

Adoptive cell Therapies

NYESO/LAGE-1 TCR

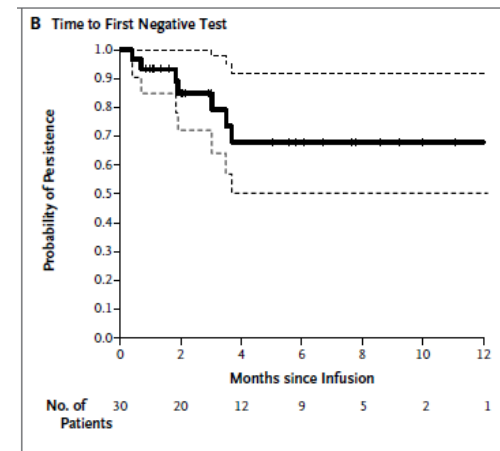
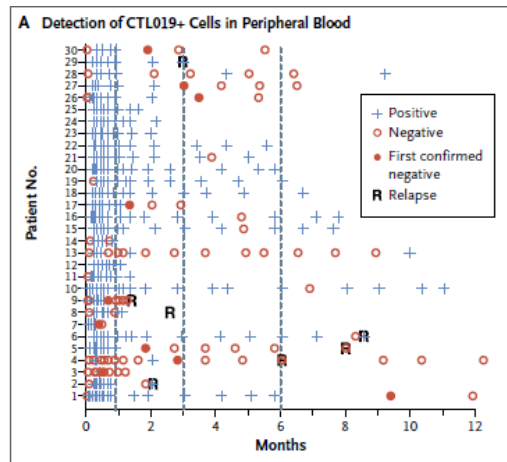
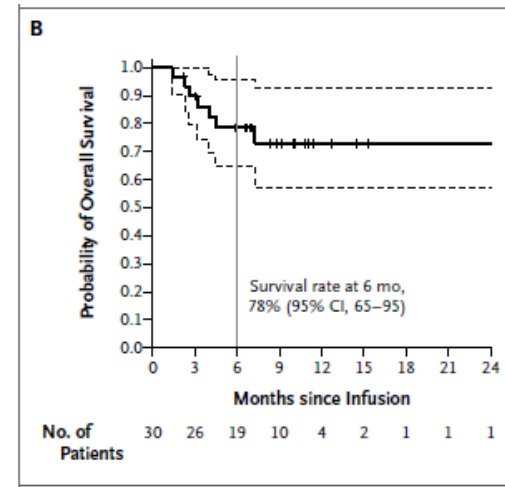
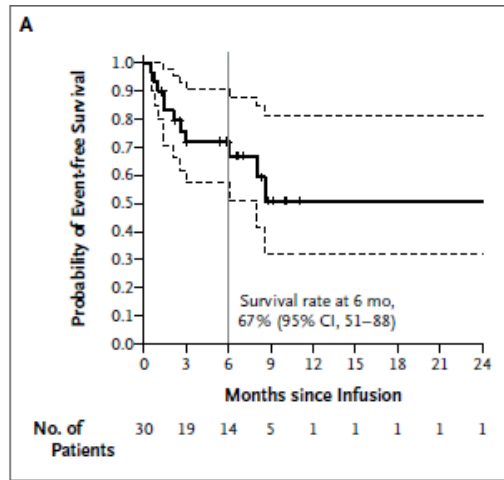
CANCER
PROGRESS
by Defined Health

