

CONVEGNO INTERREGIONALE SIE

Delegazioni Umbria e Marche

Società Italiana di Ematologia

NOVITÀ TERAPEUTICHE NEI LINFOMI NON-HODGKIN E MIELOMA MULTIPLO: FOCUS SU ANTICORPI BISPECIFICI E CAR-T

Assisi, Sala Conciliazione, Comune di Assisi
4 Novembre 2026

Il bersaglio della maggioranza degli anticorpi bispecifici e CAR-T: BCMA e il campo minato per raggiungerlo: sBCMA

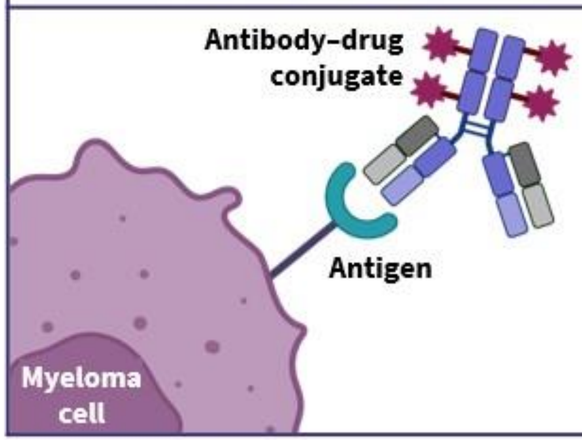
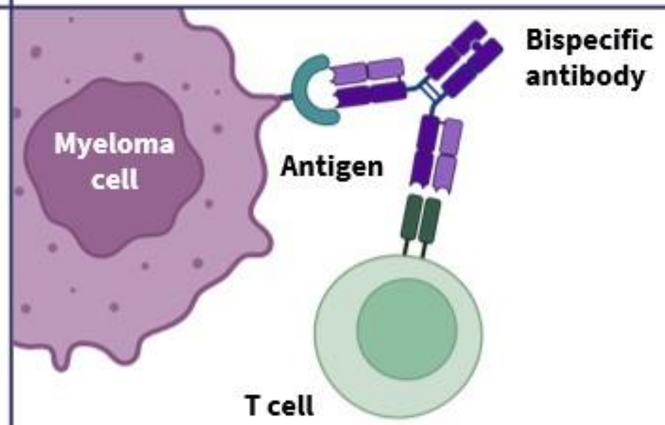
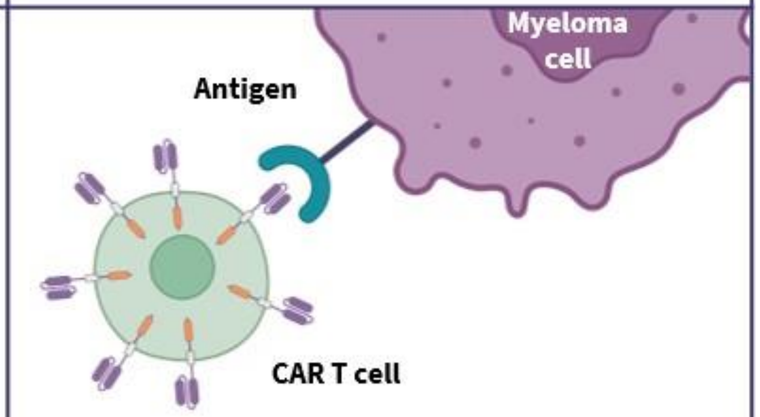
Giorgio Minotti
Università e Fondazione Policlinico Universitario Campus Bio-Medico, Roma
Fondazione Pisana per la Scienza, Pisa
Assisi, 4 novembre 2026

DISCLOSURES

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Johnson& Johnson			X		X	X	
Incyte	X		X			X	
BeiGene			X		X	X	
Servier			X			X	
Astellas	X						
Pfizer					X		
Gentili					X		
Lilly					X	X	
Daiichi Sankyo						X	

