

SITC Hot Topics

Pediatric/Young Adult ALL CD19CAR T Cell Protocol PLAT-02: Phase I Toxicity Profile

Michael Jensen, MD

Sinegal Endowed Professor of Pediatrics, UWSOM
Director, Ben Towne Center for Childhood Cancer Research



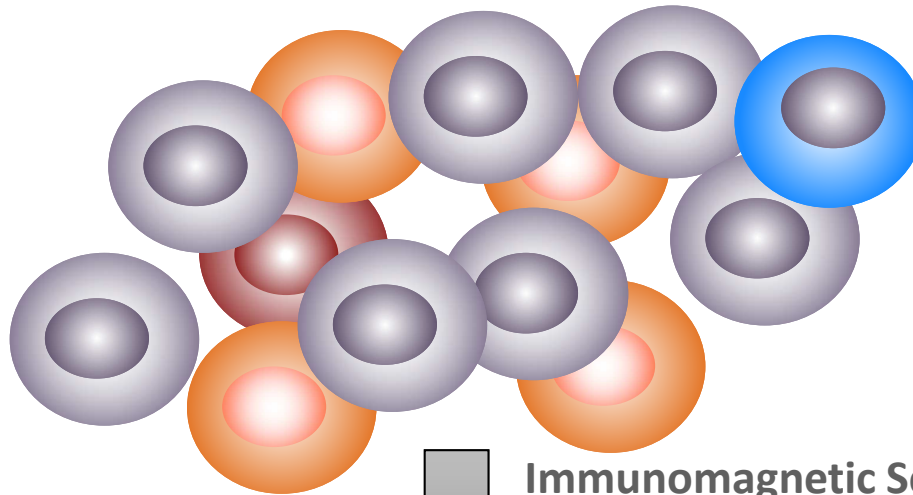
Pediatric Leukemia CD19CAR

Adoptive Therapy Trials

Site	Defined Cells	Vector	scFv	ECD Spacer	Co-stim	Selection/ Suicide
MSKCC	No	Retro	SJ251	CD28partial	CD28	No/No
CHOP	No	Lenti	FMC63	CD8hinge	4-1BB	No/No
NCI	No	Retro	FMC63	CD8hnge	CD28	No/No
Baylor	EBV	Retro	FMC63	Full IgG1	CD28	No/No
SCRI	CD4:CD8	Lenti	FMC63	IgG4hinge	4-1BB	Yes/Yes

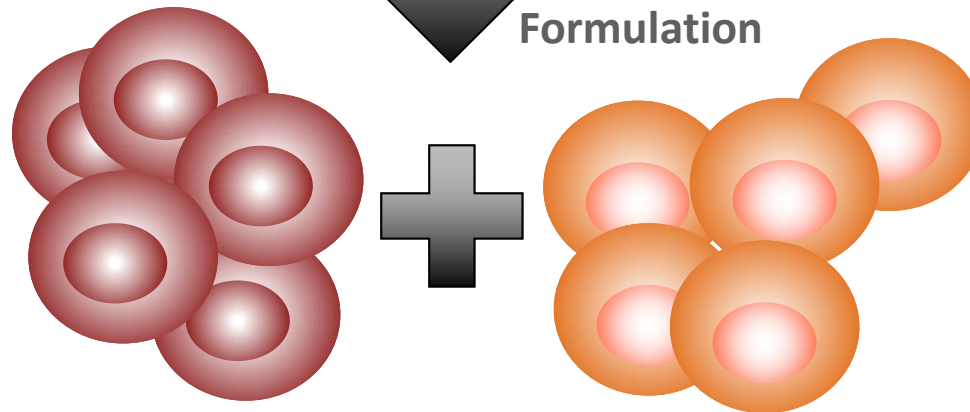
PLAT-02 Defined Product Composition:

PBMC



Immunomagnetic Selection
Lentivirus Transduction
Expansion
Formulation

**FORMULATED
CAR T CELL
PRODUCT**



100% CAR⁺CD8⁺

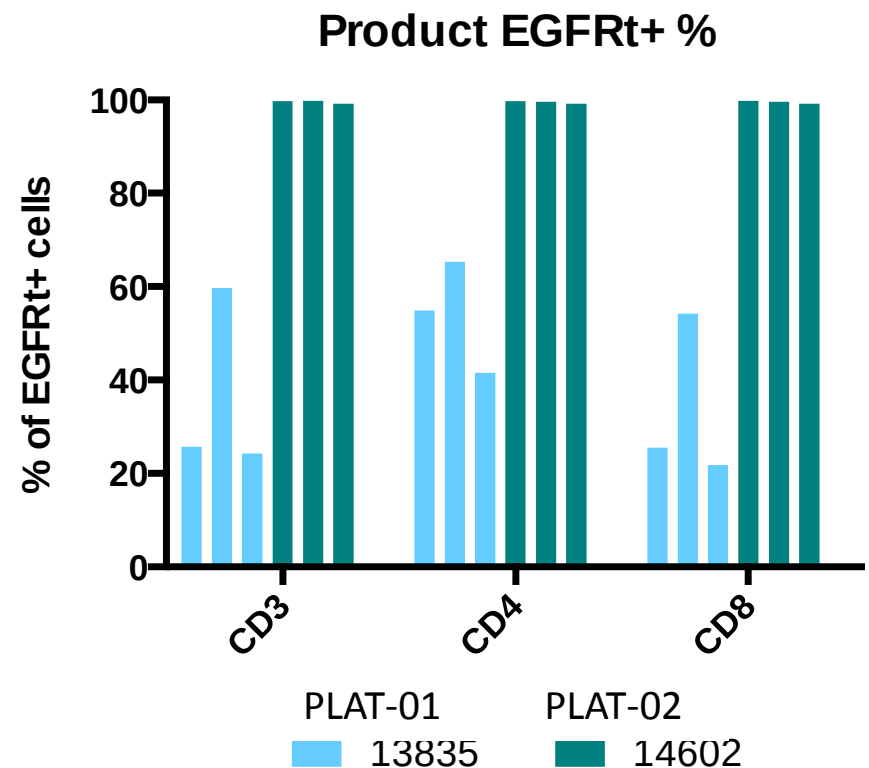
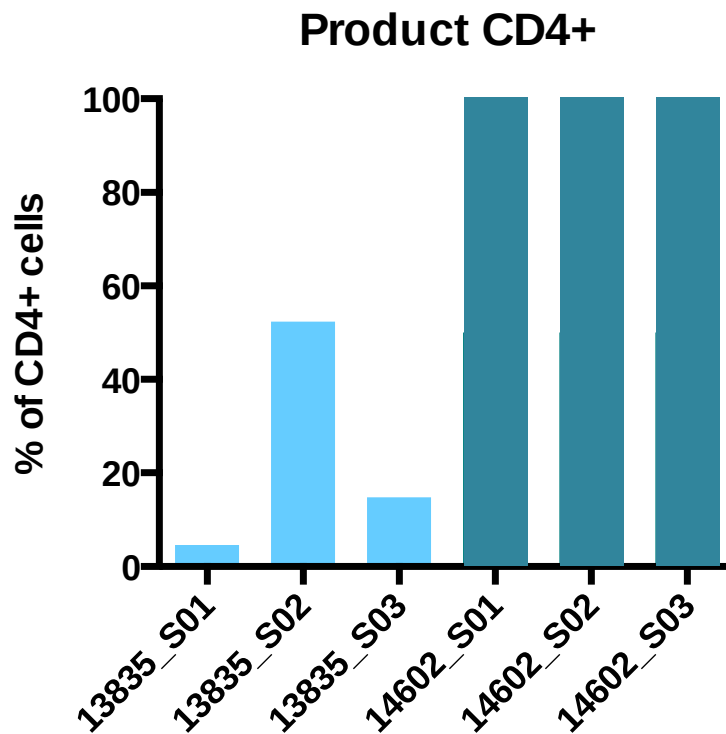
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100% CAR⁺CD4⁺