Cancer Progress by Defined Health
New York, NY | March 8-9, 2016

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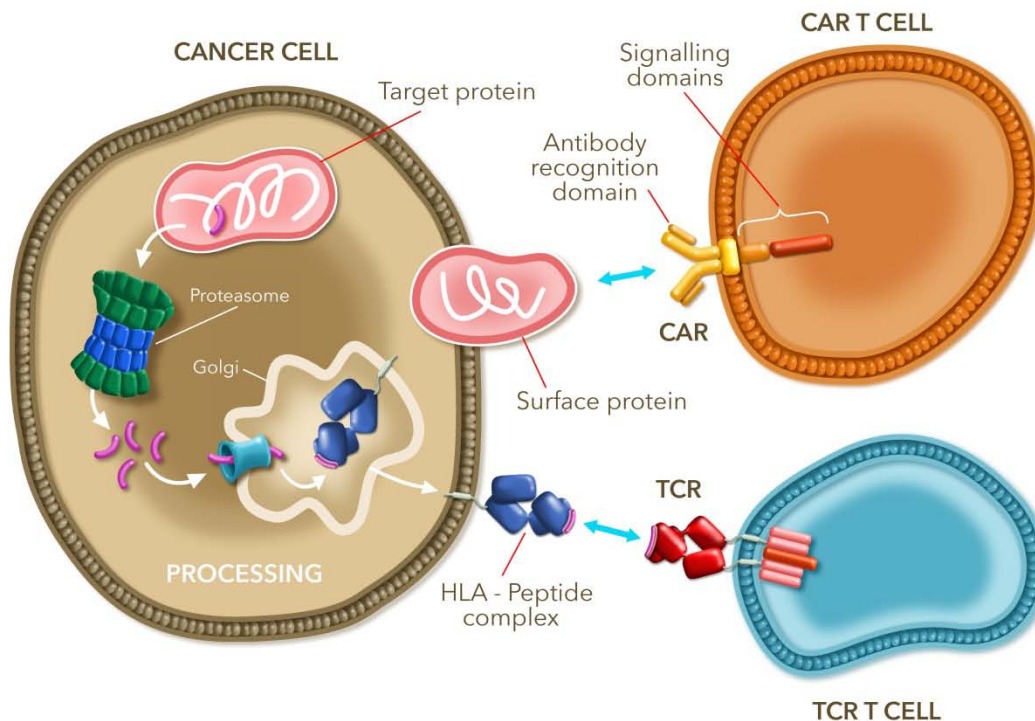
Chimeric Antigen Receptor T Cells Against CD19 Induce Sustained Remissions in ALL



