Meet The Professor
Optimizing the Management of Multiple Myeloma

Tuesday, November 15, 2022
5:00 PM – 6:00 PM ET

Faculty

Paul G Richardson, MD

Moderator

Neil Love, MD

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Commercial Support

This activity is supported by educational grants from AbbVie Inc, GlaxoSmithKline, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, and Karyopharm Therapeutics.

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI BioPharma Corp, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

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Contracted Research	Bristol-Myers Squibb Company, Celgene Corporation, Karyopharm Therapeutics, Oncopeptides, Takeda Pharmaceuticals USA Inc

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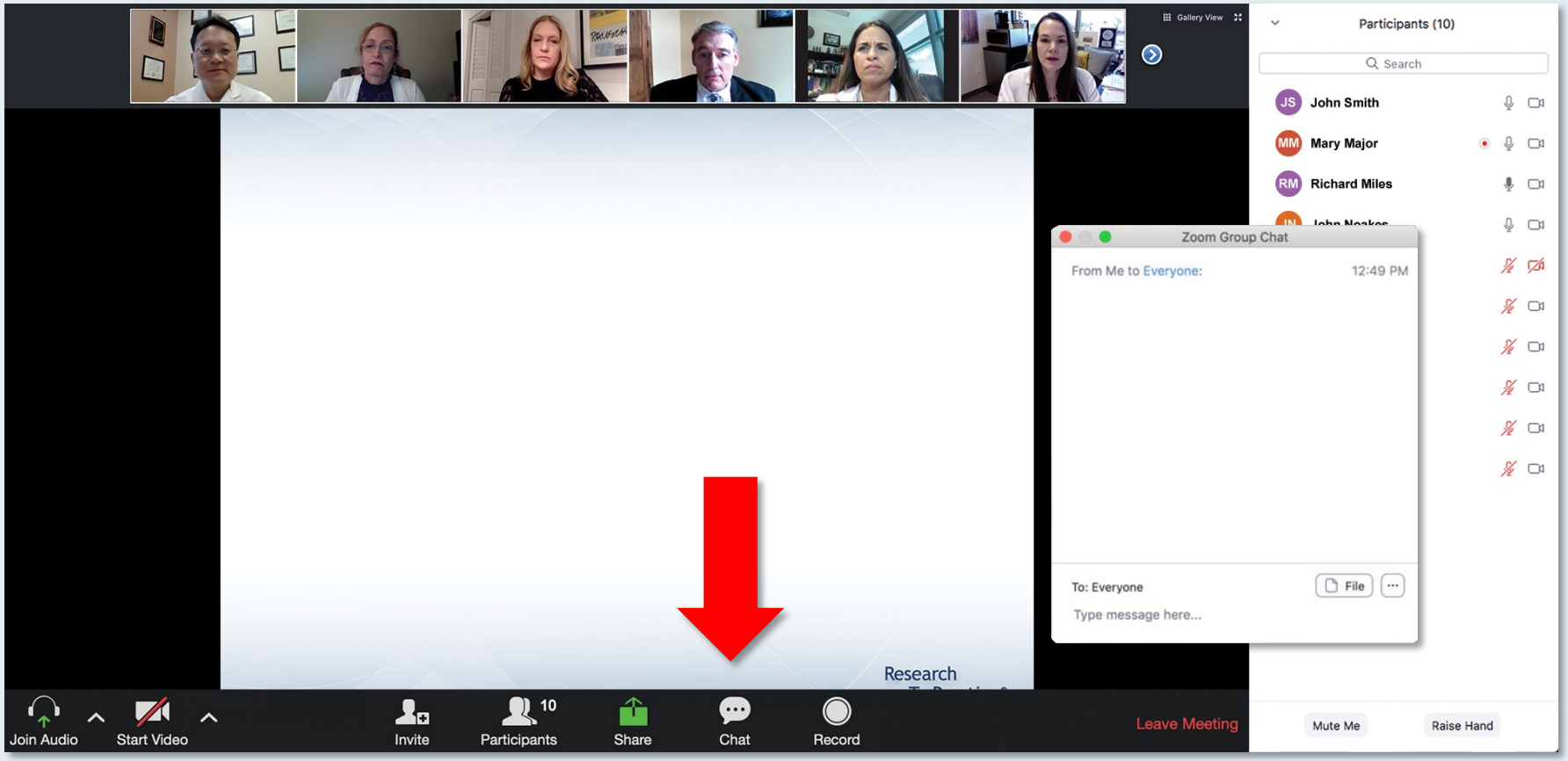

Feel free to submit questions now before the program begins and throughout the program.

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Familiarizing Yourself with the Zoom Interface

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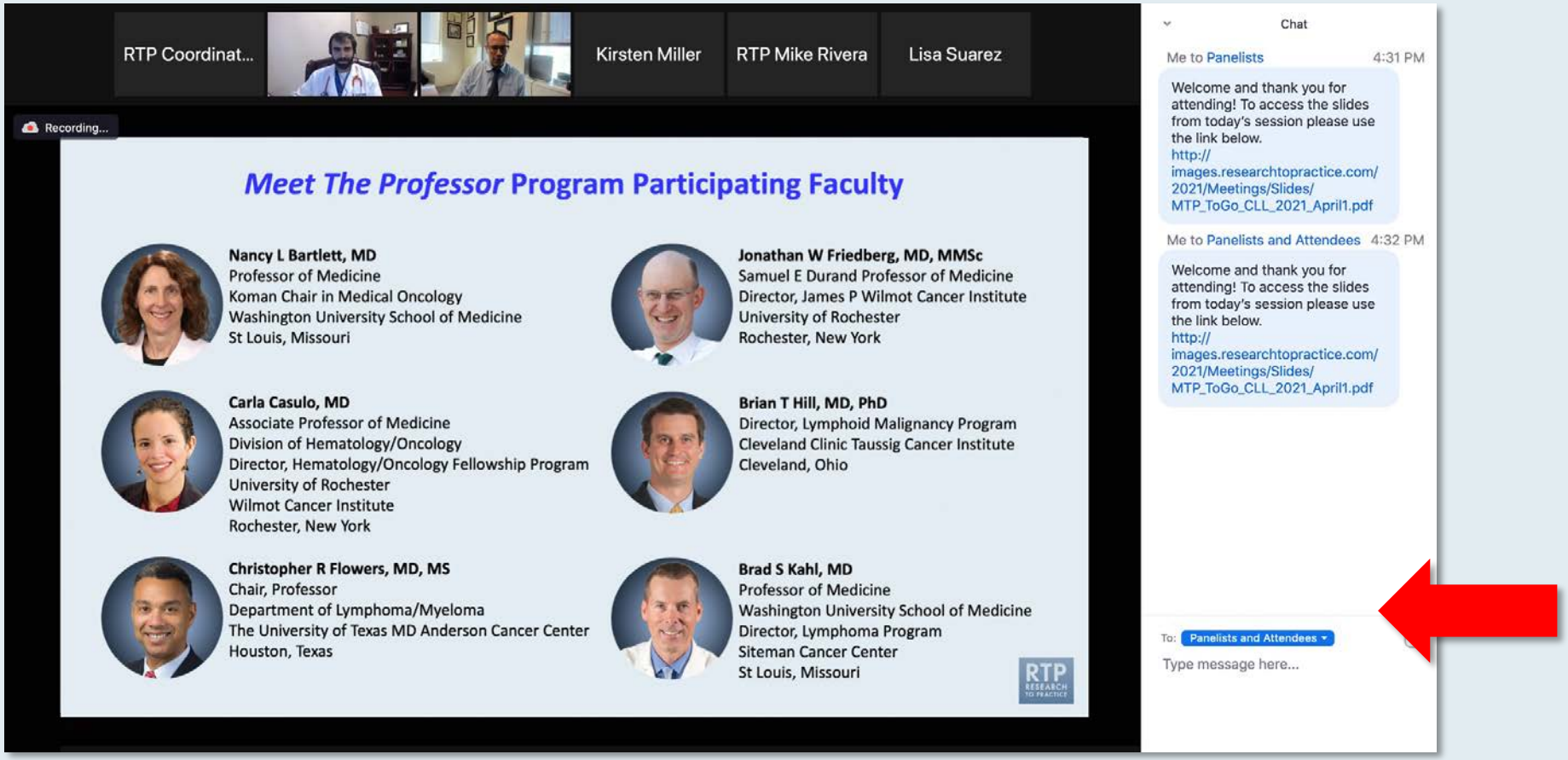

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Familiarizing Yourself with the Zoom Interface

