

ZAMASA Foundation and Myeloma Research: St Vincent's Hospital

Georgia McCaughan

Staff Specialist Haematology

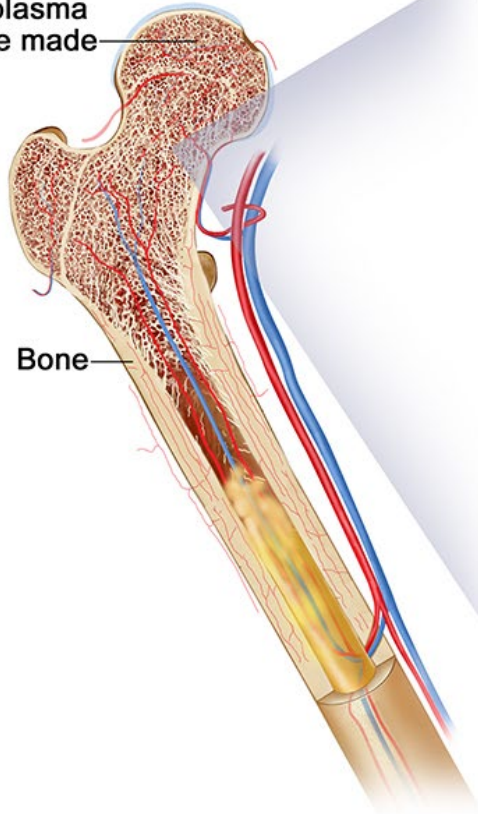
St Vincent's Hospital, Sydney



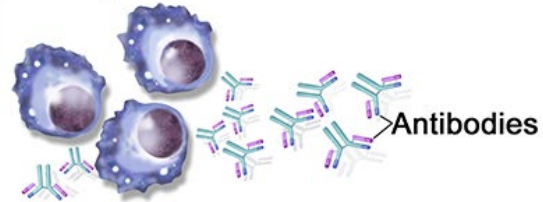
What is Multiple Myeloma?

Multiple Myeloma

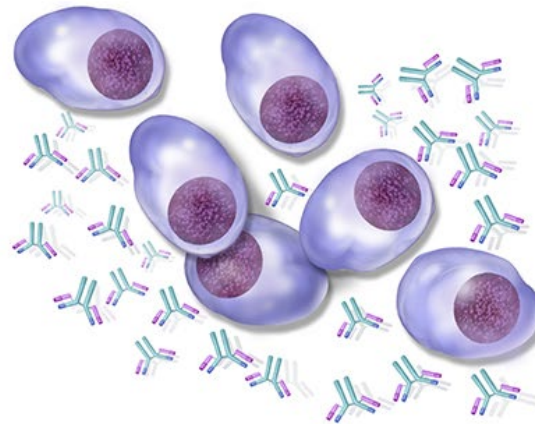
Red marrow
where plasma
cells are made



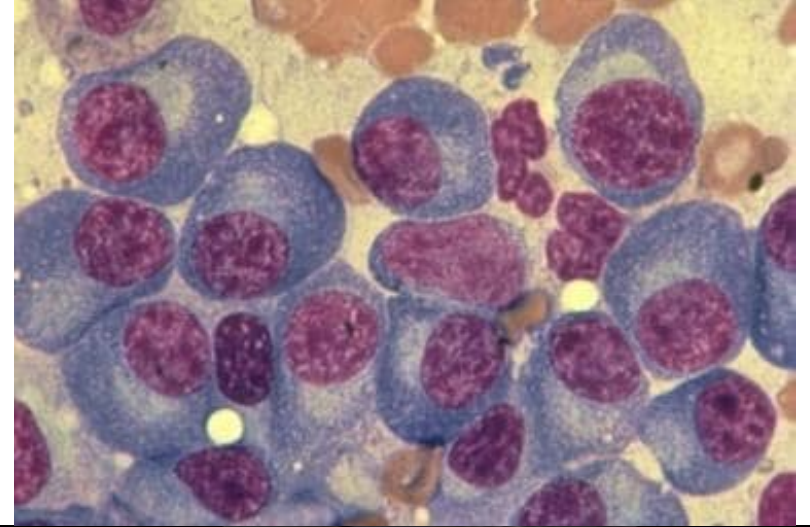
Normal plasma cells



Multiple myeloma cells (abnormal plasma cells)