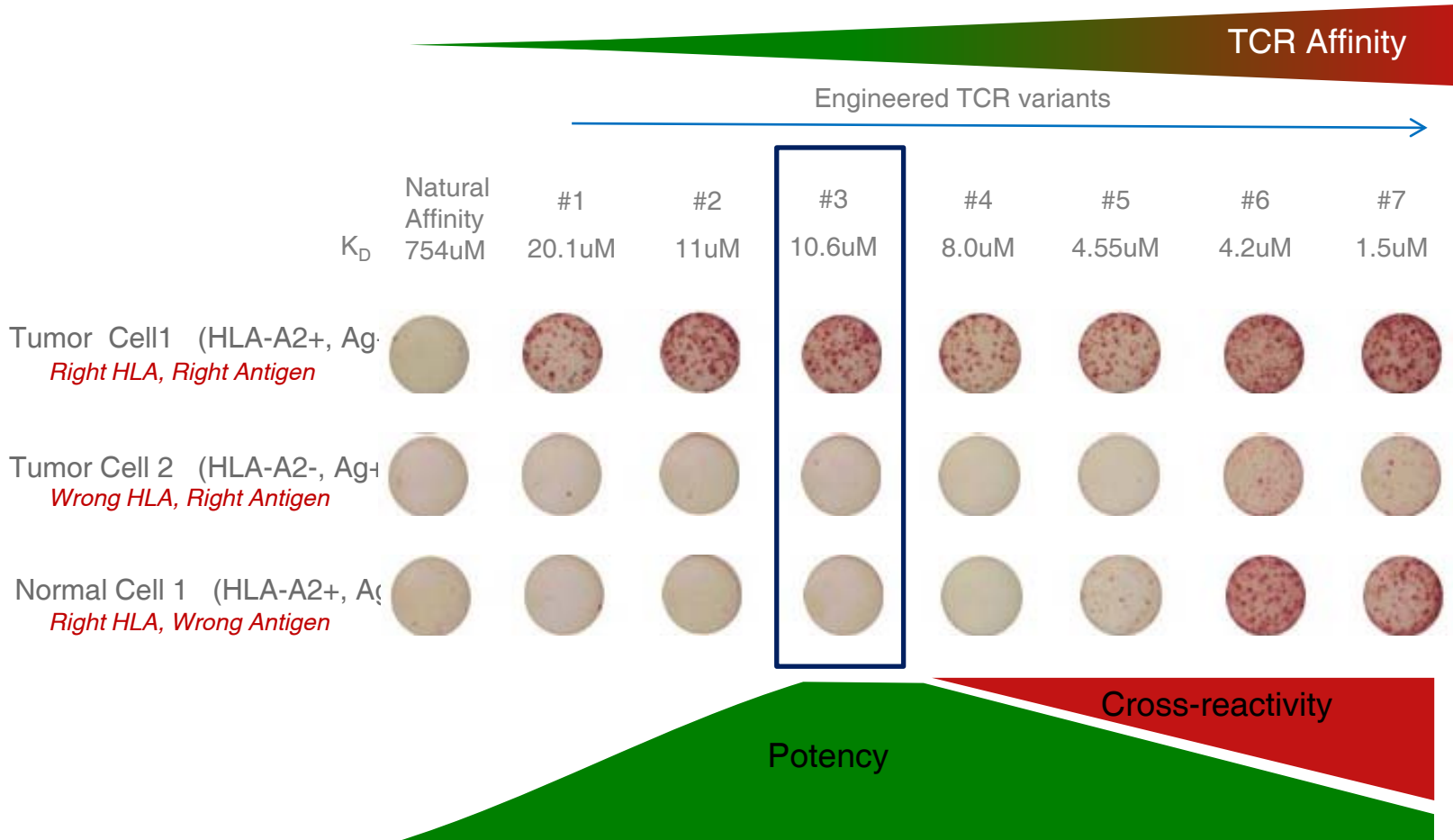
Maude S. N Eng J Med 371:1507, 2014

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TCR Therapeutics Recognize Intracellular Cancer Antigens

