

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 punto di vista del farmacologo

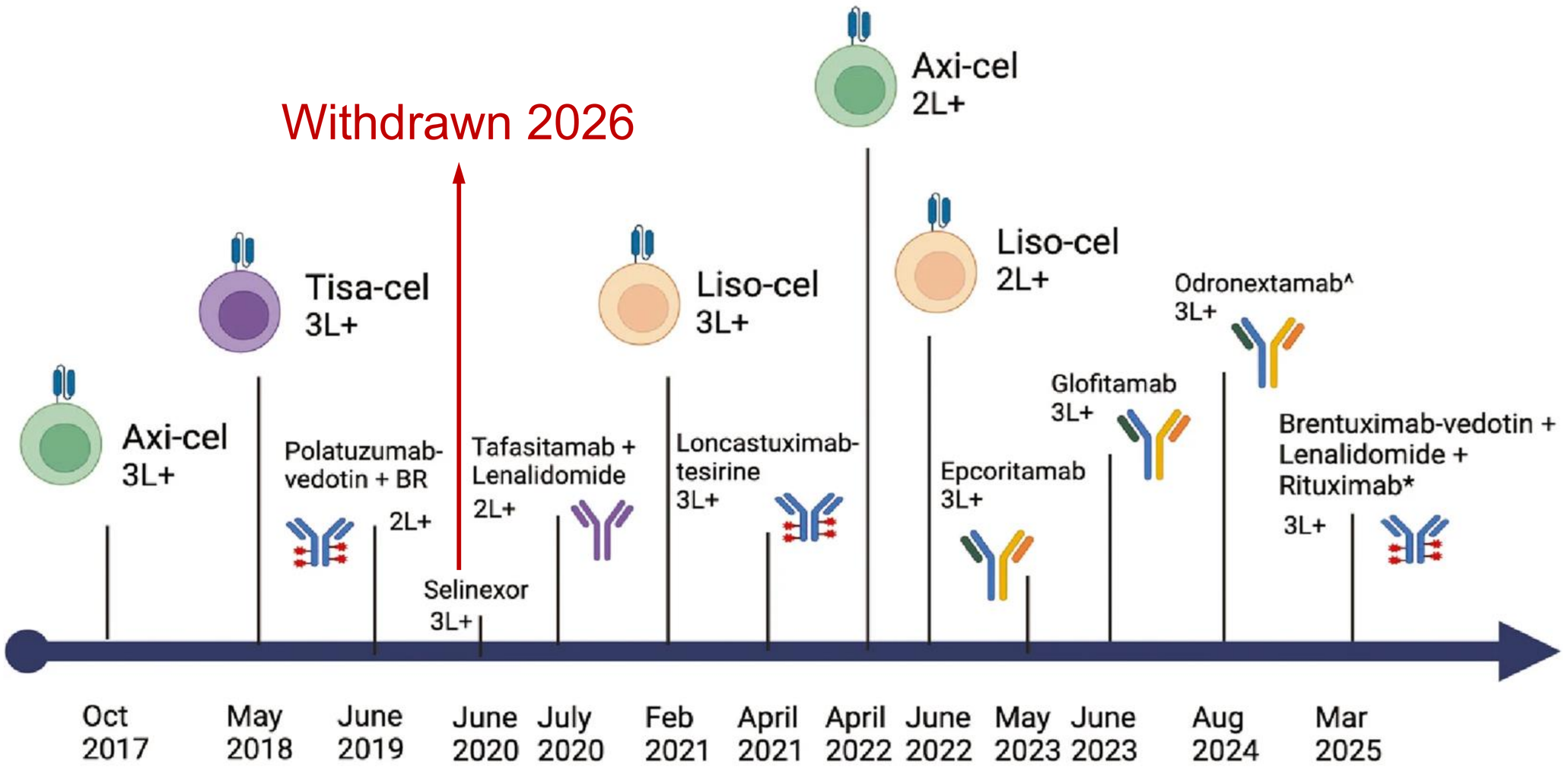
Giorgio Minotti
Università e Fondazione Policlinico Universitario Campus Bio-Medico, Roma
Fondazione Pisana per la Scienza, Pisa

Assisi, 4 novembre 2026

DISCLOSURES

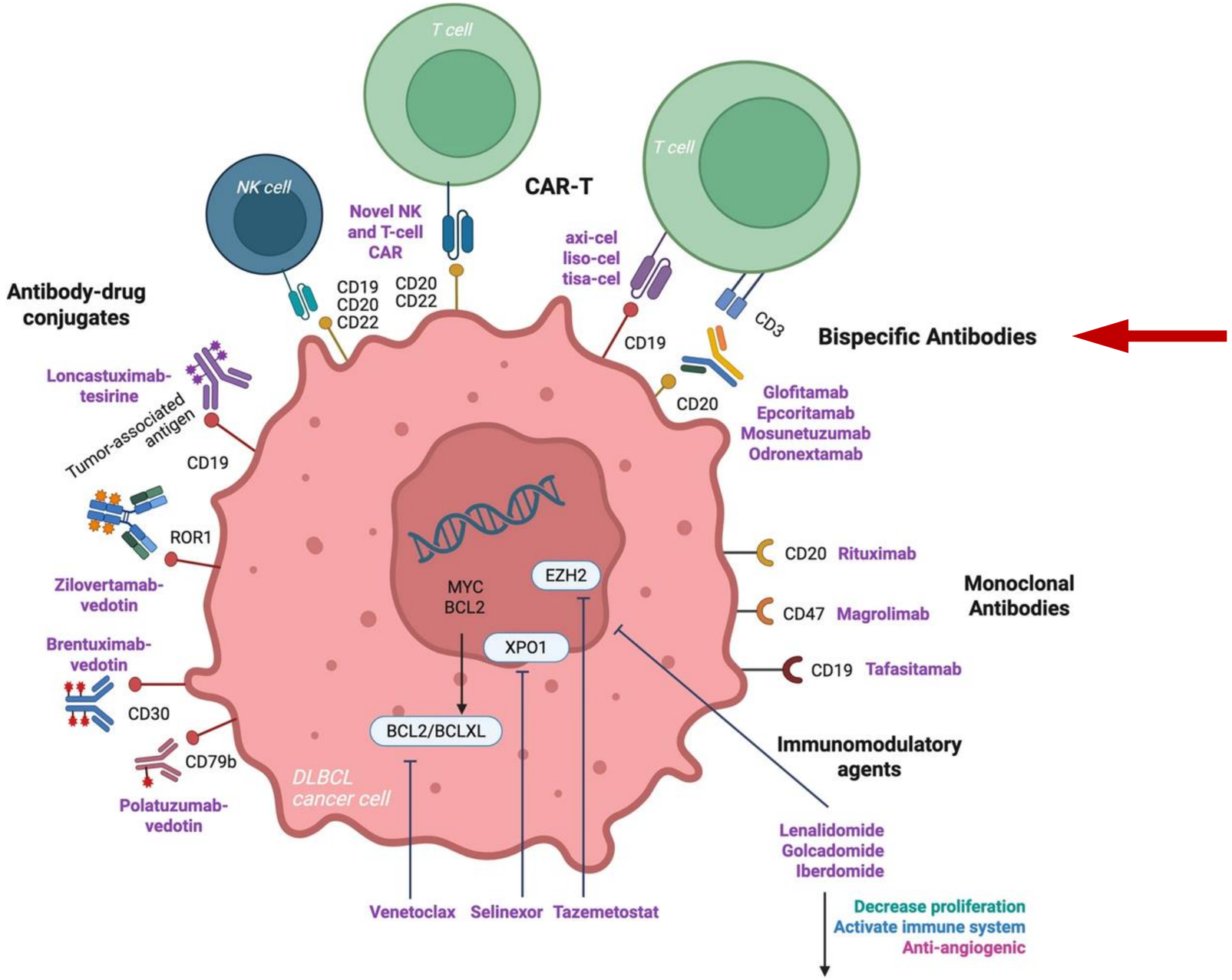
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Johnson& Johnson			X		X	X	
Incyte	X		X			X	
BeiGene			X		X	X	
Servier			X			X	
Astellas	X						
Pfizer					X		
Gentili					X		
Lilly					X	X	
Daiichi Sankyo						X	