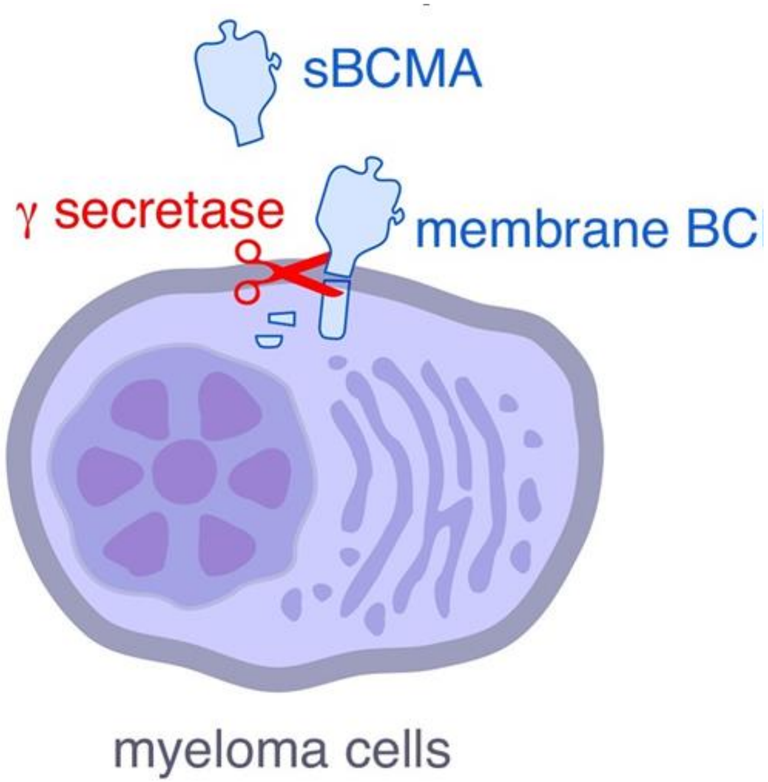
BCMA

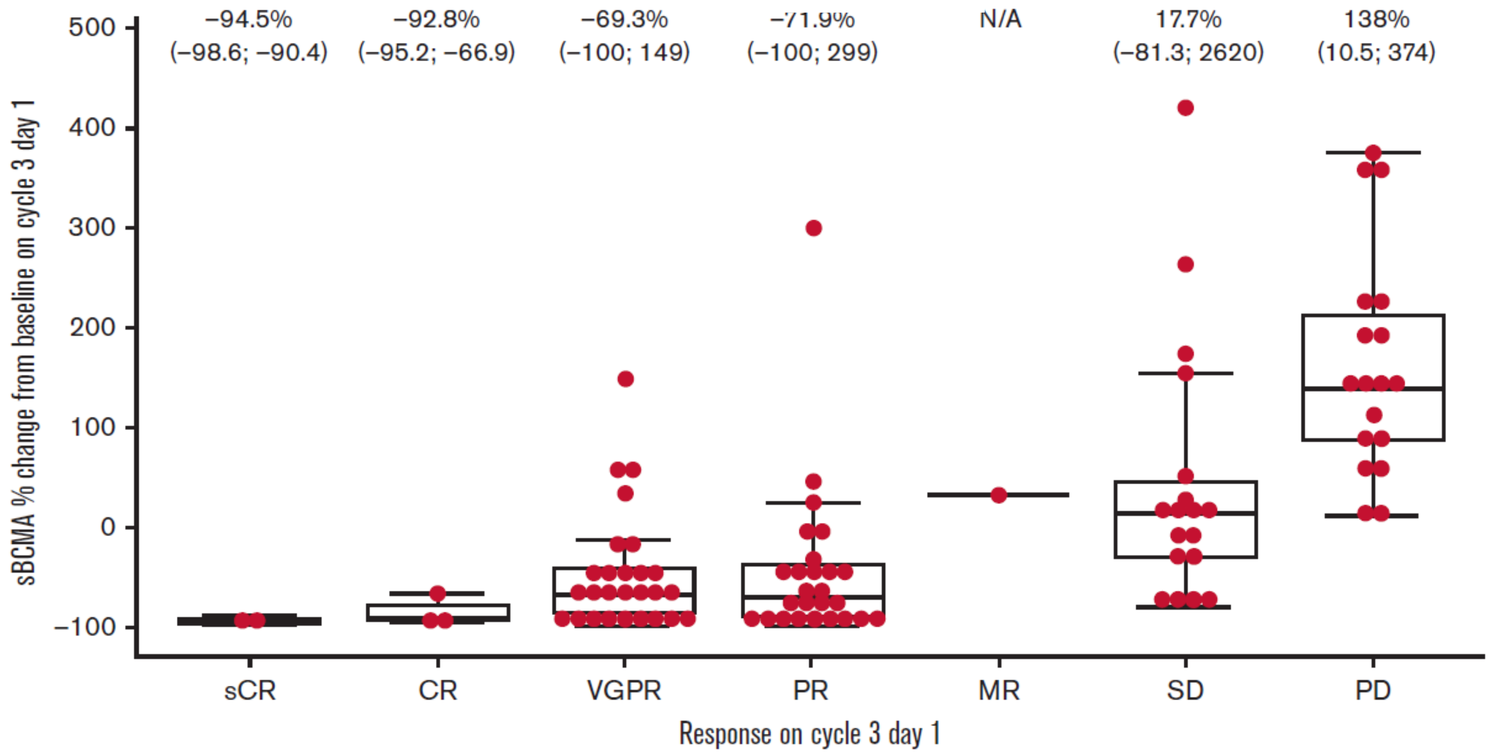
BCMA, ONE TARGET FOR MULTIPLE STRATEGIES

ADC	BsAb	CAR-T
A BCMA-targeted mAb, attached via a linker to a cytotoxic payload. Upon BCMA binding, the ADC is internalized into the myeloma cell. The payload is then released, inducing apoptosis and targeted tumor cell death.	BsAbs simultaneously bind BCMA on myeloma cells and CD3 on T cells, facilitating T-cell activation, cytokine release, and cytotoxicity directed against malignant plasma cells.	Genetically modified autologous T cells expressing a BCMA-directed CAR recognize and kill myeloma cells through T-cell activation, cytokine release, and cytotoxic effector functions.
		

Cancers, 2021;13(18):4701

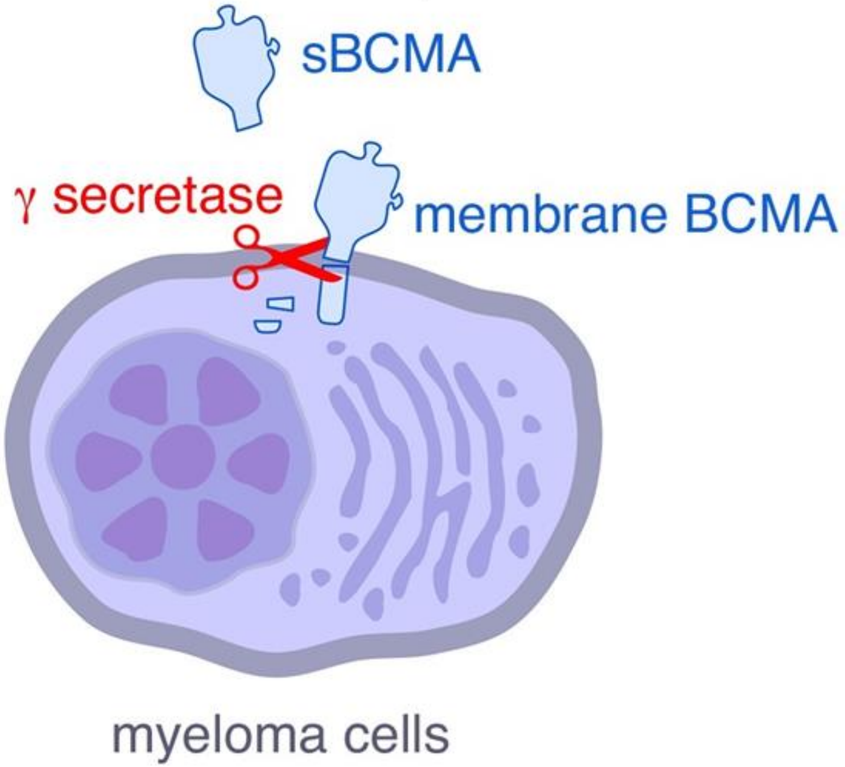
sBCMA CORRELATES WITH TUMOR BURDEN AND RESPONSE TO BiTEs