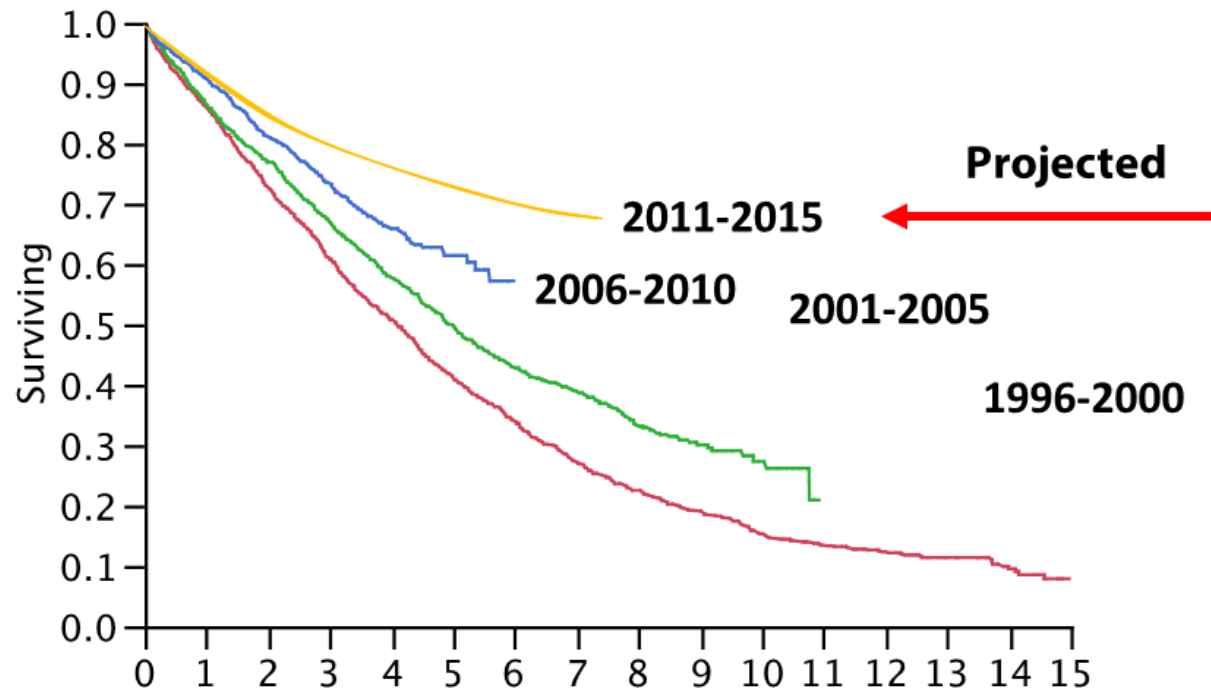
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Survival in Myeloma



Survival in Myeloma



International Myeloma Foundation

Kumar S. Blood 2008;111: 2516 – 2520; Kumar S. Leukemia (2014) 28, 1122–1128.