FDA & EMA APPROVALS IN R/R DLBCL



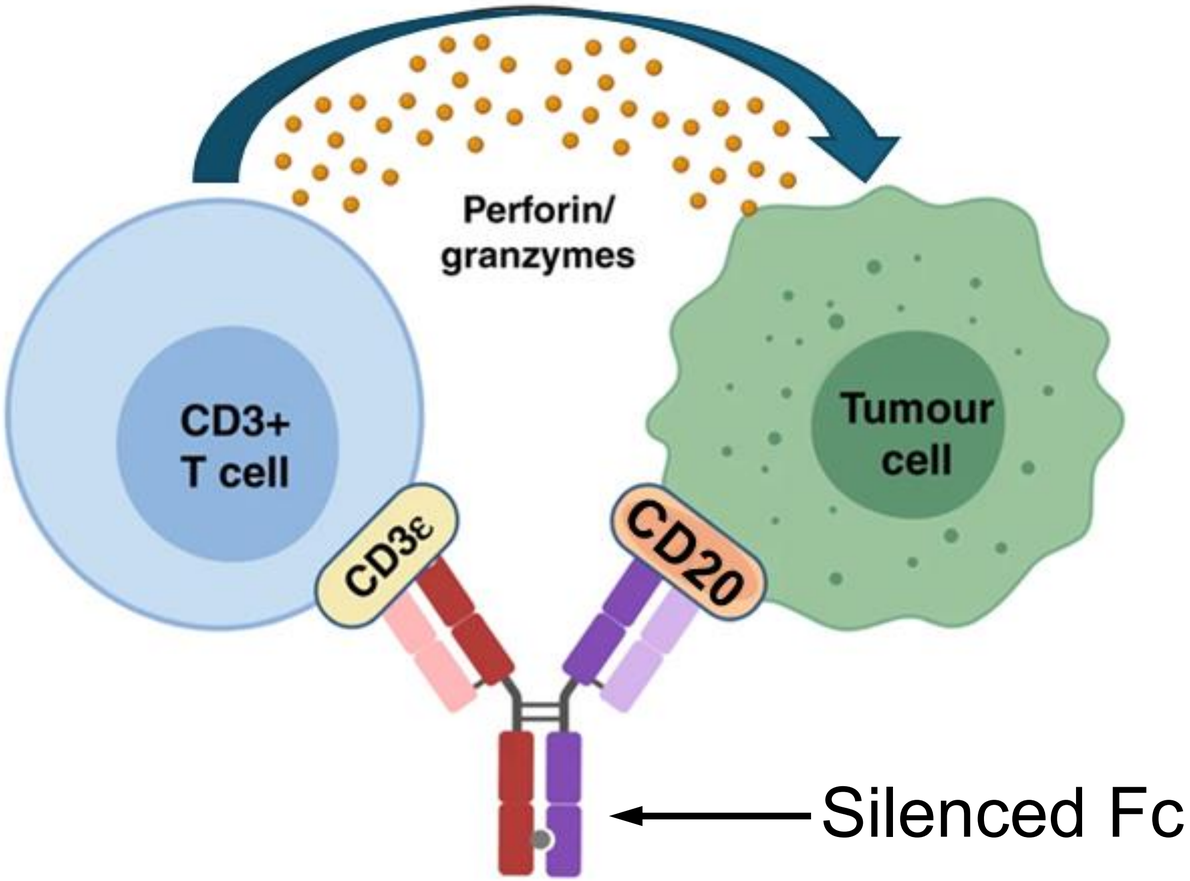
Abbreviations: axi-cel, Axicabtagene ciloleucel; liso-cel, Lisocabtagene maraleucel; tisa-cel, Tisagenlecleucel. 2L+, second line or later; 3L+, third line or later. *FDA approval only, ^EMA approval only.

Journal of Hematology & Oncology (2025) 18:68



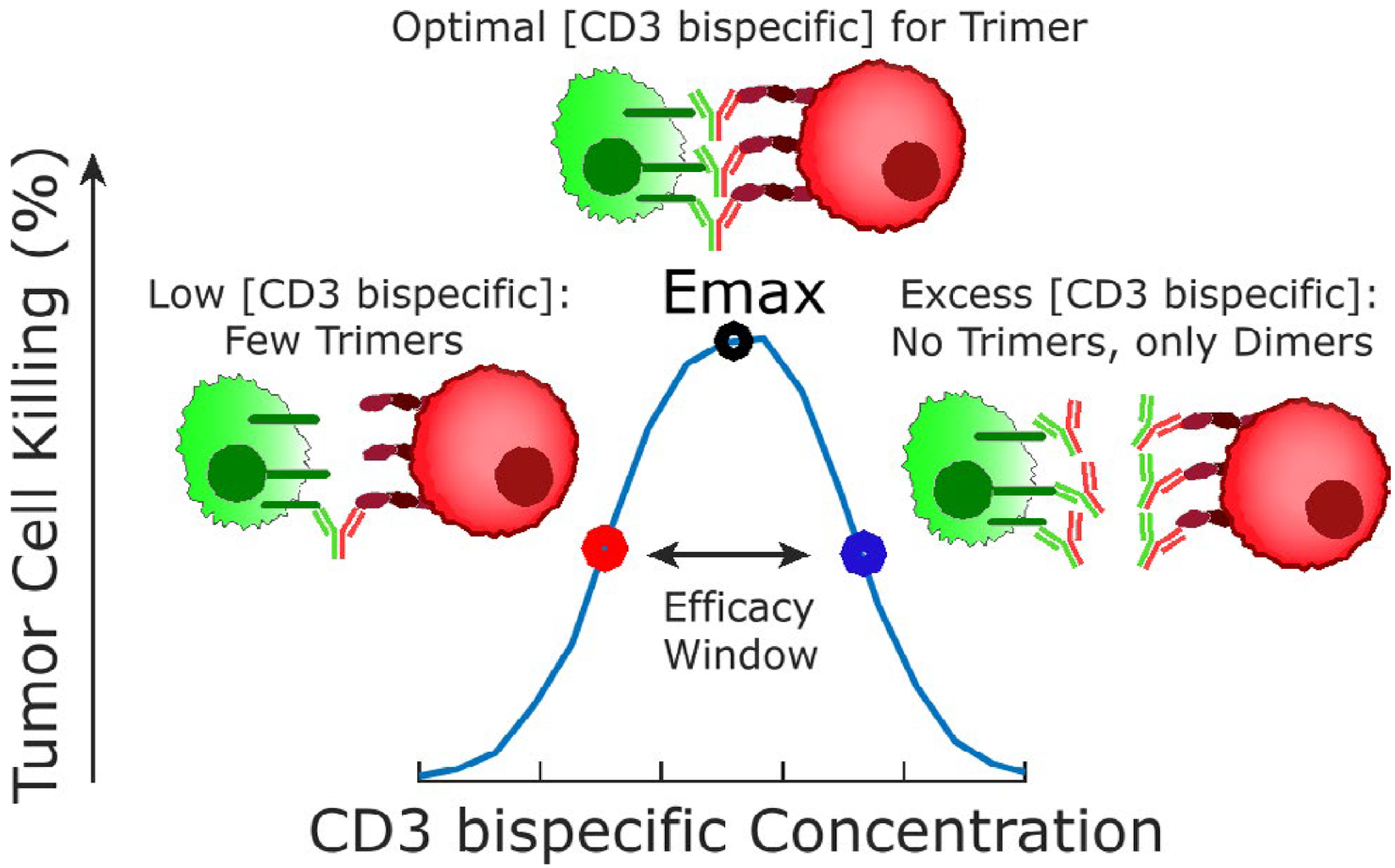
Journal of Hematology & Oncology (2025) 18:68

BiTEs and trimers



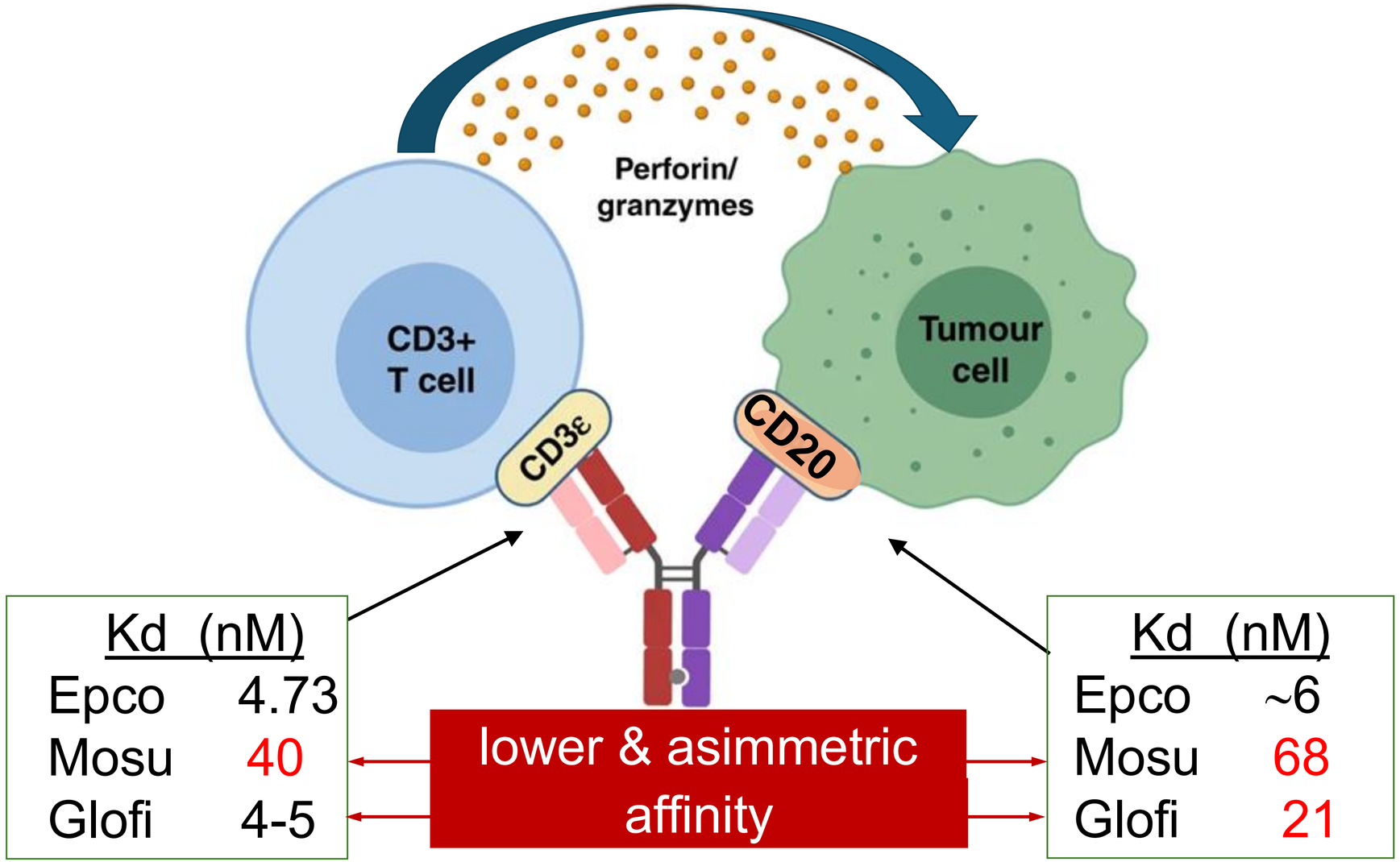
Modified after Singh et al. Br. J. Cancer (2021) 124:1037-1048