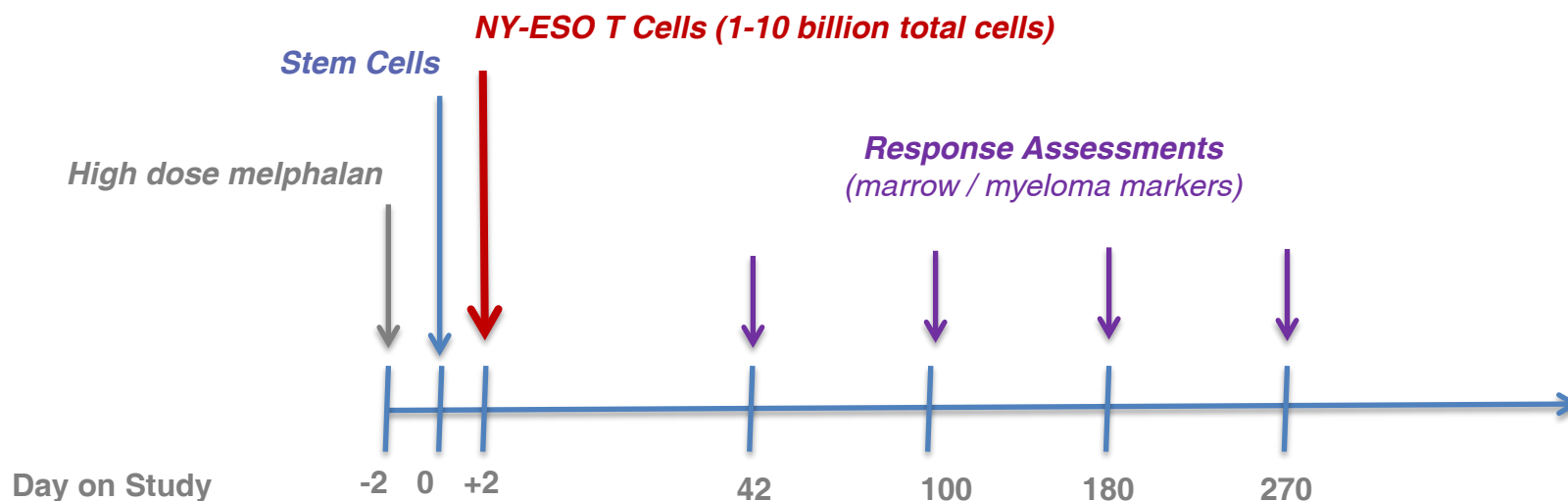


TCR Affinity Maturation



#3: Potent and specific

Phase I/II Multiple Myeloma



- All enrolled patients (n=25) had symptomatic myeloma with active disease
- High risk population
 - Average of 3 prior Rx (5 prior ASCT)
 - Twelve with cytogenetic abnormalities, including seven categorized as high-risk
- Patients conditioned with high-dose melphalan followed 2 days later by ASCT