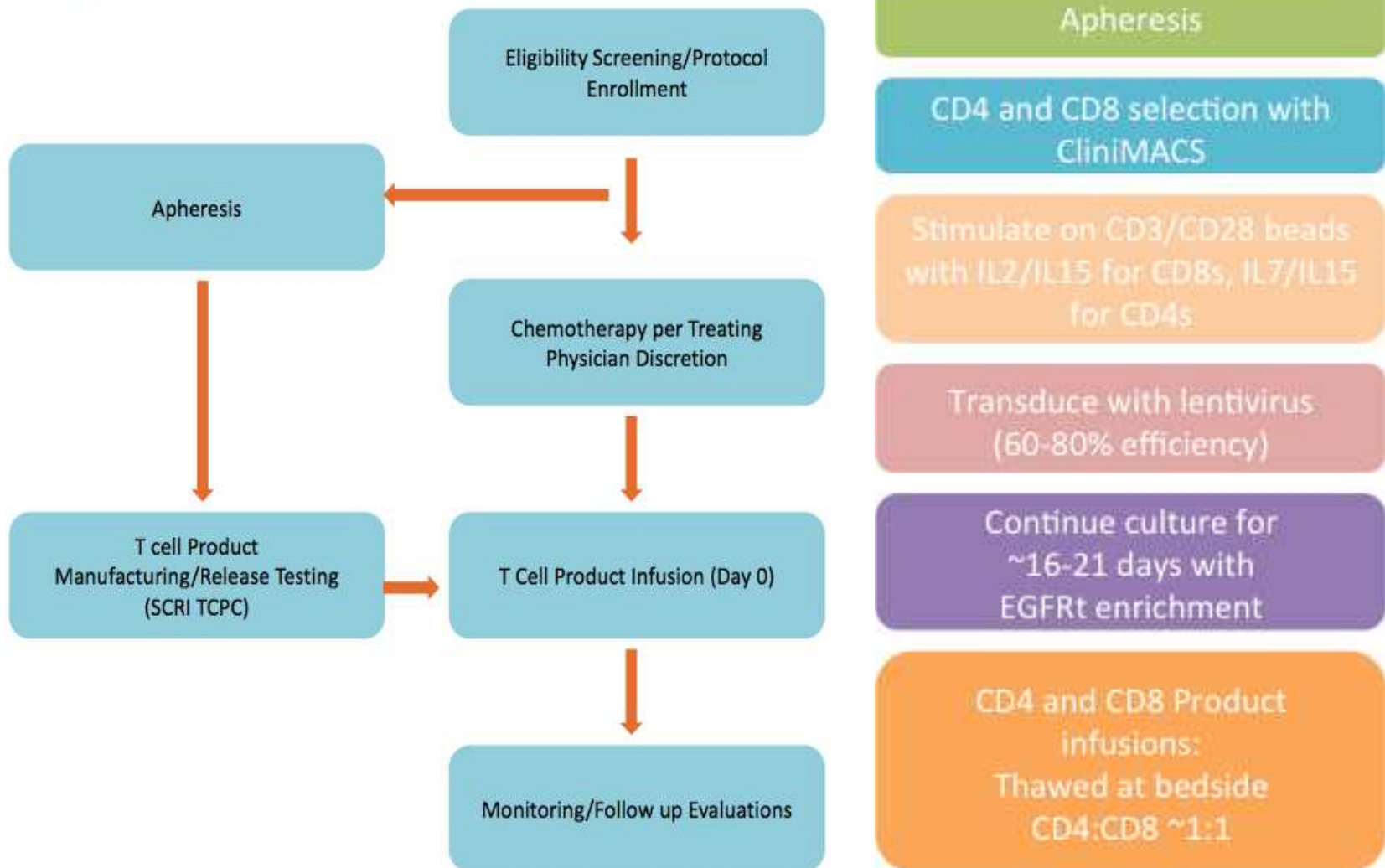
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Defined Composition CAR T Cell Product Uniformity Compared to Unformulated Products



PLAT-02: A Phase 1/2 Trial of Defined Composition CD19CAR T Cell Adoptive Therapy For Refractory Relapsed and Post-HSCT Recurrent Pediatric ALL

EXPERIMENTAL DESIGN SCHEMA



PLAT-02: Day +7 Tumor Burden vs Response

Marrow Dz Burden

Response

Dose Level 3
($5.0 \times 10^6/\text{kg}$)

Dose Level 2
($1.0 \times 10^6/\text{kg}$)

Dose Level 1
($0.5 \times 10^6/\text{kg}$)