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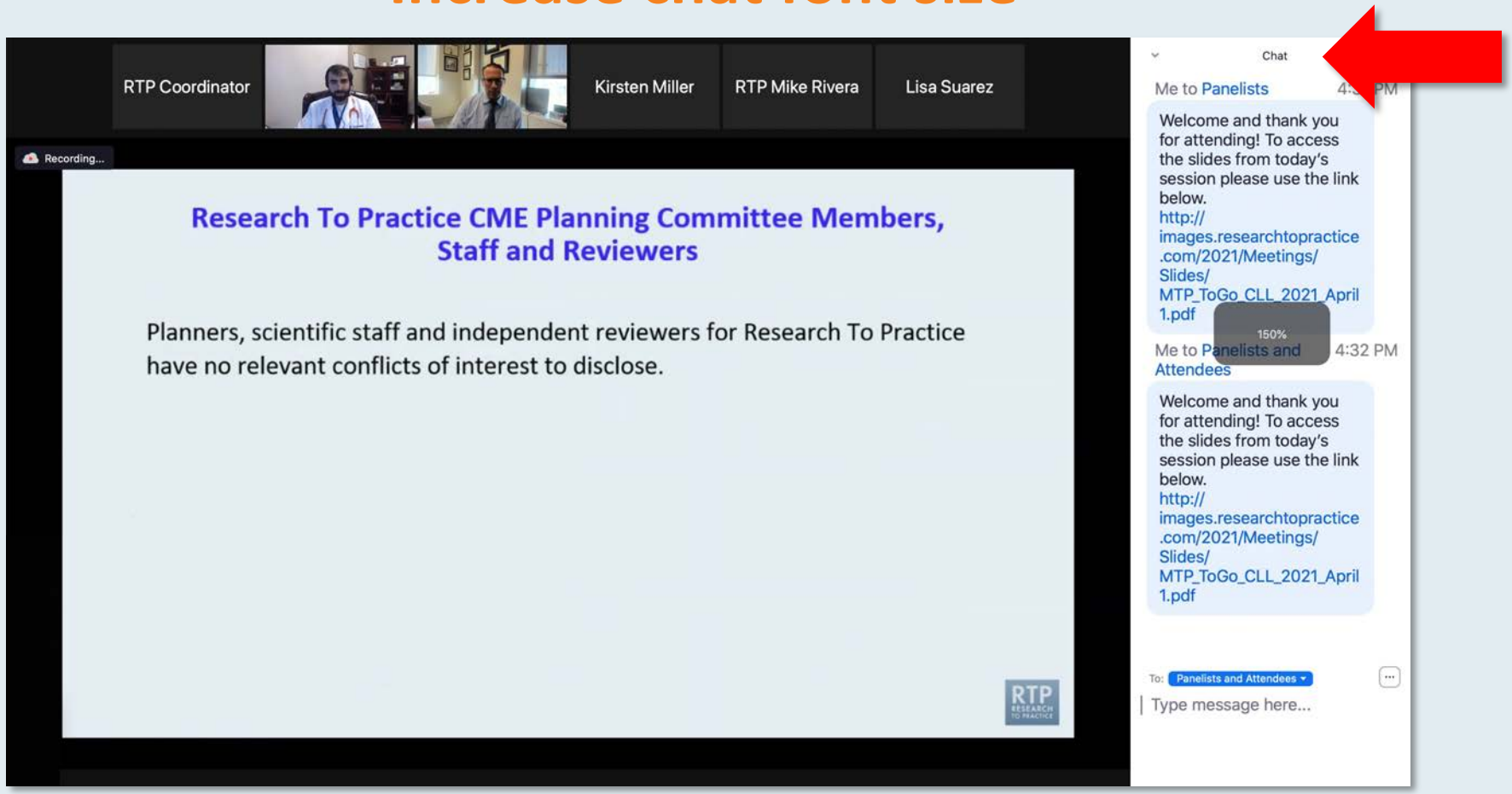

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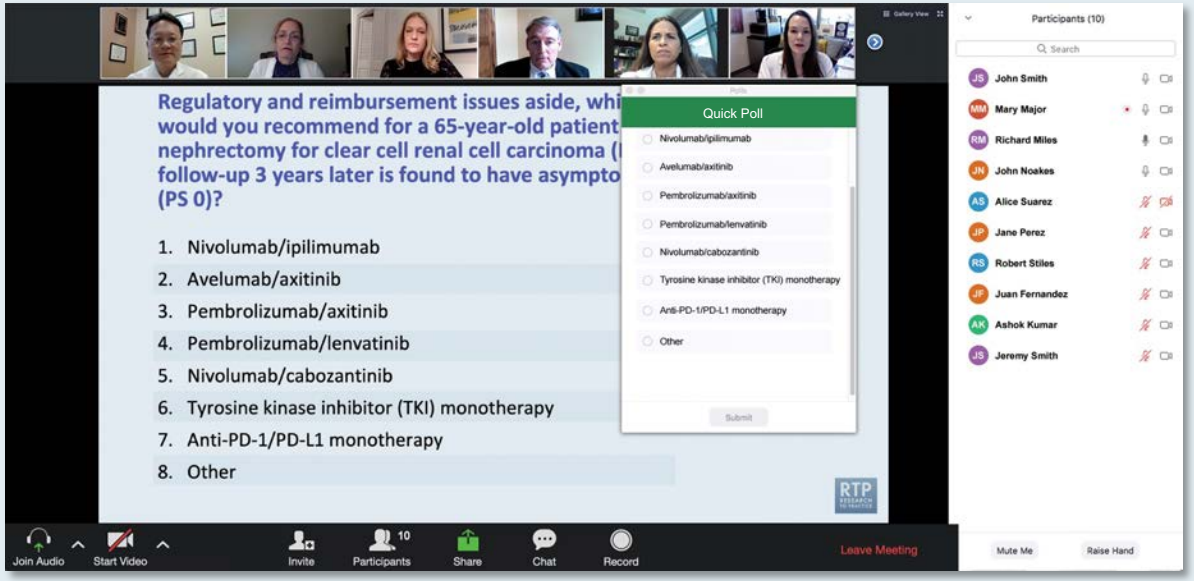

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ONCOLOGY TODAY

WITH DR NEIL LOVE

BCMA-Directed Therapies for Multiple Myeloma

DR AMRITA KRISHNAN
CITY OF HOPE CANCER CENTER

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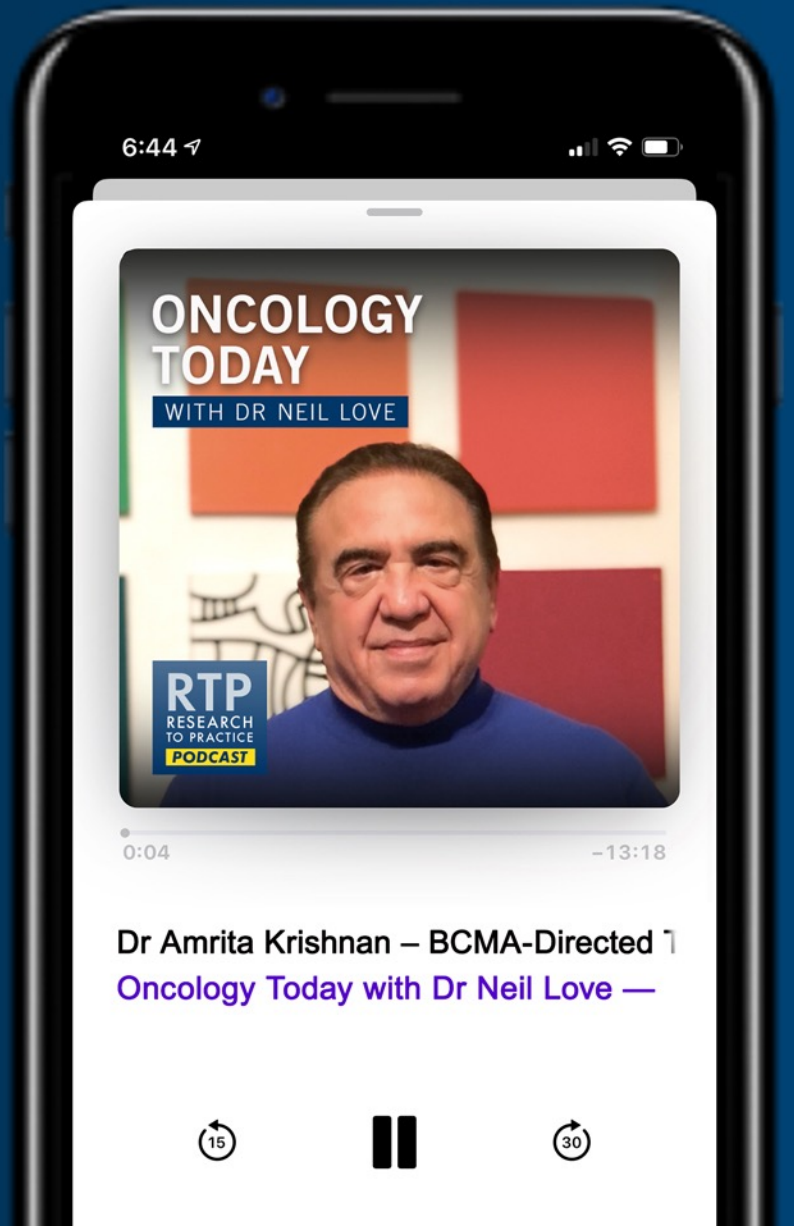

Oncology Today with Dr Neil Love — Novel Agents and Strategies in Acute Myeloid Leukemia

A CME/MOC-Accredited Virtual Event

Thursday, November 17, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel A Pollyea, MD, MS

Moderator

Neil Love, MD

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BCMA-Directed Therapy in Multiple Myeloma — Expert Opinions and Patient Perspectives

Part 2 of a 2-Part CME/MOC-Accredited Virtual Series

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Emerging Role of Antibody-Drug Conjugates in the Management of Non-Small Cell Lung Cancer

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RTP RESEARCH TO PRACTICE

What Clinicians Want to Know: Addressing Current Questions and Controversies in the Management of HER2-Positive Breast Cancer

Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the 2022 San Antonio Breast Cancer Symposium®

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7:15 PM – 9:15 PM CT (8:15 PM – 10:15 PM ET)

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Erika Hamilton, MD

Sara A Hurvitz, MD

Ian E Krop, MD, PhD

Shanu Modi, MD

Sara M Tolaney, MD, MPH

Moderator

Neil Love, MD

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Matthew P Goetz, MD

Virginia Kaklamani, MD, DSc

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RTP RESEARCH TO PRACTICE

Addressing Current Questions and Controversies in the Management of Chronic Lymphocytic Leukemia — What Clinicians Want to Know