Trimers and efficacy window



Betts et al. Clin. Pharmacol. Ther. 2020;108:528

Not all trimers are identical



FDA Access Data, Reference ID: 5100050;

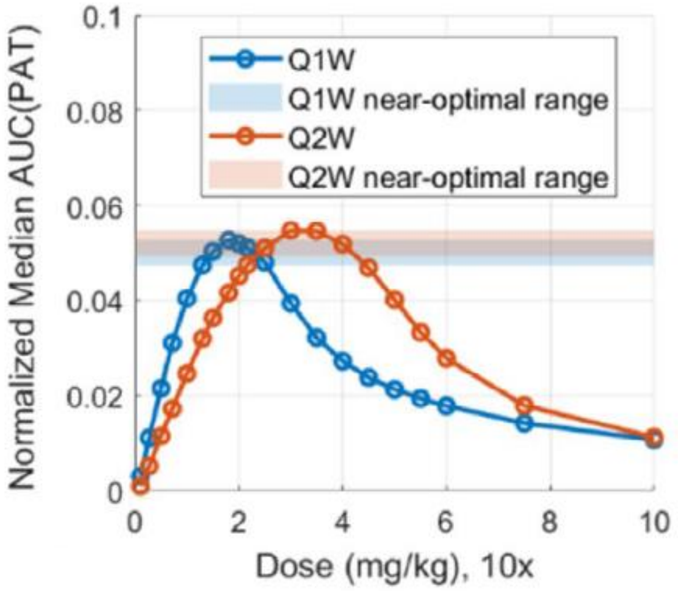
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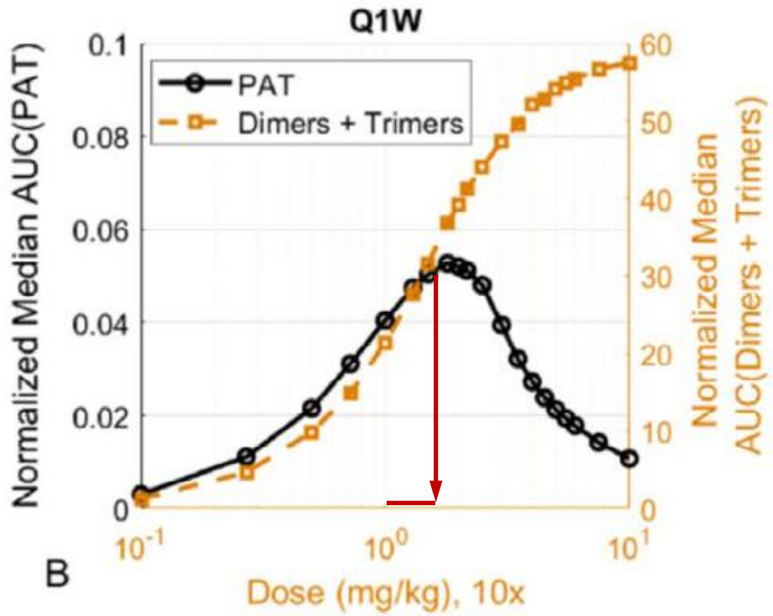
NOT ALL PATIENTS ARE IDENTICAL

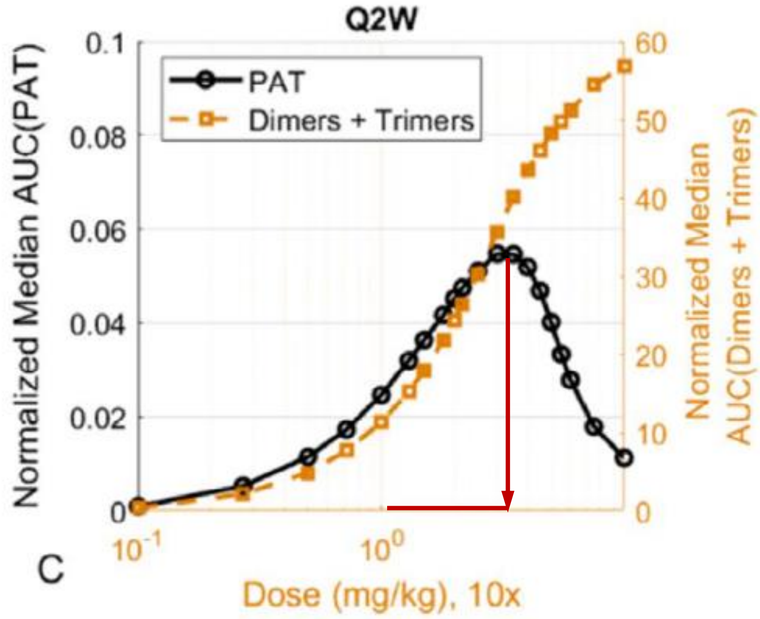
CD3	CD20
HIGH	HIGH
HIGH	low
low	HIGH
low	low

Concept from Gevertz & IKareva,
CPT: Pharmacometrics & Systems Pharmacology, 2025