Dex



CRS Grading and Management

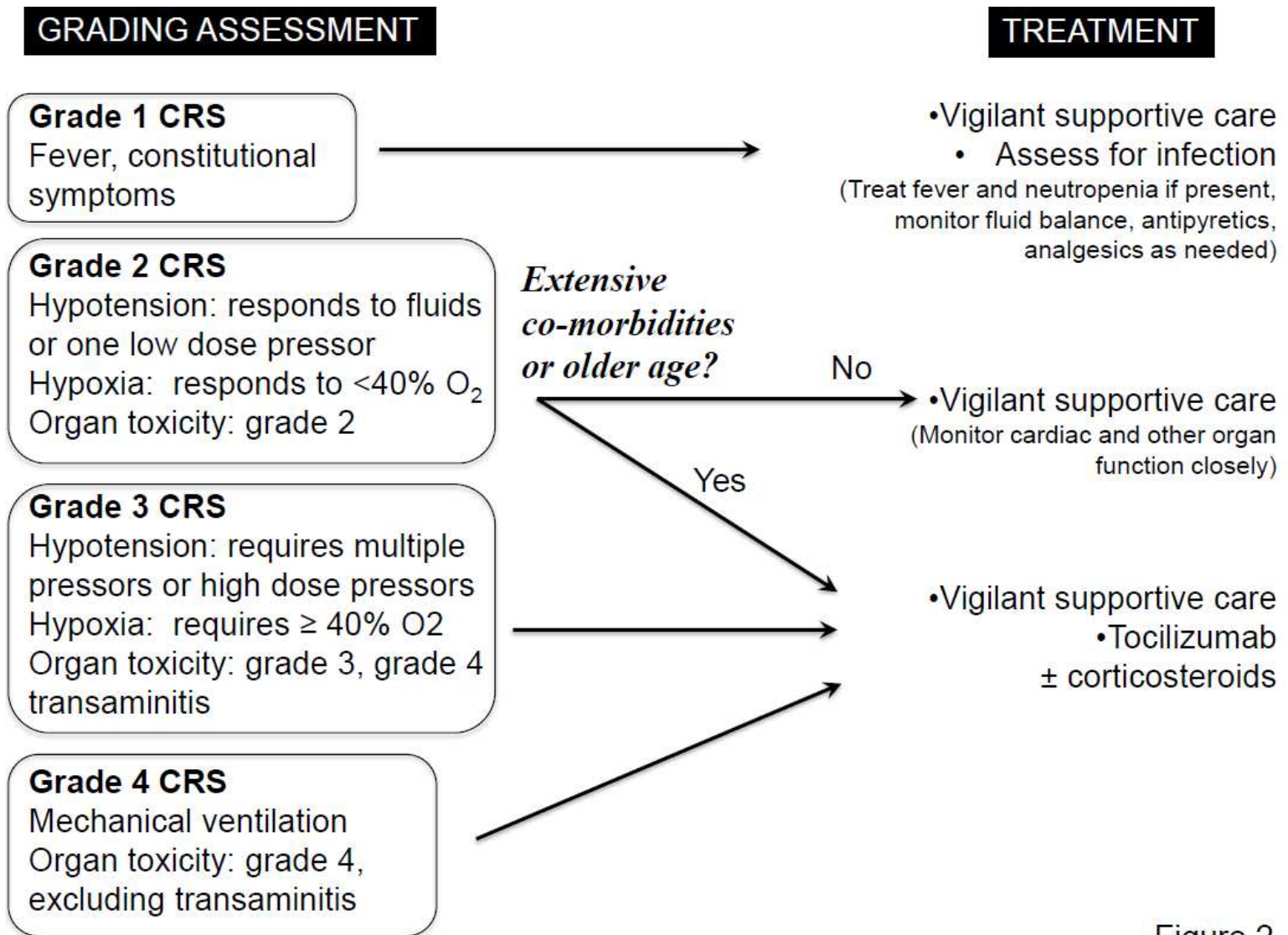