- Advanced MM frequently expresses the CT antigens NY-ESO-1 or LAGE-1
 - Associated with poor prognosis in myeloma
(Dhodapkar et al, Cancer Immun, 2003; Atanackovic et al, Clin Cancer Res, 2009; and others....)

Response Assessment

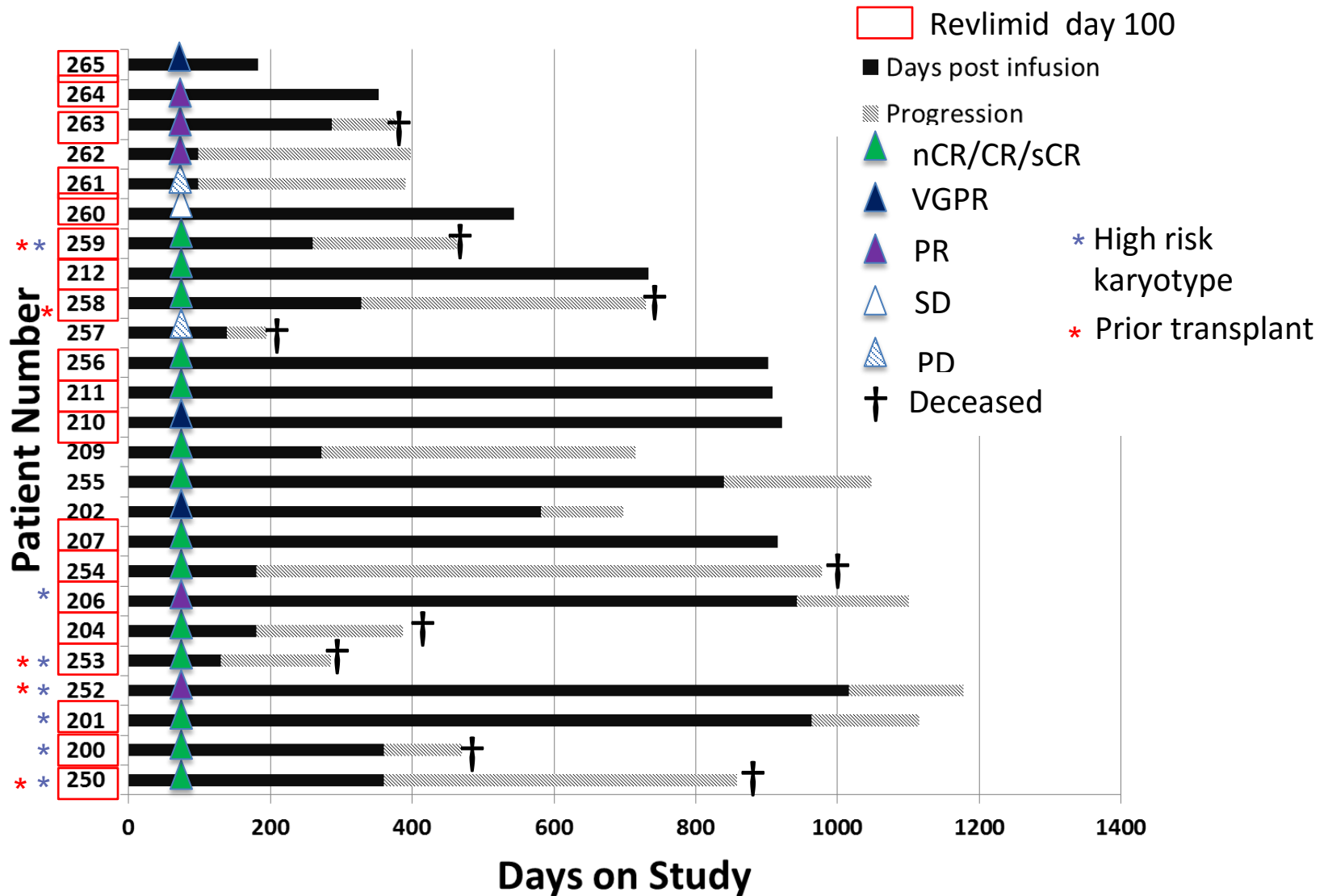
Best Response by day 100	Number of patients	% Total
CR	3	14%
nCR	10	45%
VGPR	2	9%
PR	5	23%
SD	1	5%
PD	1	5%
Not assessable*	3	NA
Total evaluable	22	100%

