Excellence in Cellular Therapies and Multiple Myeloma Research

ST VINCENT'S CURRAN FOUNDATION

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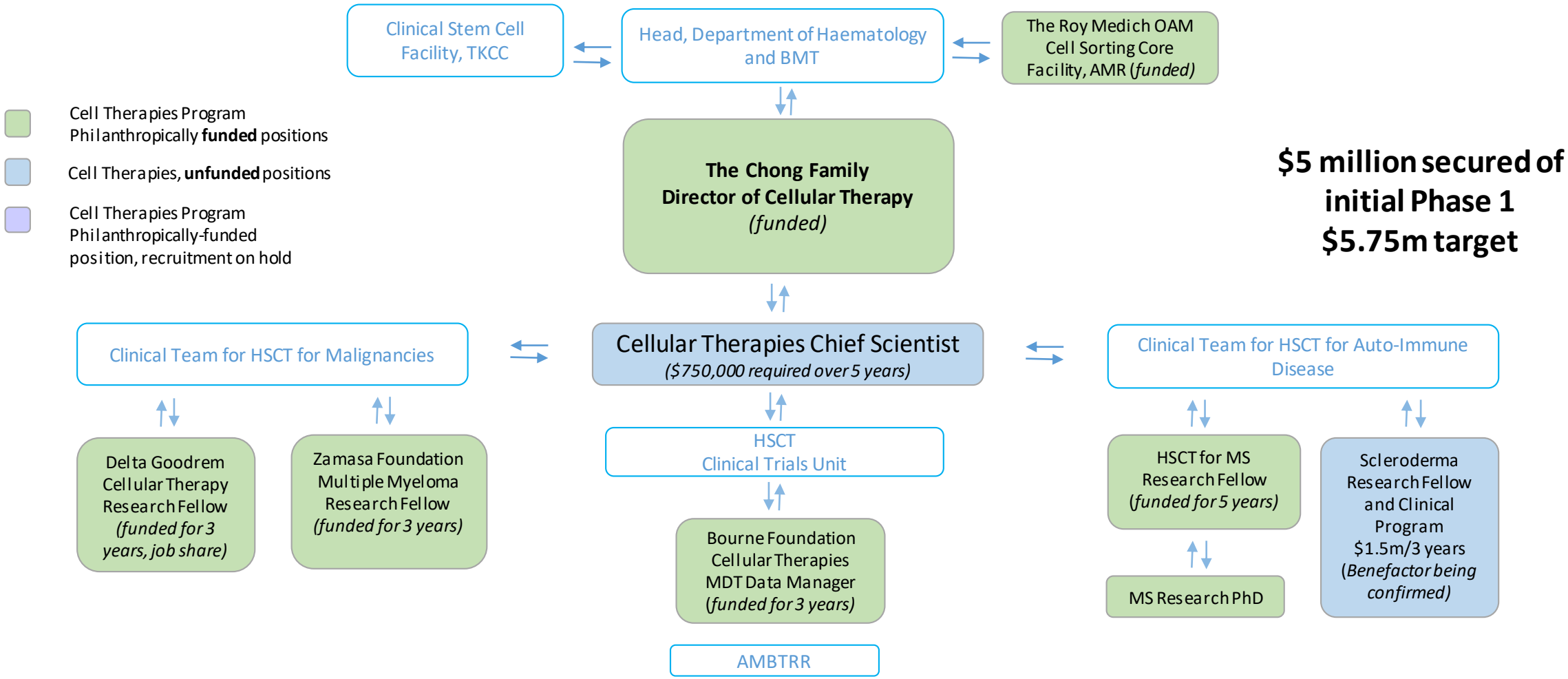
We acknowledge the traditional land owners upon which

St Vincent's Hospital Sydney is located -

The Gadigal People of the Eora Nation.

We pay our respects to Elders past, present and future.

ST VINCENT'S CELLULAR THERAPIES
STRUCTURE AS AT AUGUST 2021



Multiple Myeloma and its place in the new Cellular Therapies Unit at St Vincent's Hospital

Dr John Moore

Haematology Department

St Vincent's Hospital Sydney

Multiple Myeloma

- Plasma cell malignancy
- Median age 60-70, M > F
- 45% increase since 1940
- No.11 on cancer incidence in NSW

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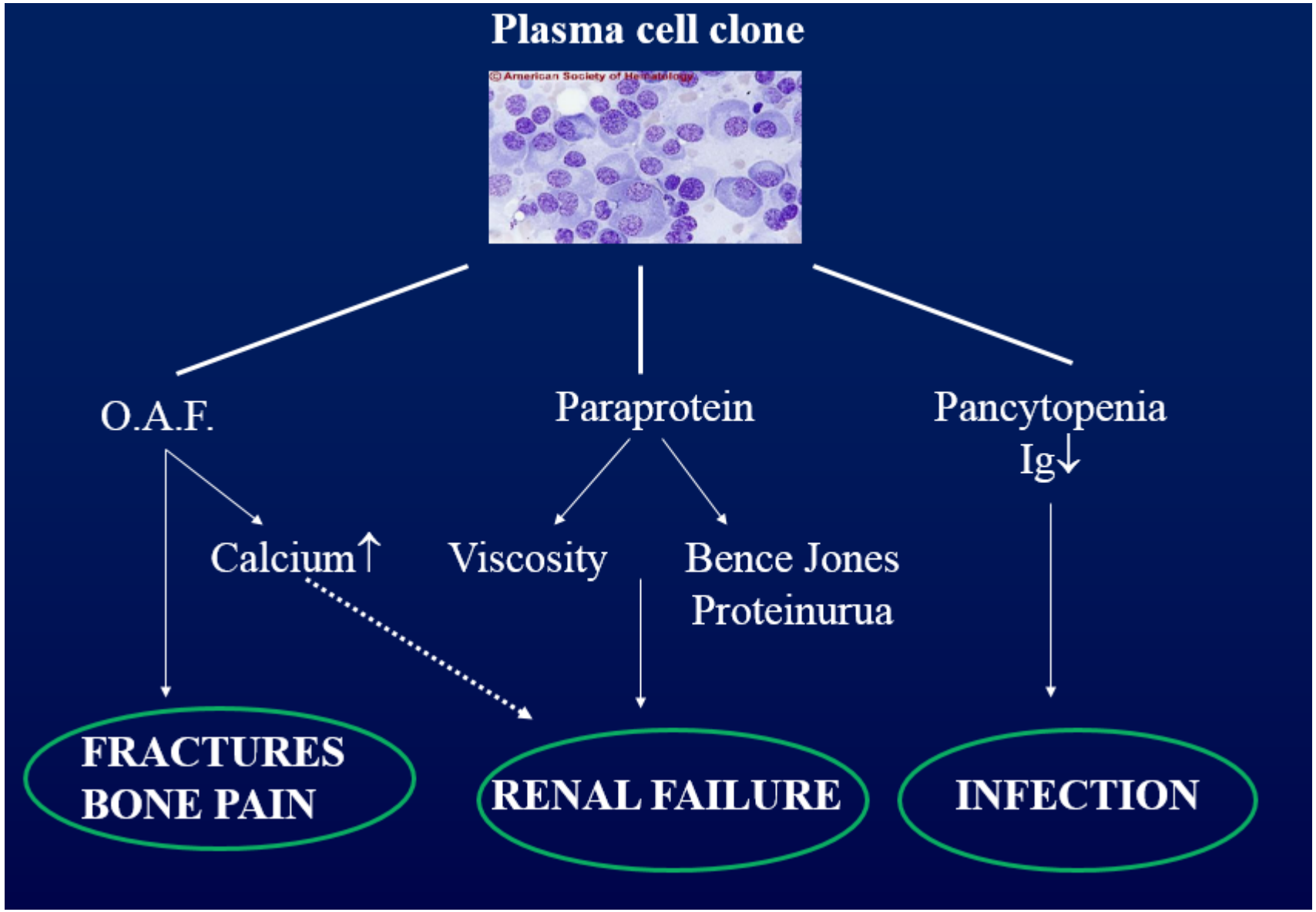


Myeloma Symptoms

- Bone pain
- Fracture
- Confusion
- Dehydration
- Fevers/Night sweats
- Lethargy