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Professor Dr Arnon P Kater, MD, PhD
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Noopur Raje, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Jerome Lipper Multiple Myeloma Center
Dana-Farber Cancer Institute
RJ Corman Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Meet The Professor Program Participating Faculty

Rafael Fonseca, MD
Chief Innovation Officer
Getz Family Professor of Cancer
Distinguished Mayo Investigator
Mayo Clinic in Arizona
Phoenix, Arizona

Shaji K Kumar, MD
Mark and Judy Mullins Professor
of Hematological Malignancies
Consultant, Division of Hematology
Professor of Medicine
Mayo Clinic
Rochester, Minnesota

Ola Landgren, MD, PhD
Professor of Medicine
Leader, Experimental Therapeutics Program
Leader, Myeloma Division
Co-Leader of Tumor Biology Program
Sylvester Comprehensive Cancer Center
University of Miami
Miami, Florida

Sagar Lonial, MD
Chair and Professor
Department of Hematology and Medical Oncology
Anne and Bernard Gray Family Chair in Cancer
Chief Medical Officer
Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia

Joseph Mikhael, MD, MEd
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Translational Genomics Research Institute (TGen)
City of Hope Cancer Center
Chief Medical Officer
International Myeloma Foundation
Consultant Hematologist and Director, Myeloma
Research, Phase 1 Program
HonorHealth Research Institute
Adjunct Professor, College of Health Solutions
Arizona State University
Phoenix, Arizona

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Meet The Professor Program Participating Faculty

Noopur Raje, MD
Director, Center for Multiple Myeloma
Massachusetts General Hospital Cancer Center
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Paul G Richardson, MD
Clinical Program Leader and Director of Clinical Research
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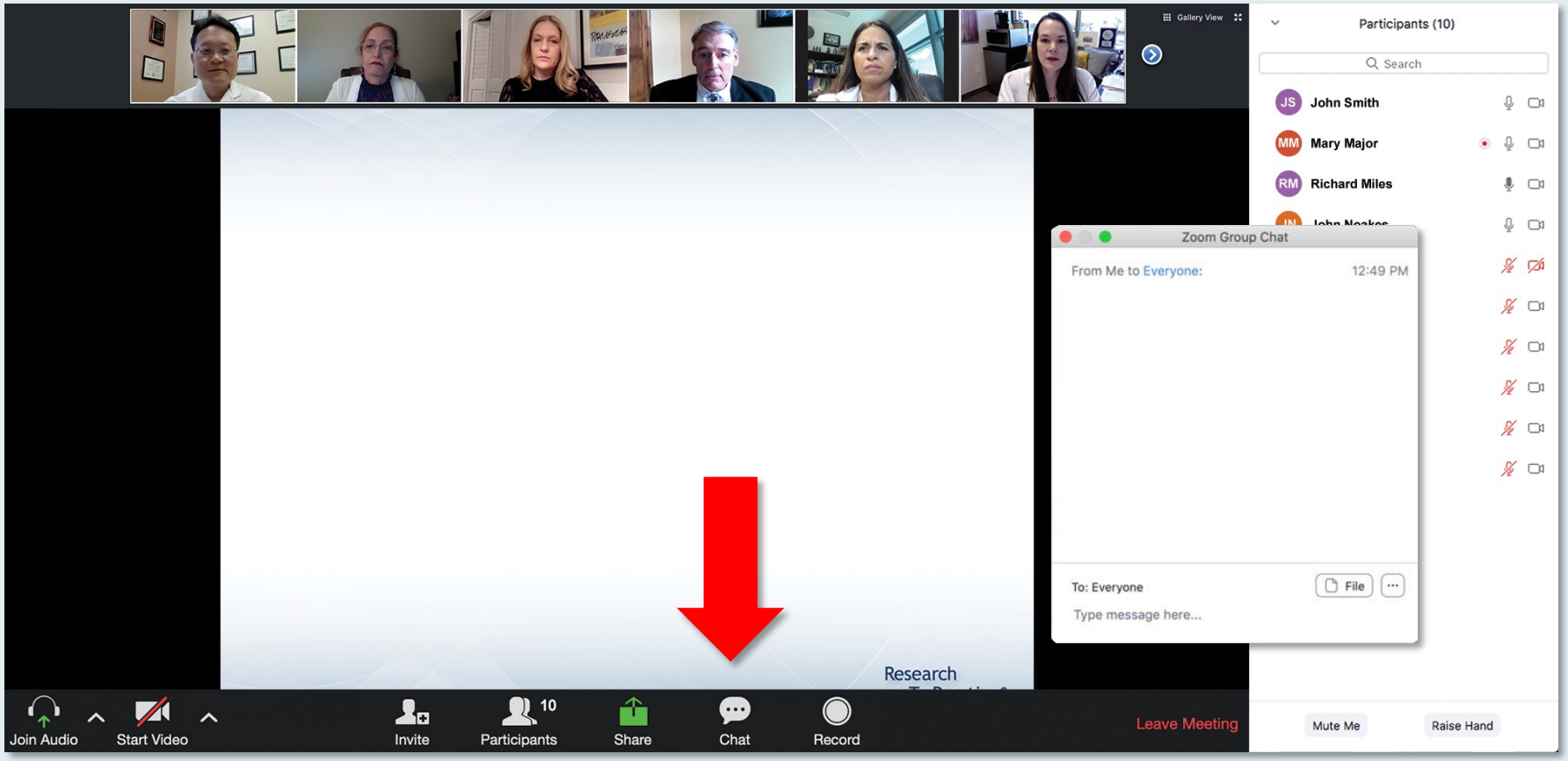

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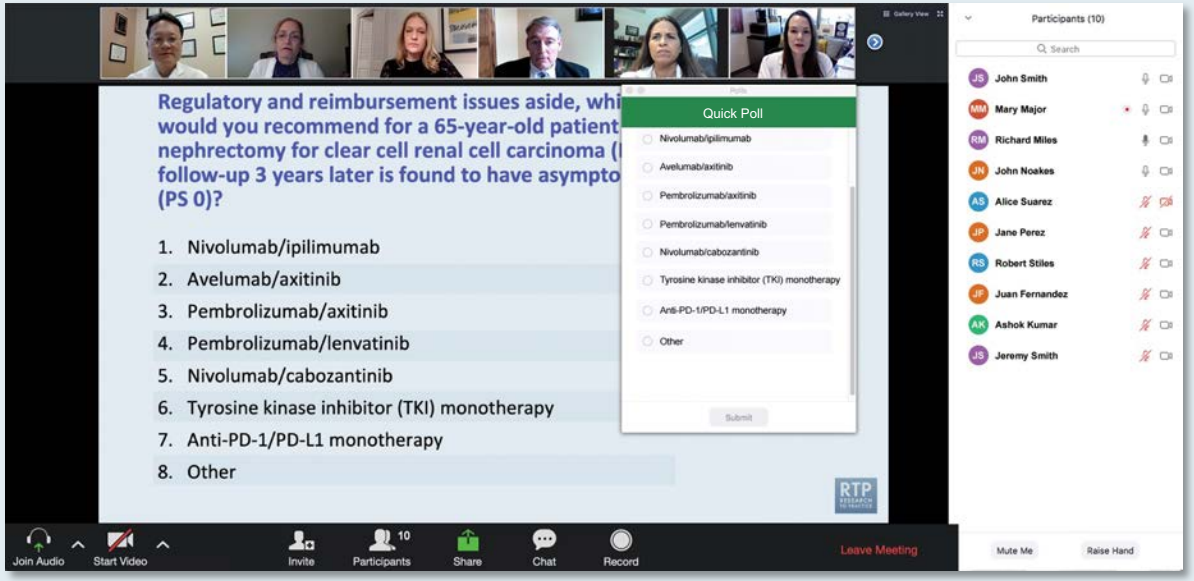

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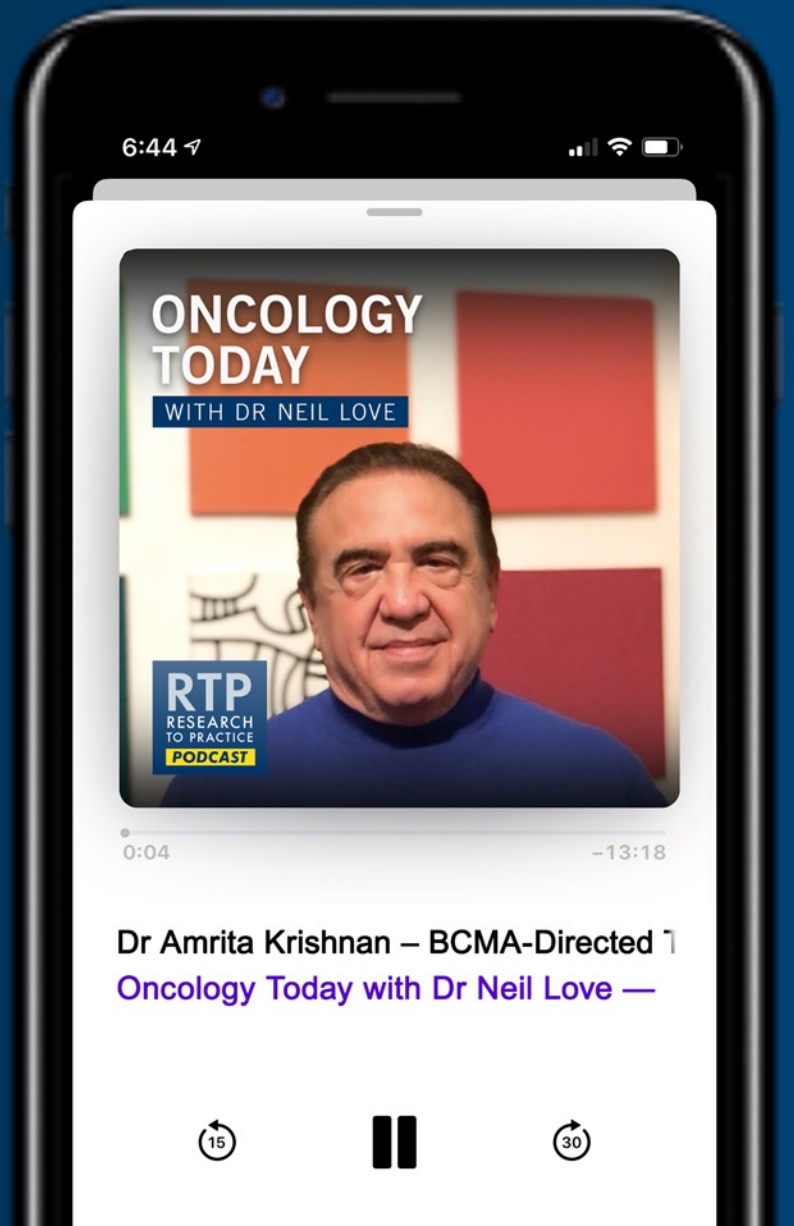