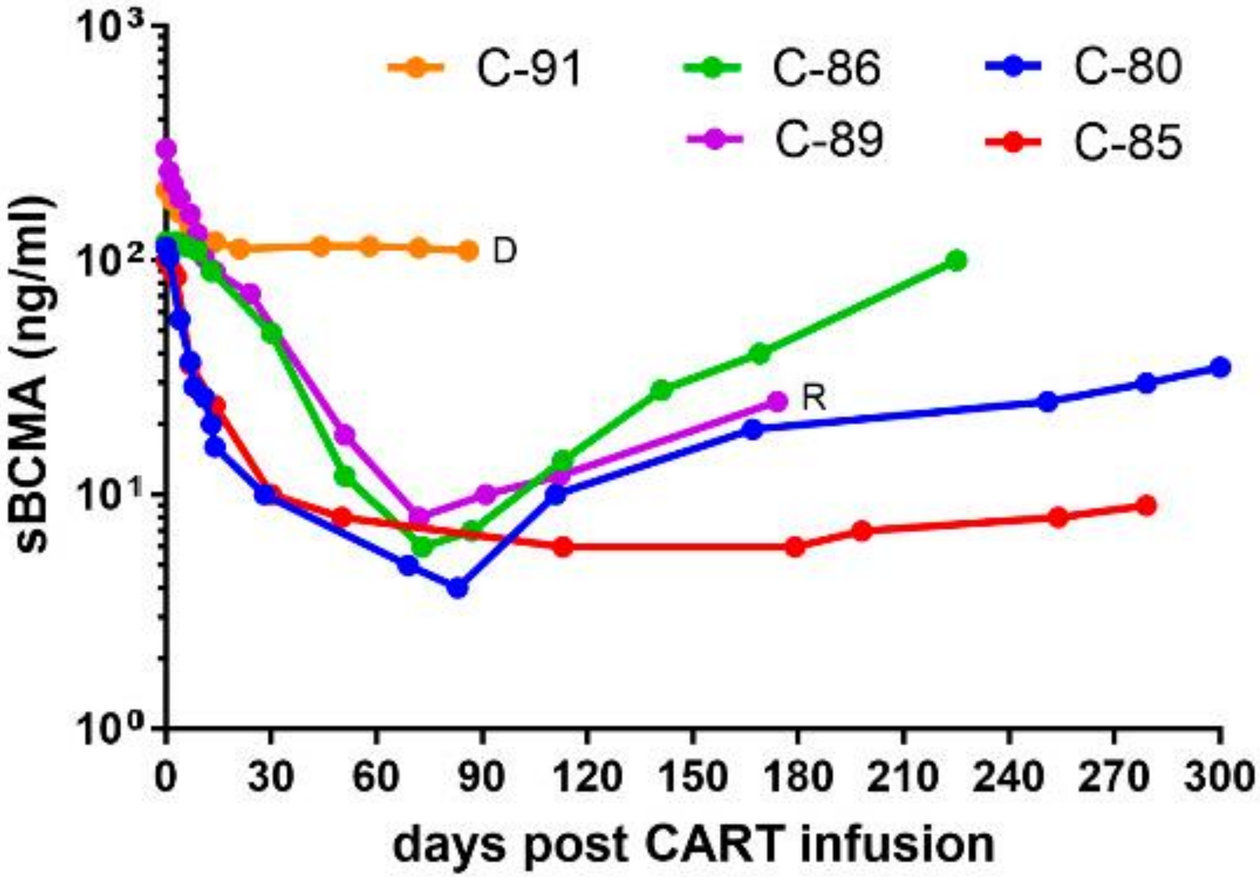




Curr Opinion Immunol 71: 117-123, 2021

Haematologica, 102 (4), 2017



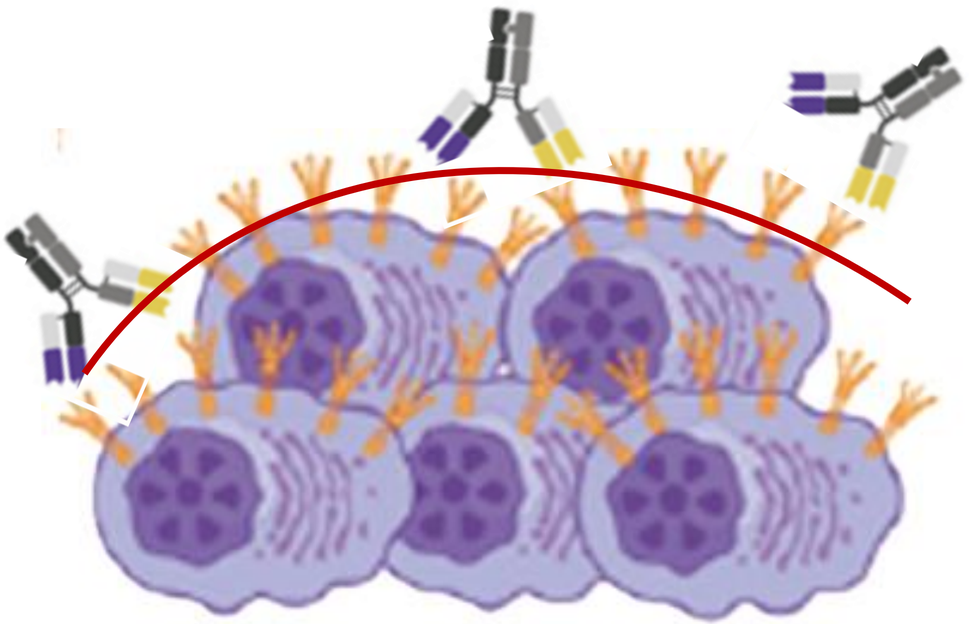


Curr Opinion Immunol 71: 117-123, 2021