Multiple Myeloma Signs

- Anaemia
- Bone pain
- Fractures, bone masses
- Cord Compression

Myeloma - Diagnosis

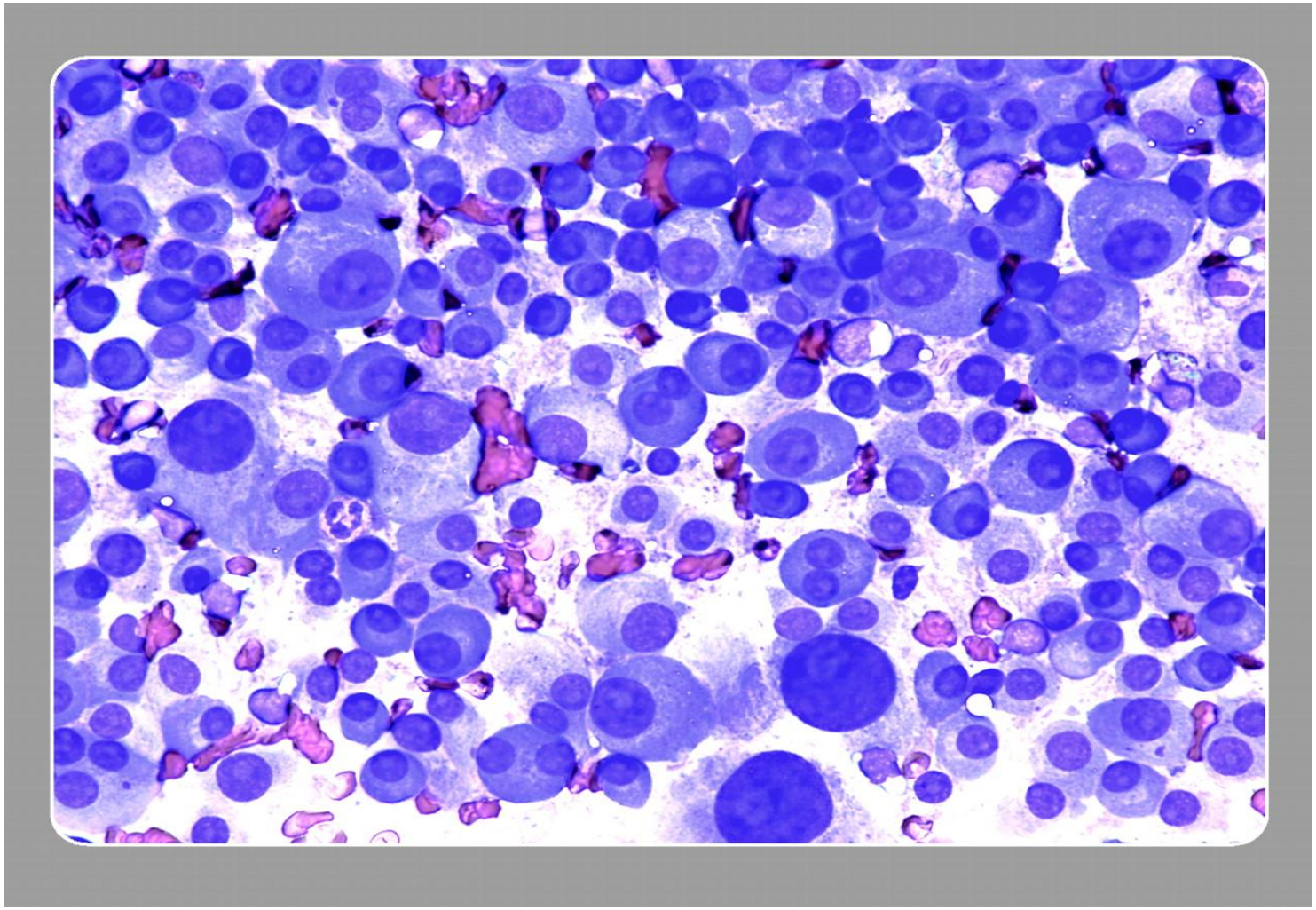
Need to distinguish:

- MM, Smoldering MM, MGUS

Laboratory:

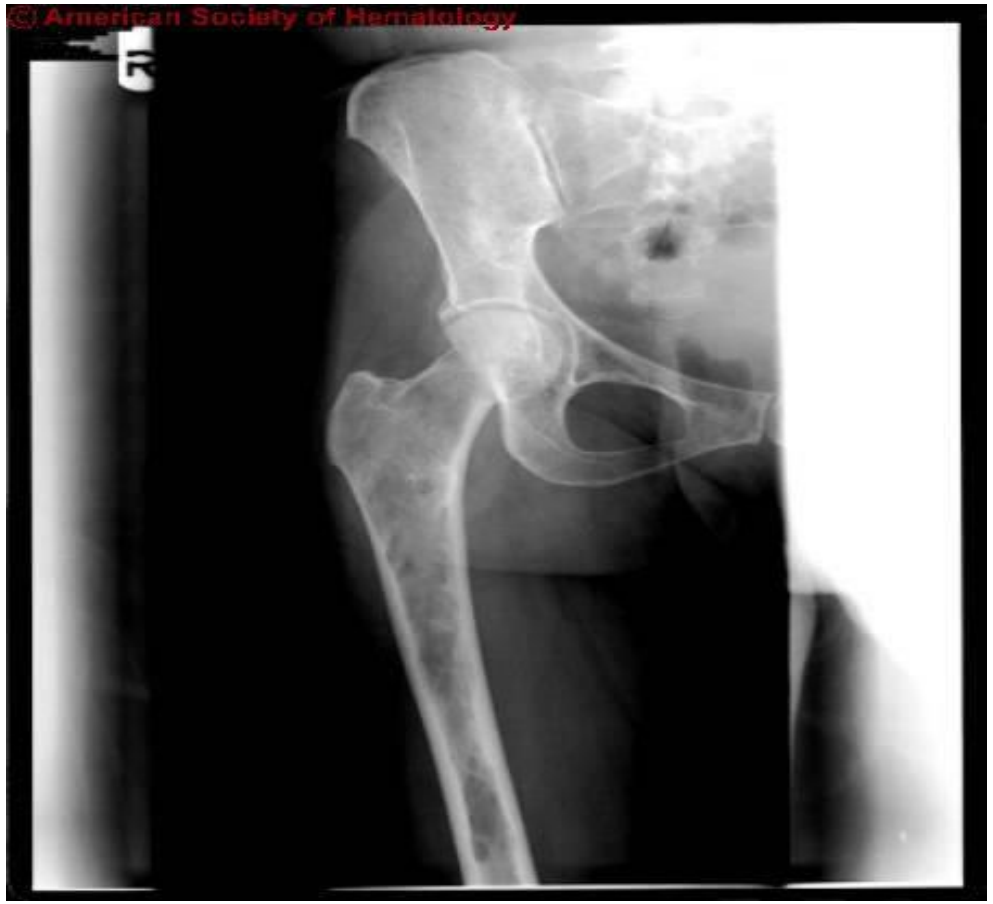
- FBC, Biochemistry
- Serum Ig, EPG/IFXN
- Serum free light chains
- Urine EPG/IFXN
- B_2M, LDH
- Bone Marrow - 30% plasma cells
- Skeletal Survey +/- MRI +/- PET

blood
JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY

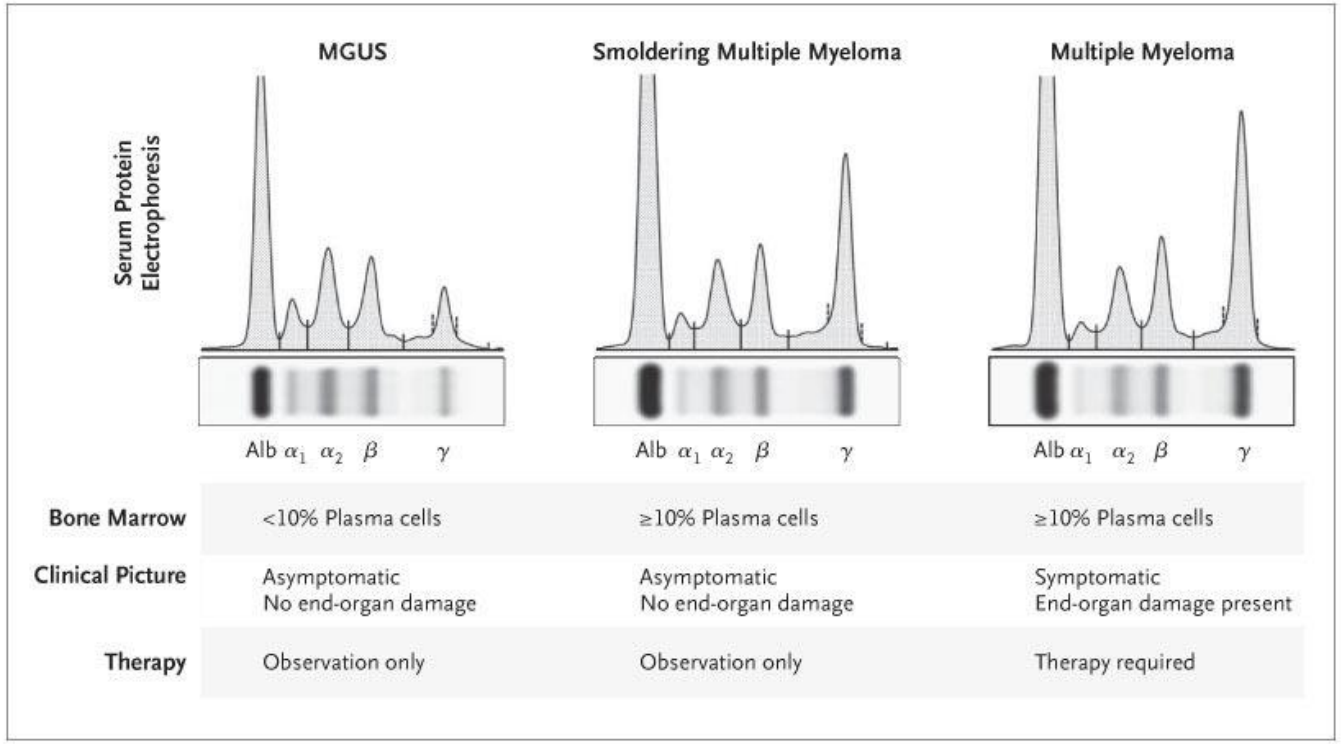


Blood 2005;105:2629

Pathological Fractures and Lytic Lesions



Characteristics of Active Multiple Myeloma and its Precursors



	MGUS	Smoldering Multiple Myeloma	Multiple Myeloma
Bone Marrow	<10% Plasma cells	≥10% Plasma cells	≥10% Plasma cells
Clinical Picture	Asymptomatic No end-organ damage	Asymptomatic No end-organ damage	Symptomatic End-organ damage present
Therapy	Observation only	Observation only	Therapy required