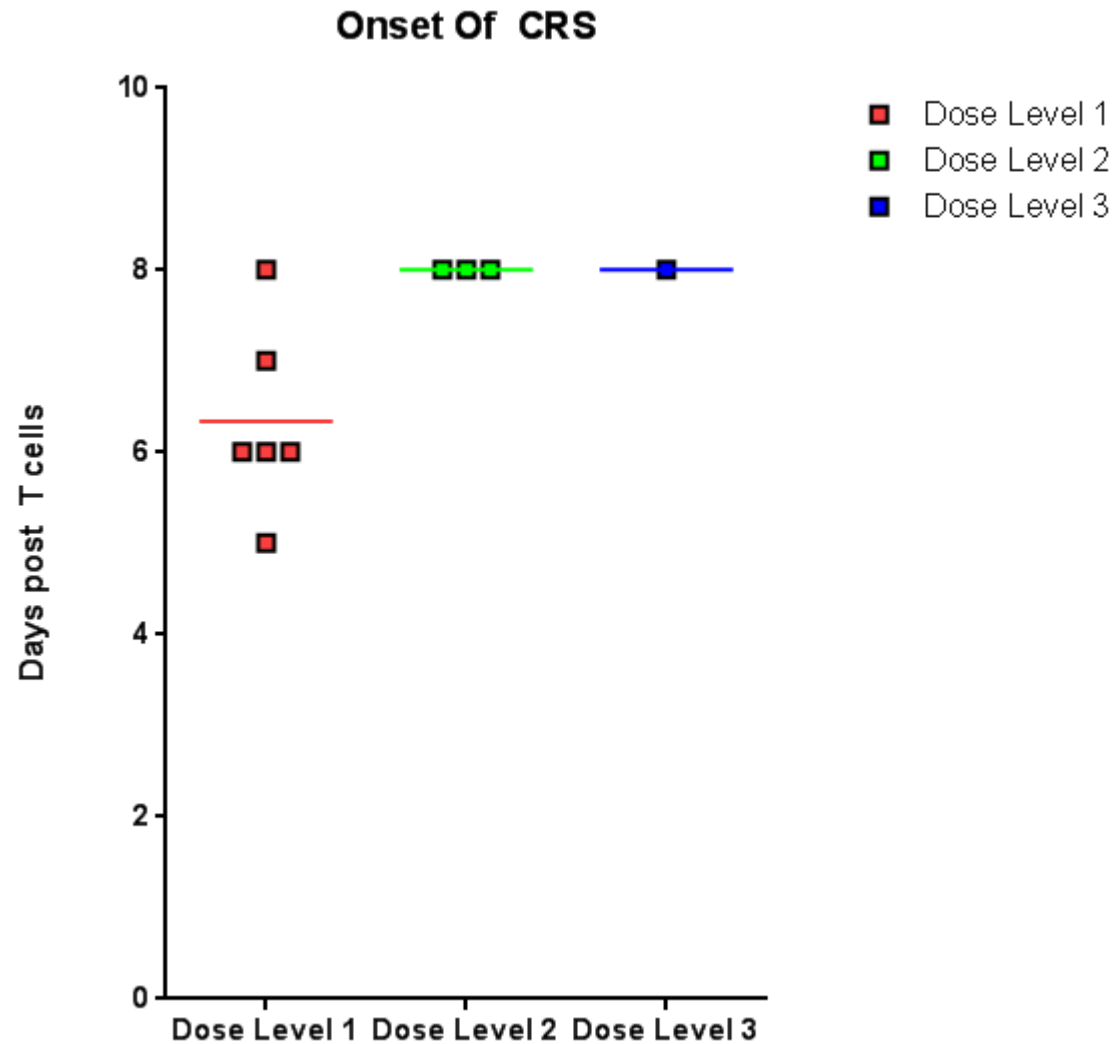
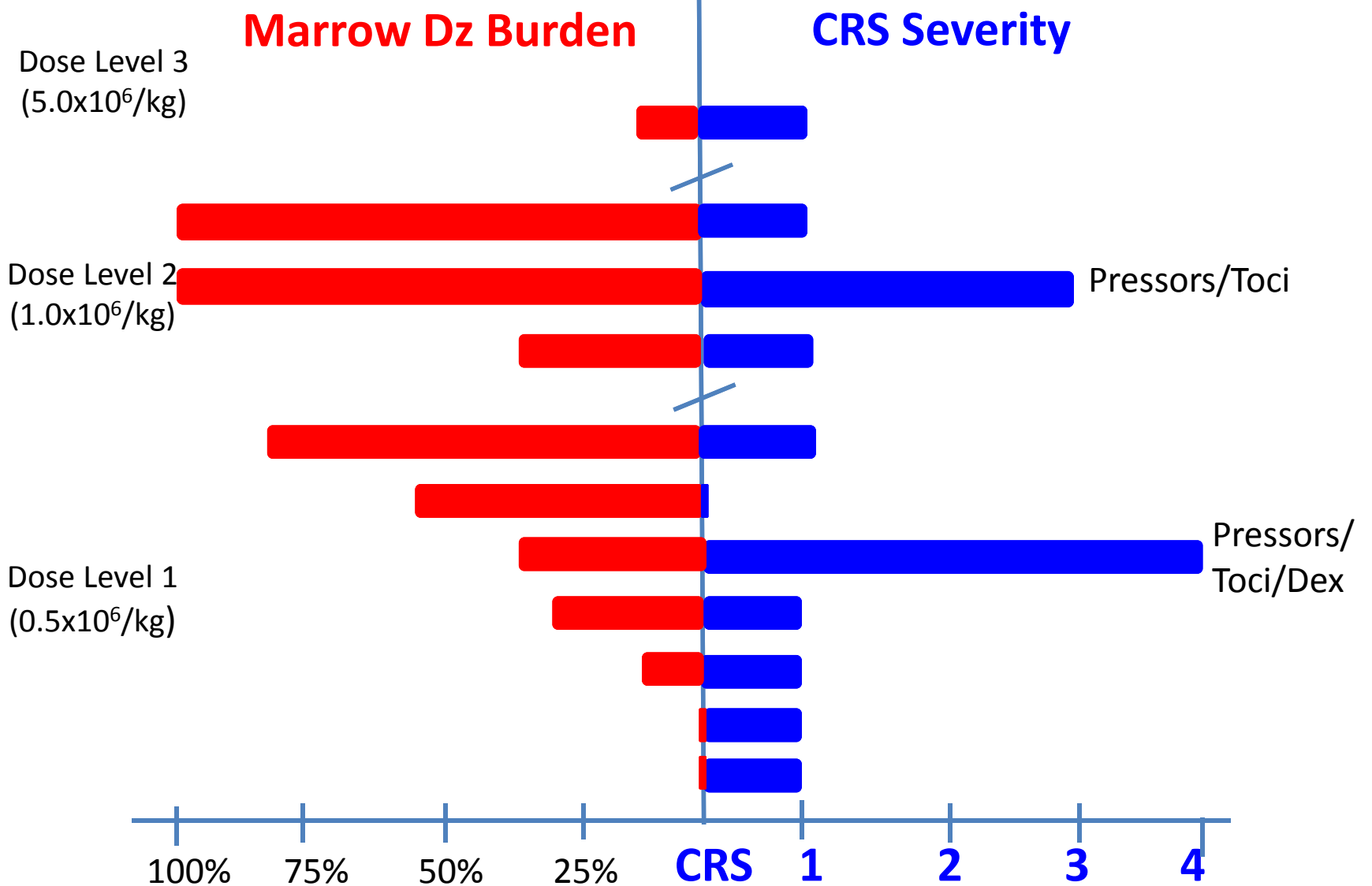


