Efficacy and safety of P-BCMA-101 CAR-T cells in patients with relapsed/refractory (r/r) multiple myeloma (MM)

C. Costello[6], A. D. Cohen[5], K. K. Patel[3], S. Abbas Ali[4],

J. G. Berdeja[2], N. Shah[7], S. Ganguly[8], M. Kocoglu[9], M. Abedi[10], A. Deol[11],

E. M. Ostertag[12], C. E. Martin[12], M. Ghoddusi[12], D. J. Shedlock[12],

J. McCaigue[12], H. Namini[12], K. McArthur[12], S. Yalamanchili[12],

M. A. Spear[12], T. K. Gregory[1]

[1]Colorado Blood Cancer Inst., Denver, CO; [2]Tennessee Oncology, Nashville, TN; [3]MD Anderson Cancer Ctr., Houston, TX;

[4]Johns Hopkins Univ., Baltimore, MD; [5]Abramson Cancer Ctr. Univ. of Pennsylvania, Philadelphia, PA;

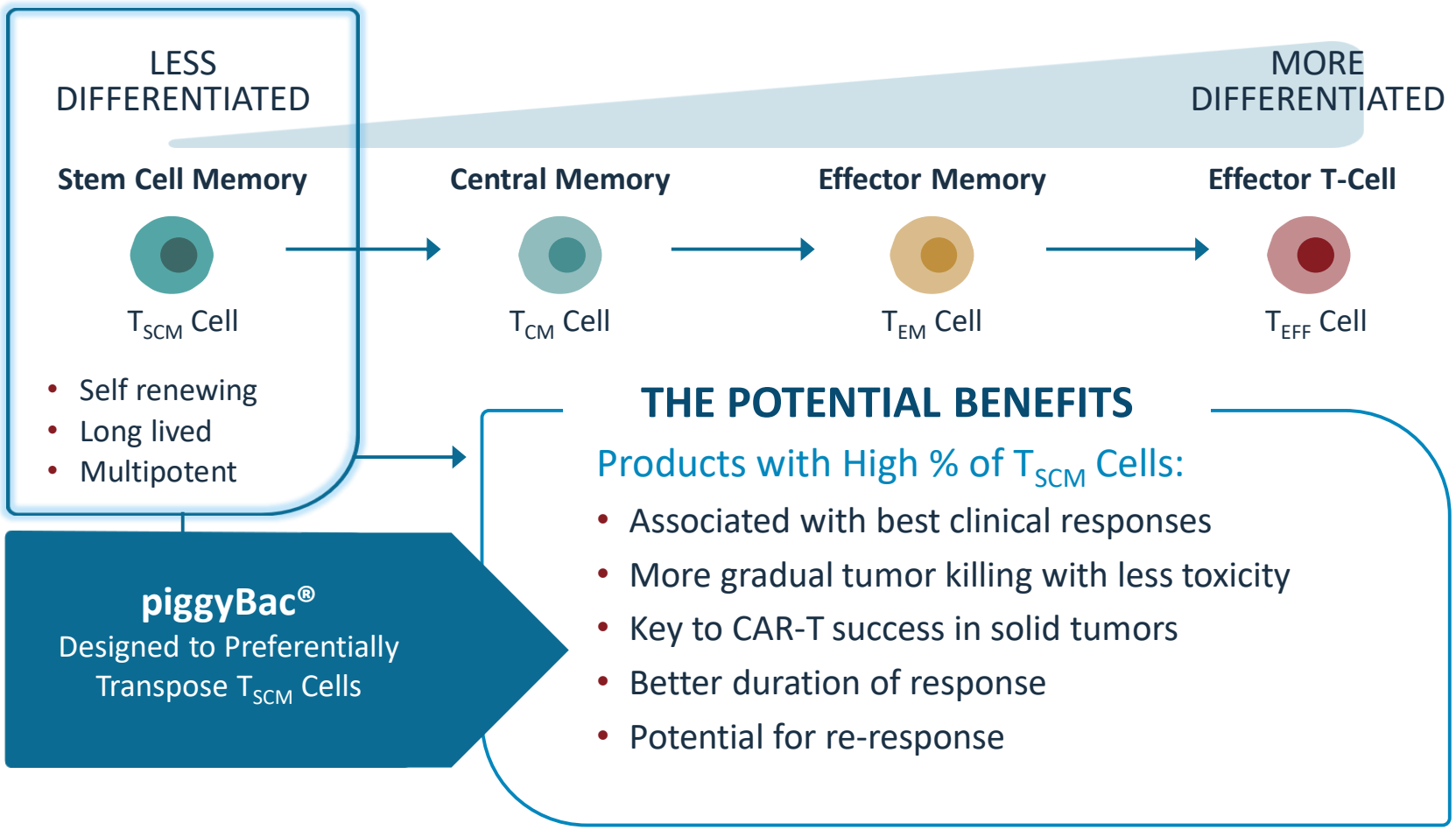
[6]Moores Cancer Ctr., UC San Diego, San Diego, CA; [7]UC San Francisco, San Francisco, CA;

[8]Univ. Kansas, Fairway, KS; [9]Univ. of Maryland, Baltimore MD [10]UC Davis, Sacramento, CA,

[11]Karmanos Cancer Center, [12] Poseida Therapeutics, Inc., San Diego, CA

Not All T-Cells are Created Equally:

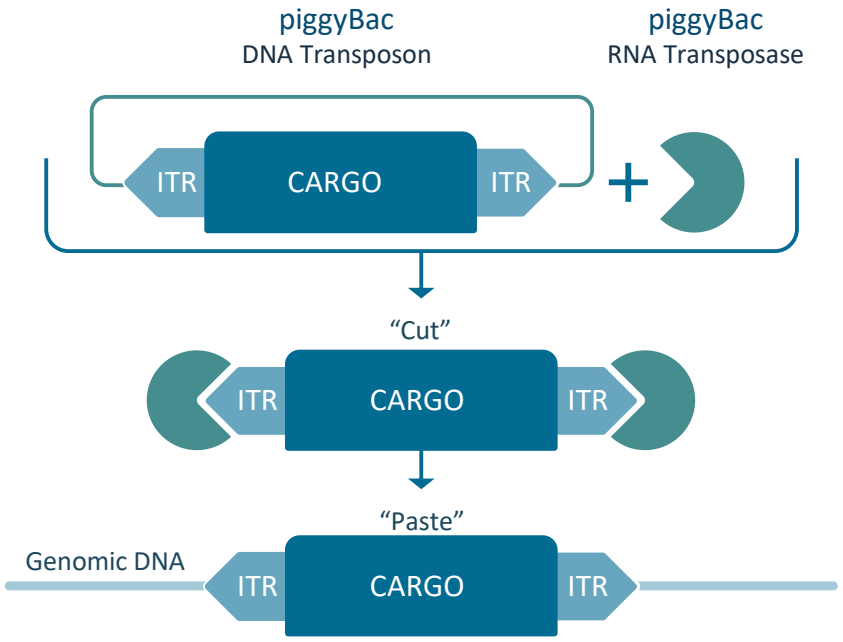
The Importance of Stem Cell Memory T Cells (T_{SCM})



Spear M., et al., Poseida (2019) CAR-TCR Summit; Melenhorst J. et al., UPenn (2017) 20th ASGCT; Basu et al., Adaptimmune (2017) CAR-TCR Summit; Bot A., et al., Kite (2019) CAR-TCR Summit; T_{cm}: Larson, Juno(2018) AACR; T_{scm} TIL: Beatty M., Moffitt (2018) SITC; T_{cm}: Fraietta J. et al., UPenn (2018) TET2 Disruption, PMID 29849141

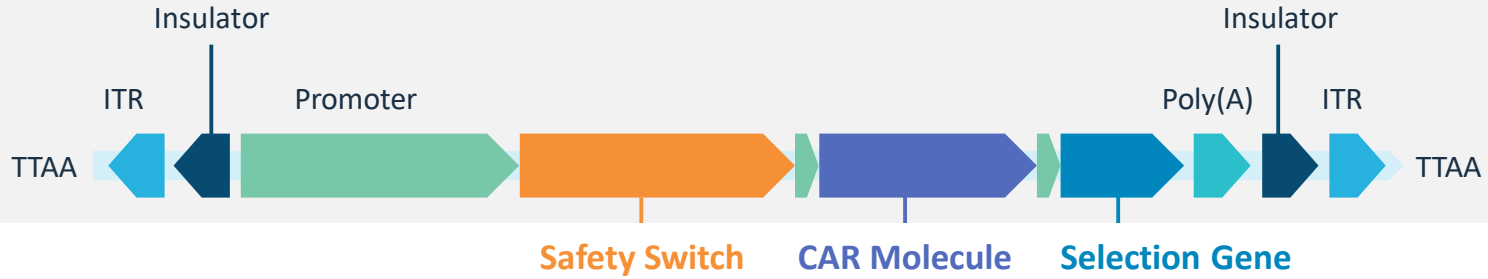
P-BCMA-101 is a Novel CAR-T Cell Made With Transposons (piggyBac®)

Very Large Cargo Capacity:
Potentially >20x Lentivirus



Large transgene with ability to carry multiple CAR or TCR molecule genes and armoring technology

Designed To Have Desirable Product Attributes



INCORPORATES PROPRIETARY SAFETY SWITCH

- Rapid, dose-dependent **elimination** of CAR-T cells with rimiducid if needed
- Potential **management of** Cytokine Release Syndrome (**CRS**) or other AEs

DIFFERENTIATED BINDING CAR-T MOLECULE

- Centyrin™ molecule with **high-specificity binding** to BCMA
- Fully human with no **tonic signaling observed to date**

DRUG RESISTANCE GENE PERMITS POSITIVE SELECTION

- **~100% of T-cells** in final product express the CAR molecule
- Predicted to result in **greater therapeutic index**

Modified Manufacturing Process Using Nanoplasmids (NP)

Small Changes in CAR-T Manufacturing Can Have a Big Impact

- Cell-based products are **living drugs** and are affected by donor and manufacturing variability. The **type and quality of cells** affect product performance

- Improving **transposition frequency** during manufacturing may improve final product
  - More CAR+ cells, less cell proliferation and cell death in culture means healthier more proliferative cells in a patient

- Improving Transposition of P-BCMA-101 with a Modified Manufacturing Process with **Nanoplasmid (NP)**
  - Reduces the backbone size to < 500 bp (less DNA = less toxicity) vs. >2000 bp for Standard Plasmid
  - Brings piggyBac® ITRs closer together (enhanced transposition efficiency)