Emerging Treatments for Multiple Myeloma



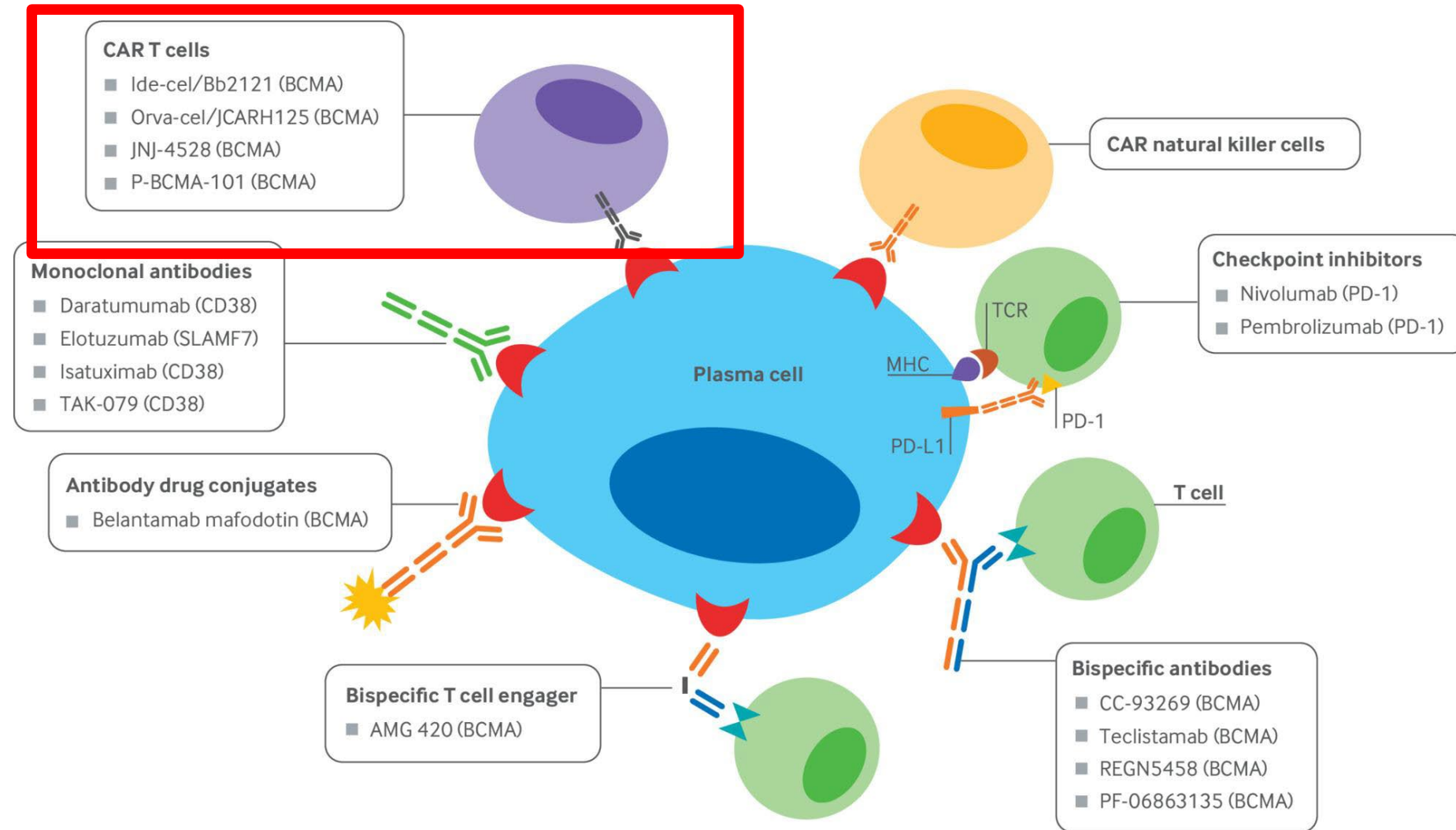
Active Drugs in Multiple Myeloma

<ul style="list-style-type: none"> Alkylators Steroids Anthracyclines 	Anti-SLAMF7 moAb <ul style="list-style-type: none"> Elotuzumab 	<ul style="list-style-type: none"> Panobinostat (histone deacetylase inhibitor) Selinexor (XPO1 inhibitor) Venetoclax (BCL-2 inhibitor) 	Anti-BCMA CAR-T <ul style="list-style-type: none"> Cilta-cel Ide-cel JCARH125
IMiDs <ul style="list-style-type: none"> Thalidomide Lenalidomide Pomalidomide 	Anti-CD38 moAbs <ul style="list-style-type: none"> Daratumumab Isatuximab Felzartamab (MOR202) TAK 079 SAR 442085 		
Proteasome Inhibitors <ul style="list-style-type: none"> Bortezomib Carfilzomib Ixazomib 	Anti-BCMA antibody drug conjugate <ul style="list-style-type: none"> Belantamab 	Novel bispecifics <ul style="list-style-type: none"> Talquetamab (GPRC5D/CD3) Cevostamab (FcRH5/CD3) 	CELMoDs <ul style="list-style-type: none"> Iberdomide CC-92480