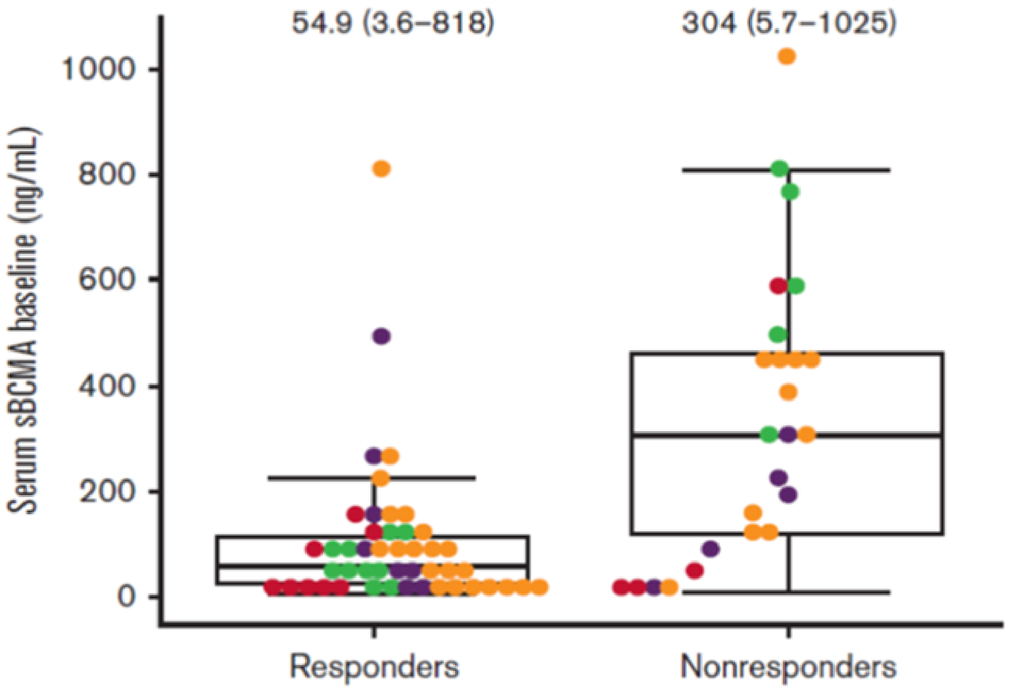
Curr. Issues Mol. Biol. 2022, 44 1465

sBCMA, NOT JUST A MARKER

WHAT WE WANT FROM BiTEs

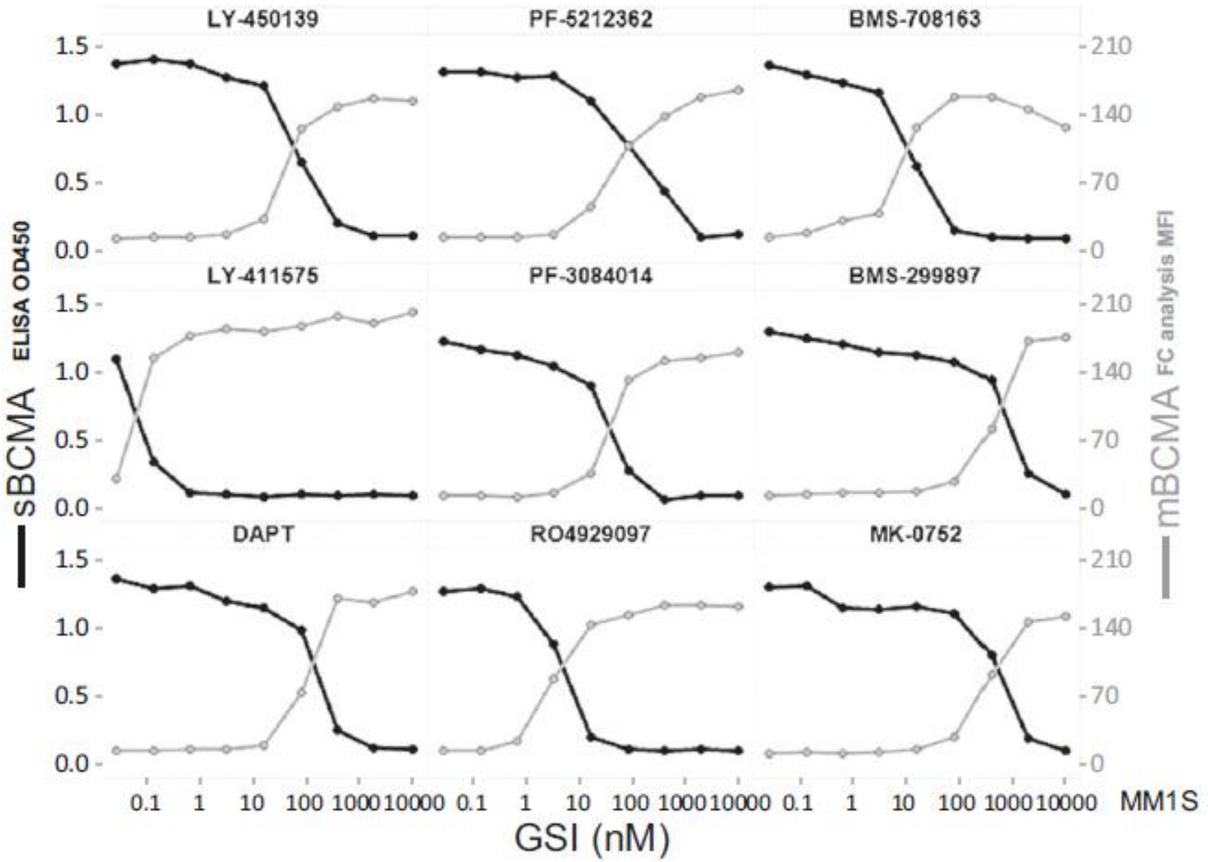