Kyle R et al. N Engl J Med 2007;356:2582-2590

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Updated IMWG Criteria for Diagnosis of Multiple Myeloma

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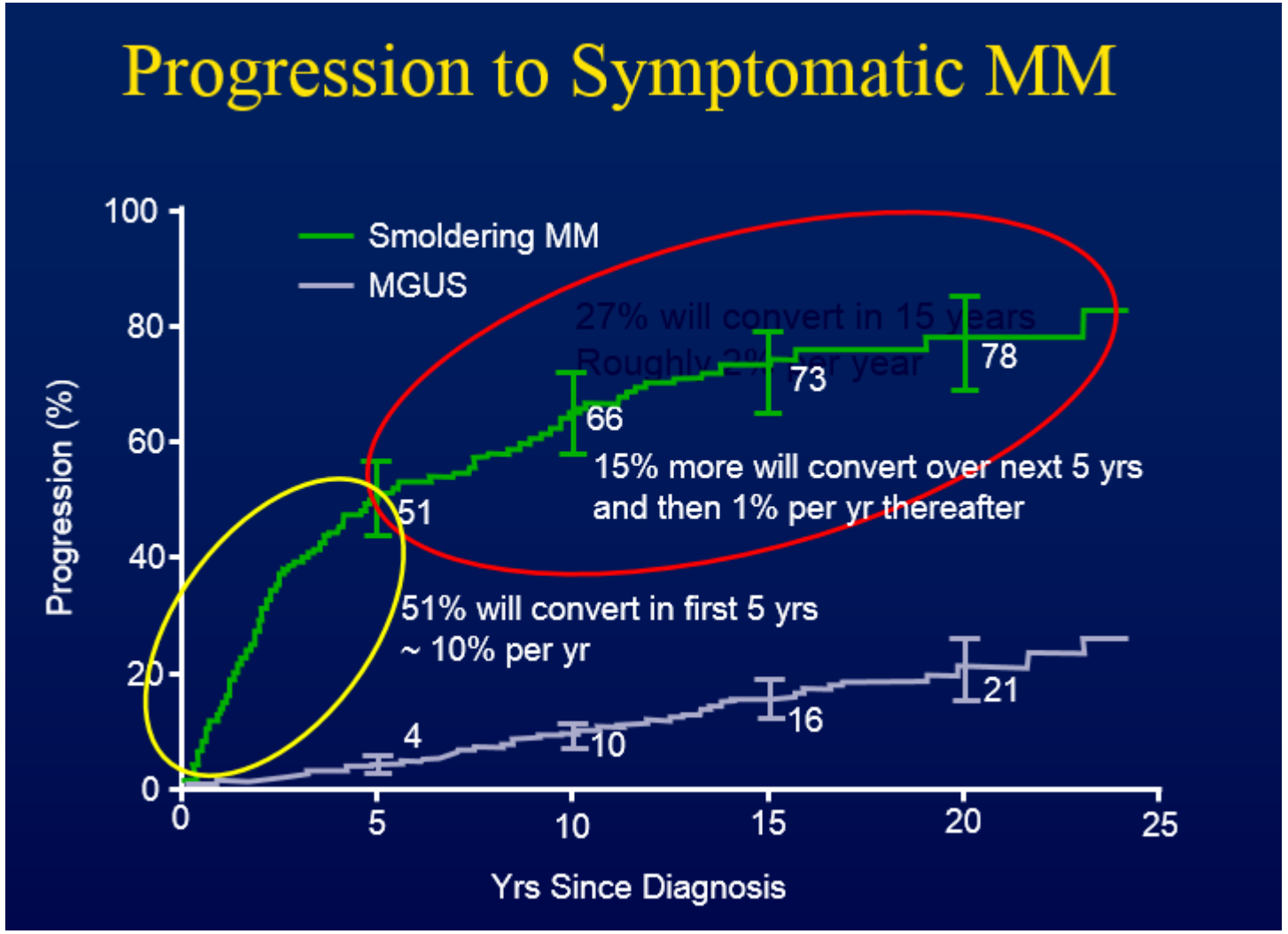
MGUS	Smoldering	Multiple Myeloma
▪ M protein < 3 g/dL ▪ Clonal plasma cells in BM < 10% ▪ No myeloma-defining events	▪ M protein ≥ 3 g/dL (serum) or ≥ 500 mg/24 hrs (urine) ▪ Clonal plasma cells in BM ≥ 10% to 60% ▪ No myeloma-defining events	▪ Underlying plasma cell proliferative disorder ▪ AND 1 or more myeloma-defining events ▪ ≥ 1 CRAB* feature ▪ Clonal plasma cells in BM ≥ 60% ▪ Serum free light-chain ratio ≥ 100 ▪ > 1 MRI focal lesion

*C: Calcium elevation (> 11 mg/dL or > 1 mg/dL higher than ULN)
R: Renal insufficiency (CrCl < 40 mL/min or serum creatinine > 2 mg/dL)
A: Anemia (Hb < 10 g/dL or 2 g/dL < normal)
B: Bone disease (≥ 1 lytic lesions on skeletal radiography, CT, or PET/CT)

Rajkumar SV, et al. Lancet Oncol. 2014;15:e538-e548.



Kyle RA, et al. N Engl J Med. 2007;356:2582-2590.

Myeloma Supportive Care

- Bone protection – zometa, prolia
- Infection prophylaxis – Bactrim, Valtrex
- IVIG if appropriate
- Watch renal function/Ca
- Analgesia/XRT as required

Myeloma - Rx

Transplant eligible

- CyBordD x4
- If response – HSCT
- If NR – other agents
- Consider maintenance

Transplant ineligible

- Lenalidomide
- CyBorD
- Carfilzomib
- Pomalidomide

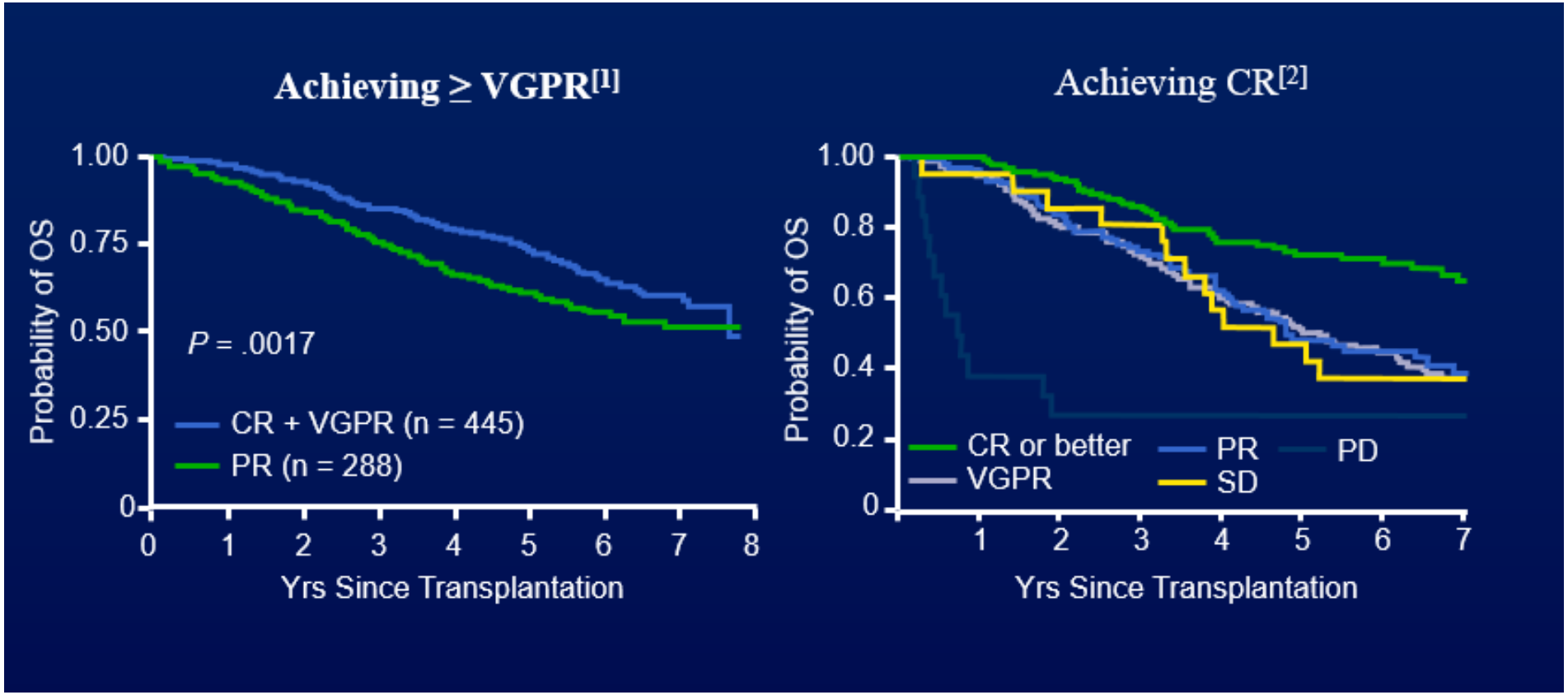
Lenalidomide

- Structurally similar to thalidomide without somnolence
- Similar strict PBS pharmacovigilance (separate section within PBS - $60,000/year)
- Very potent anti-MM therapy. Combined with weekly dexamethasone 40mg
- Similar action to thalidomide
- Normal dose: 10-25mg orally D1-D21
- Main S/E: myelosuppression, cramps