Figure 2

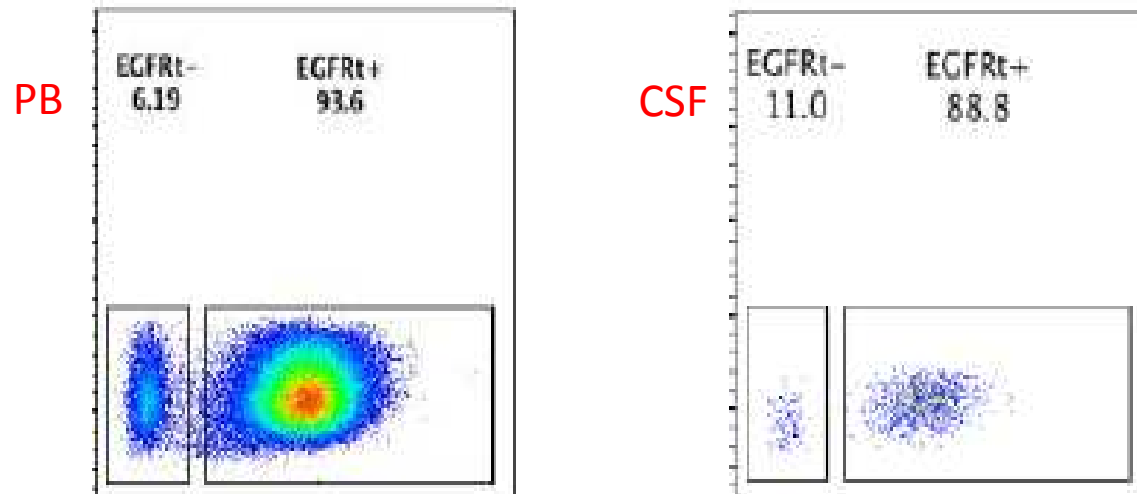
CRS Timing of Onset



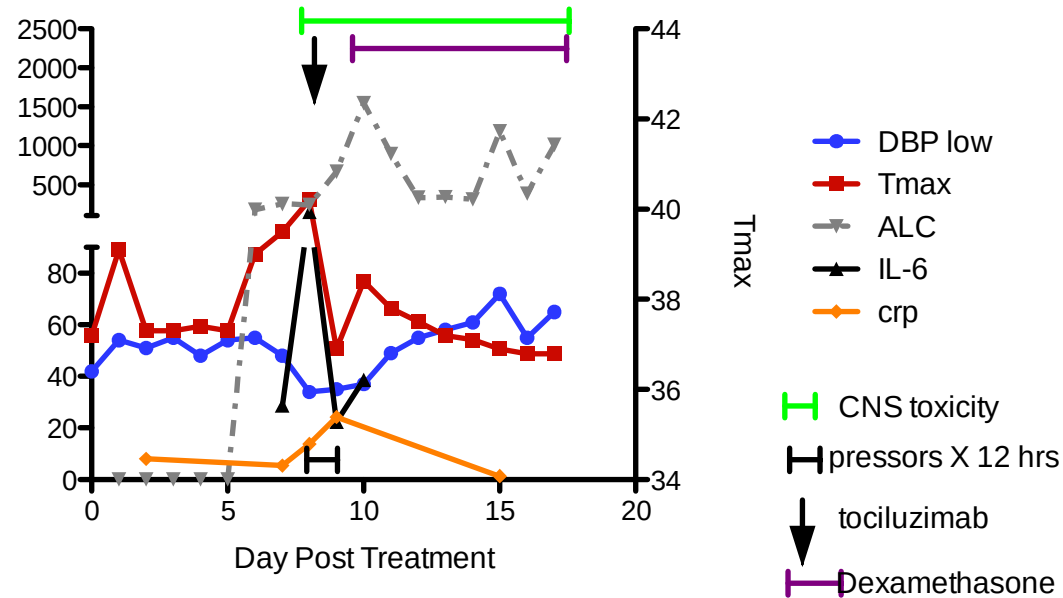
PLAT-02 CRS Profile



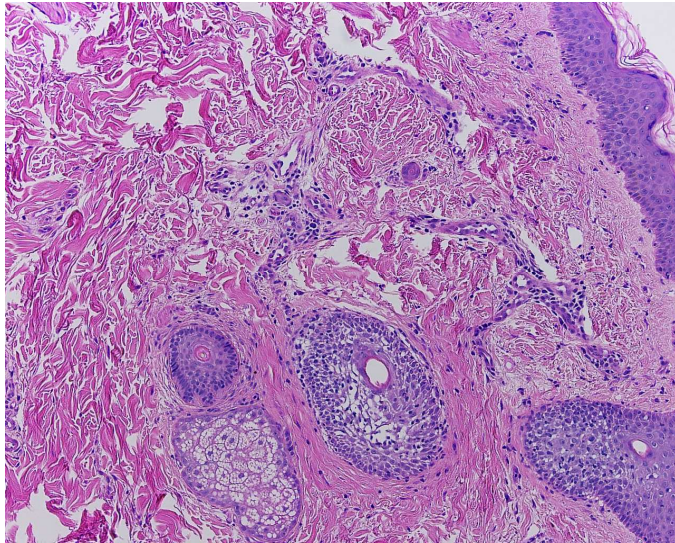
S02 CAR T Cell Engraftment-