PK/PD INFORMING OF SCHEDULE

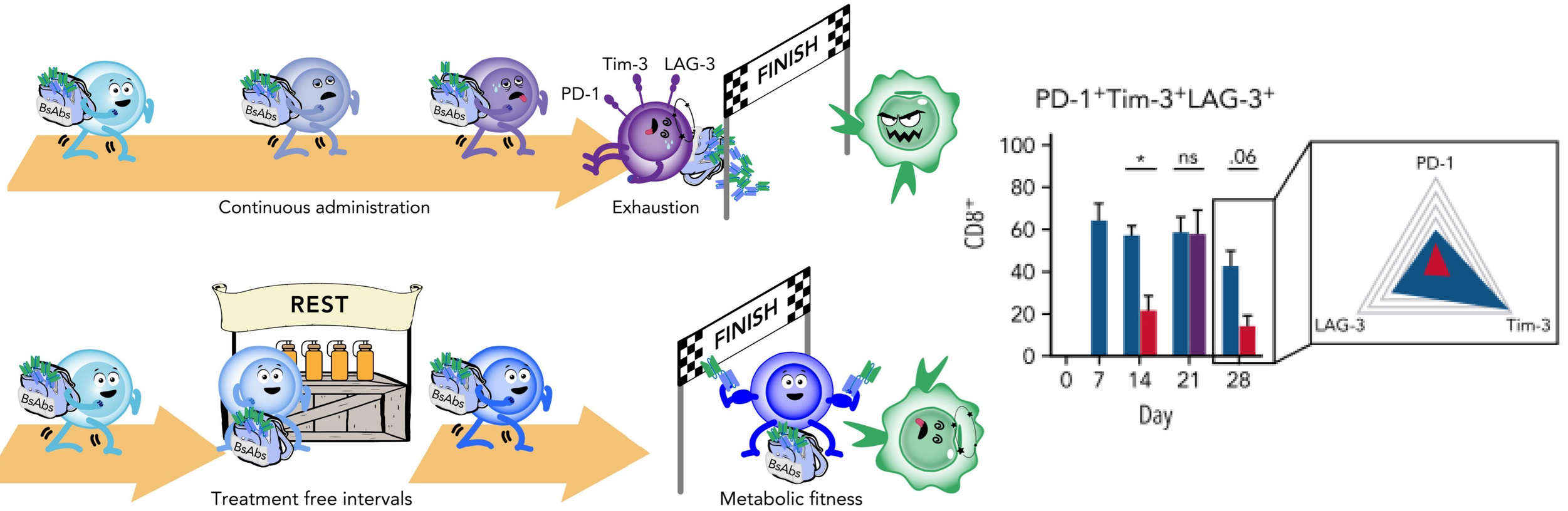




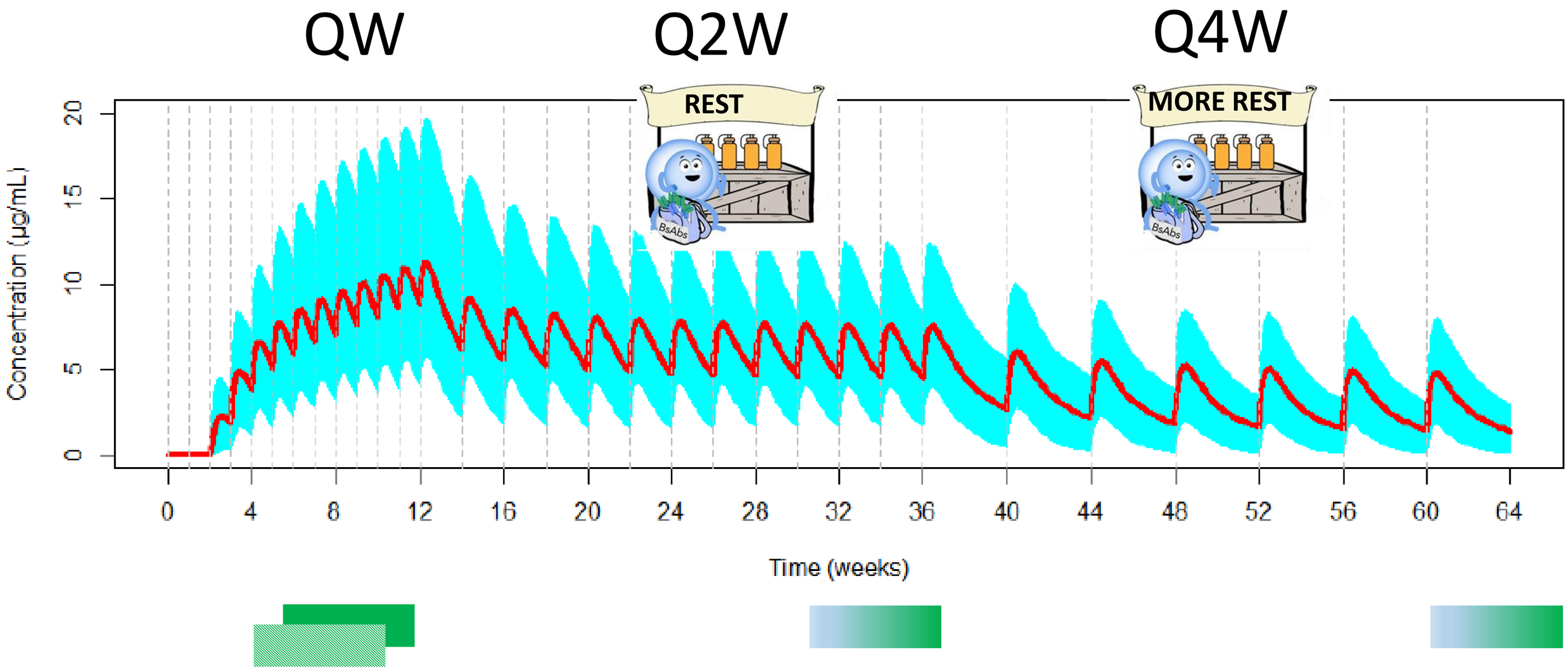


CPT: Pharmacometrics & Systems Pharmacology, 2025

Treatment induced CD8+ exhaustion: give them a rest

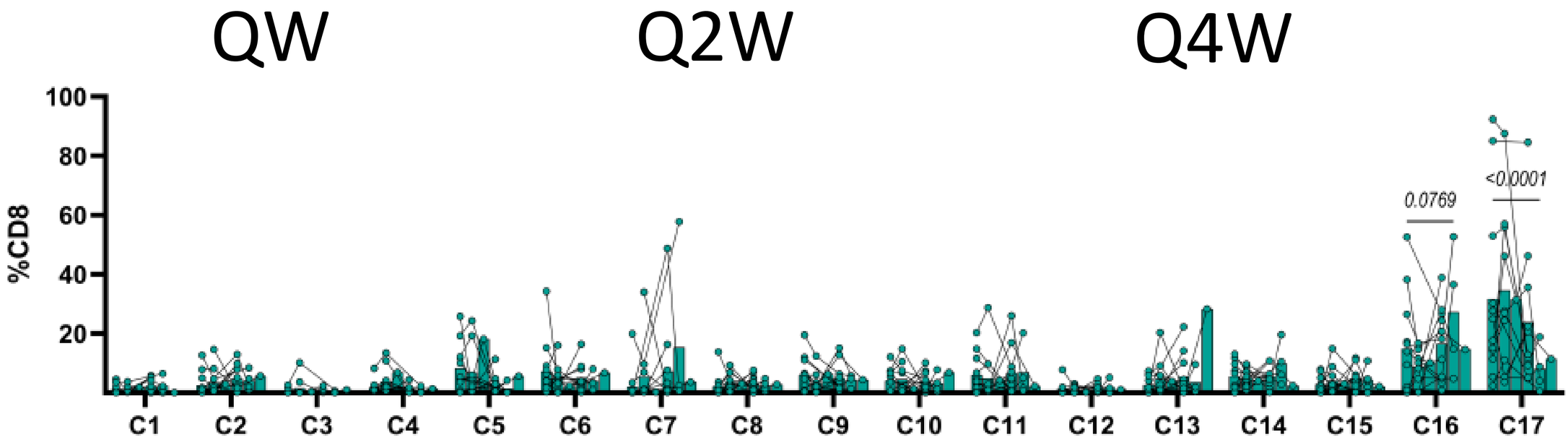


Blood. 2022;140:1104–1118

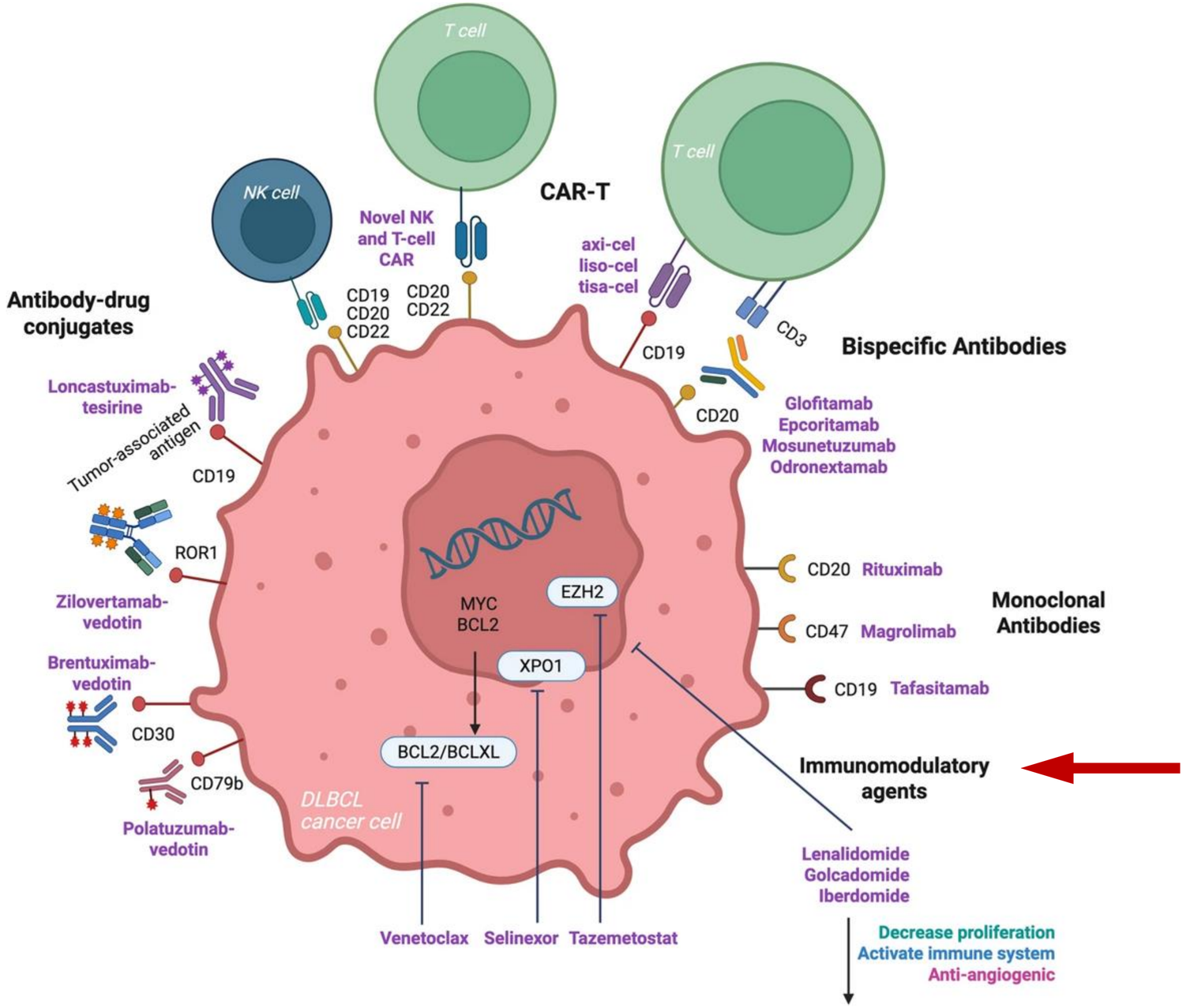


FDA Access Data, Reference ID: 5176690; Leukemia (2024) 38:2653 – 2662

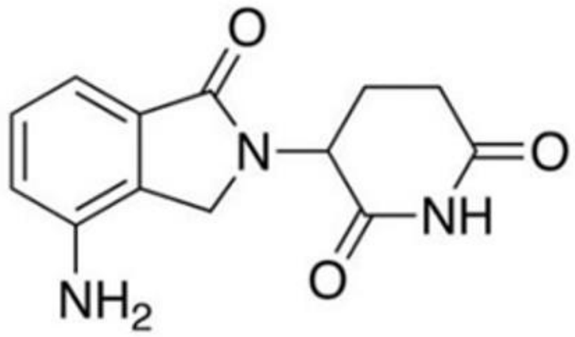
ACTIVATED EFFECTOR MEMORY CD8+ T CELLS DURING Q4W