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Contracted Research	Bristol-Myers Squibb Company, Celgene Corporation, Karyopharm Therapeutics, Oncopeptides, Takeda Pharmaceuticals USA Inc

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Lehigh Valley Topper Cancer Institute
Bethlehem, Pennsylvania

Hans Lee, MD
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kapisthalam (KS) Kumar, MD
Florida Cancer Specialists
Trinity, Florida

Muzaffar H Qazilbash, MD
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Zanetta S Lamar, MD
Florida Cancer Specialists
Naples, Florida

Erik Rupard, MD
The Reading Hospital
West Reading, Pennsylvania

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Meet The Professor with Dr Richardson

INTRODUCTION

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

MODULE 3: Journal Club with Dr Richardson

MODULE 4: Appendix of Key Publications

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2022 September 13;6(17):4967-74.
REGULAR ARTICLE

blood advances

Quality of life, psychological distress, and prognostic perceptions in caregivers of patients with multiple myeloma

Elizabeth K. O'Donnell,[1,2] Yael N. Shapiro,[1] Andrew J. Yee,[1-3] Omar Nadeem,[2,4] Jacob P. Laubach,[2,4] Andrew R. Branagan,[1,2] Kenneth C. Anderson,[2,4] Clifton C. Mo,[2,4] Nikhil C. Munshi,[2,4] Irene M. Ghobrial,[2,4] Adam S. Sperling,[2,4,5] Emerentia A. Agyemang,[1] Jill N. Burke,[1] Cynthia C. Harrington,[1] Bonnie Y. Hu,[1] Paul G. Richardson,[2,4] Noopur S. Raje,[1,2] and Areej El-Jawahri[1,2]

Cancer 2022 May 15;128(10):1996-2004.

Original Article

Quality of life, psychological distress, and prognostic perceptions in patients with multiple myeloma

Elizabeth K. O'Donnell, MD [1,2]; Yael N. Shapiro, BA[1]; Andrew J. Yee, MD[1,2,3]; Omar Nadeem, MD[2,4]; Bonnie Y. Hu, BS[1]; Jacob P. Laubach, MD[2,4]; Andrew R. Branagan, MD, PhD[1,2]; Kenneth C. Anderson, MD[2,4]; Clifton C. Mo, MD[2,4]; Nikhil C. Munshi, MD[2,4]; Irene M. Ghobrial, MD[2,4]; Adam S. Sperling, MD[2,4,5]; Emerentia A. Agyemang, NP[1]; Jill N. Burke, NP[1]; Cynthia C. Harrington, NP[1]; Paul G. Richardson, MD[2,4]; Noopur S. Raje, MD[1,2]; and Areej El-Jawahri, MD [1,2]

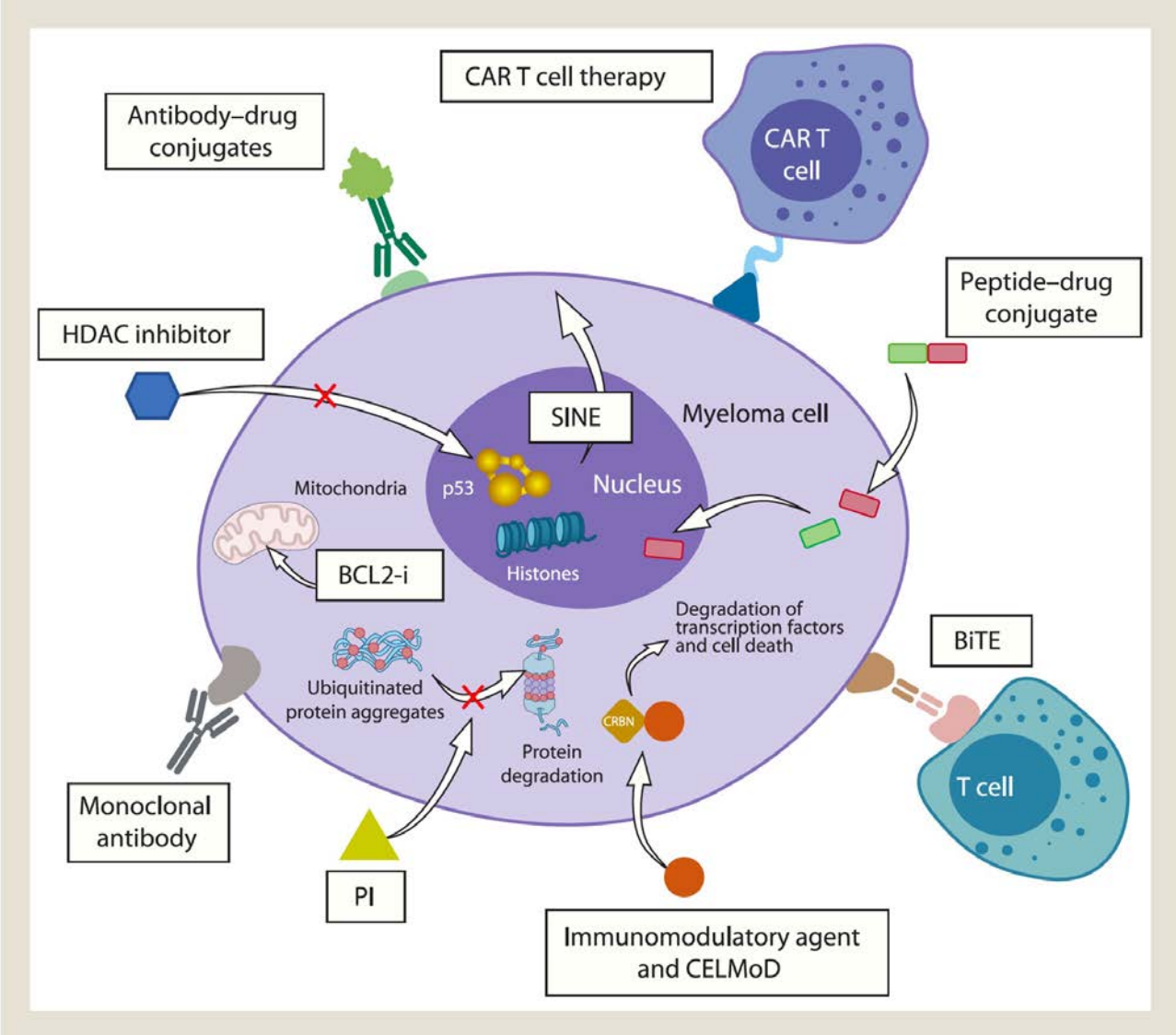
Clin Lymphoma Myeloma Leuk 2022 July;22(7):460-73.

Review Article

Treatment Options for Patients With Heavily Pretreated Relapsed and Refractory Multiple Myeloma

Meletios-Athanasios Dimopoulos,[1] Paul Richardson,[2] Sagar Lonial[3]

Mechanisms of Action of Drug Classes for the Treatment of Refractory Multiple Myeloma



Dimopoulos M-A et al. *Clin Lymphoma Myeloma Leuk* 2022 July;22(7):460-73.

Leuk Lymphoma. 2022 October ; 63(10): 2403–2412.

Risk factors for the development of orthostatic hypotension during autologous stem cell transplant in patients with multiple myeloma

Matthew Ho[a], Maria Moscvin[b], Soon Khai Low[c], Benjamin Evans[b], Sara Close[d], Robert Schlossman[d,†], Jacob Laubach[d], Claudia Paba Prada[d,‡], Brett Glotzbecker[e,$], Paul G. Richardson[d], Giada Bianchi[b]

N Engl J Med 2022 July 14;387(2):132-47.