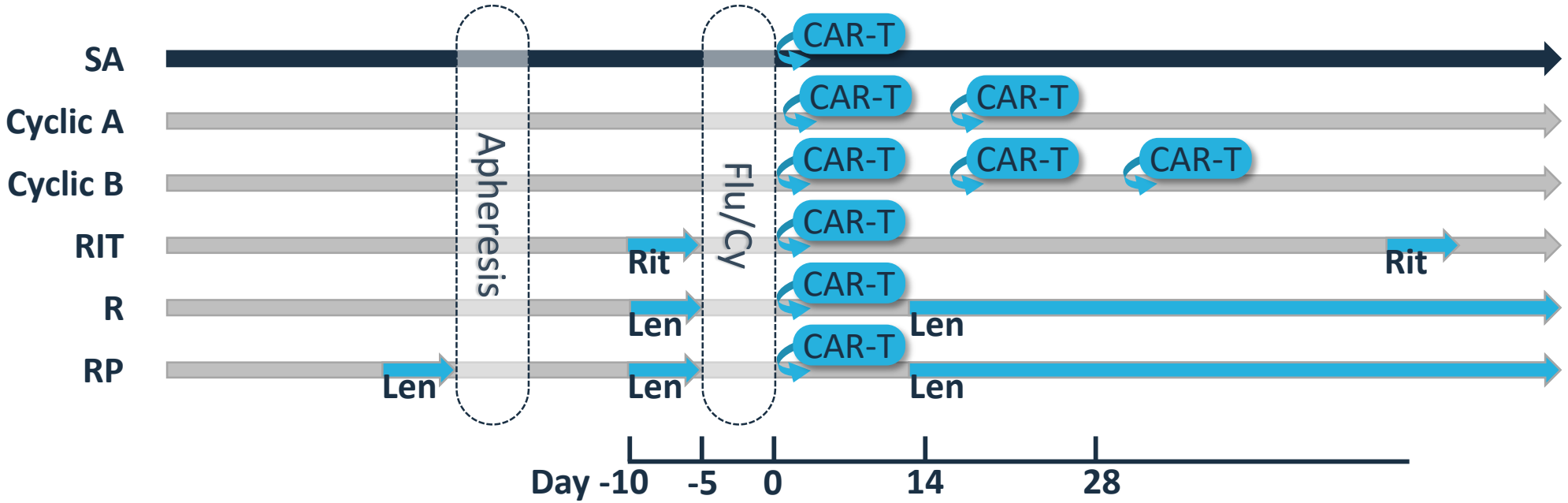
- Incorporated manufacturing changes that increased transposition frequency (2-fold) in the Phase 1 trial

Phase 1/2 Relapsed/Refractory Multiple Myeloma Clinical Trial (PRIME)

Open Label, 3+3 Design, up to 120 patients, multiple exploratory cohorts

Key eligibility criteria:

- RRMM
- ECOG PS 0-1
- ≥3 prior lines (PI+IMID)
- ≥2 prior lines IF refractory to both PI+IMID
- Prior anti-BCMA or CAR-T cell therapy allowed



Single administration (SA)