Bortezomib

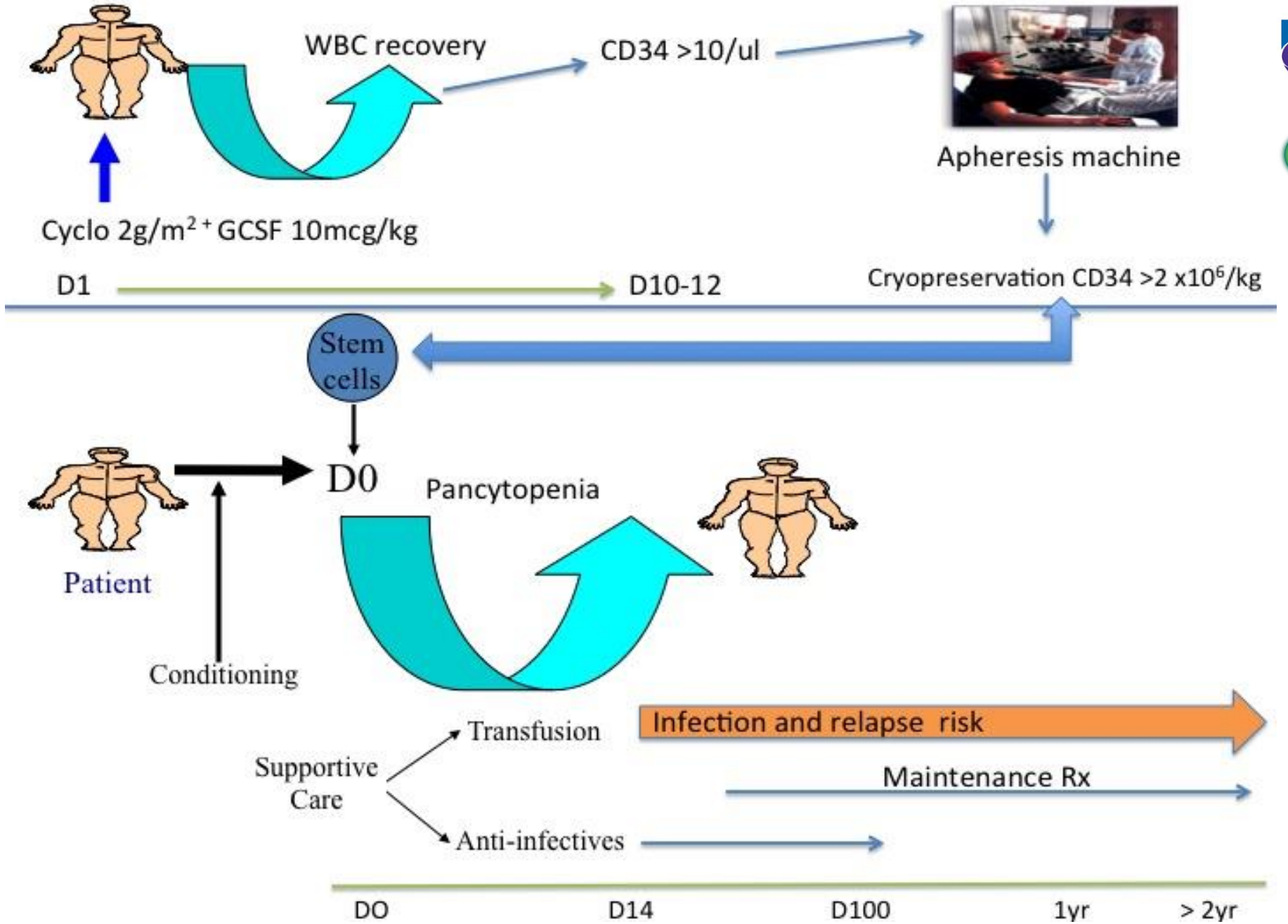
- Proteosome inhibitor
- Inhibits paraprotein packaging in proteosome.
- Very potent, combined with Dex and lenalidomide.
- s/c dose 1.3mg/m^2 D1,4,8,11 or weekly
- Main S/E: Severe painful peripheral neuropathy, mild myelosuppression.

Achieving ≥ or VGPR or CR Should Be the Goal of Therapy



1. Harousseau JL, et al. J Clin Oncol. 2009;27:5720-5726.
2. Kapoor P, et al. J Clin Oncol. 2013;31:4529-4535.

Autologous Stem Cell Transplantation


WBC recovery
CD34 >10/ul
Apheresis machine
Cyclo 2g/m² + GCSF 10mcg/kg
D1
D10-12
Cryopreservation CD34 >2 x10⁶/kg
Stem cells
D0
Pancytopenia
Patient
Conditioning
Transfusion
Supportive Care
Anti-infectives
Infection and relapse risk
Maintenance Rx
DO
D14
D100
1yr
> 2yr