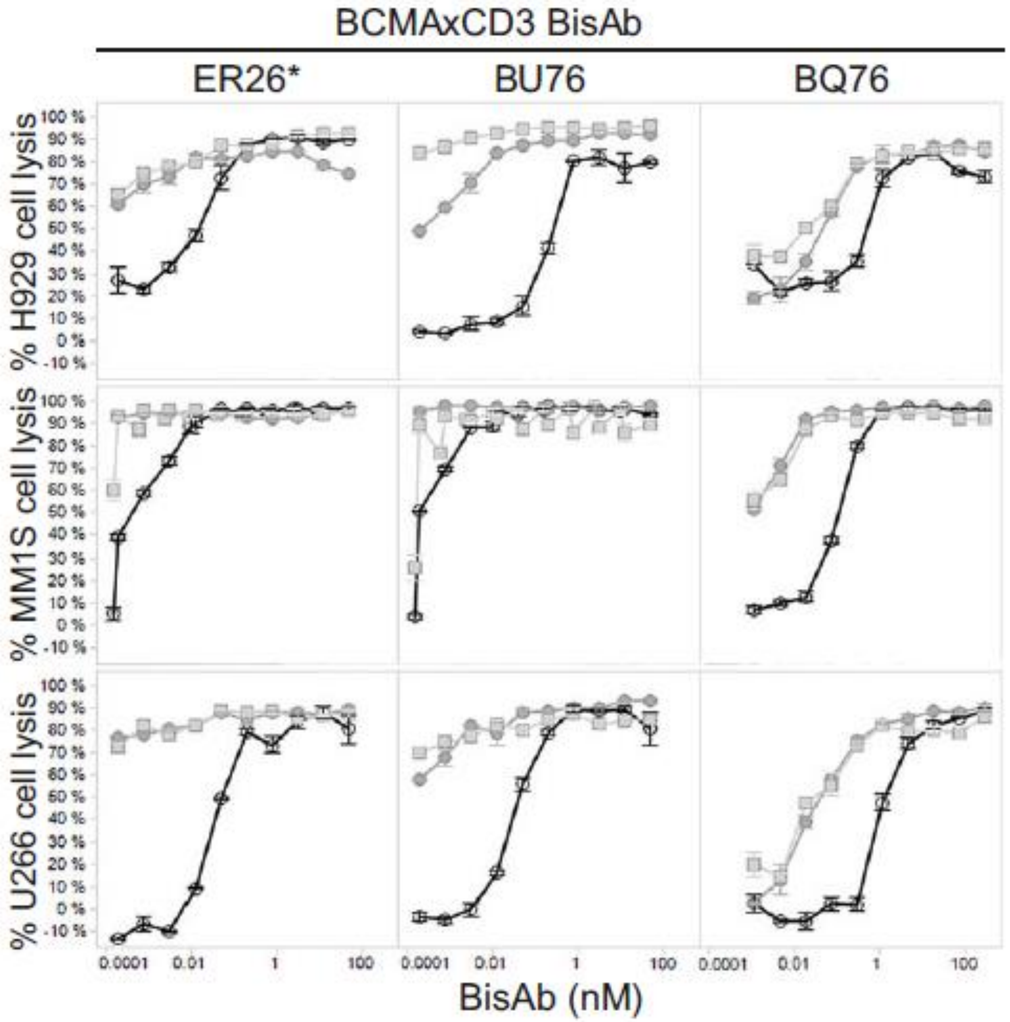
WHAT sBCMA DOES



Blood Adv 7 (4), 2023

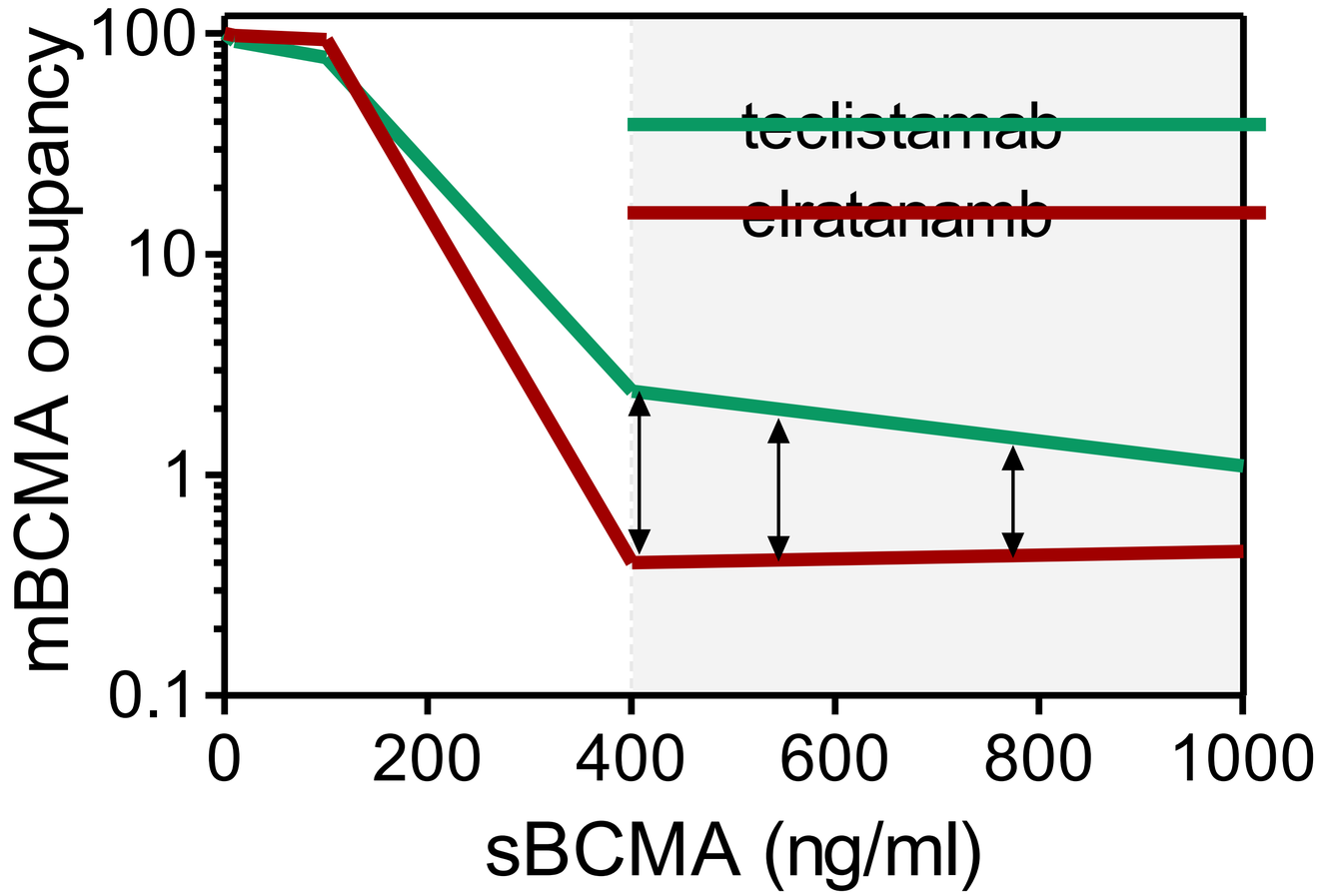
LESS sBCMA, MORE mBCMA, HIGHER EFFICACY OF ANTI BCMA BiTEs