14602-S02

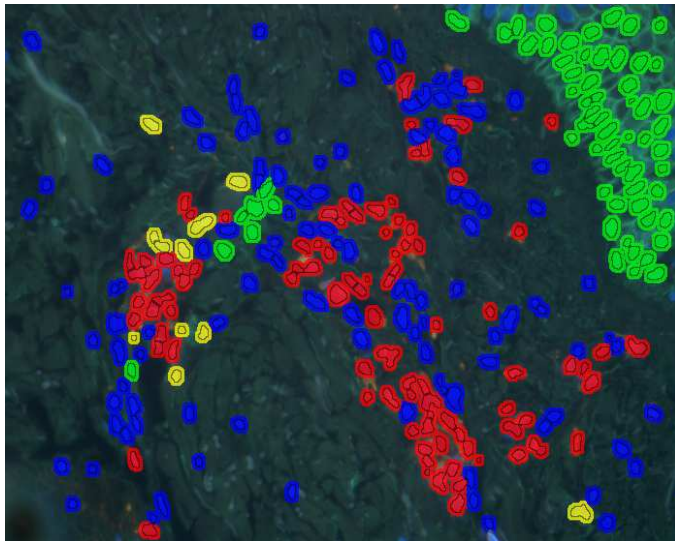


S03: De Novo Acute Skin GVHD post CRS

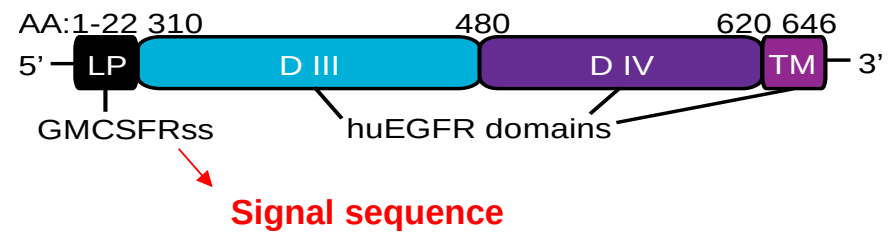
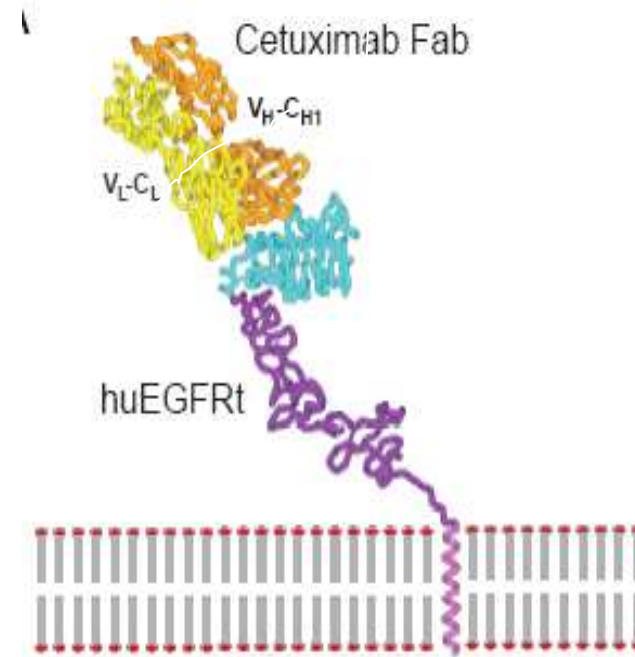
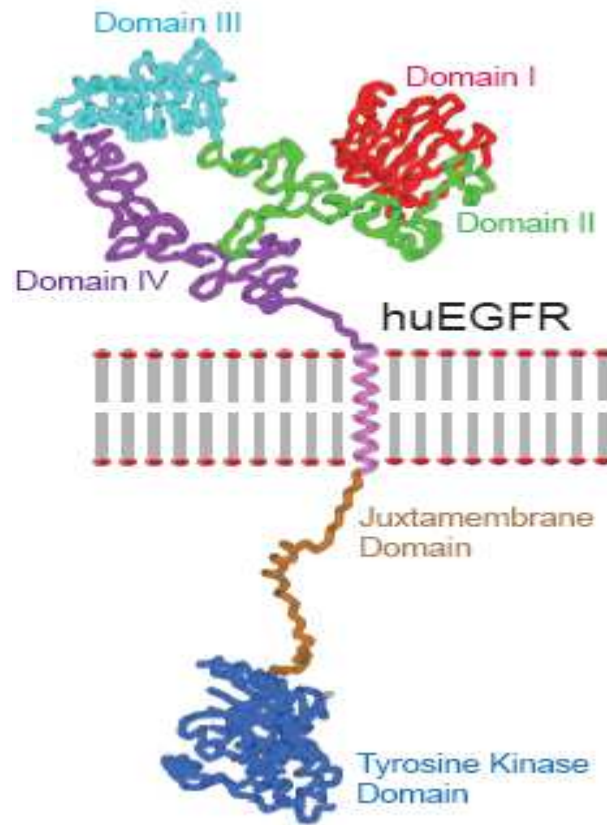