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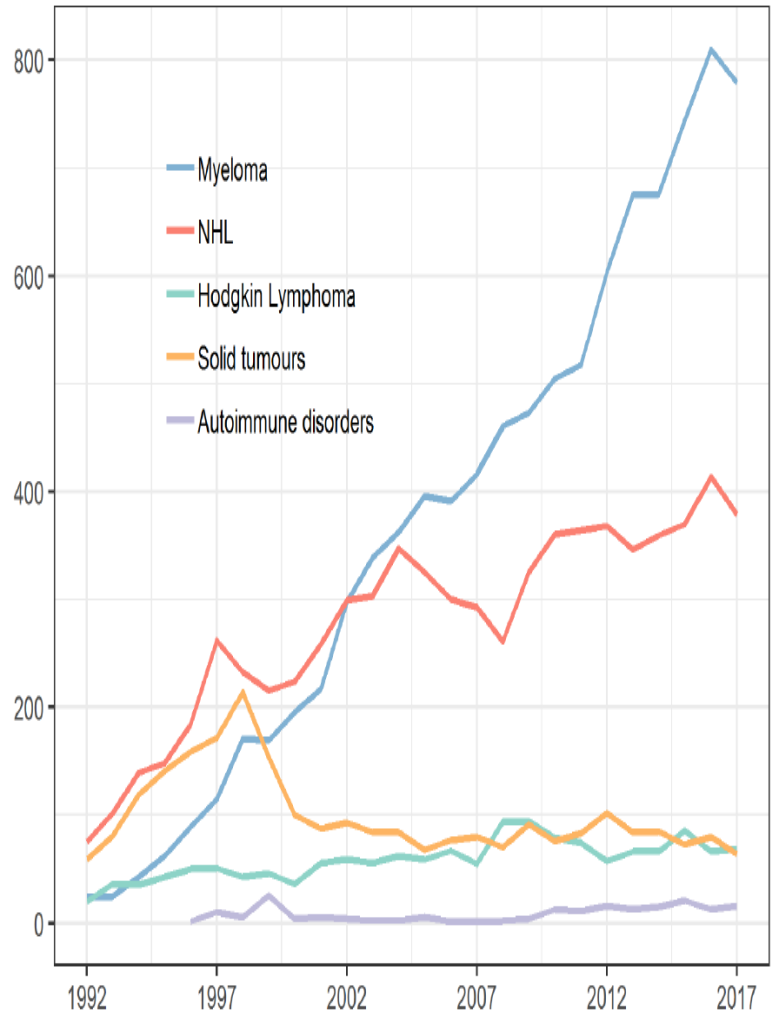
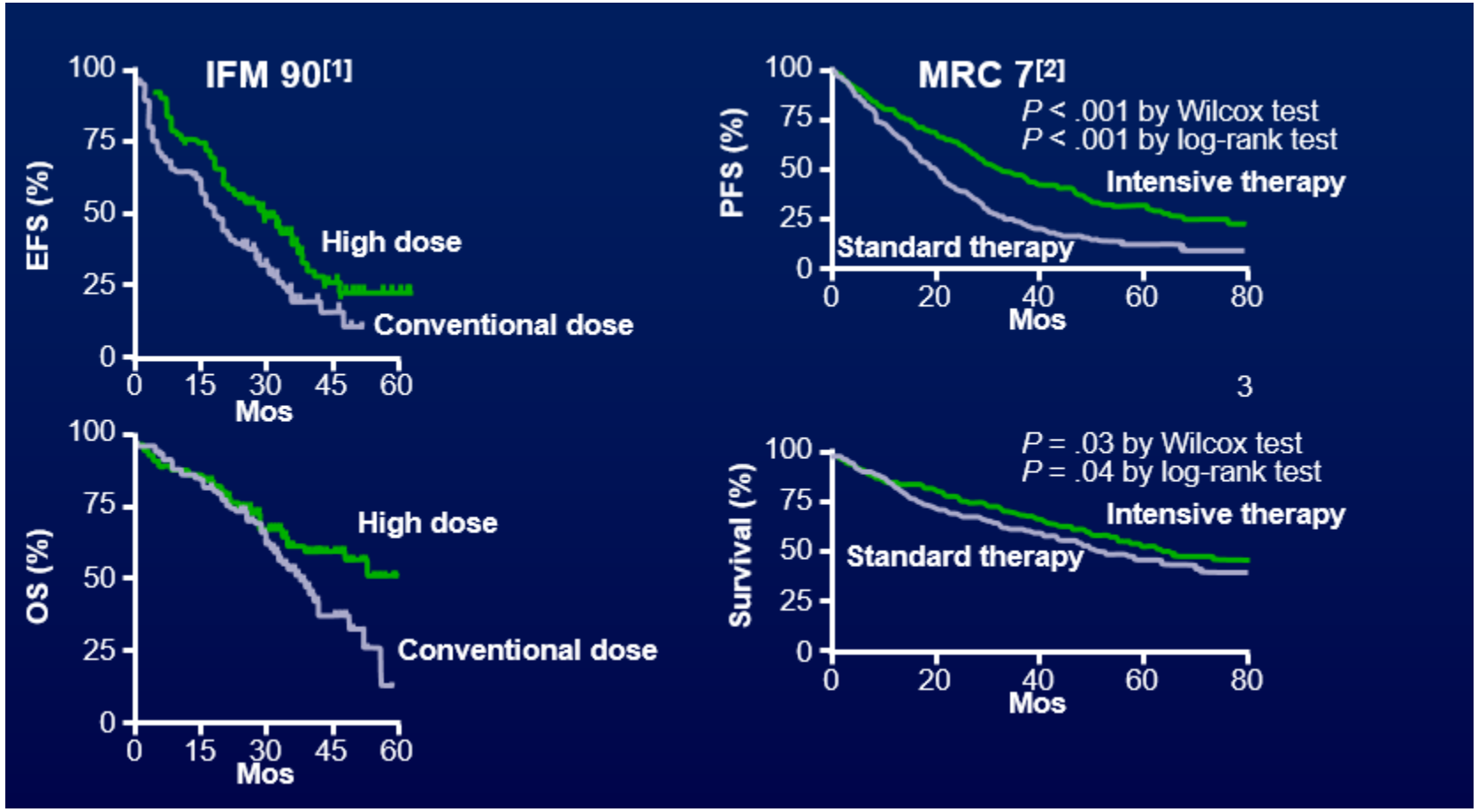
Indications for autologous transplant



Autologous Stem Cell Transplantation



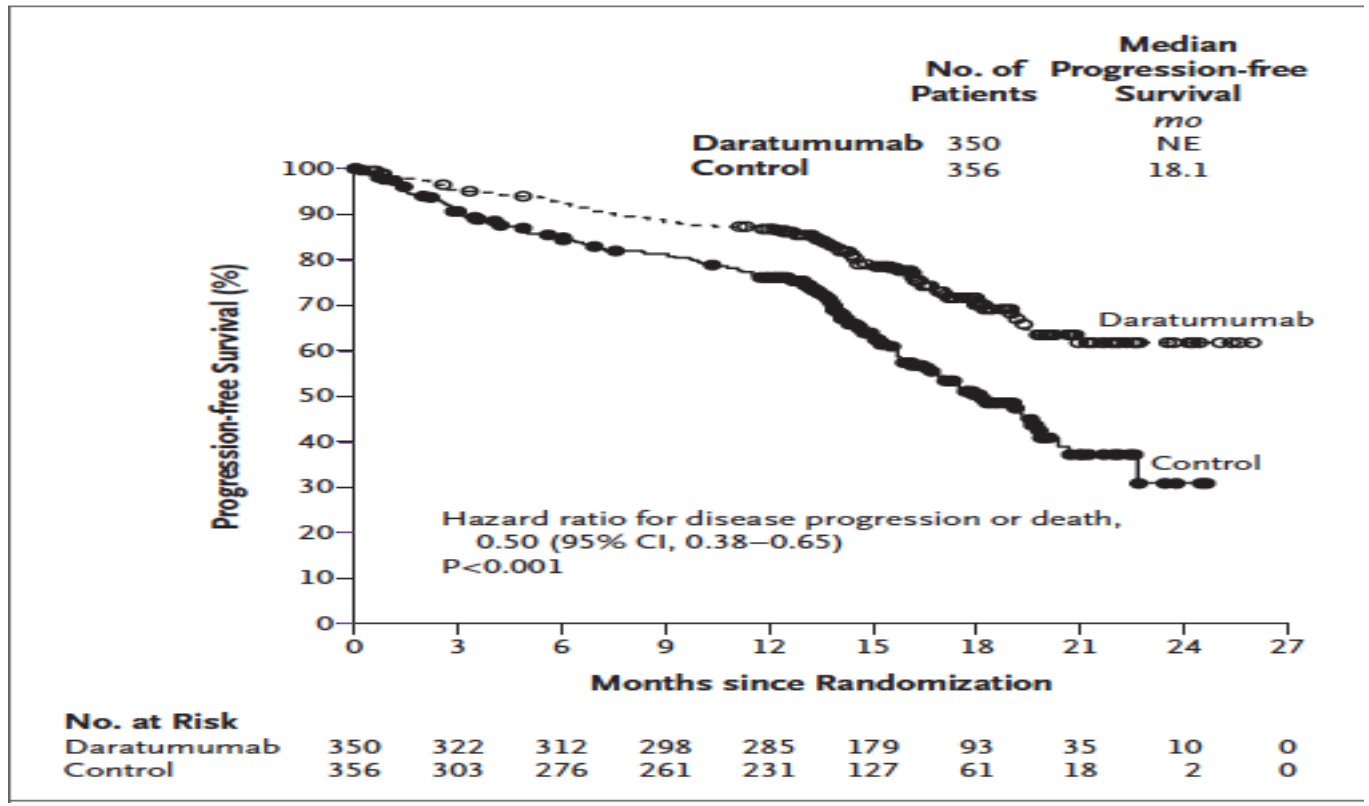
Attal M, et al. N Engl J Med. 1996;335:91-97. 2. Child JA, et al. N Engl J Med. 2003;348:1875-1883.

What's New

ORIGINAL ARTICLE

Daratumumab plus Bortezomib, Melphalan, and Prednisone for Untreated Myeloma

N Engl J Med 2018;378:518-28.