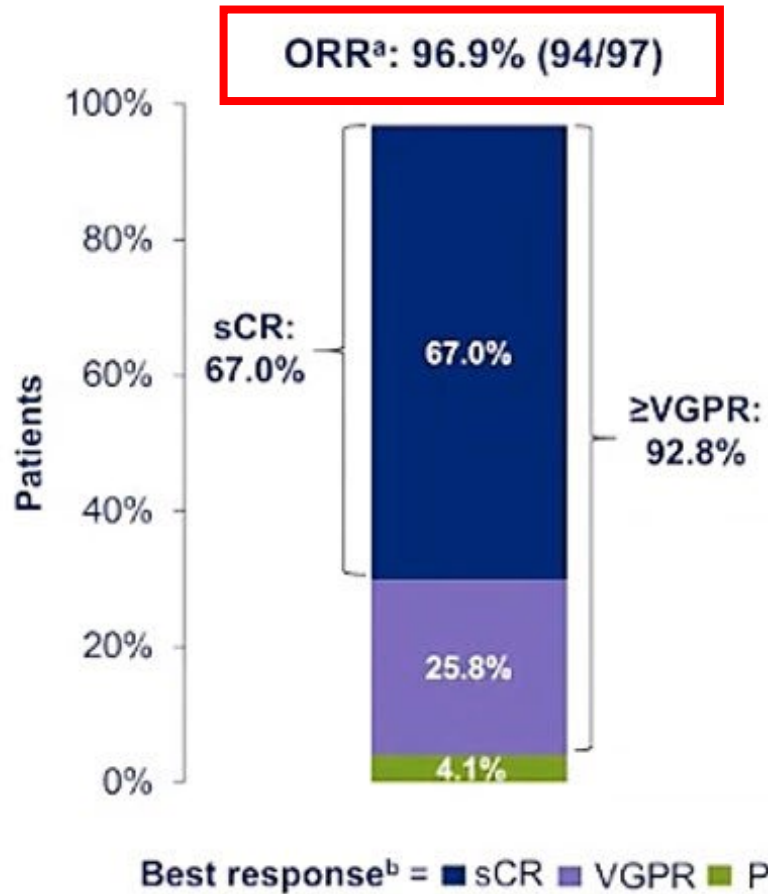
moAB: monoclonal antibody

Rajkumar SV. 2020

CAR-T Cells



CARTITUDE-1: Ciltacabtagene autoleucel

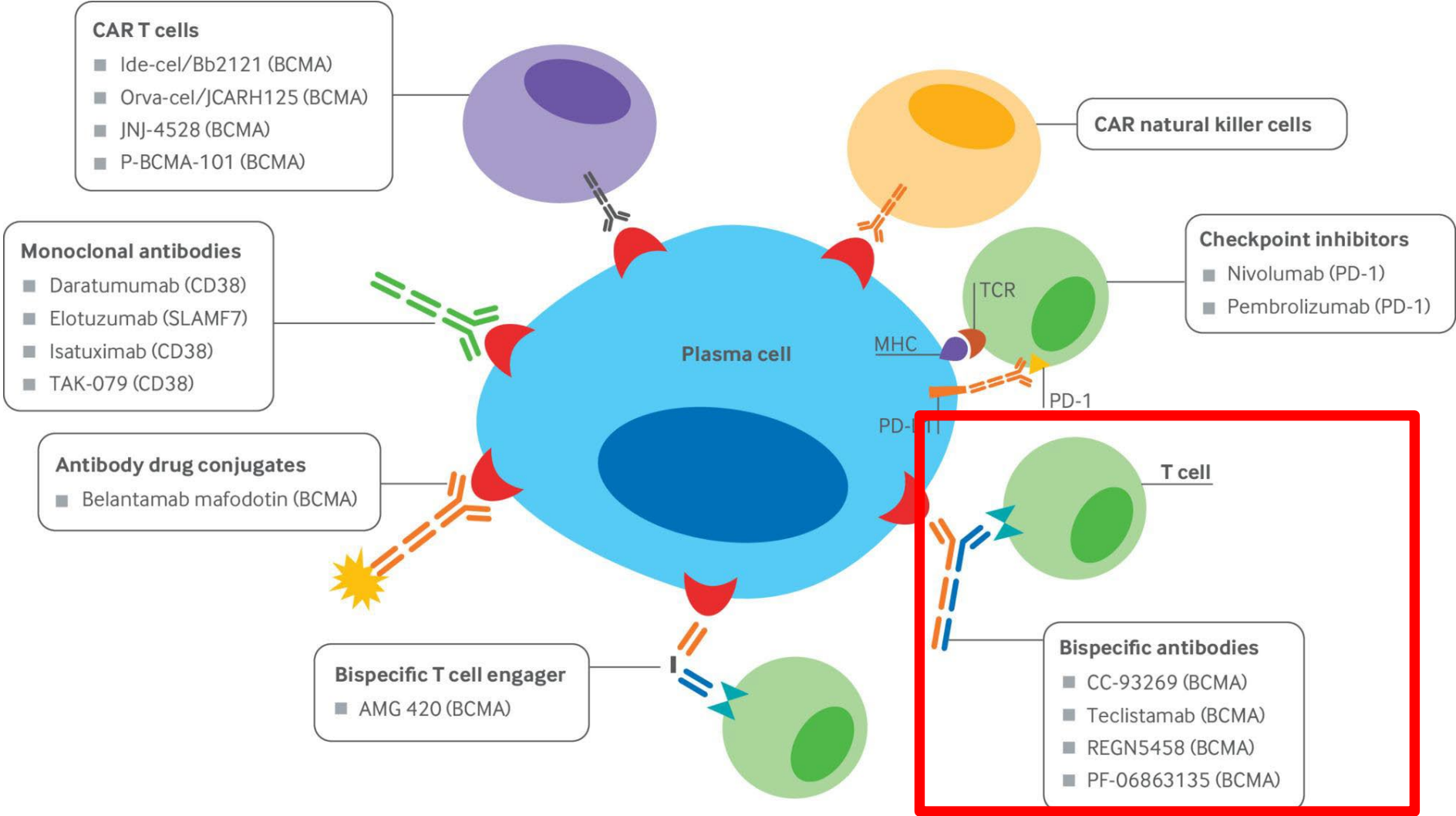


	N	Frequency in evaluable patients n=57 ^c	Frequency in all treated n=97 ^d
Overall MRD-	53	93.0%	54.6%
MRD- and sCR	33	57.9%	34.0%
MRD- and ≥VGPR	49	86.0%	50.5%

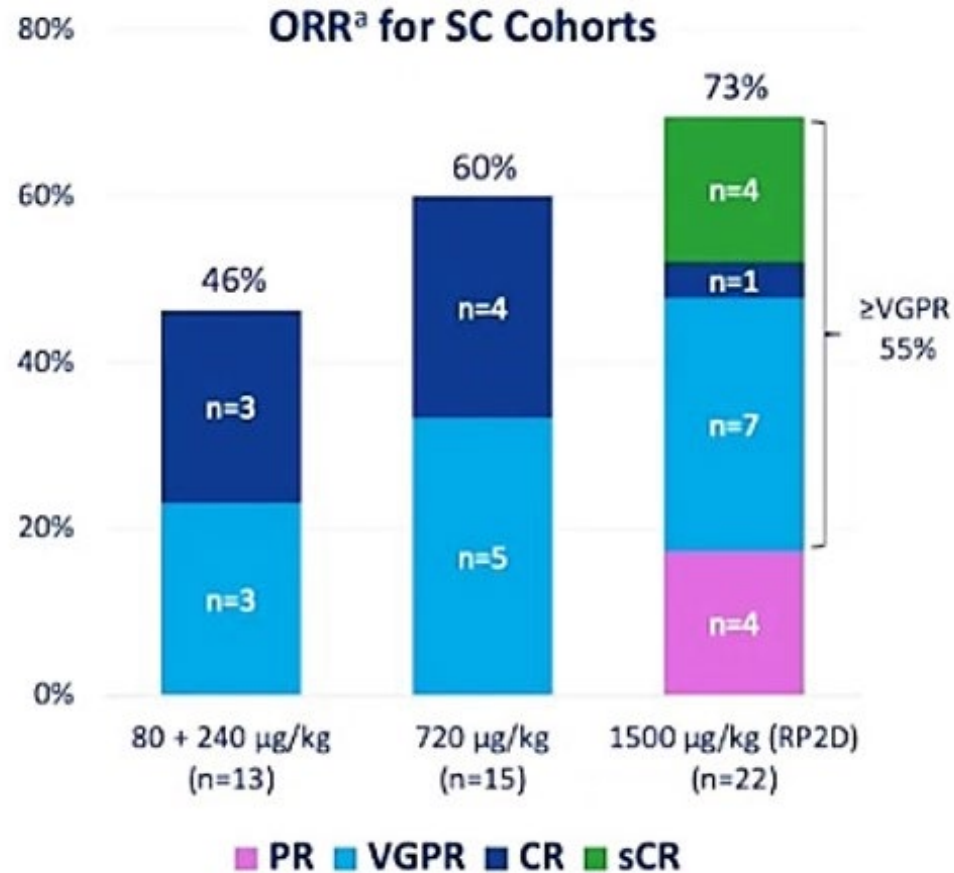
- Median time to first response: 1 month (0.9–8.5)
- Responses ongoing in 70 (72.2%) patients
- Of evaluable patients, 93.0% achieved MRD 10⁻⁵ negativity
 - Median time to MRD 10⁻⁵ negativity: 1 month (0.8–7.7)
- Among patients with 6 months individual follow-up, most had cilta-cel CAR+ T cells below the level of quantification (2 cells/μL) in peripheral blood