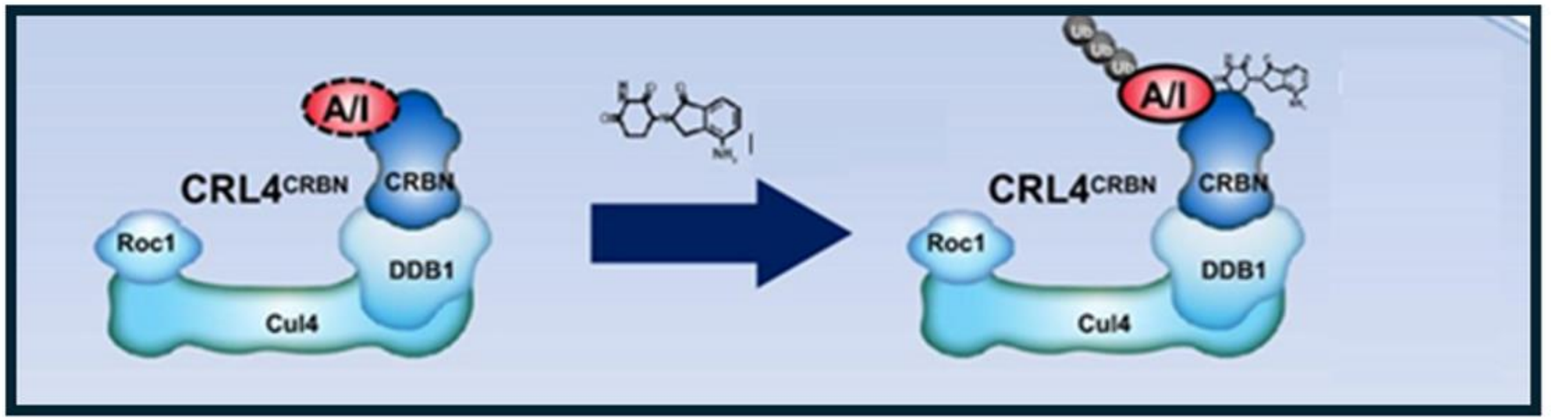


FDA Access Data, Reference ID: 5176690; Leukemia (2024) 38:2653 – 2662

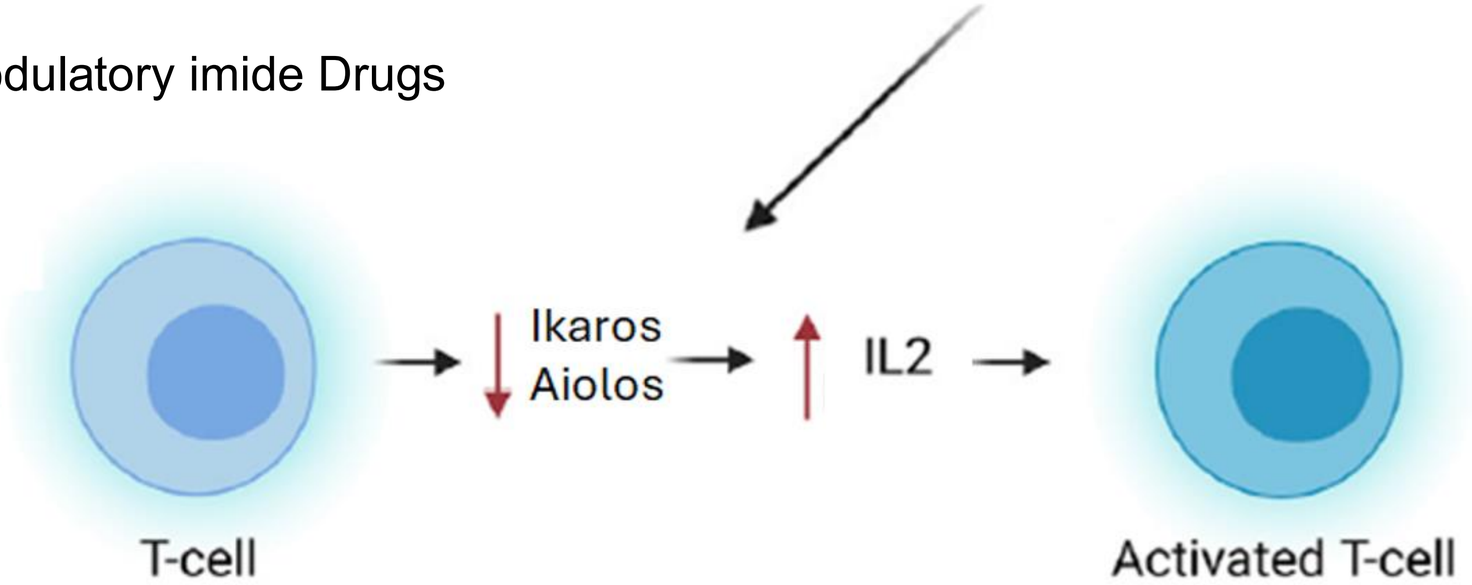


Journal of Hematology & Oncology (2025) 18:68



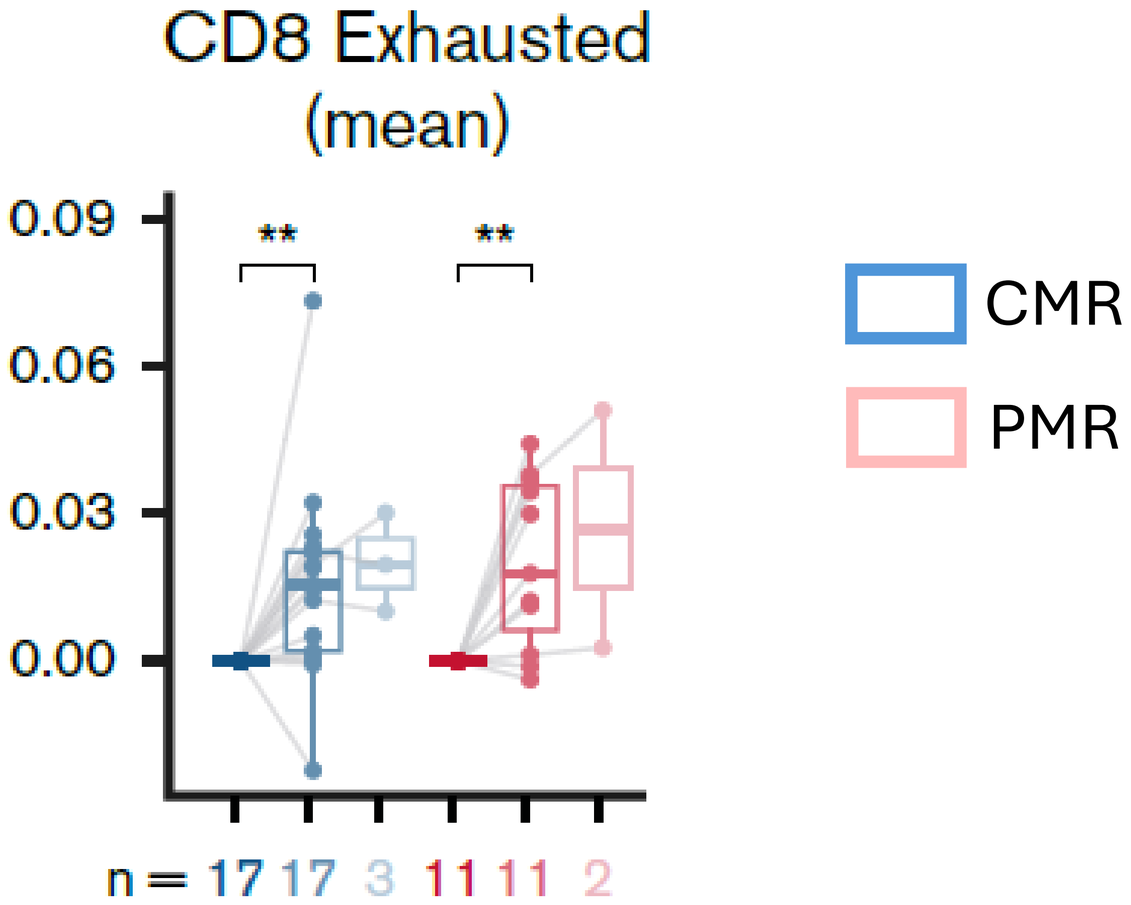


IMiDs:
Cereblon-targeting ImmunoModulatory imide Drugs



Labicki et al. Cell Chem. Biol. 2022; 29: 1245-1247

ALSO IN FD THERAPY



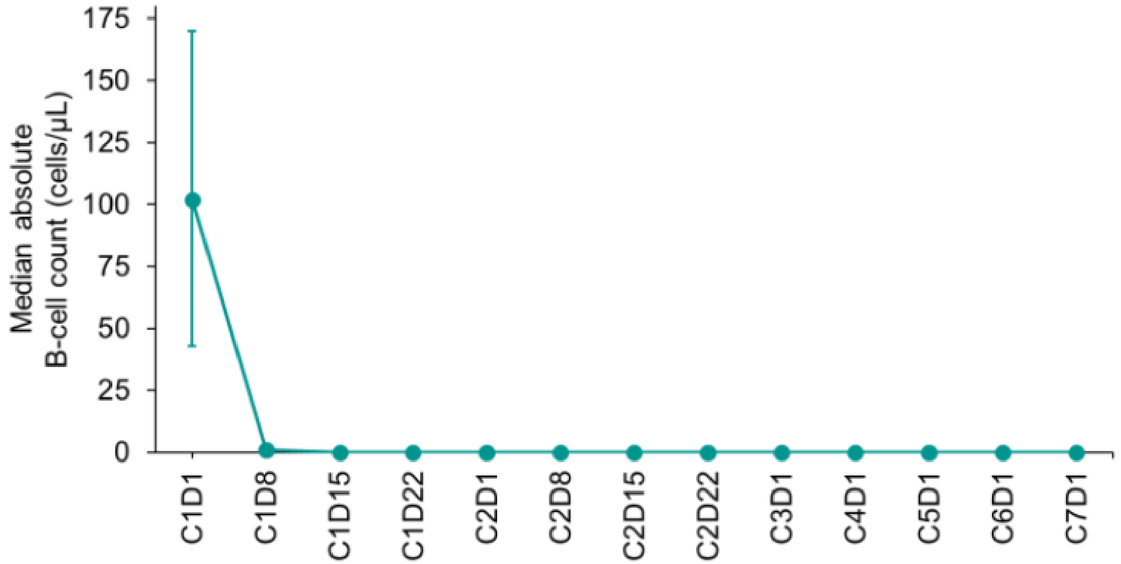
Blood Adv (2026) 10, 2976

RITUXIMAB

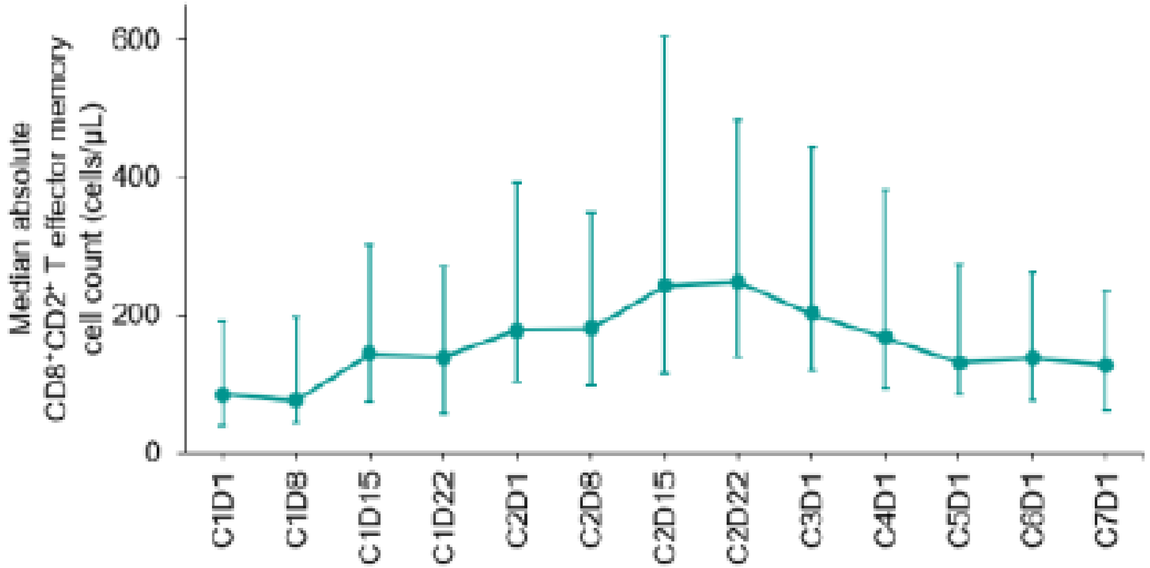
FD R² EPCO

LENALIDOMIDE

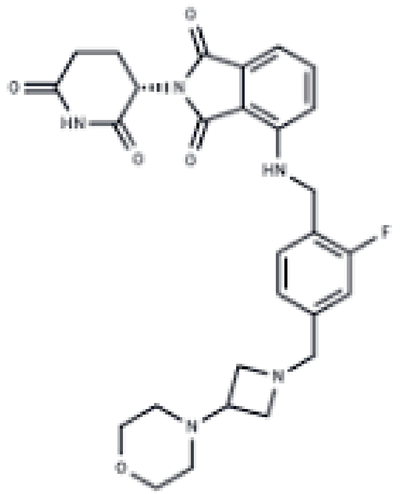