Leukemia (2022) 12: 118

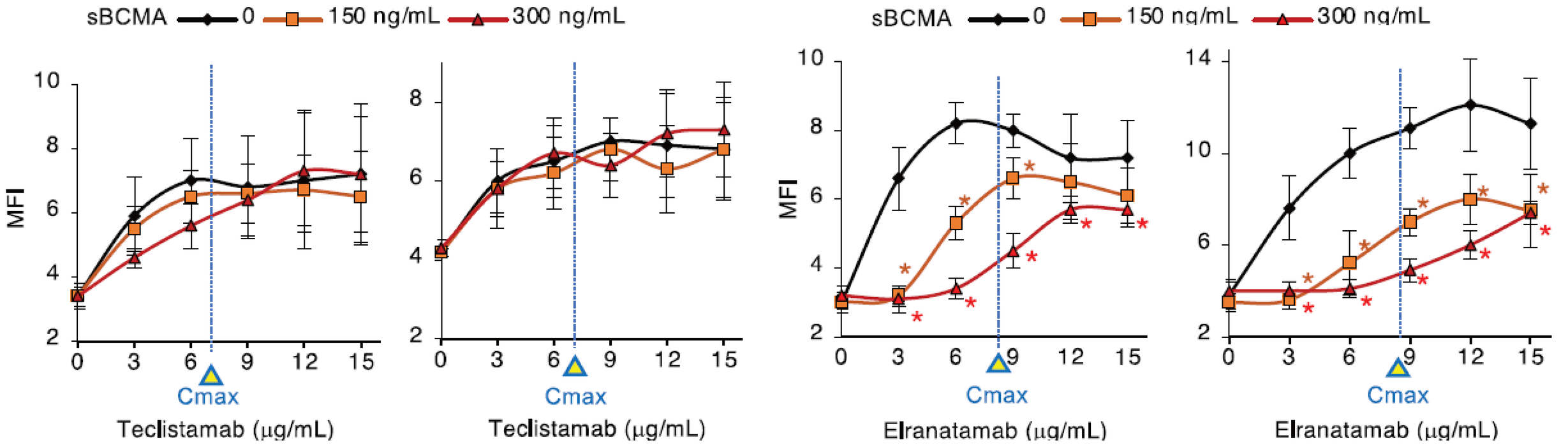
TECLISTAMAB > ELRANATAMAB @ sBCMA >200 ng/ml



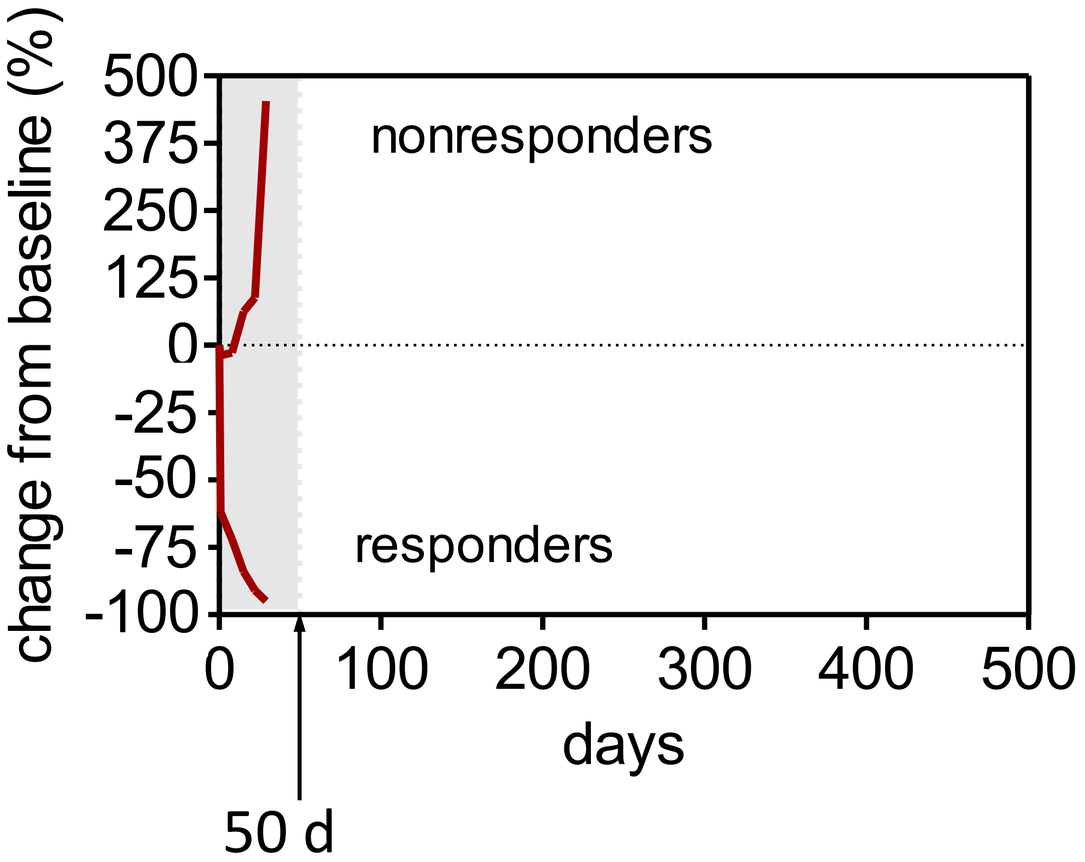
adapted from blood® 19 DECEMBER 2024 | VOLUME 144, NUMBER 25 2637

Structure-based prediction reveals a difference in the binding mode of anti-BCMA antibodies to BCMA and soluble BCMA