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ORIGINAL ARTICLE

Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma

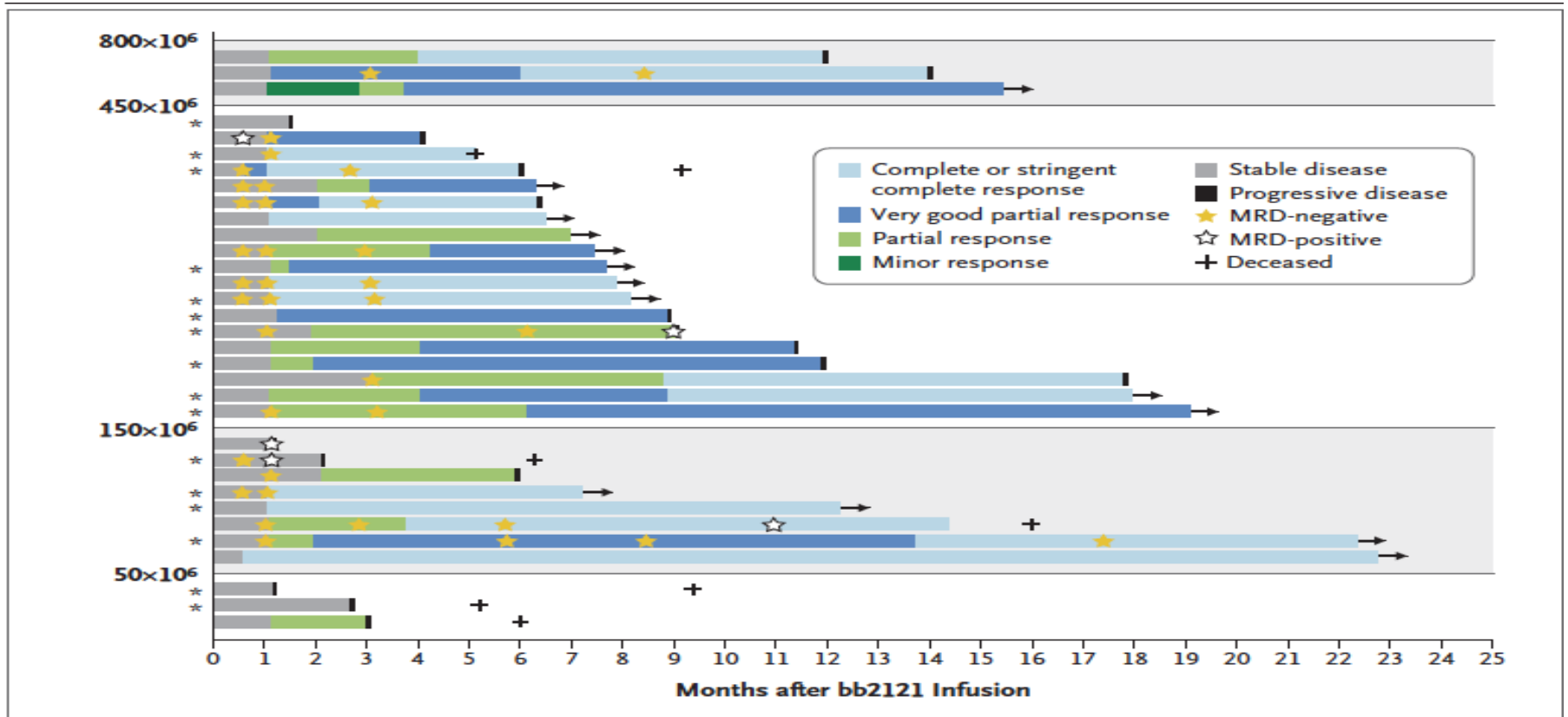
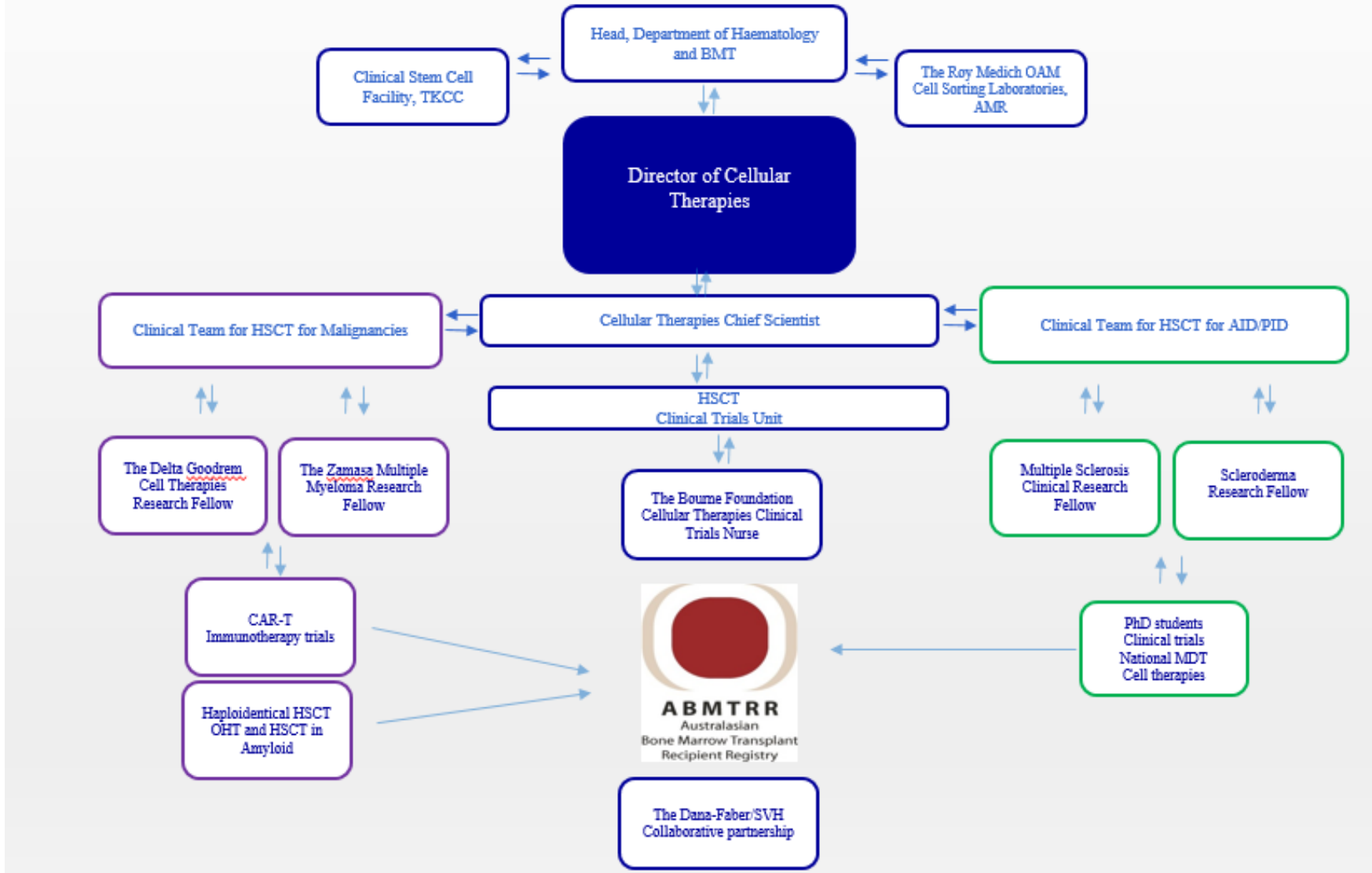


Figure 1. Response to bb2121 Infusion.

Cellular Therapies Program Structure



Conclusions

- Many new developments in Myeloma
- MM better controlled and better overall survival than 10 years ago
- New immunotherapies are likely the key to continued improvements in survival in MM
- Exciting times ahead for St Vincents Hospital with the establishment of the Zamasa Foundation Fellow, DFI/SVH collaboration and the Cellular Therapies Unit.

Acknowledgements

- Patients and guests
- St Vincent's Hospital, Sydney
- The nursing, allied health and medical staff of the Haematology Unit at St Vincent's Hospital
- The St Vincent's Curran Foundation
- The Zamasa Foundation
- The Delta Goodrem Foundation
- The Medich and Chong Families
- MS Research Australia
- The Bourne Foundation
- Kiriwina Investment Company

ZAMASA FOUNDATION AND MYELOMA RESEARCH: ST VINCENT'S HOSPITAL

Georgia McCaughan

ZAMASA Foundation Myeloma Fellow

St Vincent's Hospital, Sydney

Summary

- Establishment of the fellowship and research highlights
- Formation of local and international collaborations
- Highlights of current and future directions of immunotherapy in multiple myeloma

Fellowship Highlights

- First dedicated Myeloma Fellowship in New South Wales
- Established a dedicated myeloma clinic at St Vincent's Hospital
- Engagement with the Australian myeloma community
  - New South Wales Harmonisation Projects
  - Australasian Leukaemia and Lymphoma Group (ALLG)
  - Australian Myeloma Research Consortium (AMaRC)
- Research highlights

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

ABMTRR
Australasian
Bone Marrow Transplant
Recipient Registry

Leukaemia Foundation

ANZTCT

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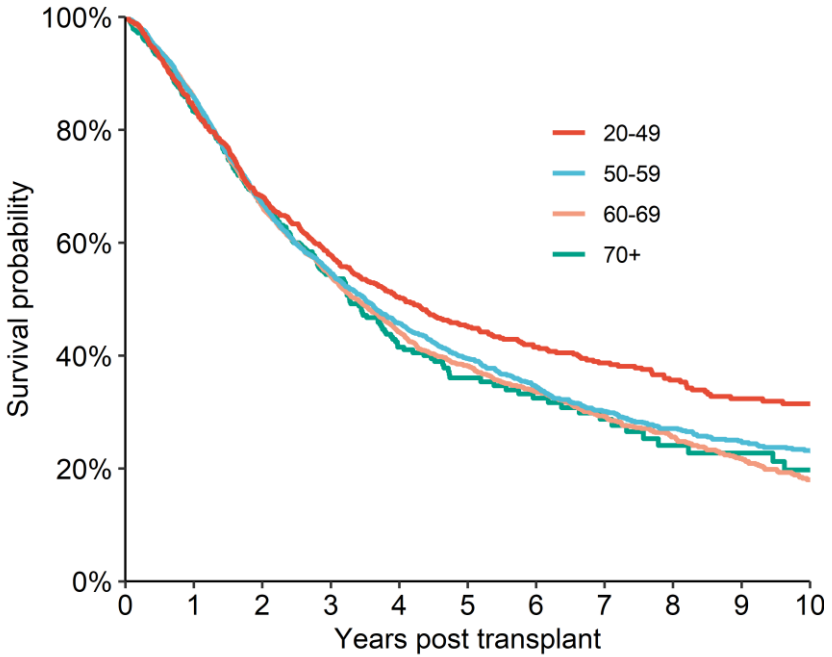
Proportion of Patients Undergoing Autologous Stem Cell Transplantation for Multiple Myeloma is Increasing