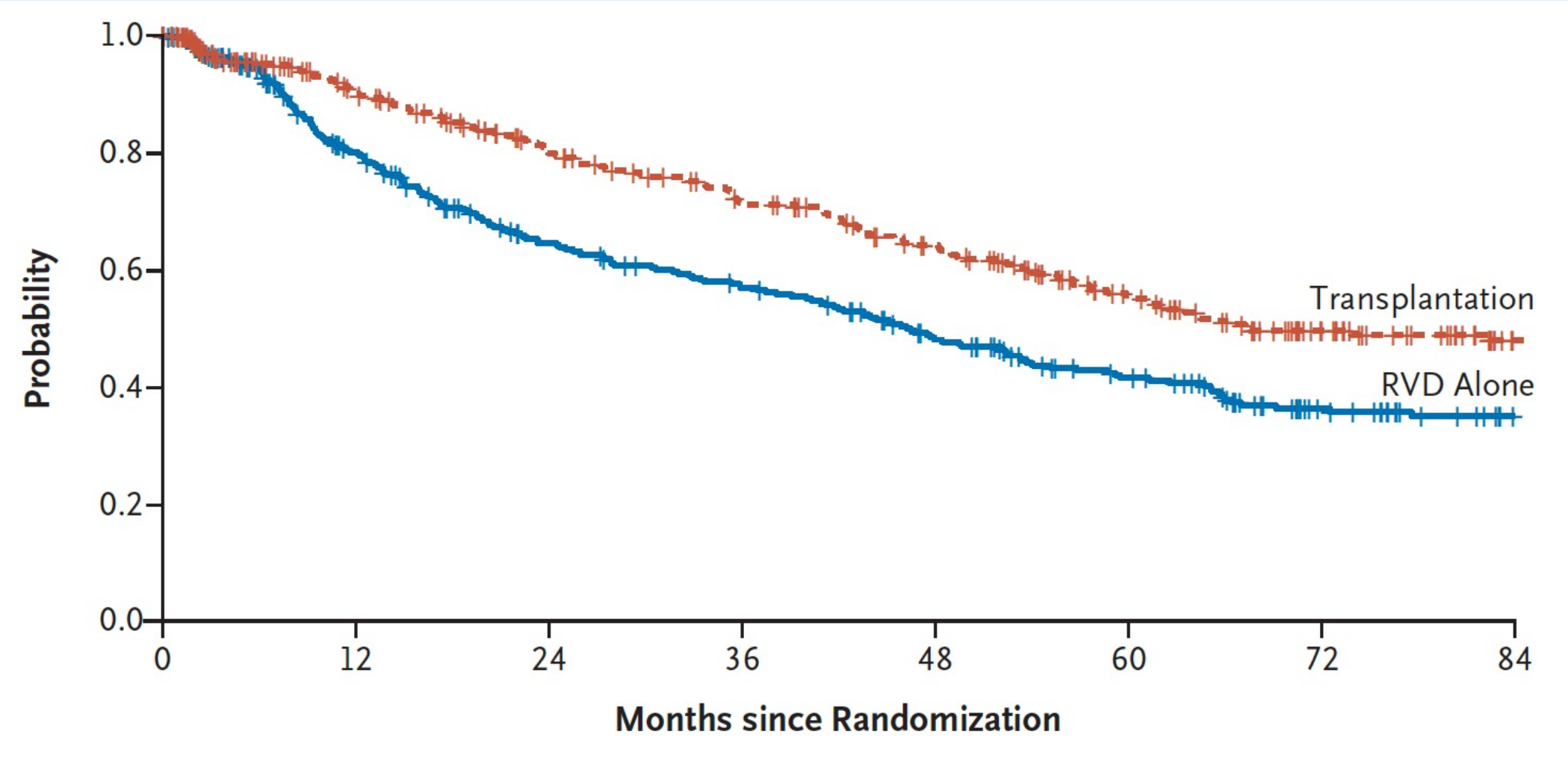
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma

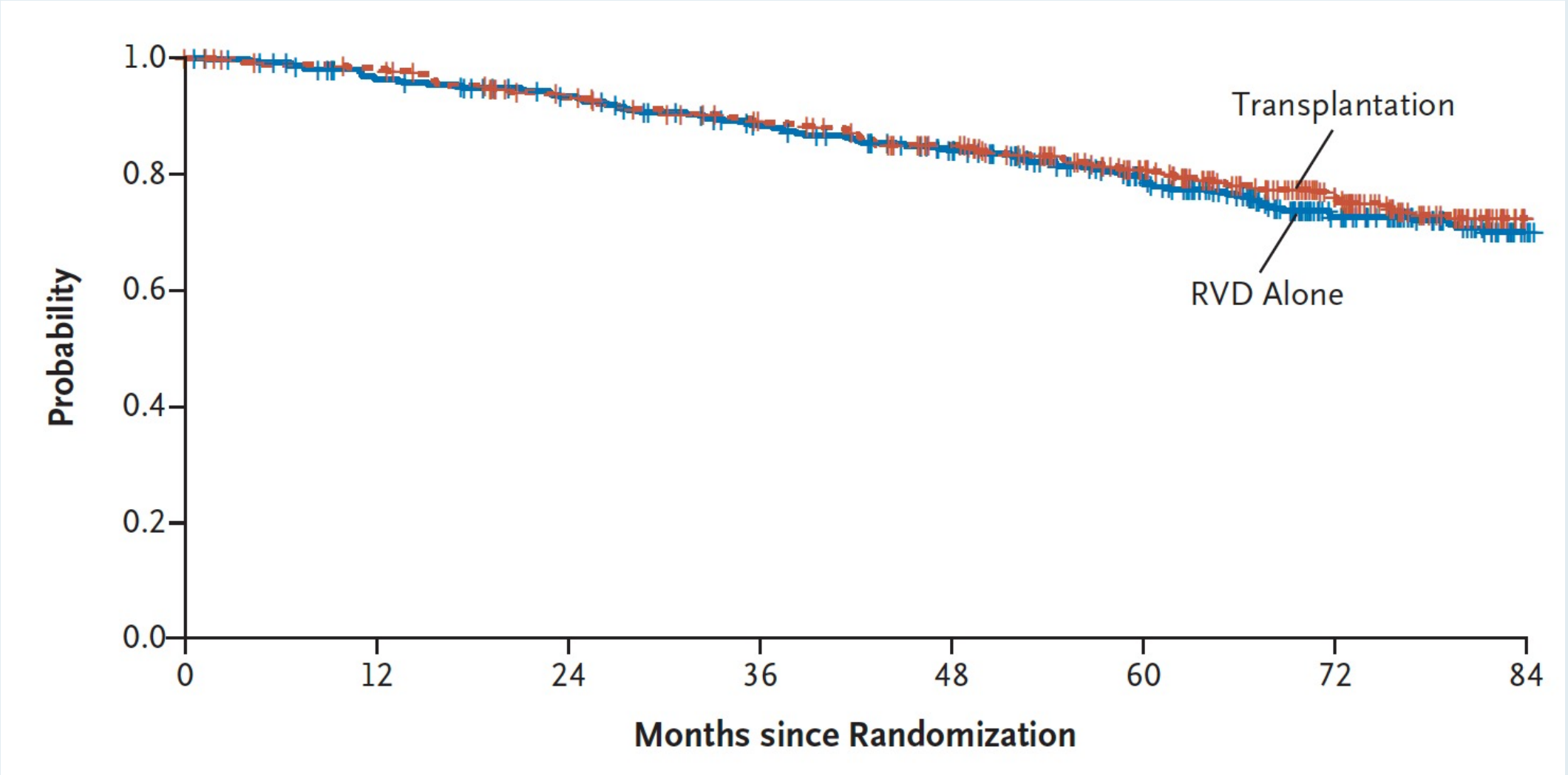
P.G. Richardson, S.J. Jacobus, E.A. Weller, H. Hassoun, S. Lonial, N.S. Raje, E. Medvedova, P.L. McCarthy, E.N. Libby, P.M. Voorhees, R.Z. Orlowski, L.D. Anderson, Jr., J.A. Zonder, C.P. Milner, C. Gasparetto, M.E. Agha, A.M. Khan, D.D. Hurd, K. Gowin, R.T. Kamble, S. Jagannath, N. Nathwani, M. Alsina, R.F. Cornell, H. Hashmi, E.L. Campagnaro, A.C. Andreescu, T. Gentile, M. Liedtke, K.N. Godby, A.D. Cohen, T.H. Openshaw, M.C. Pasquini, S.A. Giralt, J.L. Kaufman, A.J. Yee, E. Scott, P. Torka, A. Foley, M. Fulciniti, K. Hebert, M.K. Samur, K. Masone, M.E. Maglio, A.A. Zeytoonjian, O. Nadeem, R.L. Schlossman, J.P. Laubach, C. Paba-Prada, I.M. Ghobrial, A. Perrot, P. Moreau, H. Avet-Loiseau, M. Attal, K.C. Anderson, and N.C. Munshi, for the DETERMINATION Investigators*

DETERMINATION: Progression-Free Survival (ITT)



Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47.

DETERMINATION: Overall Survival (ITT)



Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47.