* Patients with VGPR or better going into transplant

- Two year overall survival (OS) and progression free survival (PFS) as of November 2015
 - 16/25 patients remain alive; 8/25 remain in remission
 - Median PFS = 19.1 months; Median OS = 32.1 months

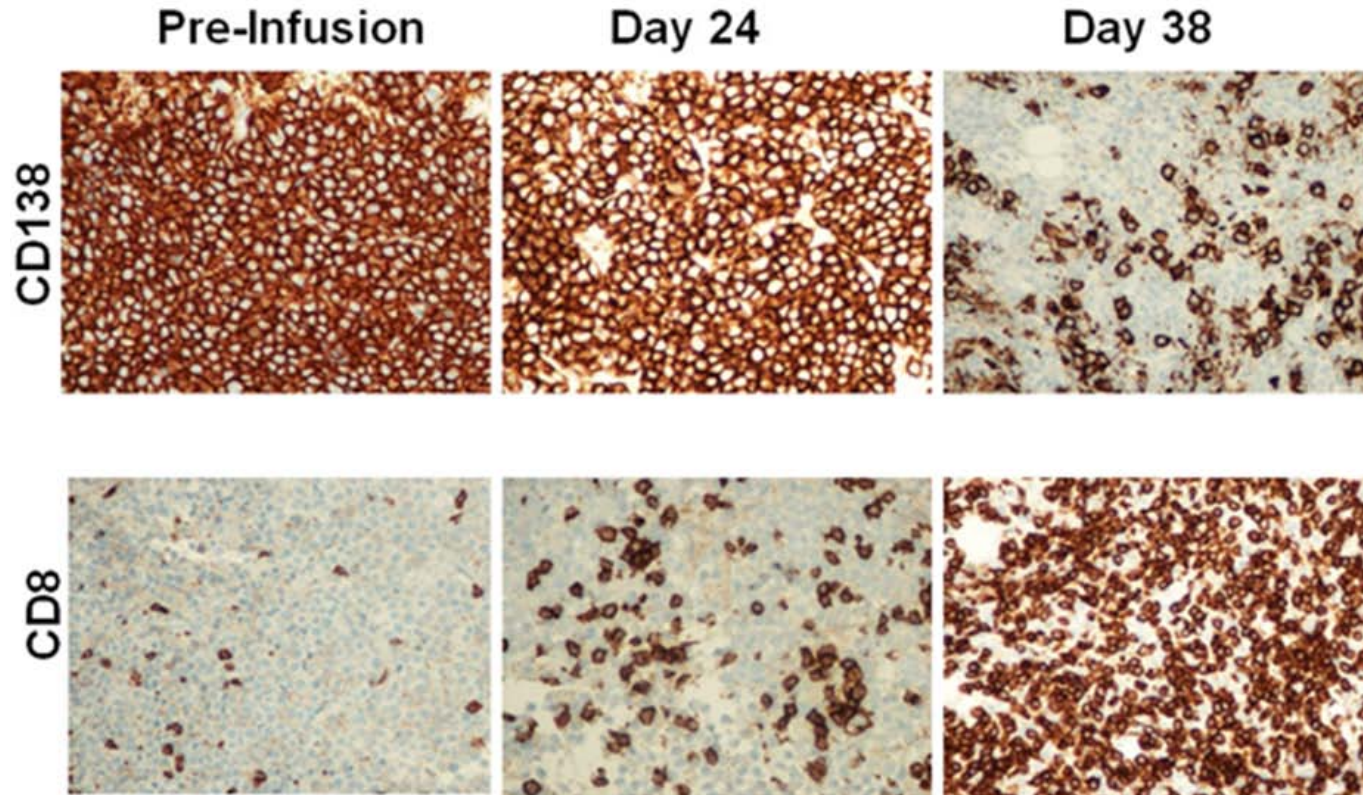
Rapoport et al. Nat Med 21(8):914-21

Duration of Response

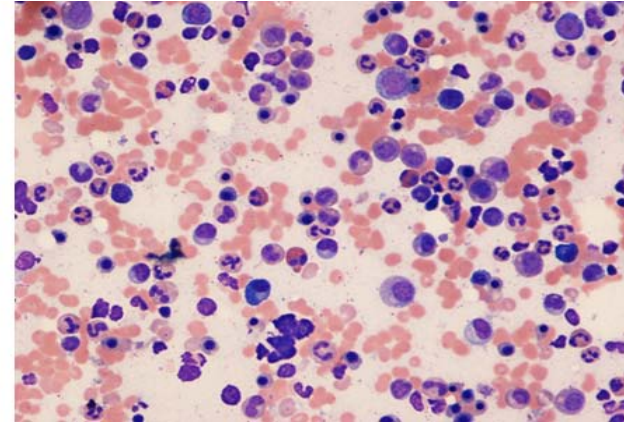
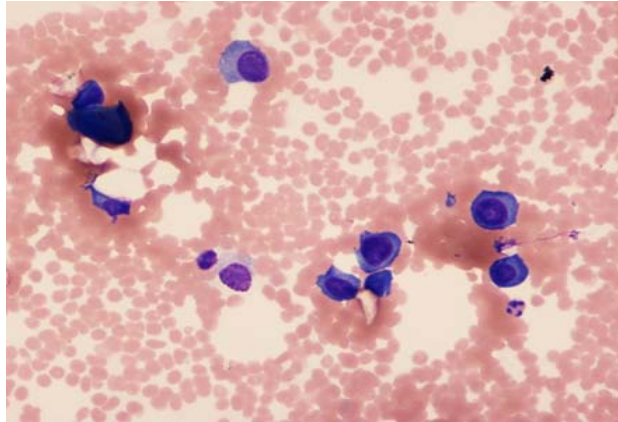


Massive Infiltration of T cells Into Marrow Correlate with Response

Patient 253



Resolution of Disease in Bone Marrow and Plasmacytoma by Day 56 Post-therapy with NY-ESO TCR in Myeloma