Cyclic administration- dose divided **A)** 1/3+2/3 or **B)** 1/3+1/3+1/3

Combination Administration

Cohort R: lenalidomide 10-25mg PO QD 21/28d

Cohort RP: lenalidomide 10-25mg PO QD 21/28d

Cohort RIT: rituximab 375 mg/m^2 via IV infusion day -12, -5, and q8w post-CART

CIRM funding RMAT status

Baseline Demographics and Clinical Characteristics

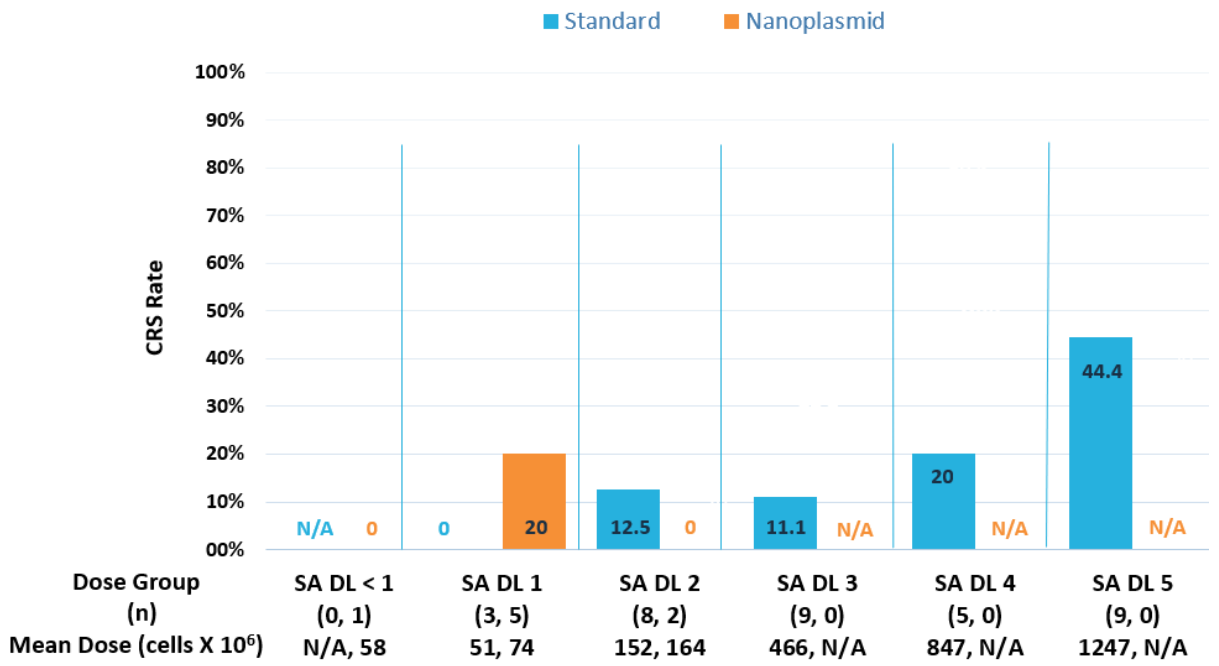
Parameter (n=55)		
Median (min, max) age, y	60 (42, 74)	
Male:Female, n (%)	37 (67):18(33)	
Median (min, max) time since diagnosis, y	4.9 (0.9, 13.9)	
ECOG PS, n (%)		
0	20 (36)	
1	35 (64)	
Median (min, max) prior lines of therapy	8 (2, 18)	
	Exposed	Refractory
Proteasome inhibitor, n (%)	55 (100)	40 (73)
Bortezomib	53 (96)	23 (42)
Carfilzomib	47 (85)	31 (56)
Ixazomib	15 (27)	10 (18)
IMiD, n (%)	55 (100)	44 (80)
Lenalidomide	55 (100)	37 (67)
Pomalidomide	50 (91)	34 (62)
Thalidomide	12 (22)	3 (5)
Daratumumab, n (%)	51 (93)	38 (69)
Triple Class (PI, IMiD and anti-CD38), n (%)	51 (93)	33 (60)
anti-BCMA, n (%)	4 (7)	4 (7)
Prior autologous SCT	37 (67)	

Safety: Adverse Events of Interest

TEAE, n (%)	Overall (n=53)	≥ Grade 3
Dose Limiting Toxicity (DLT)[a]	0 (0.0)	0 (0.0)
Cytokine Release Syndrome[a]	9 (17.0)	0 (0.0)
Administered tocilizumab	4 (7.3)	
Administered steroids	3 (5.5)	
Neurotoxicity[a]	2 (3.8)	2 (3.8)
Infection		
Overall	24 (45.3)	10 (18.9)
First month	9 (17.0)	4 (7.5)
Neutropenia/Neutrophil count decreased[b]	41 (77.4)	40 (75.5)
Thrombocytopenia/Platelet count decreased[b]	22 (41.5)	16 (30.2)
Anemia	21 (39.6)	16 (30.2)
White Blood Cell Count Decreased	21 (39.6)	19 (35.8)
Fatigue	17 (32.1)	0 (0.0)

Highest incidence TEAE were infection, neutropenia, thrombocytopenia, anemia, leukopenia and fatigue
No rimiducid use or ICU admission for CRS
16 patients treated outpatient

Cytokine Release Syndrome by Dose Level (n = 53)

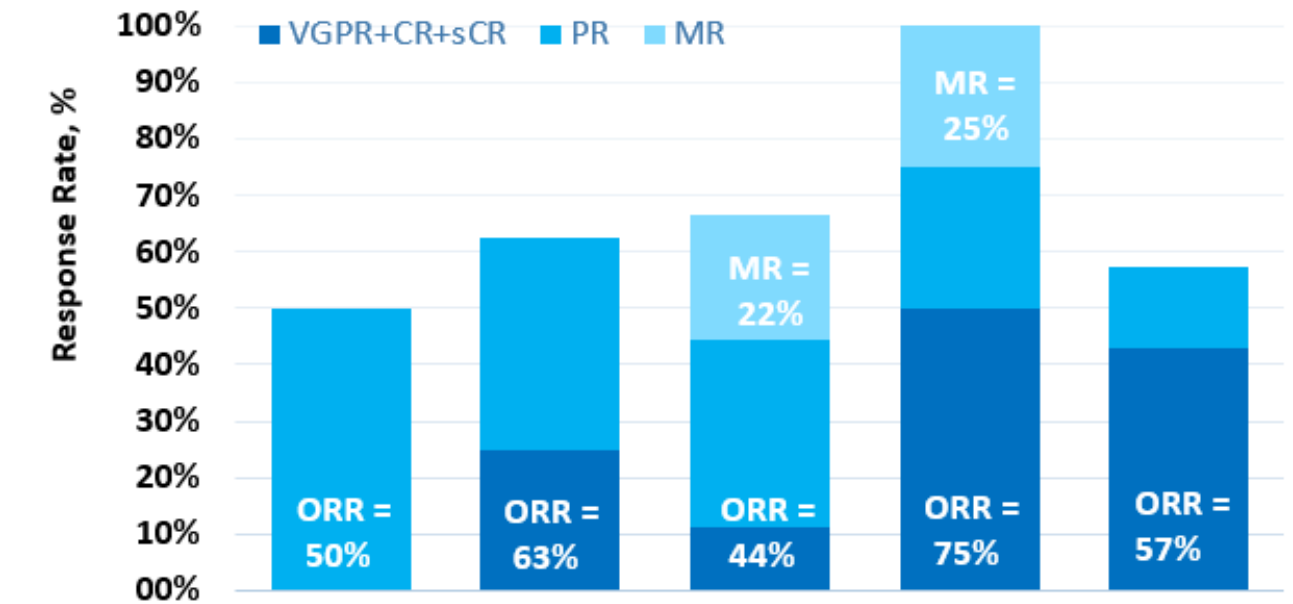


All CRS was Grade 1/2
No CRS in RIT/R/RP groups.
CRS in 1/4 patients in cyclic dosing groups (1/2 NP)

