neurosurgery, Neurology, ID) teams essential for program success

University of Maryland Experience

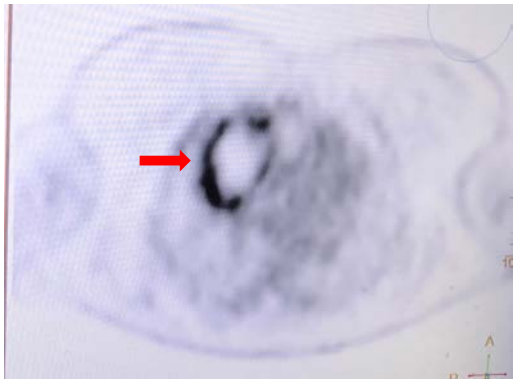
- 33 year old lady, healthy, with ABC-type large cell lymphoma.
- Progressive disease after R-CHOP X 6.
- Progressive disease after Salvage chemo with R-GDP.
- LOS- 9 days
- Grade 1 CRS, No neurotoxicity



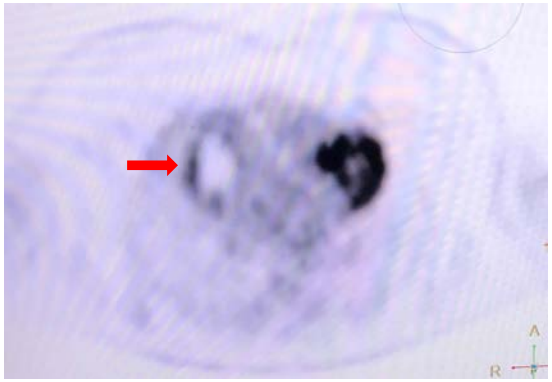
Baseline- pre-CAR-T



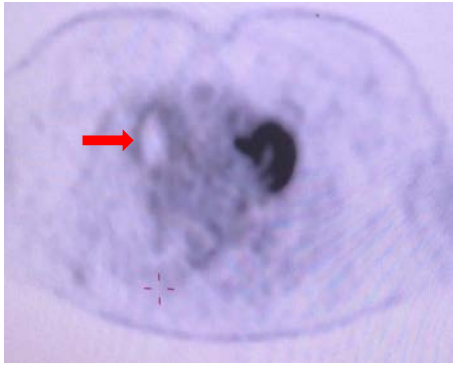
Baseline- pre-CAR-T



Day 30, PR



Day 80



Day 120, CR

CD20-Directed AT-CAR-T (Developing Trial)

- **A**ntibody-**T**agged “universal” CAR therapy
- First-in-Human trial planned using Biotin-tagged-anti-CD20 MoAb and AT-CAR cells for B cell lymphoma
- Collaboration with Miltenyi/Lentigen which purchased Living-Pharma company established by Dr. Eduardo Davila

Questions

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