Pre-treatment

Day 56

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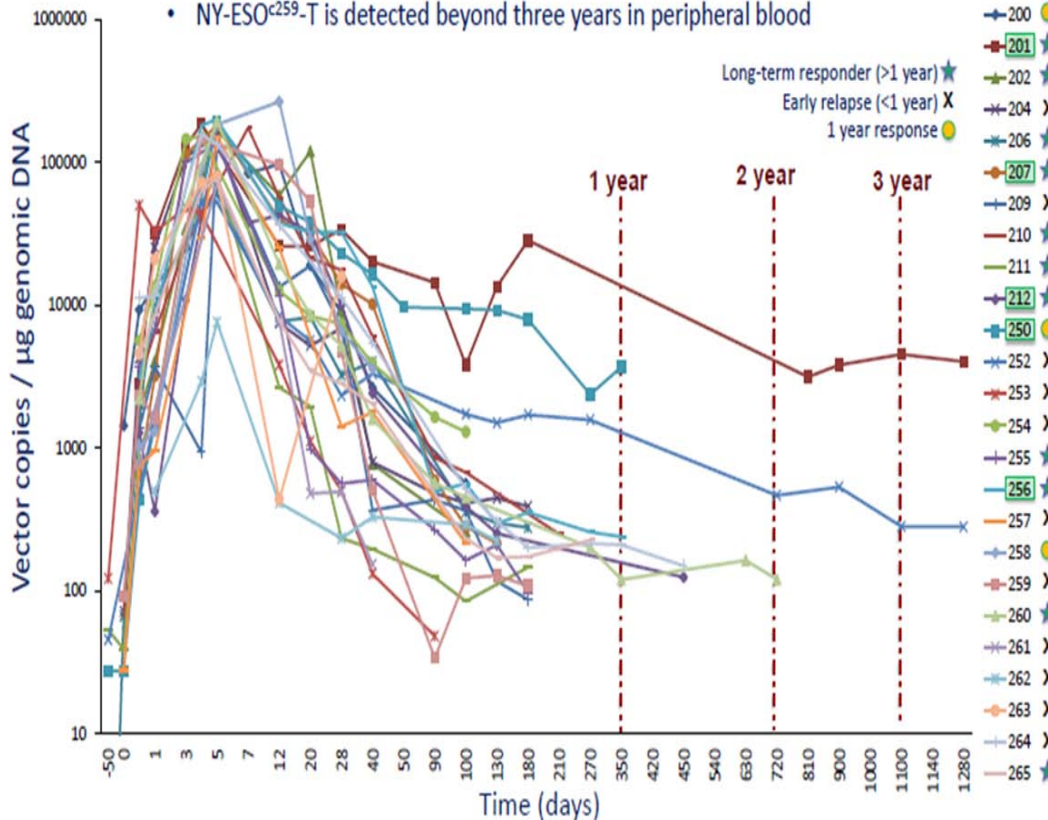
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Phase I/II Study in Multiple Myeloma: *Persistence and Relapse Correlation*

- NY-ESO-1^{c259T} cell persistence in peripheral blood as measured by PCR
- NY-ESO^{c259}-T is detected beyond three years in peripheral blood



- At the time of relapse, blood and tumor were evaluated for NY-ESO-1^{c259T} persistence and antigen, respectively
- Relapse corresponds to loss of persistence or loss of antigen

Patient ID	Timepoint at relapse	Best response	Persistence of NY-ESO T at relapse?	Antigen expression on tumor at relapse?
250	1 year	sCR	Y	N
200	1 year	nCR	Y	N
252	2.75 year	PR	N	Y
253	4 months	nCR	N	Y
204	6 months	nCR	N	Y
254	6 months	PR	Y	N
255	1.75 year	nCR	N	Y
209	8 months	**	N	Y
257	4 months	nCR	N	Y
258	9 months	nCR	N	Y
259	9 months	sCR	N	Y
261	3 months	PR	N	Y
262	5 months	PR	N	Y
263	9 months	PR	N	Y