[a]By investigator assessment [b]Patient counted once for either term

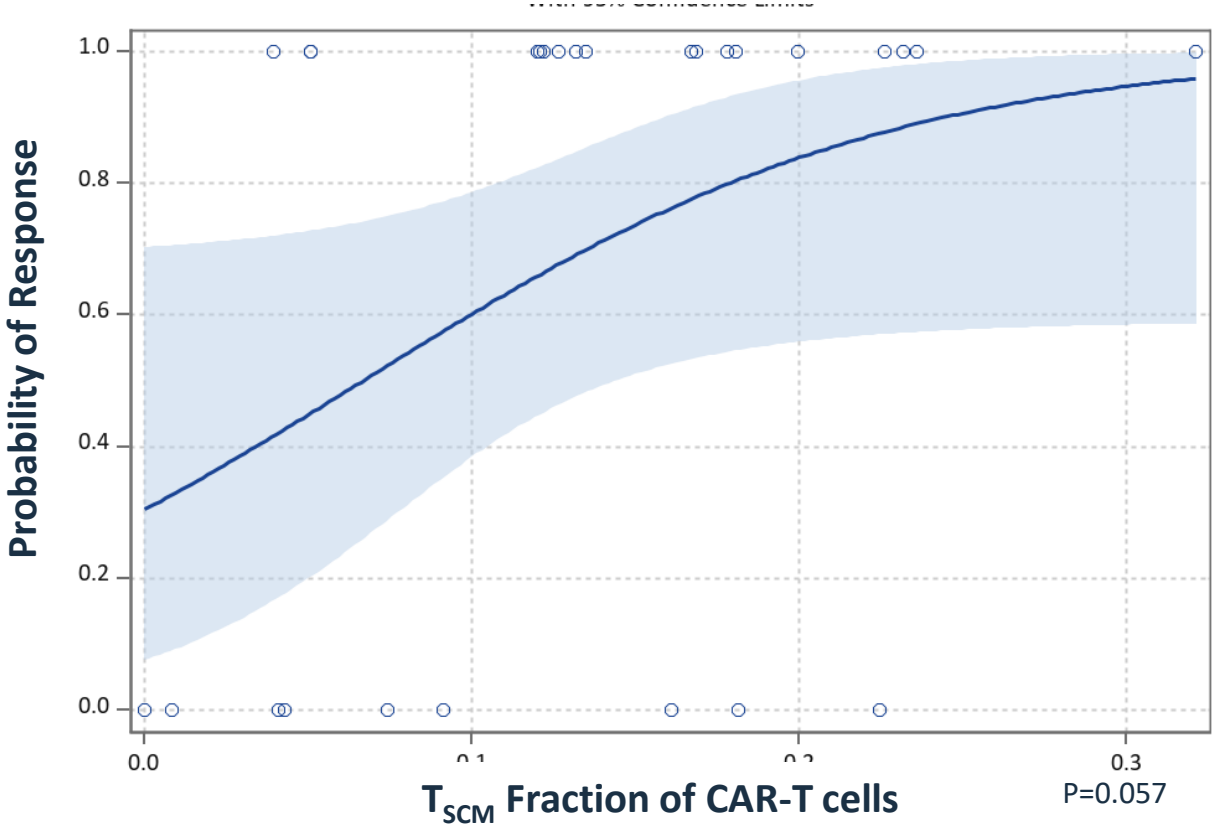
Dose Escalation with Original Manufacturing Process: High Response Rates