2022;3(1):1-10

Exploration of Targeted Anti-tumor Therapy

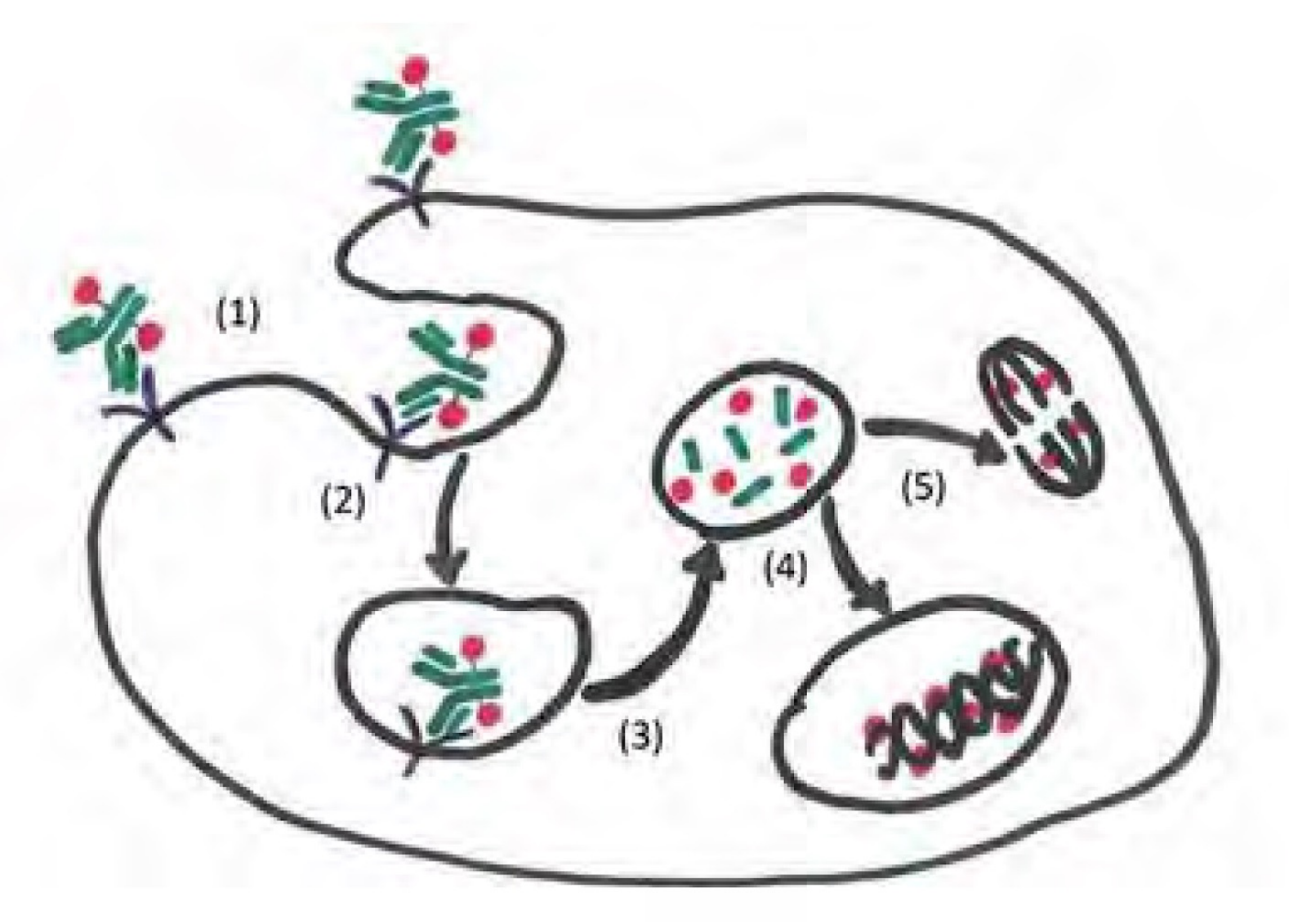
Open Exploration

Open Access Review

Antibody-drug conjugate therapies in multiple myeloma—what's next on the horizon?

Monique Hartley-Brown*, Paul Richardson

Mechanism of Action of Antibody-Drug Conjugates



Hartley-Brown M, Richardson P. *Explor Target Antitumor Ther* 2022;3(1):1-10.

2022 ASCO® ANNUAL MEETING

Abstract 8019

Synergistic Effects of Low-dose Belantamab Mafodotin in Combination with a Gamma-Secretase Inhibitor (Nirogacestat) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM): DREAMM-5 Study

Poster No. 443

Speaker: Sagar Lonial, MD, FACP

Acknowledgments

This study was funded by GlaxoSmithKline (GSK Study 208887). Drug linker technology licensed from Seagen, Inc.; monoclonal antibody produced using POTELLIGENT Technology licensed from BioWa; nirogacestat (gamma-secretase inhibitor) is manufactured and provided by SpringWorks Therapeutics as part of a collaborative agreement with GSK. On behalf of all authors, and with their permission, an audio recording was prepared by Sagar Lonial who did not receive any payment for this recording. Writing assistance was provided by Elisabeth Walsby, PhD and Sharon Bryant, DPT of Fishawack Indicia, part of Fishawack Health and funded by GSK.

Authors and Affiliations

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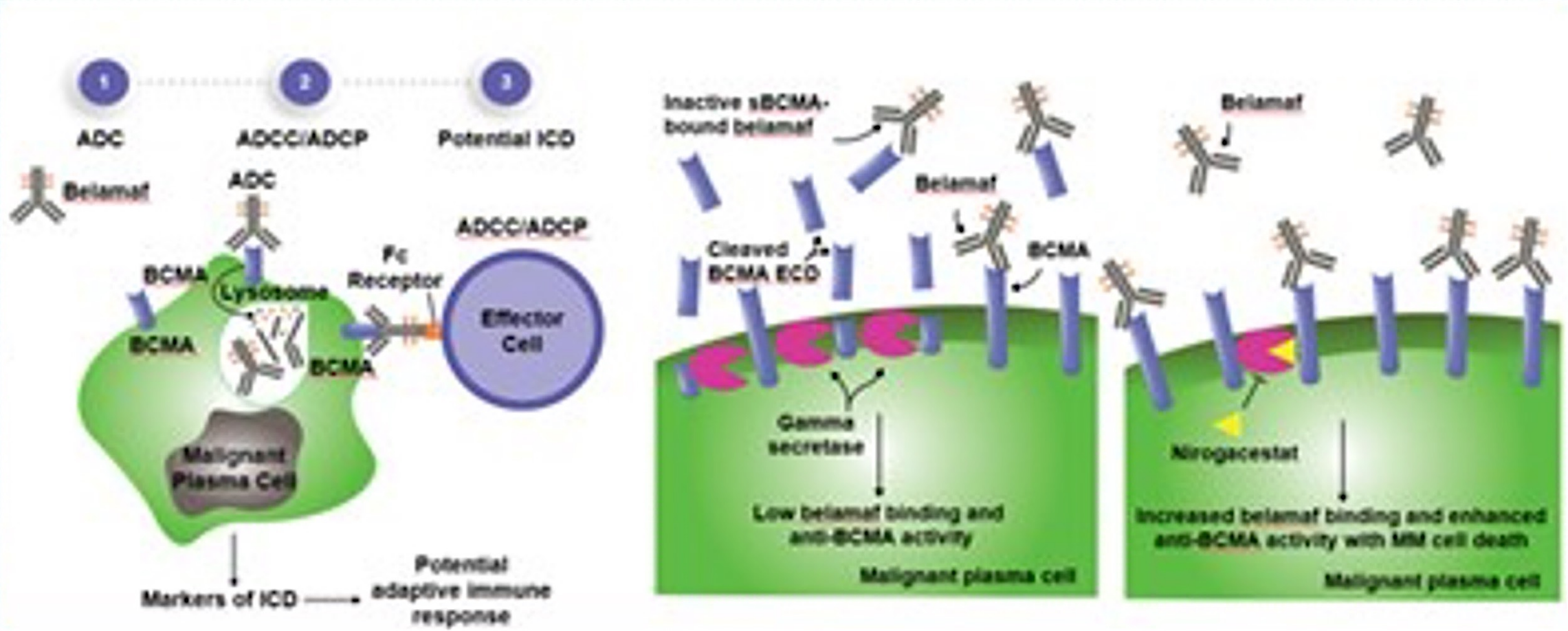
Mechanisms of Action of Belantamab Mafodotin (Belamaf) and Belamaf Combined with Nirogacestat



Lonial S et al. ASCO 2022;Abstract 8019.

Phase III DREAMM-3 Trial of Belantamab Mafodotin Monotherapy versus Pomalidomide in Combination with Low-Dose Dexamethasone Does Not Meet Its Primary Endpoint

Press Release: November 7, 2022

The DREAMM-3 Phase III open-label, randomized, head-to-head superiority trial of belantamab mafodotin monotherapy versus pomalidomide in combination with low dose dexamethasone (PomDex) for patients with relapsed or refractory multiple myeloma did not meet its primary endpoint of progression-free survival (PFS).

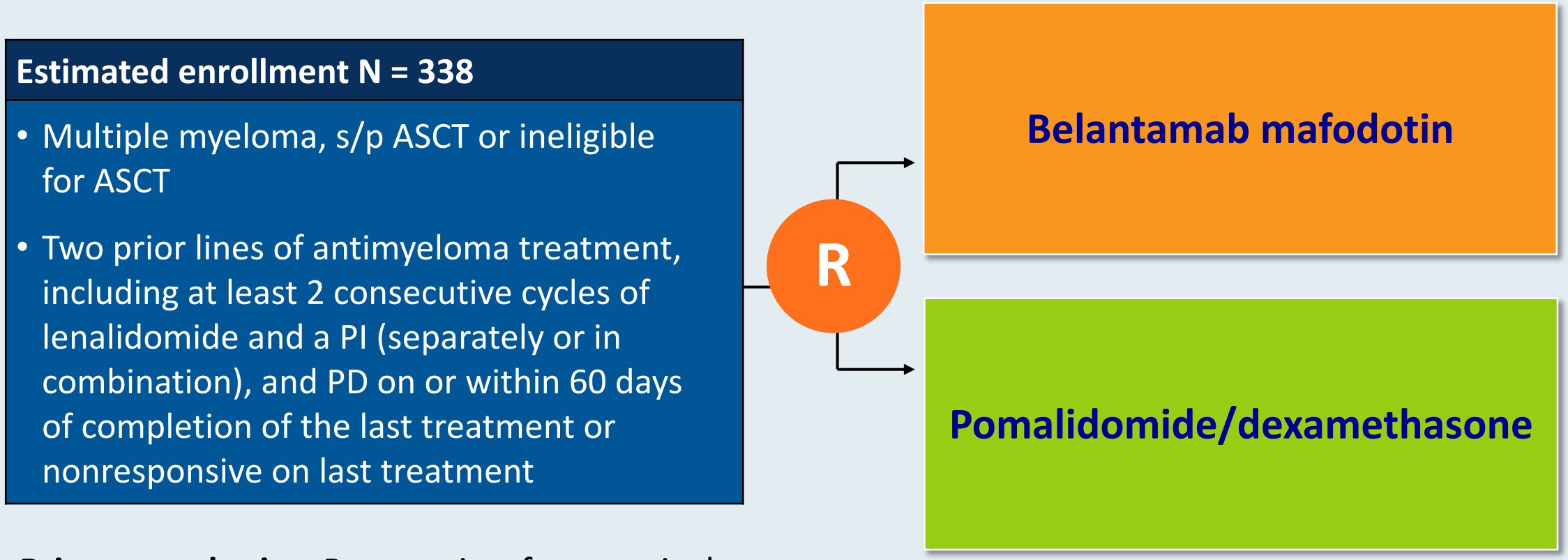
“In the DREAMM-3 trial, the primary endpoint of PFS demonstrated a hazard ratio of 1.03 (95% CI: 0.72, 1.47). The observed median progression-free survival was longer for belantamab mafodotin vs PomDex (11.2 months vs 7 months).”