Leukemia (2026) 40:211–214; https://doi.org/10.1038/s41375-025-02792-3

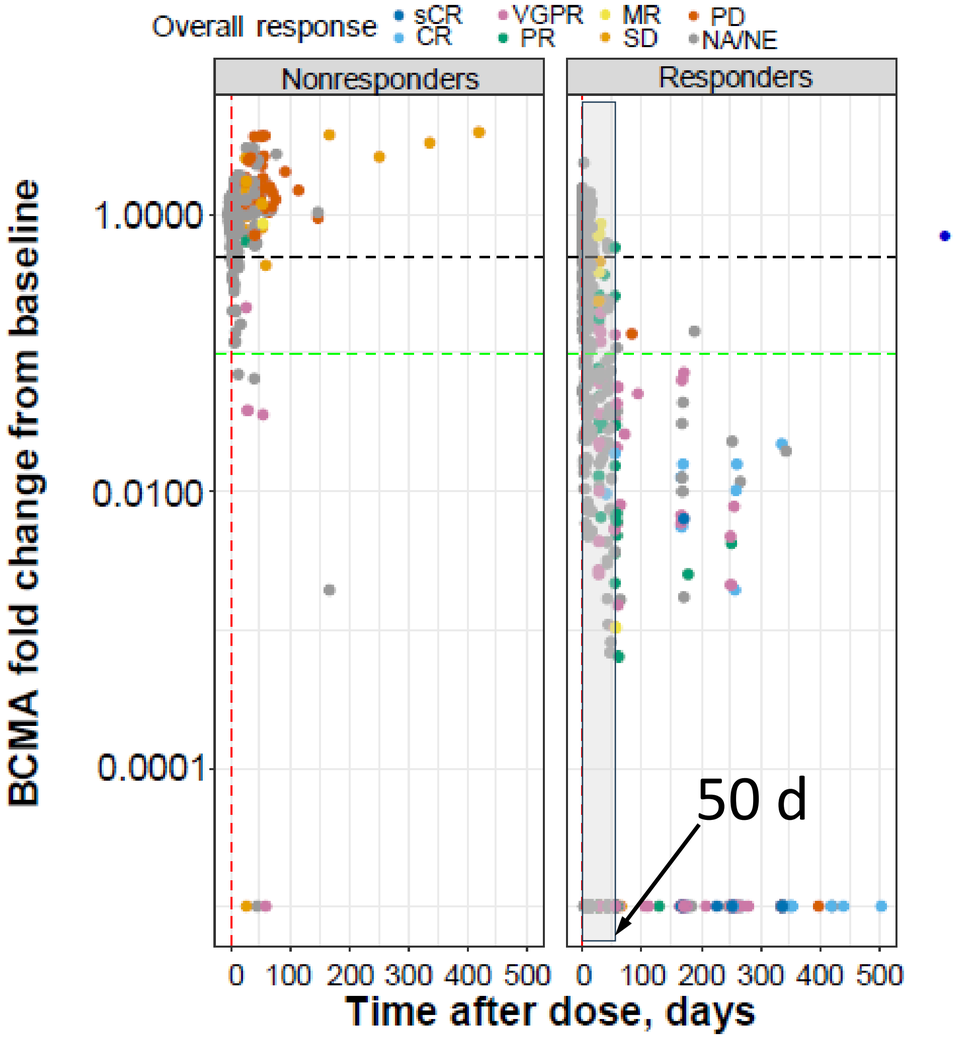


TECLISTAMAB



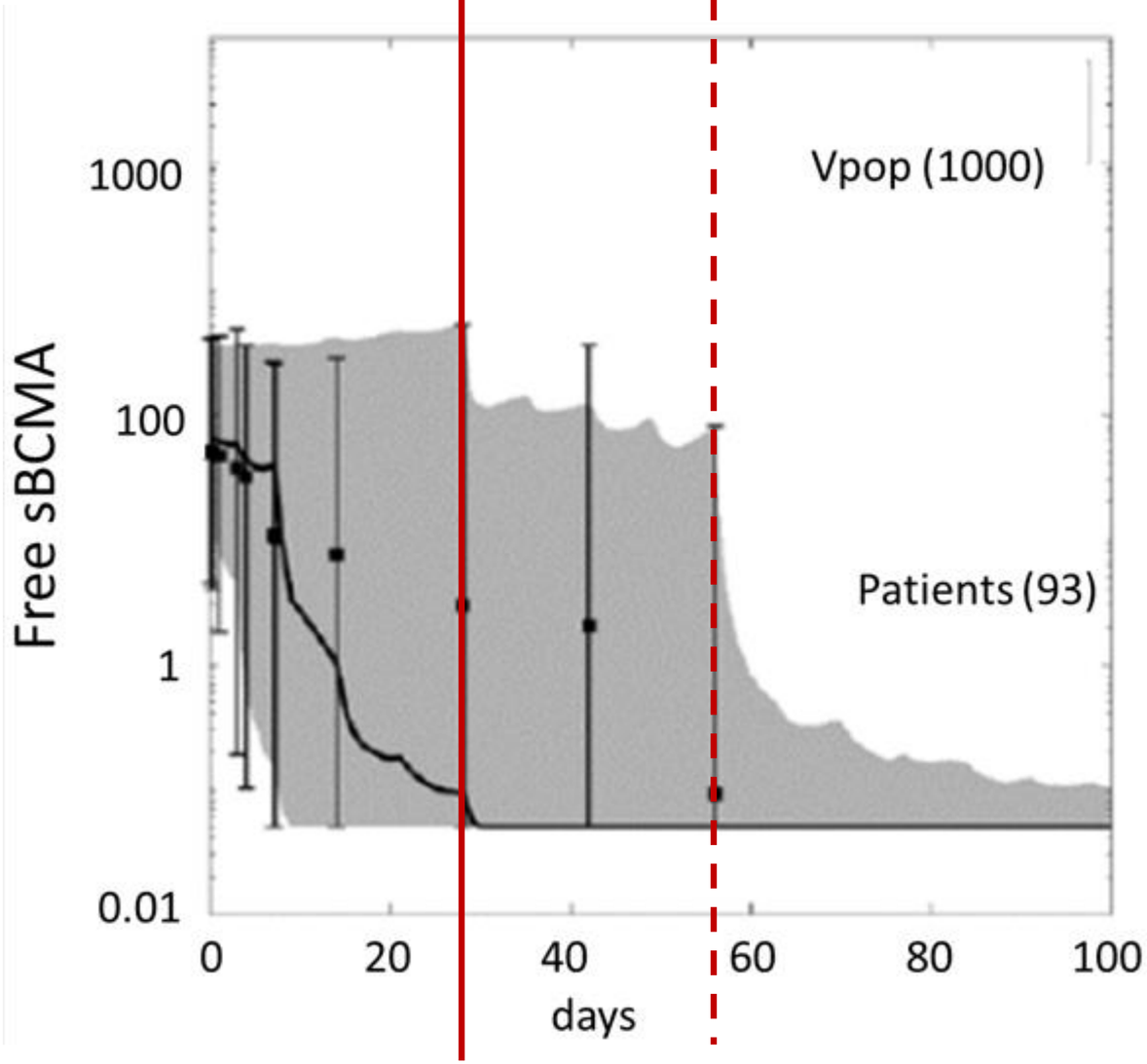
FDA Reference ID: 5065872

ELRANATAMAB



Blood 142 (Suppl. 1): 3345, 2023

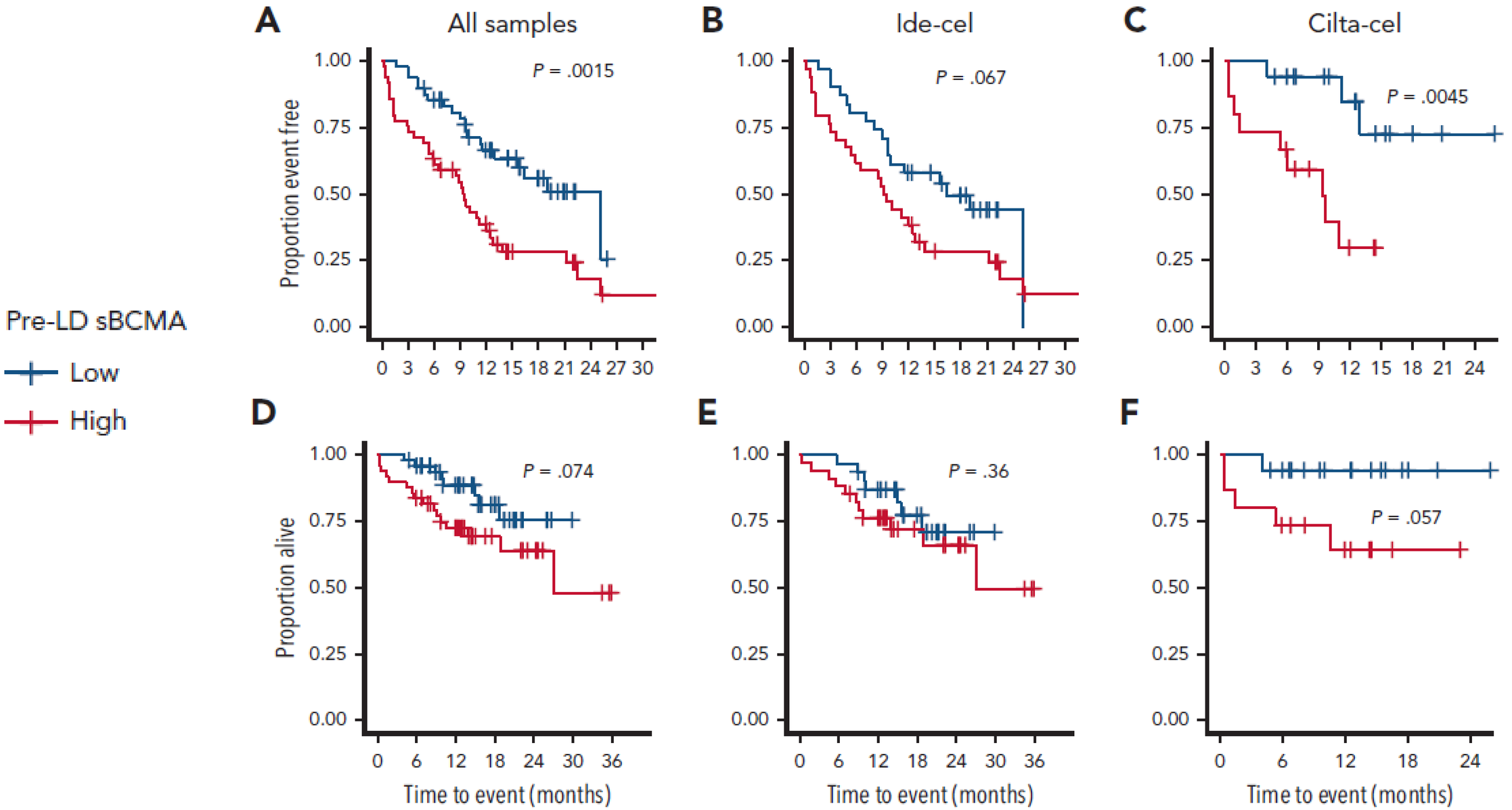
Membrane BCMA exposed, switch to less intense schedule