Two fold increase in patients ≥ 70 undergoing autologous stem cell transplantation for MM

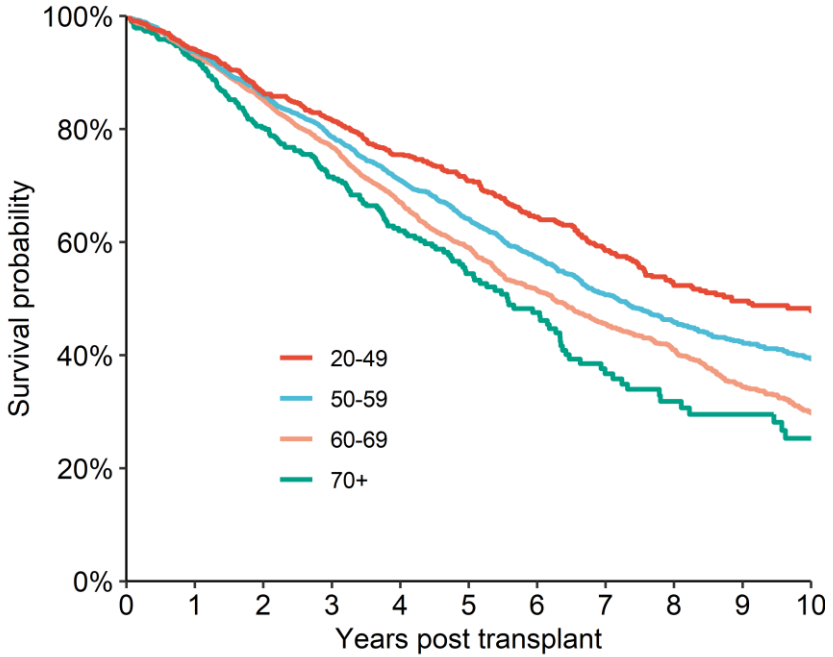
Similar Outcomes Regardless of Age

Progression Free Survival by Age Group



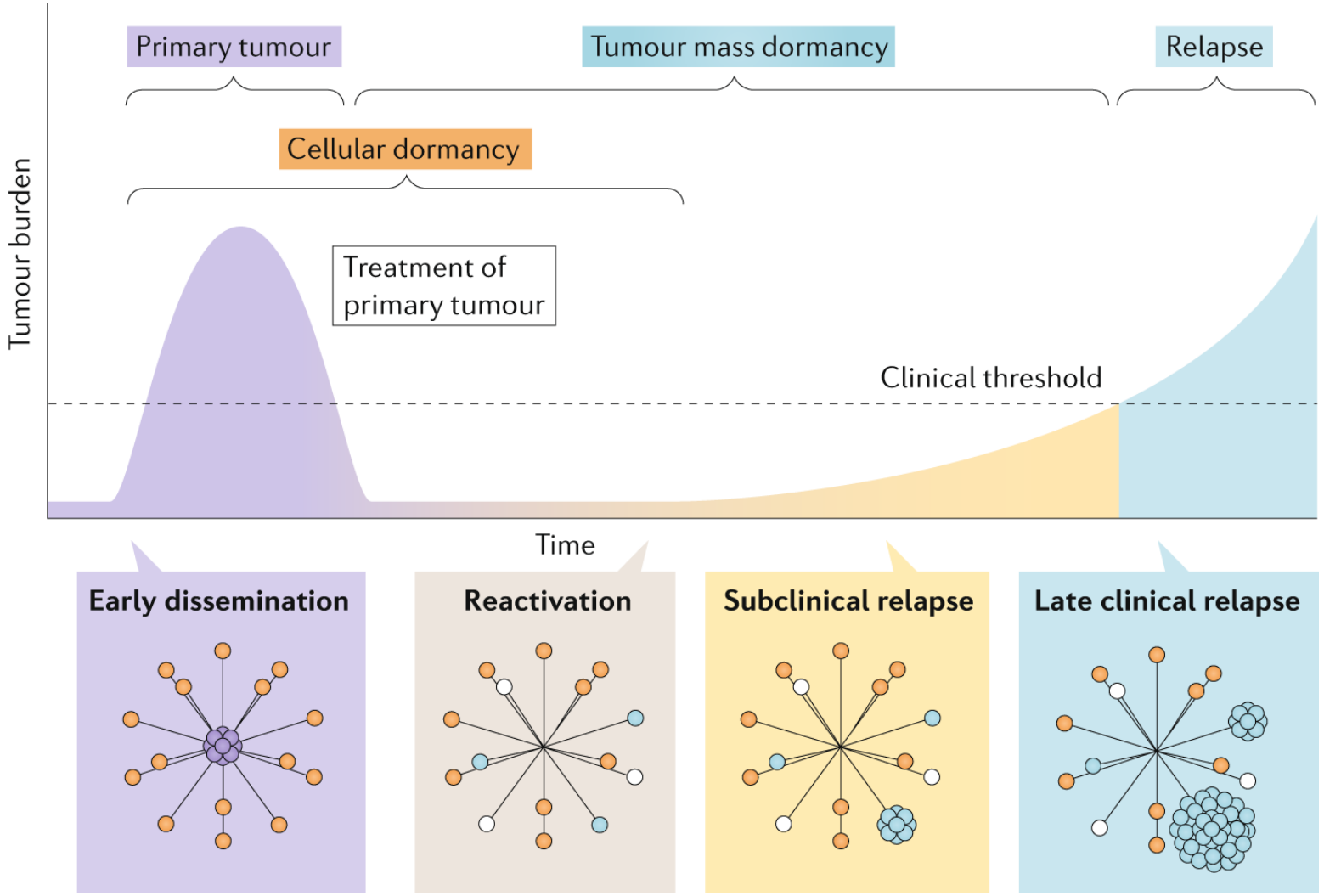
Median PFS:
Age ≥70: 3.3 years (95% CI 2.9-3.8)
Age 60-69: 3.4 years (95% CI 3.3-3.6)

Overall Survival by Age Group



Median OS:
Age ≥70: 5.6 years (95% CI 4.9-6.3)
Age 60-69: 6.2 years (95% CI 5.8-6.6) (P = 0.01)

St Vincent's/Garvan Collaboration



Phan, T.G., Croucher, P.I. The dormant cancer cell life cycle. *Nat Rev Cancer* **20,** 398–411 (2020). https://doi.org/10.1038/s41568-020-0263-0

St Vincent's/Dana Faber Collaboration

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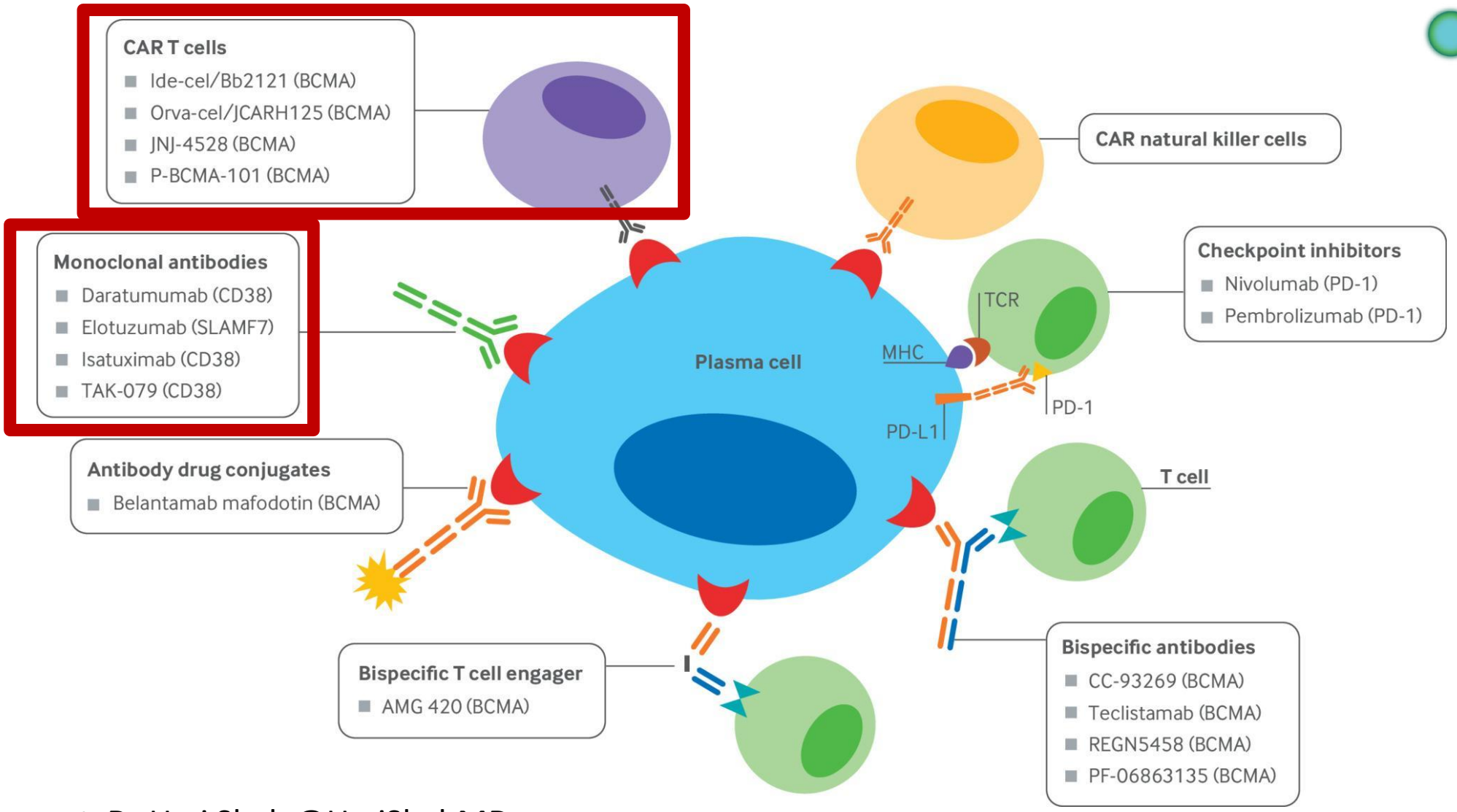
Dana-Farber Cancer Institute