“Data from DREAMM-3 is in the process of being shared with health authorities. Discussions with health authorities are currently ongoing. Additional trials within the DREAMM (DRiving Excellence in Approaches to Multiple Myeloma) clinical trial programme will continue.”

“Data from the DREAMM-7 and DREAMM-8 phase III trials are anticipated in the first half of 2023.”

https://www.gsk.com/en-gb/media/press-releases/gsk-provides-update-on-dreamm-3-phase-iii-trial-for-blenrep/

DREAMM-3 Phase III Trial Design



Primary endpoint: Progression-free survival

Secondary endpoints: Overall survival, overall response rate, clinical benefit rate, duration of response, time to response, time to disease progression, others

PI = proteasome inhibitor; PD = disease progression

https://clinicaltrials.gov/ct2/show/NCT04162210. Accessed November 2022.

Safety and Efficacy of Belantamab Mafodotin in Combination with Rd in Newly Diagnosed, Transplant Ineligible Multiple Myeloma Patients: A Phase 1/2 Study by the Hellenic Society of Hematology

Terpos E et al.

EHA 2022;Abstract S178.

DREAMM-9: Phase I Study of Belantamab Mafodotin plus Standard of Care in Patients with Transplant-Ineligible Newly Diagnosed Multiple Myeloma

Usmani SZ et al.

EHA 2022;Abstract P942.

Ongoing Phase III Trials of Belantamab Mafodotin

Study	N	Setting	Treatment arms	Estimated primary completion
DREAMM-8 (NCT04484623)	450	• RRMM • ≥1 prior line of treatment, including a lenalidomide-containing regimen	• Belantamab mafodotin + Pomalidomide/dexamethasone • Bortezomib + Pomalidomide/dexamethasone	March 2023
DREAMM-7 (NCT04246047)	575	• RRMM • ≥1 prior line of treatment	• Belantamab mafodotin + Bortezomib/dexamethasone • Daratumumab + Bortezomib/dexamethasone	April 2023

www.clinicaltrials.gov. Accessed August 2022.

Corneal Events: Mitigation Strategy

- Corticosteroid eye drops are not beneficial for prophylaxis or treatment
- Lubricating eye drops ≥4 times per day throughout duration of the treatment period
- No contact lens use during treatment period
- Eye examination with BCVA assessment and slit lamp examination with fluorescein staining prior to each planned dose
- Dose delays and dose reductions per recommendations

Lonial S et al. *Blood Cancer J* 2021;11:103.

RTP RESEARCH TO PRACTICE

Belantamab Mafodotin Dose Modifications for Corneal Toxicity

	Exam findings per KVA scale	Recommended dose modifications
Grade 1	Corneal exam: Mild superficial keratopathy	Continue treatment at the current dose
	Change in BCVA: Decline from baseline of 1 line on the Snellen visual acuity chart	
Grade 2	Corneal exam: Moderate superficial keratopathy	Withhold treatment until improvement in both corneal examination findings and changes in BCVA to Grade 1 or better, and resume at same dose
	Change in BCVA: Decline from baseline of 2 or 3 lines (and Snellen visual acuity not worse than 20/200)	
Grade 3	Corneal exam: Severe superficial keratopathy	Withhold treatment until improvement in both corneal examination findings and changes in BCVA to Grade 1 or better, and resume at a reduced dose
	Change in BCVA: Decline from baseline by more than 3 lines (and Snellen visual acuity not worse than 20/200)	
Grade 4	Corneal exam: Corneal epithelial defect	Consider treatment discontinuation. Based on a benefit-risk ratio assessment, if continuing belantamab mafodotin is considered, treatment may be resumed at a reduced dose after the event has improved to Grade 1 or better
	Change in BCVA: Snellen visual acuity worse than 20/200	

Farooq AV et al. *Ophthalmol Ther* 2020;9(4):889-911; Lonial S et al. *Blood Cancer J* 2021;11:103.

Meet The Professor with Dr Richardson

INTRODUCTION

MODULE 1: Case Presentations

- Dr Gupta: 61-year-old man with newly diagnosed Stage II standard-risk multiple myeloma
- Dr Rupard: 72-year-old woman with Stage IIIA multiple myeloma who receives RVd → ASCT and discontinues maintenance lenalidomide after 3 years
- Dr Lamar: 73-year-old woman with relapsed myeloma s/p tandem ASCT who receives CyBorD, achieves MRD negativity and is now on maintenance ixazomib
- Dr Lee: 72-year-old woman with triple-class refractory t(11;14) multiple myeloma
- Dr Qazilbash: 65-year-old man with high-risk relapsed multiple myeloma s/p KRd induction, ASCT and maintenance KRd and 2 additional lines of therapy
- Dr Kumar: 71-year-old man with multiple myeloma who develops secondary ALL during maintenance lenalidomide

MODULE 2: Faculty Survey

MODULE 3: Journal Club with Dr Richardson

MODULE 4: Appendix of Key Publications

RTP RESEARCH TO PRACTICE

Case Presentation: 61-year-old man with newly diagnosed Stage II standard-risk multiple myeloma

Dr Ranju Gupta (Bethlehem, Pennsylvania)

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TO PRACTICE

Case Presentation: 72-year-old woman with Stage IIIA multiple myeloma who receives RVd → ASCT and discontinues maintenance lenalidomide after 3 years

Dr Erik Rupard (West Reading, Pennsylvania)

RTP RESEARCH TO PRACTICE

Case Presentation: 73-year-old woman with relapsed myeloma s/p tandem ASCT who receives CyBorD, achieves MRD negativity and is now on maintenance ixazomib

Dr Zanetta Lamar (Naples, Florida)

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RESEARCH
TO PRACTICE

Case Presentation: 72-year-old woman with triple-class refractory t(11;14) multiple myeloma

Dr Hans Lee (Houston, Texas)

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RESEARCH
TO PRACTICE

Case Presentation: 65-year-old man with high-risk relapsed multiple myeloma s/p KRd induction, ASCT and maintenance KRd and 2 additional lines of therapy

Dr Muzaffar Qazilbash (Houston, Texas)

RTP RESEARCH TO PRACTICE

Case Presentation: 71-year-old man with multiple myeloma who develops secondary ALL during maintenance lenalidomide

Dr KS Kumar (Trinity, Florida)

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RESEARCH
TO PRACTICE

Meet The Professor with Dr Richardson

INTRODUCTION

MODULE 1: Case Presentations

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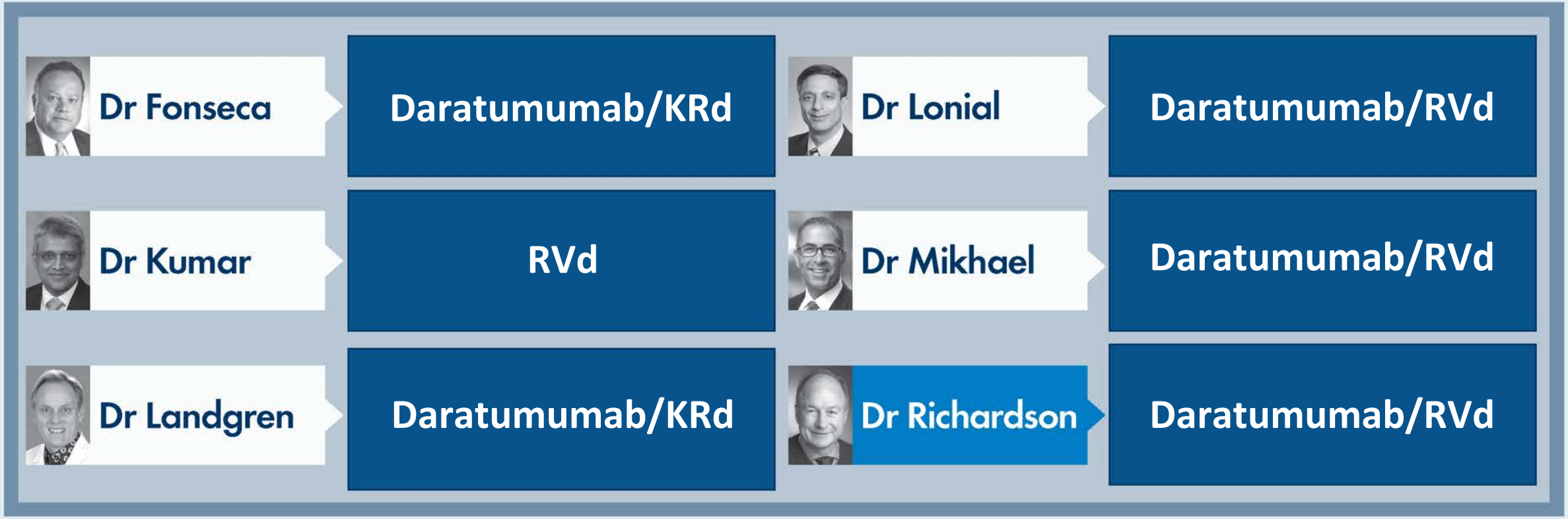
TO PRACTICE

Regulatory and reimbursement issues aside, what is your preferred pretransplant induction regimen for a younger patient with MM and no high-risk features?