Tumor Response in Evaluable Patients by Dose



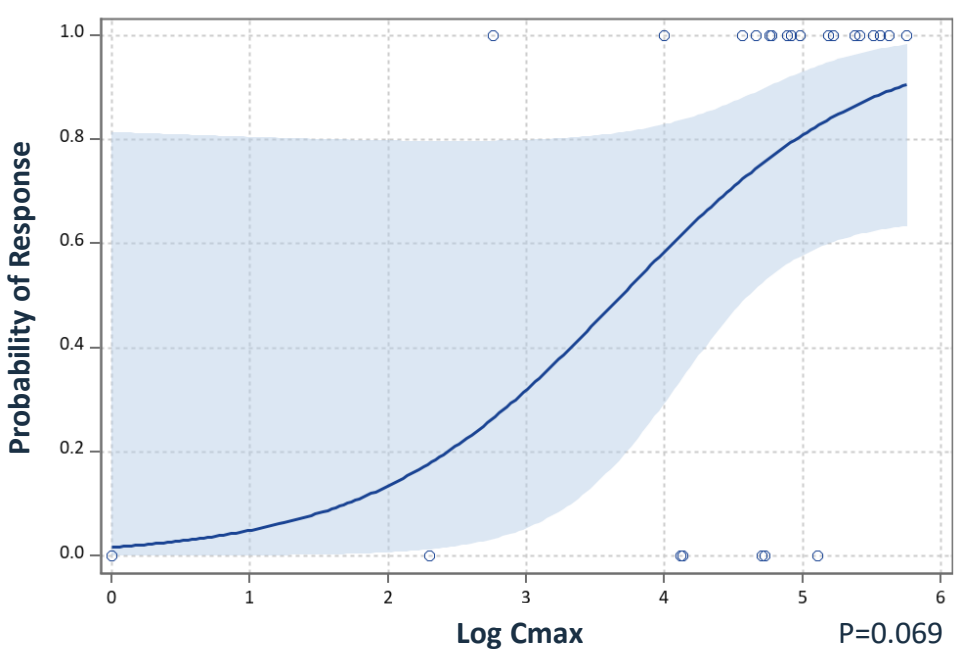
Data cutoff: November 11th, 2020. ORR, objective response rate, attaining sCR (inc. MRD-), CR, VGPR or PR, including confirmed and unconfirmed responses.
Evaluable patients: evaluable first response assessment by IMWG m-protein criteria or PD/death.

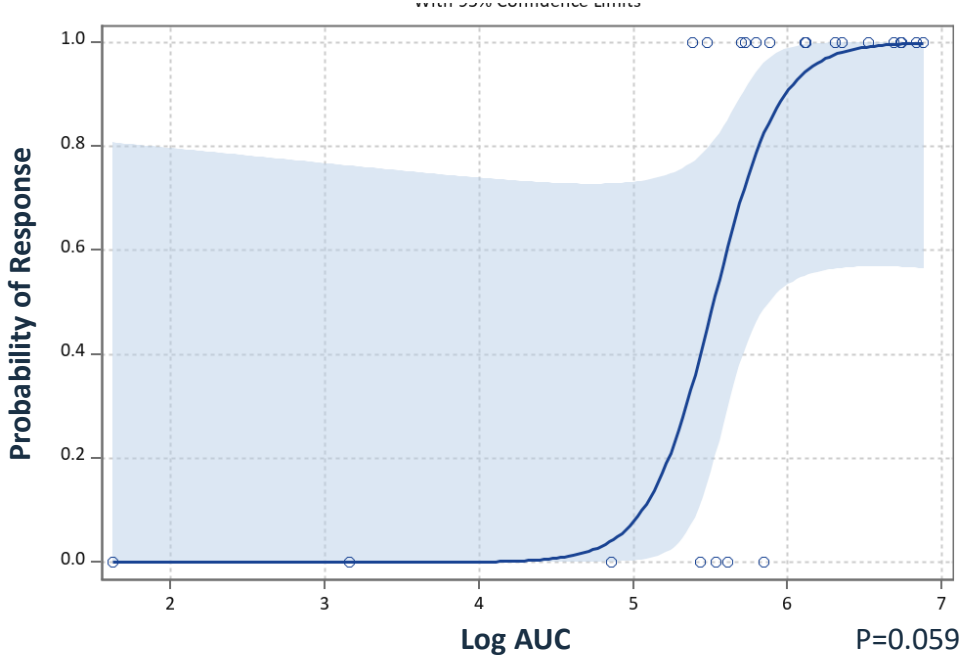
T_{SCM} Correlates with Response in Patients Treated with P-BCMA-101



The percentage (fraction) of a P-BCMA-101 CAR-T cell dose that were T_{SCM} correlated with the probability of response by IMWG criteria