CAR, chimeric antigen receptor; CR, complete response; MRD, minimal residual disease; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response. ^aPR or better. Independent Review Committee assessed. ^bNo patient had CR or stable disease as best response. ^cMRD was assessed in evaluable samples at 10⁻³ threshold by next-generation sequencing (clonoSEQ, Adaptive Biotechnologies) in all treated patients at Day 28, and at 6, 12, 18, and 24 months regardless of the status of disease measured in blood or urine; patients were not evaluable primarily due to lack of an

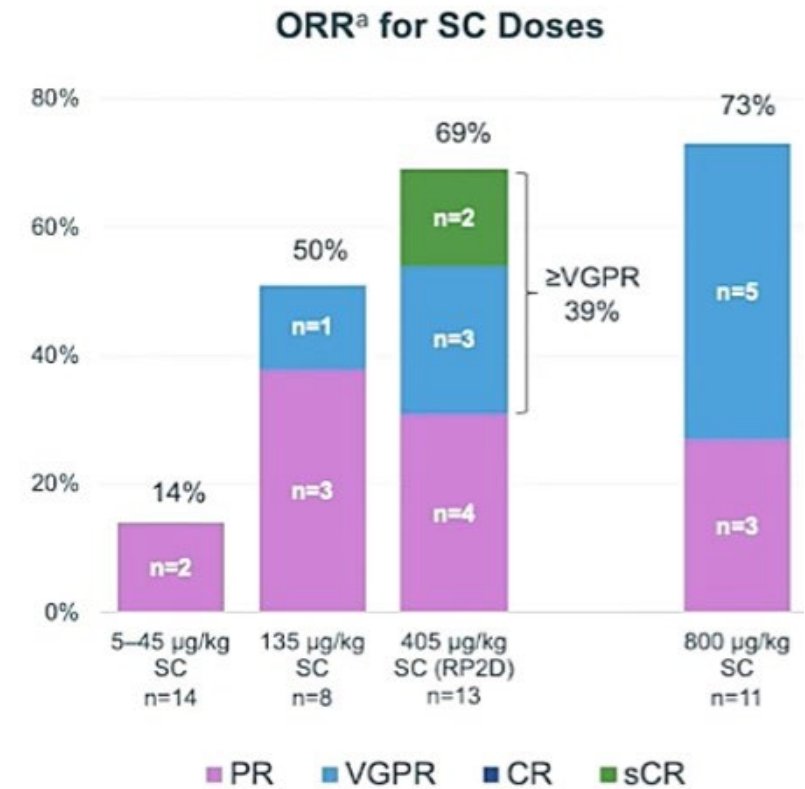
Bispecific Antibodies



Teclistamab



Talquetamab



^aAmong response-evaluable patients who had at least 1 study treatment and 1 postbaseline disease

Alfred L. Garfall et al. Updated Phase 1 Results of Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Relapsed and/or Refractory Multiple Myeloma (RRMM). *Blood* 2020; 136 (Supplement 1): 27. doi: <https://doi.org/10.1182/blood-2020-138831>

Ajai Chari et al. A Phase 1, First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D (GPCR5D) x CD3 Bispecific Antibody, in Patients with Relapsed and/or Refractory Multiple Myeloma (RRMM). *Blood* 2020; 136 (Supplement 1): 40-41. doi: <https://doi.org/10.1182/blood-2020-133873>

What is Already Happening on Campus?



ZAMASA
FOUNDATION



Garvan Institute
of Medical Research



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SYDNEY

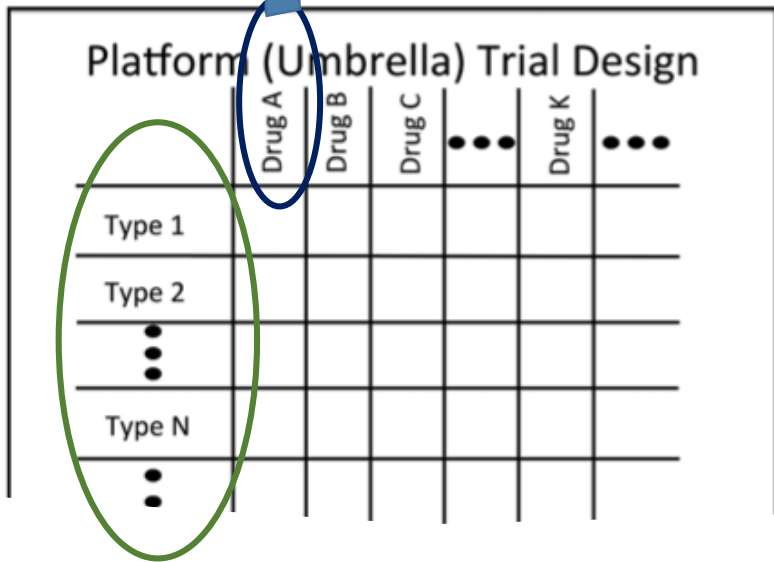


Dana-Farber
Cancer Institute

Trends and Outcomes in Australia and New Zealand for Older Patients with Multiple Myeloma undergoing Autologous Stem Cell Transplantation: An Australasian Bone Marrow Transplant Recipient Registry Study