Peripheral Blood:
70% of CD3⁺ T cells are
EGFRt⁺

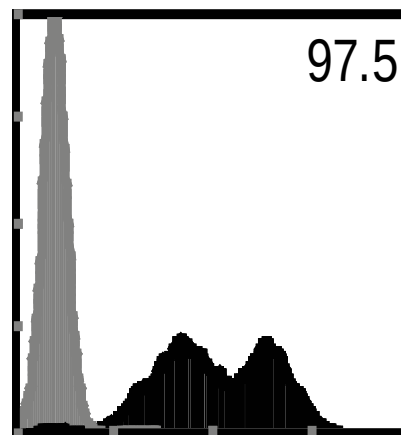
Skin Bx:
7% of CD3⁺ T cells are
EGFRt⁺



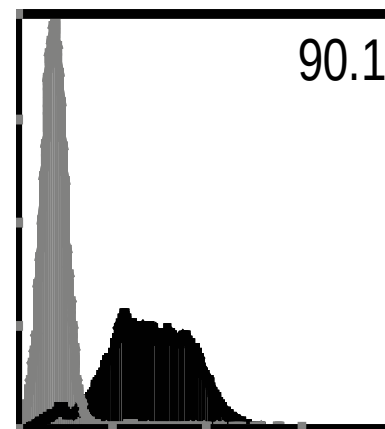
Construction of truncated human EGFR (huEGFRt) with retention of Cetuximab binding epitope



huEGFRt can be incorporated into lenti-viral vector for co-expression with CD19 chimeric antigen receptor (CD19CAR)

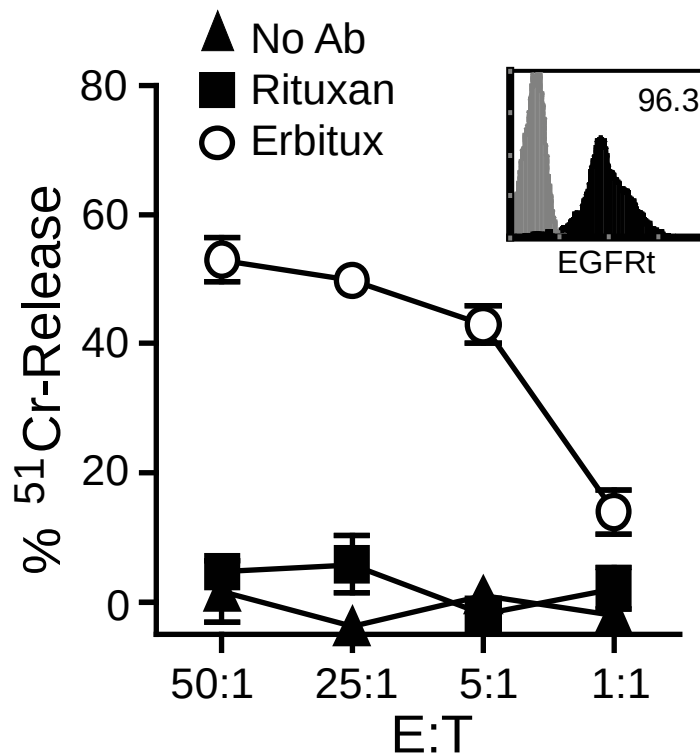


CD19CAR
(anti-Fc-Bio+SA-PE)



EGFRt
(Ctxmb-Bio+SA-PE)

huEGFRt sensitizes huEGFRt⁺ human T cells to Cetuximab mediated ADCC



Targets: ⁵¹Cr-labeled huEGFRt⁺ T cells;

Effectors: GM-CSF stimulated huPBMC

Mixed with 1ug/mL Cetuximab or RituxanTM(anti-CD20) for 4hr

In vivo: Depletion of EGFRt+ cells

Frequency of transferred cells in blood (FACS analysis)

24h post Erbitux

24h post Rituxan