Correlations Between Cmax/AUC and Response



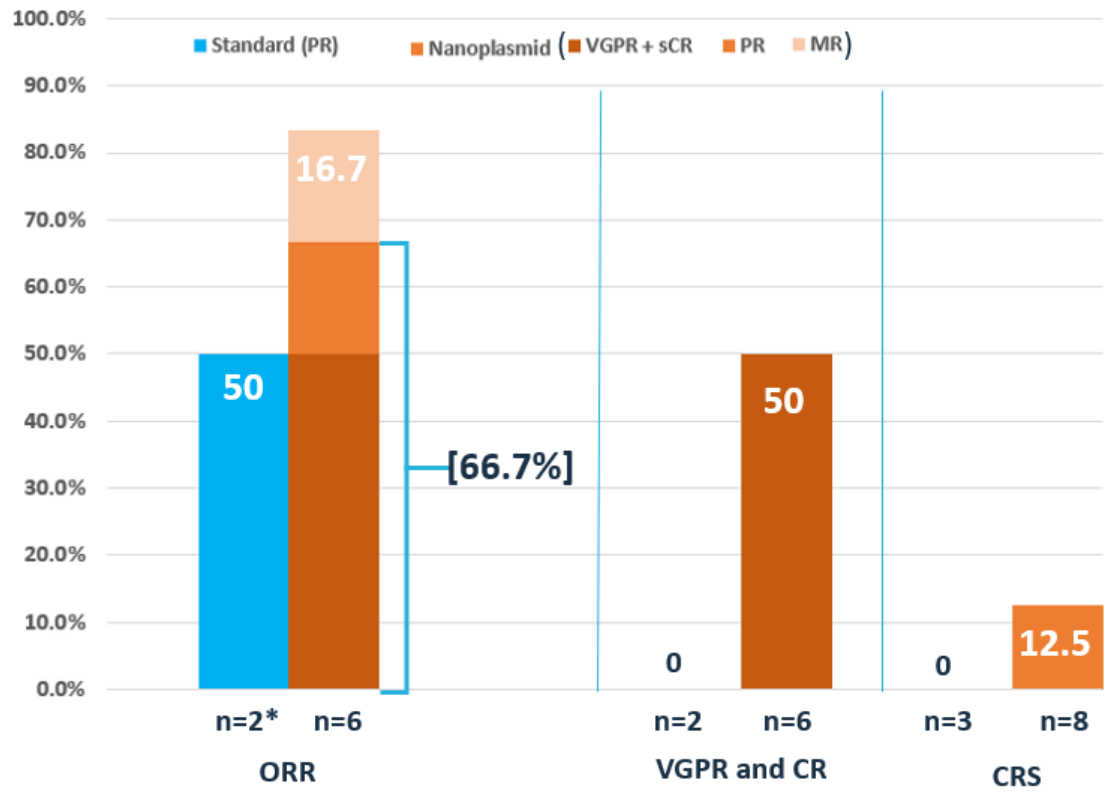


The Cmax and AUC of P-BCMA-101 expansion assessed by PCR in peripheral blood correlated with the probability of response by IMWG criteria

Initial Dose Escalation with Nanoplasmid (NP) Manufacturing Process: Equal Safety and Better Response Compared to Standard Plasmid

- P-BCMA-101 **with Nanoplasmid demonstrated higher ORR** than P-BCMA-101 with standard plasmid
  - 66.7% vs 50% by IMWG
- P-BCMA-101 **Nanoplasmid delivered deeper responses** than P-BCMA-101
  - 3 P-BCMA-101 Nanoplasmid patients at VGPR or CR compared to zero for standard plasmid
- **Safety profile** was preserved with **one Grade 1 CRS** observed with either product in these patients

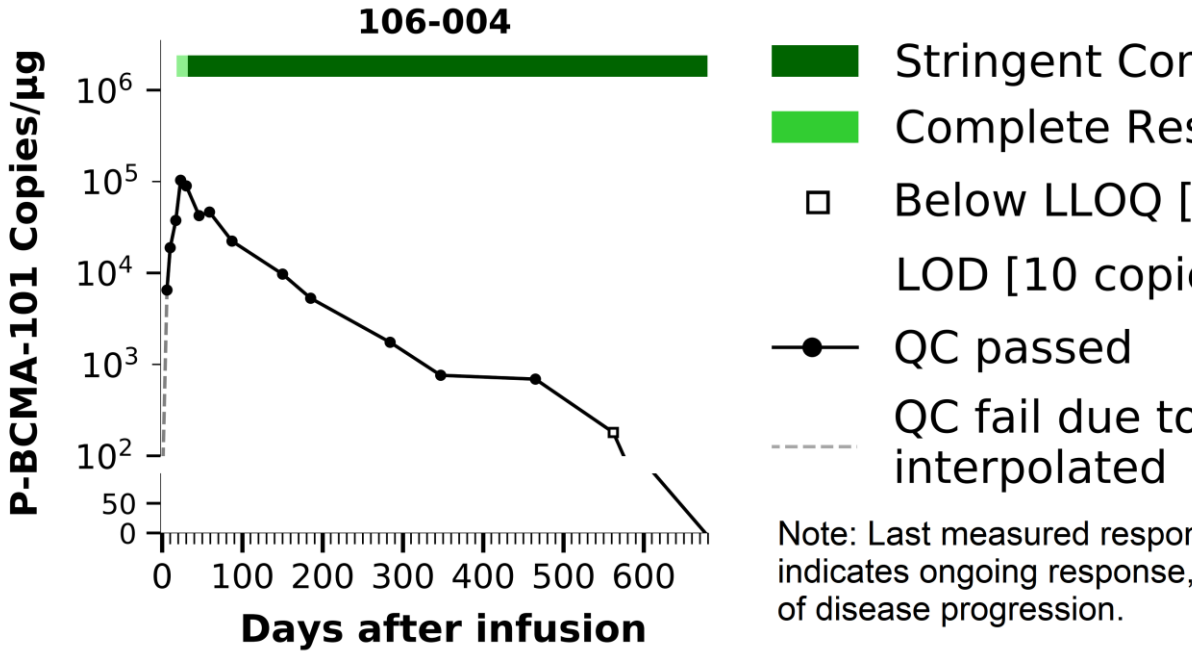
Standard Plasmid vs. Nanoplasmid @ Cohort 1 Dose Level



ORR for cyclic dosing was 1/4 (PR), Cmax was low and followed individual administrations without expanding AUC
*3 patients dosed but only 2 evaluable by IMWG criteria. 3rd patient had plasmacytomas and had significant response by PET scan.
Data cutoff: November 11th, 2020. ORR Objective Response Rate, attaining sCR, CR, VGPR or PR, including confirmed and unconfirmed responses. Evaluable patients: Obtained first response assessment by IMWG m-protein criteria or PD/death.