B cells

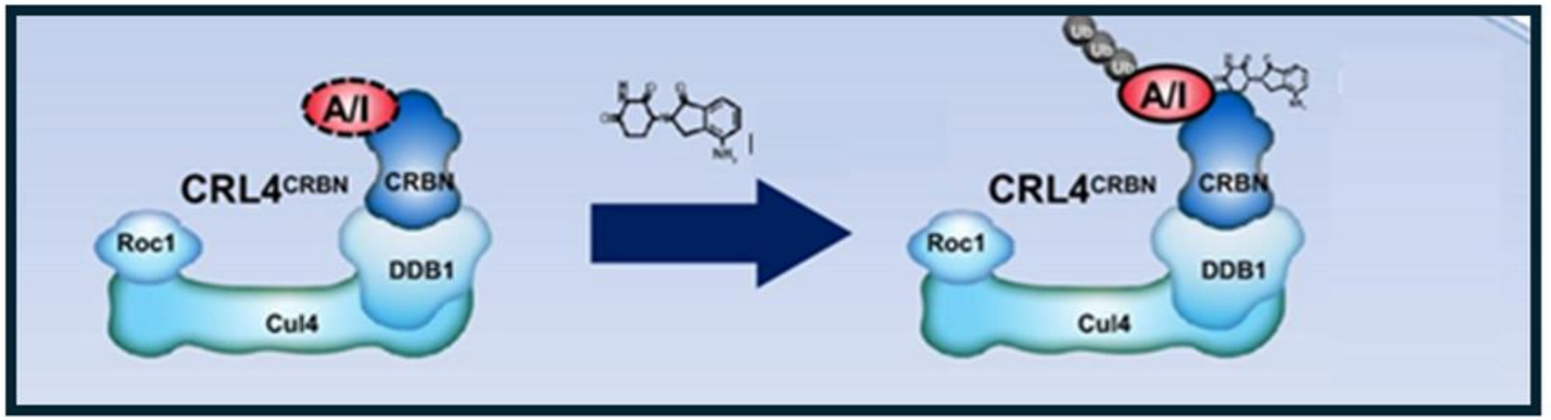


CD8+ T effector memory cells



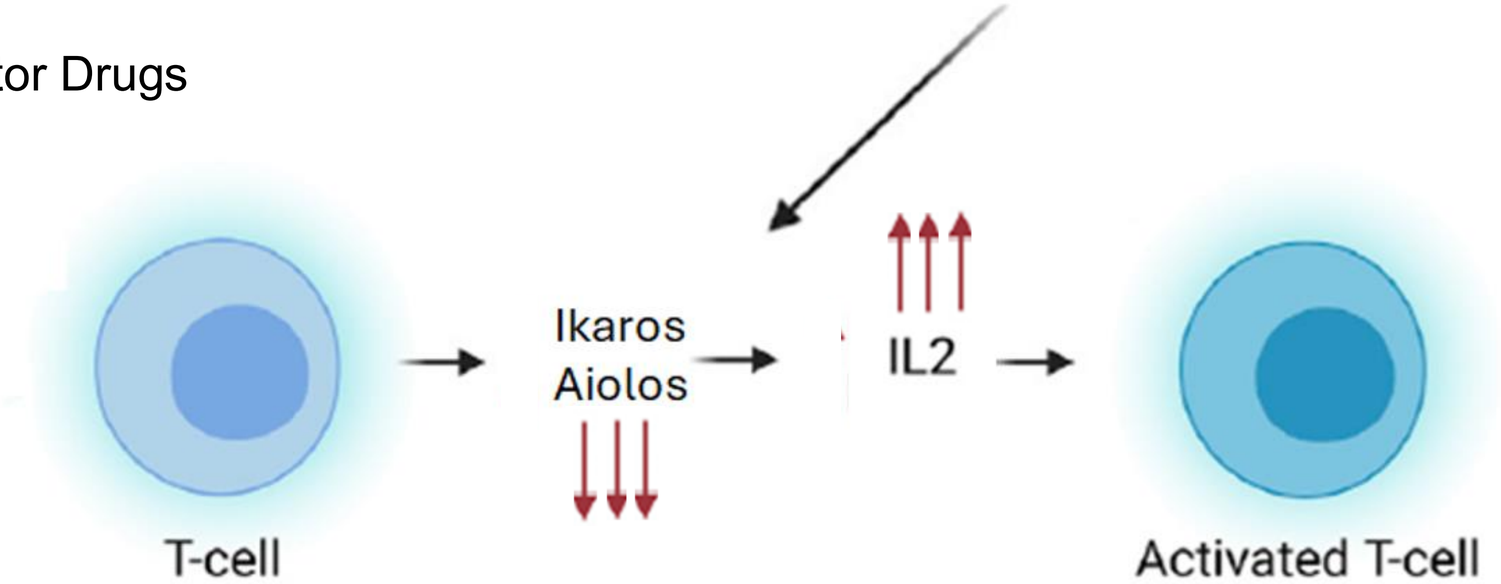
Blood 2025, 146:2630





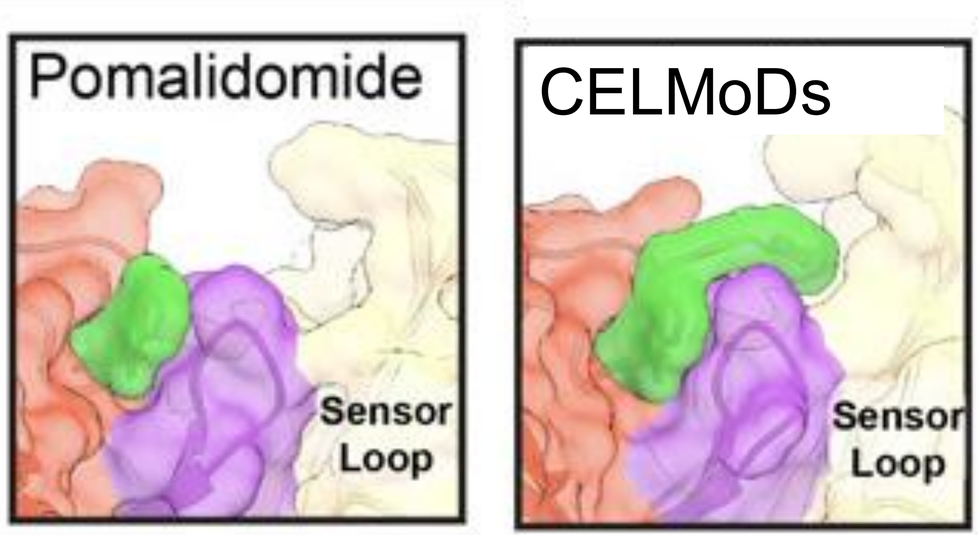
CELMoDs:
Cereblon E3 Ligase Modulator Drugs

~10-20-fold higher affinity
~10-100 fold potency



Labicki et al. Cell Chem. Biol. 2022; 29: 1245-1247

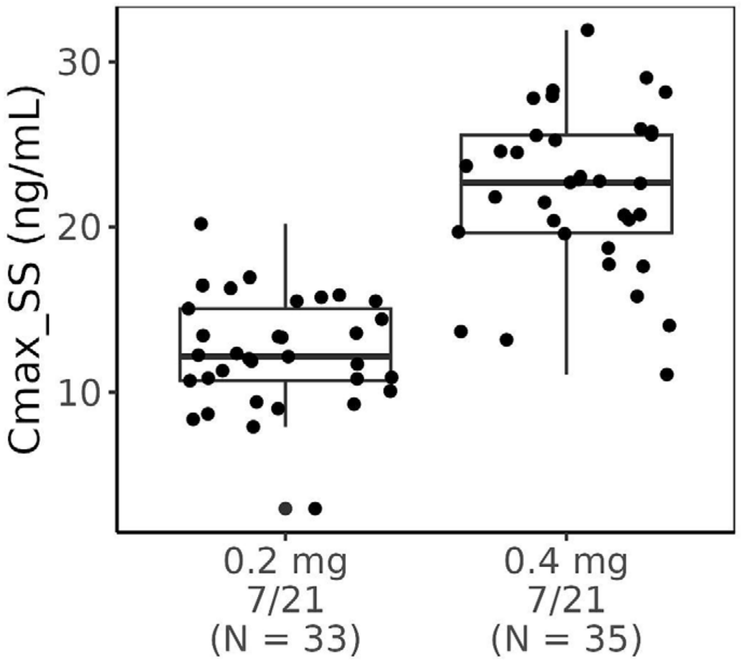
Potency of CELMoDs in the induction of Ikaros degradation compared to classical IMiDs: golcadomide > iberdomide > avadomide > pomalidomide > lenalidomide.