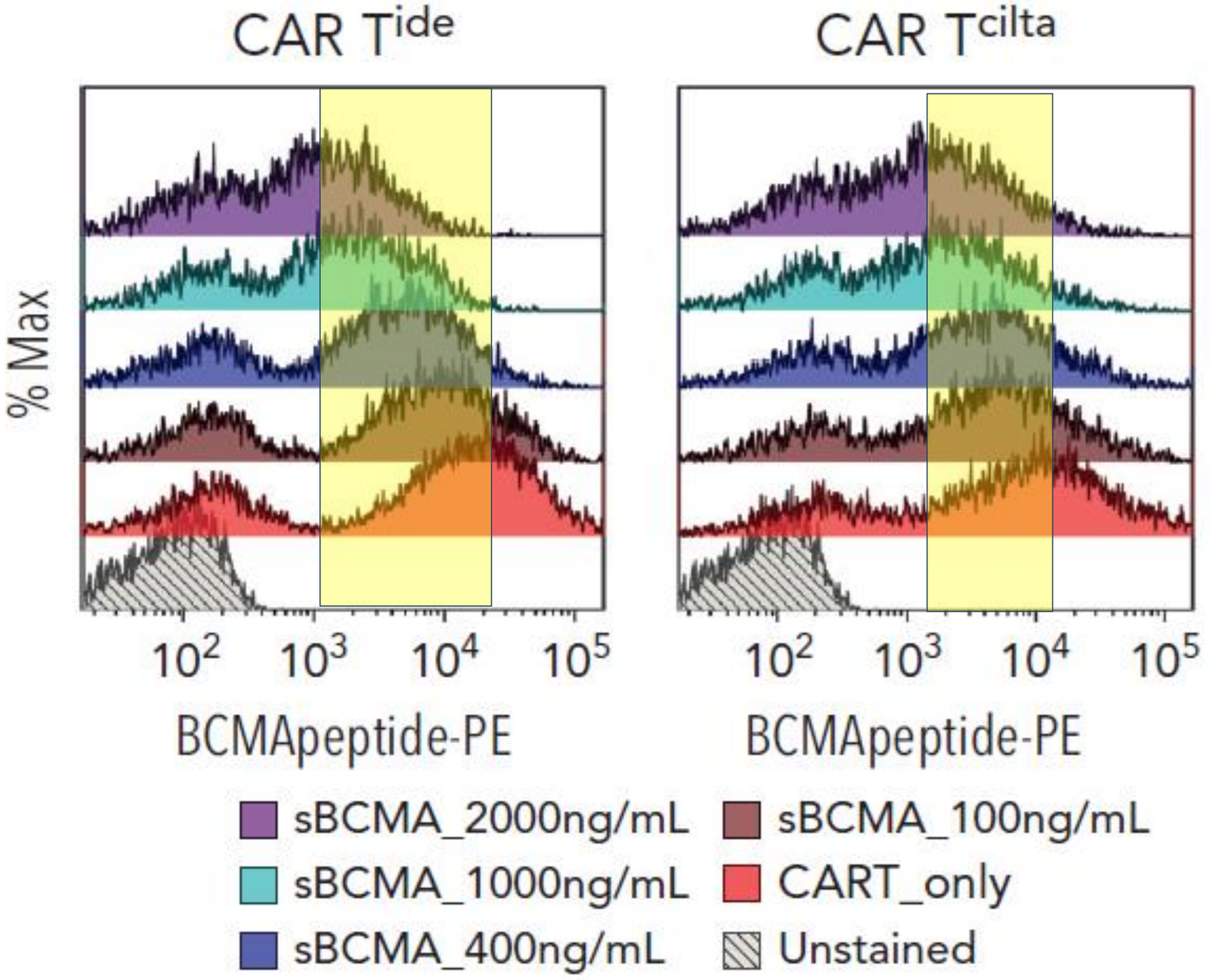


FDA Reference ID: 5226136

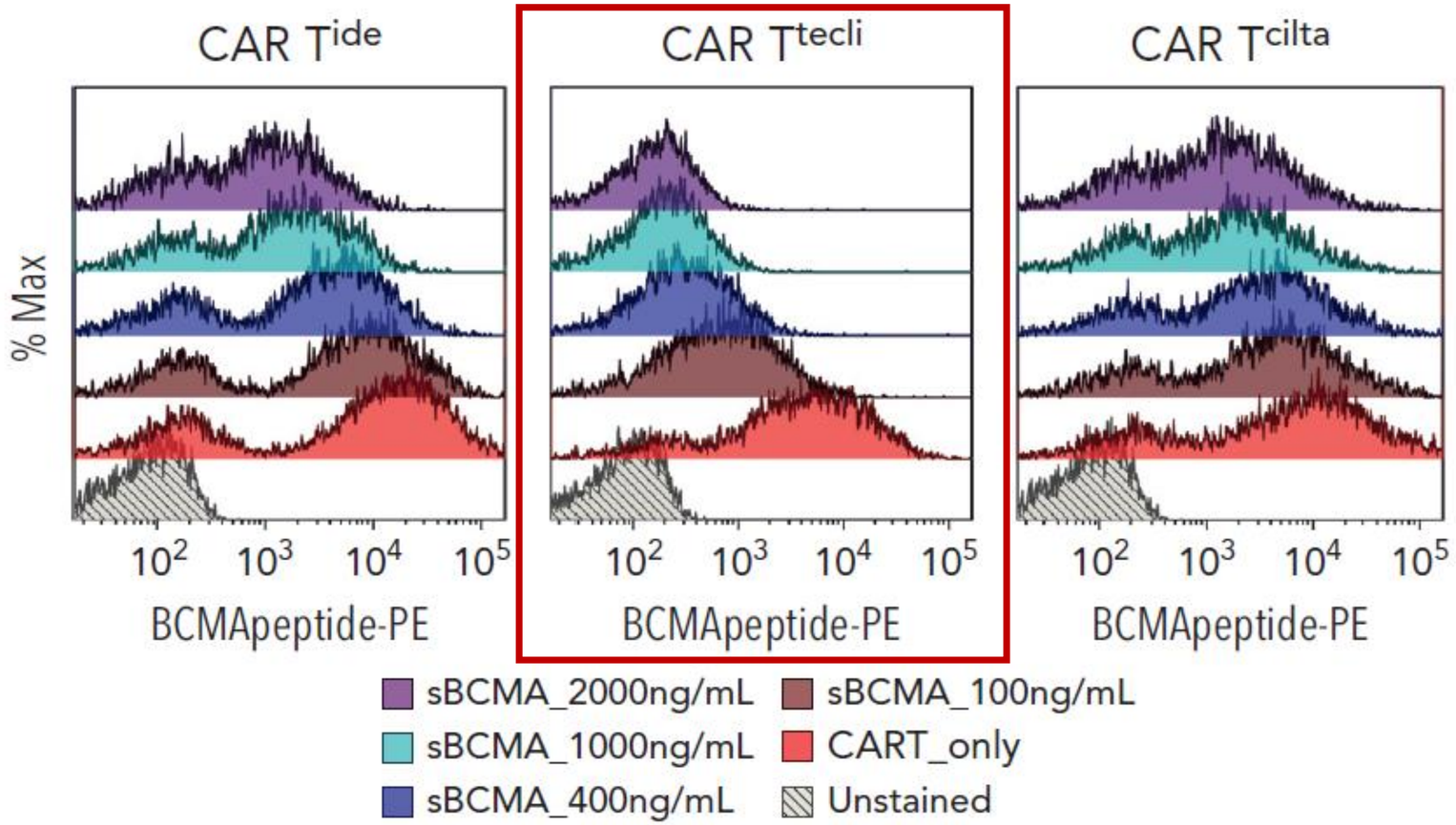
AME WITH CAR-T?

SAME WITH CAR-T?


A
All samples
P = .0015
B
Ide-cel
P = .067
C
Cilta-cel
P = .0045
D
P = .074
E
P = .36
F
P = .057
Proportion event free
Proportion alive
Time to event (months)
Pre-LD sBCMA
Low
High

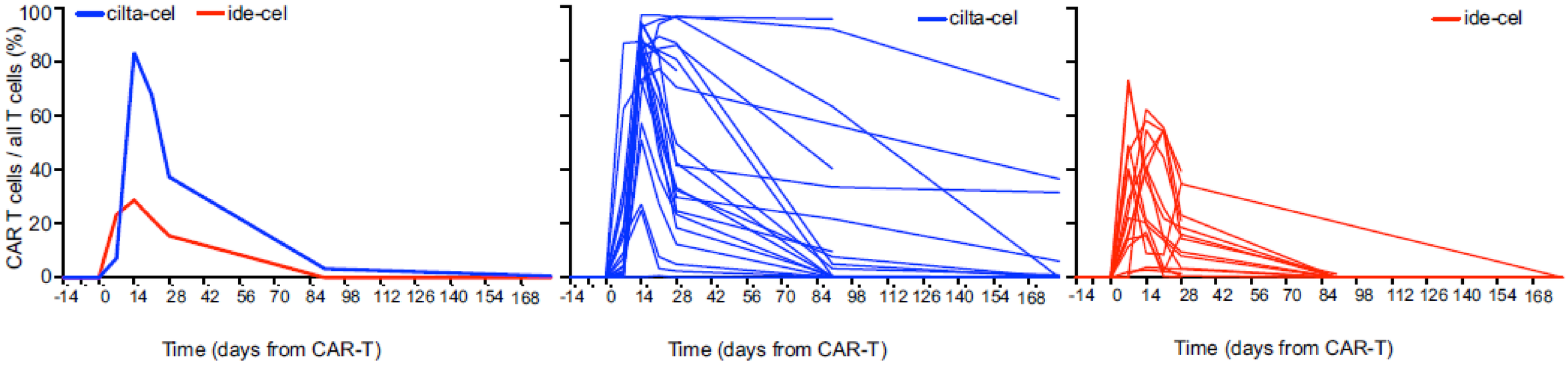

CAR T^ide
CAR T^cilta
% Max
10^2
10^3
10^4
10^5
BCMApeptide-PE
sBCMA_2000ng/mL
sBCMA_1000ng/mL
sBCMA_400ng/mL
sBCMA_100ng/mL
CART_only
Unstained

Kd 3 nM Kd 0.18-1.4 nM Kd 14-30 nM



Blood, 2025; 145:1645

AN IMPORTANT VARIABLE



Nature Comm. 2025; 16: 6154

CONCLUSIONS

- sBCMA, prognostic and outcome marker?
- Possible differentiation between anti-BCMA BiTEs
- Need for prof-of-concept studies of sBCMA-guided schedule adjustment
- CAR-T # BiTEs?

grazie