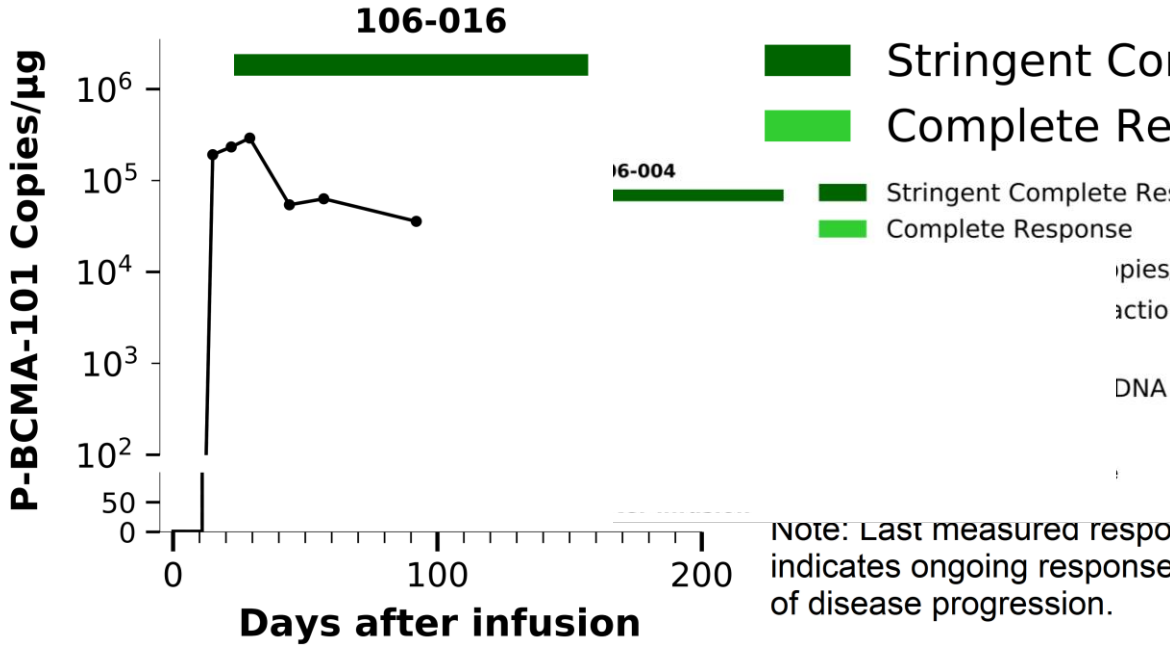
CAR-T Expansion is Associated with Best Responses

Patient 106-004: Long Term sCR



- 59 yo male with 5 prior lines
- Treated with P-BCMA-101 in August 2018
- Rapidly reached VGPR then sCR, continues on study at > 2 years
- Clinical evidence of engraftment and persistence of CAR+ cells at ~22 months

Patient 106-016: sCR recently treated with NP



- Patient: 69 yo female TP53mut with 4 prior lines
- Treated with P-BCMA-101 (NP) in June 2020
- Rapidly reached sCR
- Similar evidence of expansion and engraftment at early timepoints

Summary

Safety & Efficacy with a Novel BCMA CAR-T Cell Product

- **Excellent safety and efficacy profile demonstrated in a standard dose escalation, doses up to ~1200 x 106 CAR-T cells**
  - Very low rates of CRS (17%, no Grade 3+), CRES and usage of tocilizumab/steroids, no ICU admissions
    - May allow for greater patient access (e.g., administration at community hospitals and/or outpatient sites)
  - Early memory T cell phenotype (TSCM) may result in greater safety and efficacy
- **Manufacturing matters, use of modified process may improve expansion and efficacy**
  - PiggyBac with Nanoplasmid exemplifies continuous innovation in manufacturing
  - Current process at .75X10E6 dose results in 67% ORR, 50% VGPR/sCR with 12.5% CRS
- **Preliminary results with novel dosing methods and combinations suggest unique outcomes**
  - Safety profile is preserved with all strategies
  - Multiple doses do not appear to improve PK or efficacy, but increase logistical complexity
  - Rituximab and lenalidomide treated patient numbers are too low to assess differences at this time
  - Dose escalation is continuing in Nanoplasmid groups

Acknowledgements

Funding

Poseida

CIRM
(California Institute for Regenerative Medicine)

Manufacturing

Lonza

Clinical Sites

Banner MD Anderson Cancer Center – Rajneesh Nath, M.D.
Colorado Blood Cancer Institute – Tara Gregory, M.D.
Hackensack University Medical Center – David Siegel, M.D.
Johns Hopkins – Syed Abbas Ali, M.D.
Karmanos Cancer Institute – Abhinav Deol, M.D.
MD Anderson Cancer Center – Krina Patel, M.D.
Swedish Cancer Institute – William Bensinger, M.D.
Tennessee Oncology – Jesus G. Berdeja, M.D.
UC Davis – Comprehensive Cancer Center – Mehrdad Abedi, M.D.
UC San Diego Moores Cancer Center – Caitlin Costello, M.D.
UC San Francisco – Nina Shah, M.D.
University of Chicago - Benjamin Derman, M.D.
University of Kansas Cancer Center – Siddhartha Ganguly, M.D.
University of Maryland - Mehmet Hakan Kocoglu, M.D.
University of Pennsylvania – Adam Cohen, M.D.
Vanderbilt-Ingram Cancer Center – Bhagirathbhai Dholaria, M.D.

With the greatest appreciation to all of the patients


Thank You