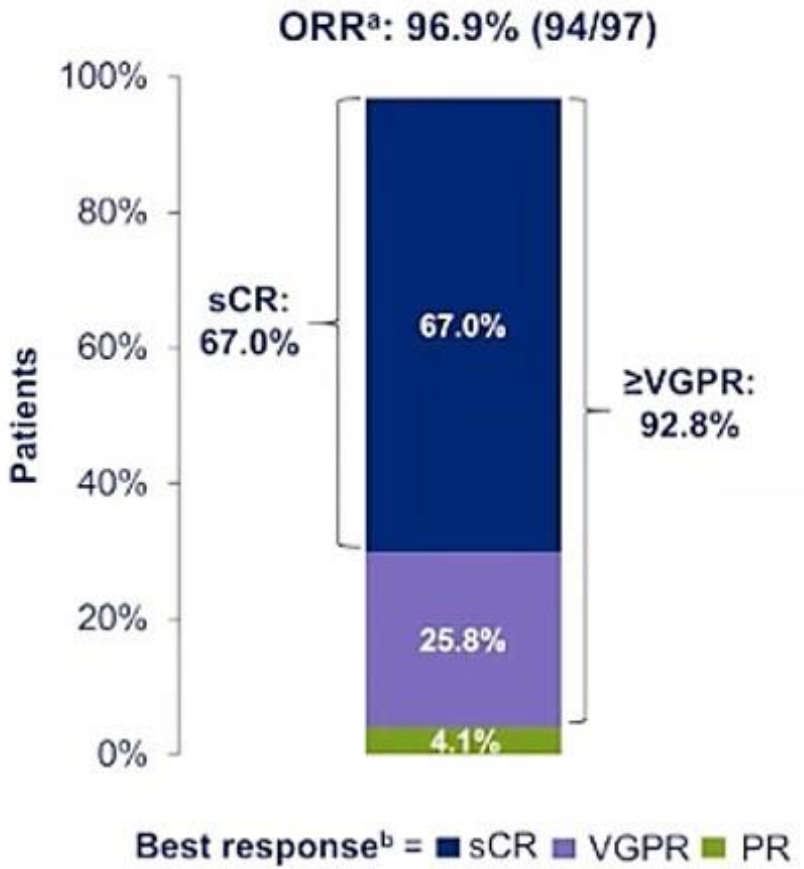
ST VINCENT'S HOSPITAL SYDNEY

Immunotherapy in Myeloma – Current and Future



Acknowledgment: Dr Urvi Shah @UrviShahMD

CARTITUDE-1: Response Rates



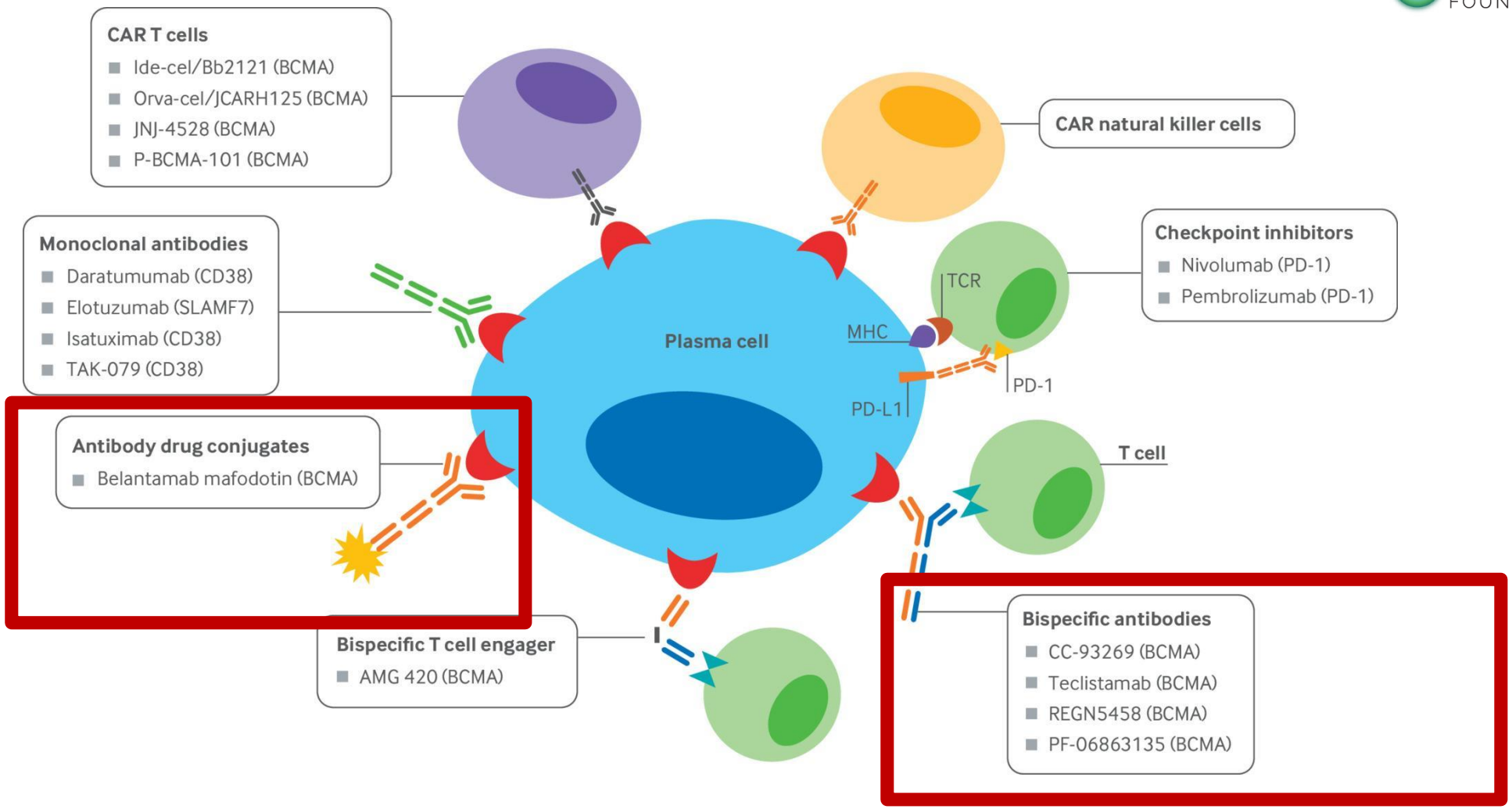
	N	Frequency in evaluable patients n=57[c]	Frequency in all treated n=97[d]
Overall MRD-	53	93.0%	54.6%
MRD- and sCR	33	57.9%	34.0%
MRD- and ≥VGPR	49	86.0%	50.5%

- 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.
[a]PR or better, Independent Review Committee assessed. [b]No patient had CR or stable disease as best response. [c]MRD was assessed in evaluable samples at 10^{-5} 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

Madduri et al. CARTITUDE-1: Phase 1b/2 Study of Ciltacabtagene Autoleucel, a B-Cell Maturation Antigen-Directed Chimeric Antigen Receptor T Cell Therapy, in Relapsed/Refractory Multiple Myeloma. *Blood* 2020; 136 (Supplement 1): 22–25. doi: https://doi.org/10.1182/blood-2020-136307

Immunotherapy in Myeloma – Current and Future



Acknowledgment: Dr Urvi Shah @UrviShahMD

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We would like to thank our presenters

Mr Barry Du Bois
Network Ten Living Room Presenter

A/Prof John Moore
Chong Family Director of Cellular Therapy, St Vincent's Hospital Sydney

Dr Georgia McCaughan
ZAMASA Myeloma Fellow - St Vincent's Hospital Sydney

and our hosts for this special Zoom presentation

Shanthini Naidoo
CEO, St Vincent's Curran Foundation
and
Greg Arandt
Chairman of Zamasa Foundation

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Thank you for joining

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https://www.supportstvincents.com.au/ways-to-give/donate/

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