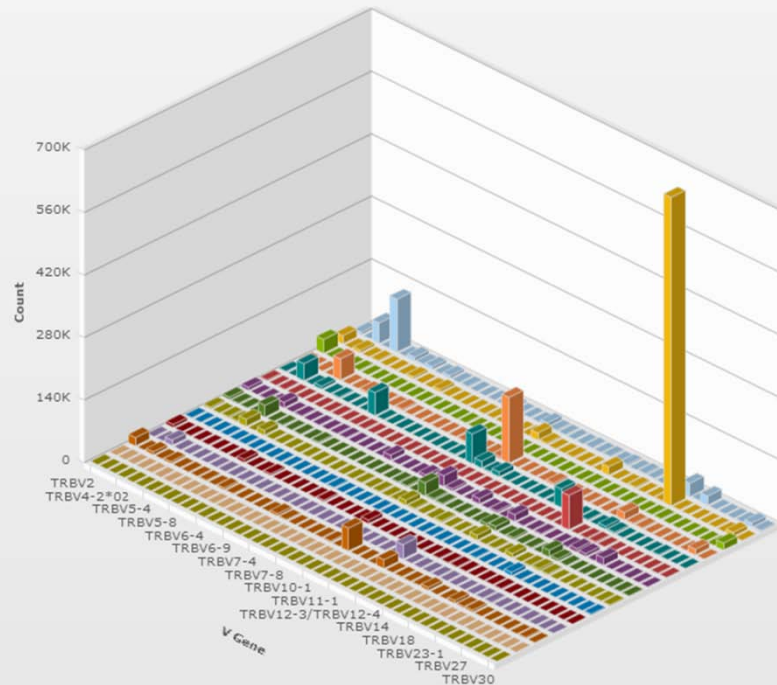
**ongoing response at transplant

Antigen Spreading: Clonal Expansion of Two TCR Clonotypes

Patient 253

3D Histogram: UPCC01411-253-D_28_2_

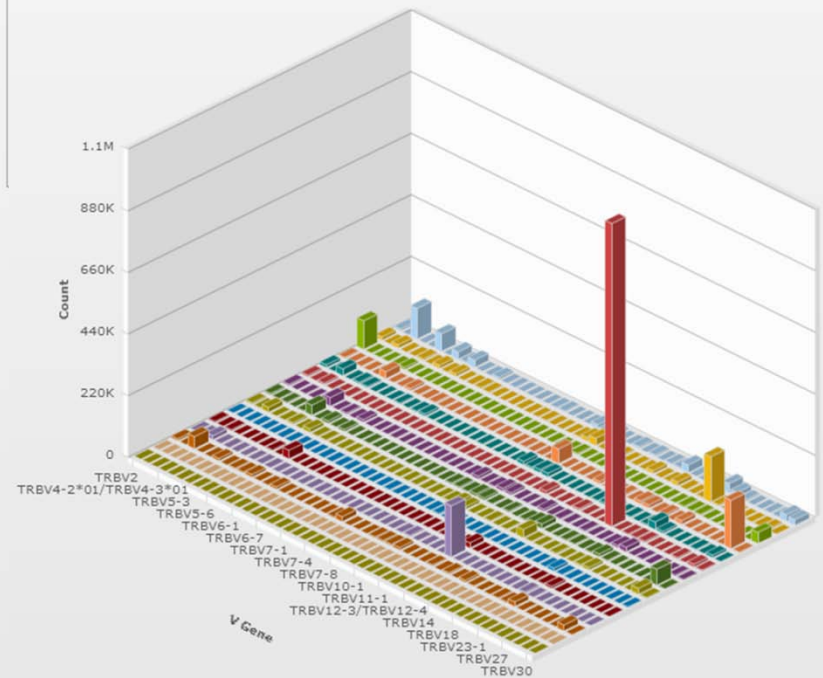
Count: total, Status: productive, normalized



Day 28 post infusion

3D Histogram: UPCC01411-253-D_68_2_

Count: total, Status: productive, normalized



Day 68 post infusion

CD19 CAR-T-Cell Therapy

Patient ID #	# of Lines of Therapy Prior to Trial	Results of Stem Cell Transplant #1		Results of Stem Cell Transplant #2 + CTL019 Therapy		
		Time to Progression (days)	Best Response Post Transplant #1	Pro-gression Yet?	Length of Follow-up (days)	Best Response Post Transplant #2
1	10	190	PR	No	339	sCR, MRD-
2	7	342	PR	Yes (Day 42)	-	N.A.
3	3	210	uCR	Yes (Day 176)	-	uCR, MRD+
4	7	137	VGPR	No	150	VGPR
5	2	100	PR	No	74	PR

Abbreviations: MRD-/+, minimal residual disease negative / positive; N.A., not applicable; PR, partial response; sCR, stringent complete response; uCR, unconfirmed complete response; VGPR, very good partial response.

- Administered in the context of ASCT
- Poor persistence of gene modified cells

Garfall A, J Clin Oncol 33,2015 (suppl; abstr 8517)

BCMA CAR-T-Cell Therapy

- N=12: 5 with amyloid light chain only, 3 with IgA disease, and 4 with IgG disease.
- They received CAR-BCMA doses of 0.3×10^6 to 9×10^6 T-cells/kg
- 1 CR, 1 VGPR, 2 PR, 8 SD
- Severe CRS preceding CR: fever, tachycardia, hypotension
- Elevated liver enzymes, and creatinine kinase
- Platelet-transfusion dependent for 9 weeks before CR
- Each of the symptoms/signs resolved within 2 weeks
- ANC < 500/mcl at the time of CAR-BCMA infusion and remained at that level for 40 days after infusion

Ali SA, ASH December 5-8, 2015. LBA-1

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