Georgia J McCaughan, Steven Tran, Simon Durrant, Simon J Harrison, James Morton, Noemi Horvath, Andrew Spencer, Ian H. Kerridge, Jeremy An Ke Er, Luani Barge, Adam Bryant, Robin J Filshie, Emily Choong, Hock Choong Lai, Campbell Tiley, Anthony K Mills, Andrew Butler, John Moore, Mark Hertzberg, Glen A Kennedy, P. Joy Ho, M Hasib Sidiqi, John Bashford, David Routledge, Kerry Taylor, Cindy H. Lee, Anna Kalff, Wei Xia, and Nada Hamad

Study Design



Selinexor 60mg weekly + Pomalidomide 4mg days 1-21
Dexamethasone 40mg weekly* (*20mg weekly if age > 75)

Stratum

Strata A

RRMM with **CrCL <30umol/min.**

Strata B

RRMM myeloma with **oligosecretory/non-secretory disease:**
defined as involved LC <100mg/L; paraprotein
<5g/L and urinary BJP <200mg/24hrs.

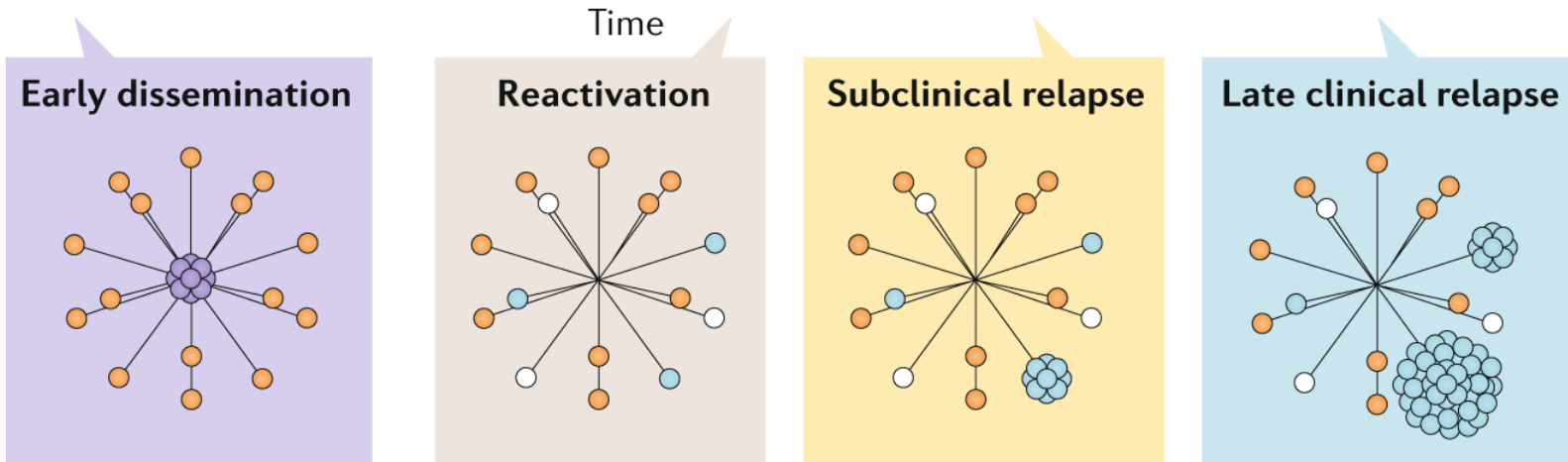
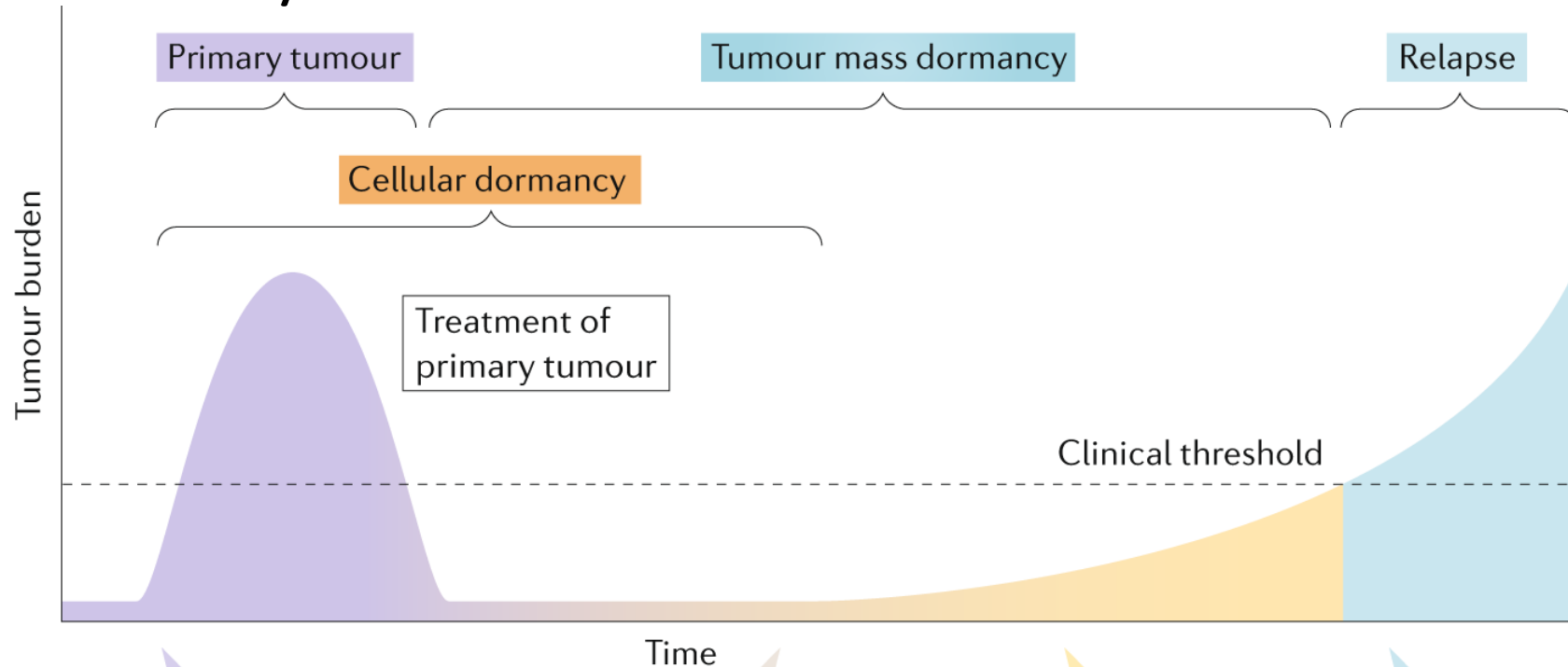
Strata C

RRMM with **extramedullary plasmacytomas.**

Strata D

RRMM with **CNS myeloma.**

St Vincent's/Garvan Collaboration: Dormancy



St Vincent's/Garvan Collaboration: Sclerostin

B



Michelle M. McDonald, Michaela R. Reagan, Scott E. Youtlen, Sindhu T. Mohanty, Anja Seckinger, Rachael L. Terry, Jessica A. Pettitt, Marija K. Simic, Tegan L. Cheng, Alyson Morse, Lawrence M. T. Le, David Abi-Hanna, Ina Kramer, Carolyn Falank, Heather Fairfield, Irene M. Ghobrial, Paul A. Baldock, David G. Little, Michaela Kneissel, Karin Vanderkerken, J. H. Duncan Bassett, Graham R. Williams, Babatunde O. Oyajobi, Dirk Hose, Tri G. Phan, Peter I. Croucher; Inhibiting the osteocyte-specific protein sclerostin increases bone mass and fracture resistance in multiple myeloma. *Blood* 2017; 129 (26): 3452–3464. doi: <https://doi.org/10.1182/blood-2017-03-773341>

St Vincent's/Dana Farber Collaboration

- Enhance clinical research through clinical trials
- Travelling fellowships
- Translational Research



ST VINCENT'S
HOSPITAL
SYDNEY



Dana-Farber
Cancer Institute

Moving Forward

- Increase our clinical trial portfolio
- Deliver state of the art therapies including bispecific and CAR-T cells