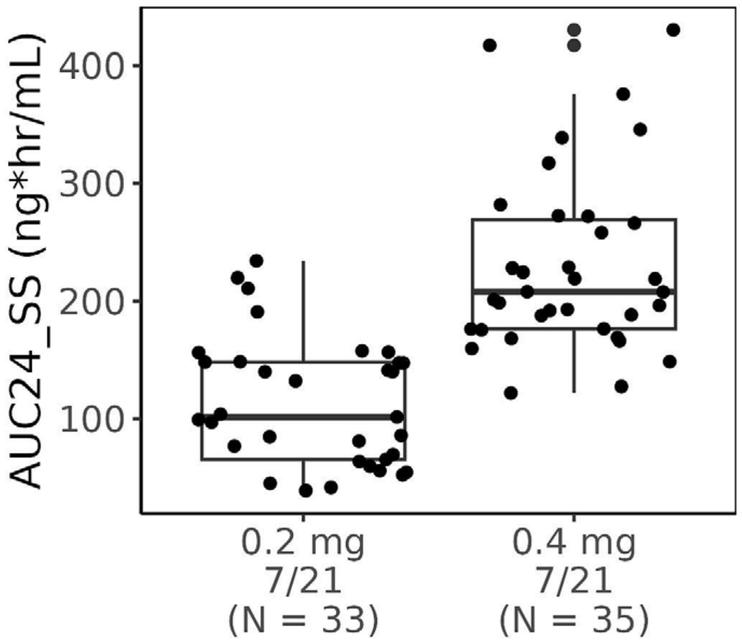


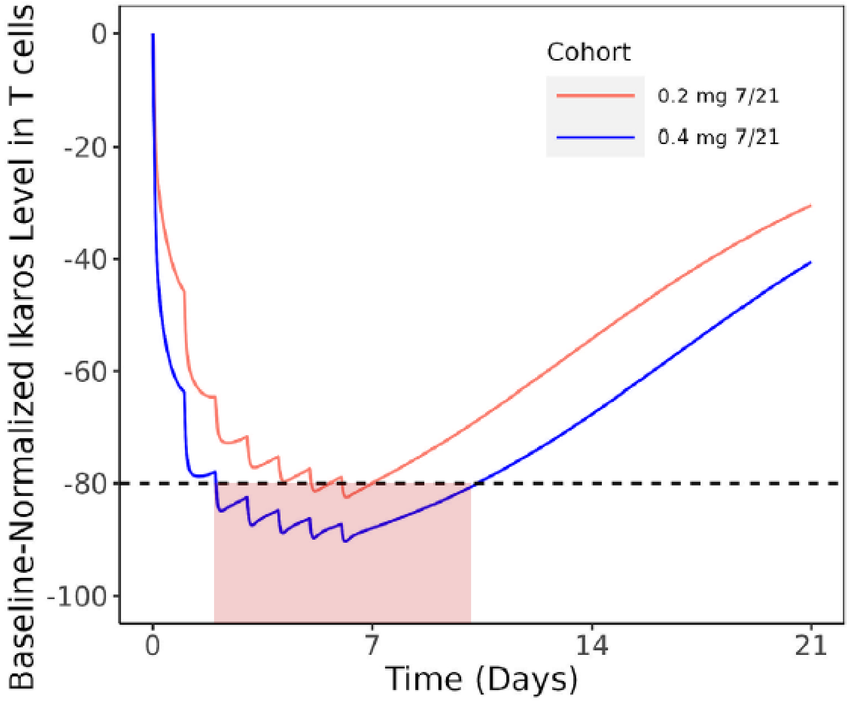
Fuchs O. Blood Reviews 57 (2023) 100994

Watson et al., (2022) BioRxiv

PK/PD informing of GOLCA dose







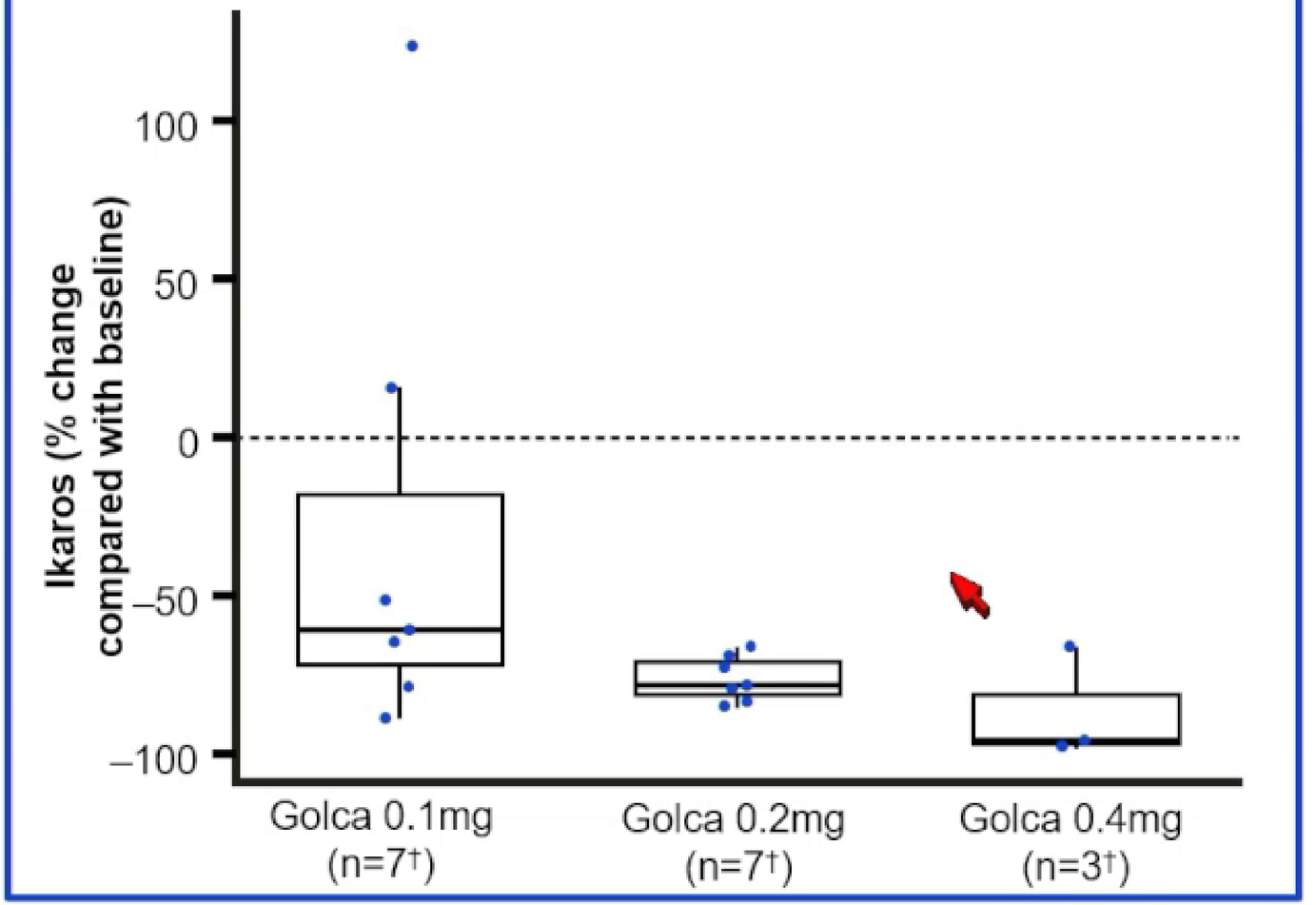
Br J Clin Pharmacol. 2026;1–13.

Mosunetuzumab (Mosun) or glofitamab (Glofit) in combination with golcadomide (Golca) demonstrates a manageable safety profile and encouraging efficacy in patients with relapsed or refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL)

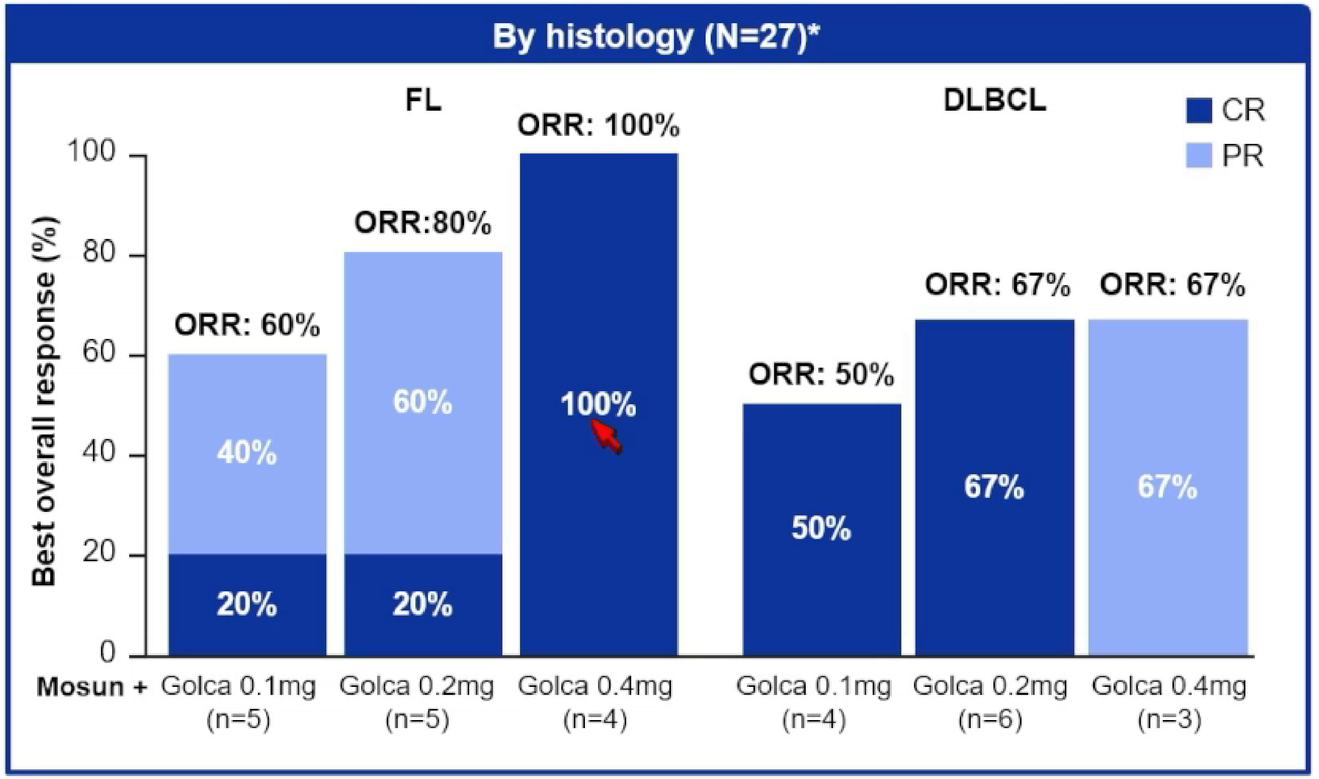
Charalambos Andreadis,[1] Irit Avivi,[2] Neta Goldschmidt,[3] William Townsend,[4] Mariana Bastos-Oreiro,[5] Abraham Avigdor,[6] Peter A. Riedell,[7] Inna Tzoran,[8] Toby A. Eyre,[9] Pamela McKay,[10] Pau Abrisquesta,[11] Eva Gonzales Barca,[12] Alejandro Martin Garcia-Sancho,[13] Sara Galimberti,[14] Antonia Kwan,[15] James Relf,[16] Wilfred Leung,[15] Francis Mussai,[16] Connie Y. Ma,[15] Adrien Petel,[17] Patrick Y. Muller,[17] Xuefeng Hou,[15] Christopher P. Fox[18]

Presented at the 67th ASH Annual Meeting | December 6–9, 2025

Maximum Ikaros on treatment (Mosun + Golca)*

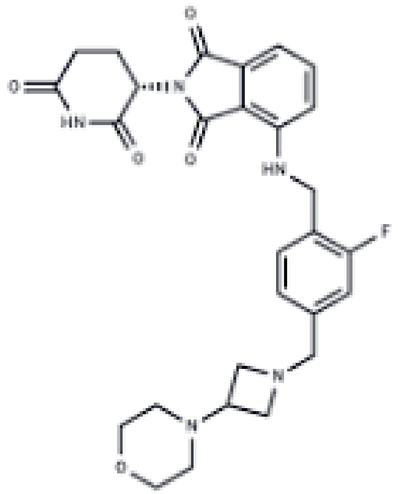


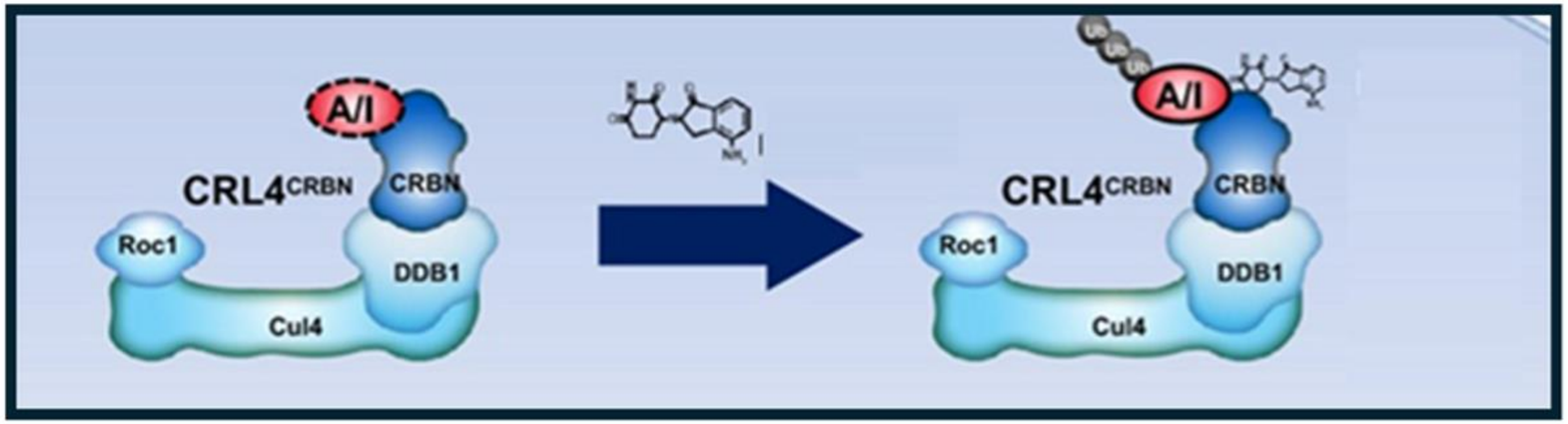
Best overall response in Arm 1: Mosun + Golca



- Median time to first response for all patients (N=27)*: 2.6 months (range: 2–4)
- Response in patients who received prior CAR T-cell therapy (n=8):
  - Overall, 5 patients achieved a CR
    - Two patients had FL and one achieved CR
    - Six patients had DLBCL and four achieved a CR

High response rates were observed in patients with FL and DLBCL including those who received prior CAR T-cell therapy



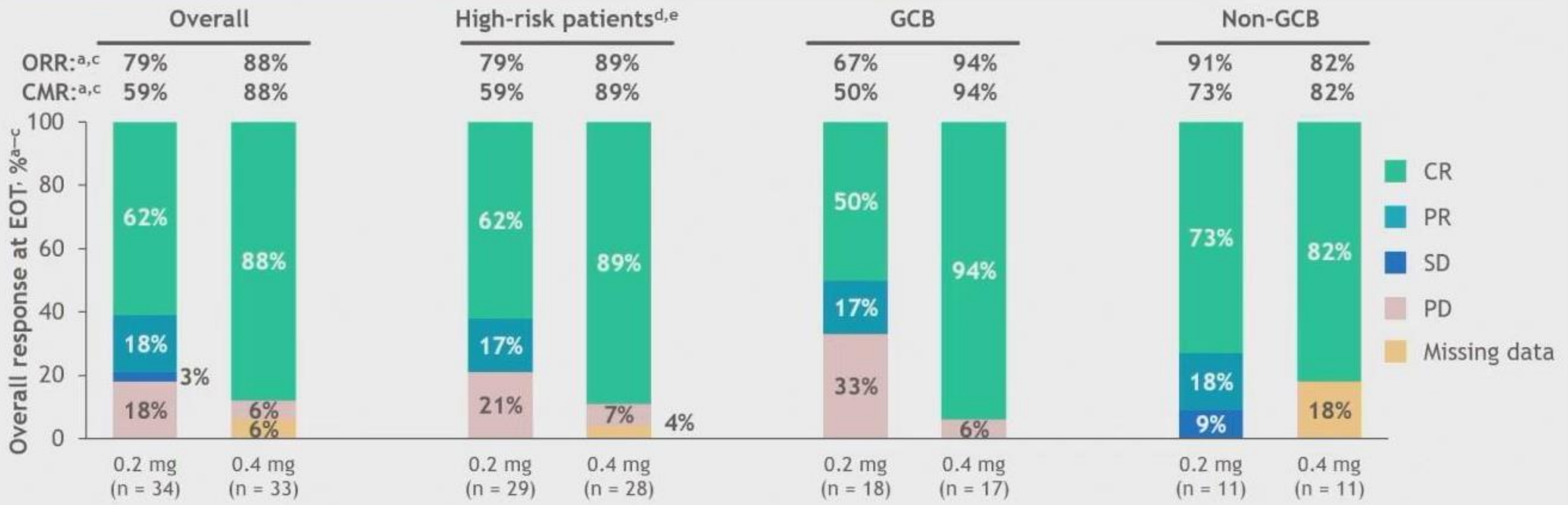


CELMoDs:
Cereblon E3 Ligase Modulator Drugs

~10-20-fold higher affinity
~10-100 fold potency

c-Myc/IRF-4 proliferation

Golcadomide 0.4 mg + R-CHOP resulted in high complete response rates



Nowakowski et al., ASH 2025

Some conclusions

- BiTEs vs PK/PD: PAT vs dimers
- Patients vs BiTEs: exhaustion
- Degrade old targets with new immunomodulators
- PK/PD informing of schedule, dose & selectivity

Grazie