KRd = carfilzomib/lenalidomide/dexamethasone; RVd = lenalidomide/bortezomib/dexamethasone

Regulatory and reimbursement issues aside, what is your preferred initial regimen for an 80-year-old patient with MM who is transplant ineligible with normal renal function and no high-risk features?

 Dr Fonseca	Daratumumab/Rd	 Dr Lonial	Daratumumab/Rd
 Dr Kumar	Daratumumab/Vd	 Dr Mikhael	Daratumumab/Rd
 Dr Landgren	Daratumumab/Rd	 Dr Richardson	Daratumumab/RVd or Daratumumab/RVd lite

Rd = lenalidomide/dexamethasone; Vd = bortezomib/dexamethasone

Regulatory and reimbursement issues aside, what would be your preferred induction treatment for a transplant-eligible patient with high-risk (del[17p]) MM?

 Dr Fonseca	Daratumumab/KRd	 Dr Lonial	KRd
 Dr Kumar	Daratumumab/RVd	 Dr Mikhael	Daratumumab/KRd
 Dr Landgren	Daratumumab/KRd	 Dr Richardson	Daratumumab/KRd

RTP RESEARCH TO PRACTICE

In general, for a patient with standard-risk MM who is receiving maintenance therapy with lenalidomide after autologous stem cell transplant (ASCT), would you offer to discontinue the lenalidomide if a minimal residual disease (MRD) assessment were negative?

 Dr Fonseca	Yes, for select patients	 Dr Lonial	No
 Dr Kumar	Yes, for select patients	 Dr Mikhael	No
 Dr Landgren	No	 Dr Richardson	No

RTP RESEARCH TO PRACTICE

When you administer daratumumab to patients with MM, do you generally use the subcutaneous formulation?

 Dr Fonseca	Yes	 Dr Lonial	Yes
 Dr Kumar	Yes	 Dr Mikhael	Yes
 Dr Landgren	Yes	 Dr Richardson	Yes

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, how would you compare the efficacy of idecabtagene vicleucel to that of ciltacabtagene autoleucel for patients with R/R MM?

 Dr Fonseca	Efficacy is similar with both agents	 Dr Lonial	Efficacy is similar with both agents
 Dr Kumar	Ciltacabtagene autoleucel is more efficacious	 Dr Mikhael	Ciltacabtagene autoleucel is more efficacious
 Dr Landgren	Ciltacabtagene autoleucel is more efficacious	 Dr Richardson	Ciltacabtagene autoleucel is more efficacious

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, how would you compare the tolerability of ciltacabtagene autoleucel to that of idecabtagene vicleucel for patients with R/R MM?

 Dr Fonseca	Tolerability is similar with both agents	 Dr Lonial	Tolerability is similar with both agents
 Dr Kumar	Idecabtagene vicleucel is more tolerable	 Dr Mikhael	Tolerability is similar with both agents
 Dr Landgren	Tolerability is similar with both agents	 Dr Richardson	Idecabtagene vicleucel is more tolerable

RTP RESEARCH TO PRACTICE

Reimbursement issues aside, what do you currently believe is the optimal point at which CAR T-cell therapy should be administered for MM (ie, at what point would you like to see your patients enter a trial or receive it off protocol)?

 Dr Fonseca	At first relapse	 Dr Lonial	At second relapse
 Dr Kumar	At first relapse	 Dr Mikhael	At first relapse
 Dr Landgren	At first relapse	 Dr Richardson	After second relapse and beyond

RTP RESEARCH TO PRACTICE

Currently, how available is CAR T-cell therapy commercially for the treatment of R/R MM?

 Dr Fonseca	Very poorly	 Dr Lonial	Manufacturing remains a major roadblock
 Dr Kumar	Limited	 Dr Mikhael	Very limited; not an option for most patients
 Dr Landgren	Way too limited	 Dr Richardson	Waiting list up to 6 months

RTP RESEARCH TO PRACTICE

FDA Approved CAR T-Cell Therapies for Relapsed or Refractory Multiple Myeloma

February 28, 2022: Ciltacabtagene autoleucel approved for the treatment of relapsed or refractory multiple myeloma in adult patients after 4 or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, based on the CARTITUDE-1 study.

March 26, 2022: Idecabtagene vicleucel approved for the treatment of relapsed or refractory multiple myeloma in adult patients after 4 or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 monoclonal antibody. This is the first FDA-approved cell-based gene therapy for multiple myeloma, based on the KarMMA study.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ciltacabtagene-autoleucel-relapsed-or-refractory-multiple-myeloma
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-idecabtagene-vicleucel-multiple-myeloma

RTP RESEARCH TO PRACTICE

Key Select Ongoing Studies of BCMA-Directed CAR T-Cell Therapy with Ide-cel and Cilta-cel

Study	Phase	N	Setting	Treatments
CARTITUDE-4	III	419	Relapsed and lenalidomide-refractory	• Pomalidomide/bortezomib/dexamethasone or daralutamide/pomalidomide/dexamethasone • Cilta-cel
CARTITUDE-5	III	650	NDMM, with no ASCT planned	• VRd → cilta-cel • VRd → lenalidomide/dexamethasone
CARTITUDE-6	III	750	NDMM, ASCT eligible	• DVRd → cilta-cel • DVRd →k ASCT
KarMMa-4	I	13	NDMM, high risk	• Ide-cel → lenalidomide maintenance
KarMMa-2	II	235	RRMM, high risk NDMM	• Ide-cel • Ide-cel + lenalidomide

NDMM = newly diagnosed multiple myeloma; ASCT = autologous stem cell transplant; VRd = bortezomib/lenalidomide/dexamethasone; RRMM = relapsed/refractory multiple myeloma; PI = proteasome inhibitor; IMiD = immunomodulatory drug

www.clinicaltrials.gov. Accessed August 2022.

Regulatory and reimbursement issues aside and assuming you had access to CAR T-cell therapies and bispecific antibodies, how would you generally sequence these 2 treatments for a patient with multiregimen-relapsed MM who is eligible to receive CAR T-cell therapy?

 Dr Fonseca	Bispecific antibody → CAR T-cell therapy	 Dr Lonial	CAR T-cell therapy → bispecific antibody
 Dr Kumar	CAR T-cell therapy → bispecific antibody	 Dr Mikhael	CAR T-cell therapy → bispecific antibody
 Dr Landgren	CAR T-cell therapy → bispecific antibody	 Dr Richardson	Bispecific antibody → CAR T-cell therapy

BCMA x CD3 Bispecific Antibodies: Summary

Therapy	Characteristics	N	Population	Safety	Response
Teclistamab[1]	▪ Bispecific ▪ IV/SC (RP2D: 1500 µg/kg SC) ▪ Weekly and every other week in f/u	157	▪ At SC cohorts: ▪ Median of 5PL ▪ 79% triple refractory ▪ 38% penta refractory	▪ At RP2D: ▪ CRS 70% G1-2 ▪ Neurotox 1% (G1) ▪ Infections 50%	At RP2D, ORR: 65% with 40% sCR/CR
AMG 701[2]	▪ BiTE modified ▪ IV ▪ Weekly	82	▪ Median of 6PL ▪ 62% triple refractory	▪ CRS 55%, G3-4: 9% ▪ No ICANS ▪ 20% cytopenias	83% ORR at the top dose level and 50% VGPR
REGN5458[3]	▪ Bispecific ▪ IV ▪ Weekly and every other week C4→	49	▪ Median of 5PL ▪ 100% triple refractory ▪ 57% penta refractory	▪ CRS 39%, no G3-4 ▪ ICANS 12% ▪ Cytopenias 47% and infections 18%	62.5% at 96 mg and 95% of responders were VGPR. Some CR in lower dose levels
TNB-383B[4]	▪ Triple chain anti-BCMA bispecific ▪ IV fixed doses ▪ Every 3 weeks	58	▪ Median of 6PL ▪ 64% triple refractory ▪ 34% penta refractory	▪ CRS 45% and no G3-4 ▪ No ICANS ▪ Cytopenias 21% and infections 14%	80% (13% CR) at the dose levels 40-60 mg
Elranatamab (PF-3135[5])	▪ Bispecific ▪ SC and weekly ▪ RP2D: 1000 µg/kg	30	▪ Median of 8PL ▪ 87% triple refractory ▪ 23% prior BCMA-based therapy	▪ CRS 73% and no G3-4 ▪ ICANS 20% ▪ ISR 50%	83% ORR at RP2D

1. Usmani SZ et al. *Lancet* 2021. 2. Harrison SJ et al. ASH 2020;Abstract 181. 3. Madduri D et al. ASH 2020;Abstract 291.
4. Rodriguez C et al. ASH 2020;Abstract 293.5. Bahlis NJ et al. ASCO 2021;Abstract 8006.

Content courtesy of Noopur Raje, MD

ASCO 2022;Abstract 8007.

Teclistamab, a B-Cell Maturation Antigen (BCMA) x CD3 Bispecific Antibody, in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): Updated Efficacy and Safety Results From MajesTEC-1

Ajay K Nooka (anooka@emory.edu)[1], Philippe Moreau[2], Saad Z Usmani[3], Alfred L Garfall[4], Niels WCJ van de Donk[5], Jesús San-Miguel[6], Albert Oriol[7], Ajai Chari[8], Lionel Karlin[9], Maria-Victoria Mateos[10], Rakesh Popat[11], Joaquín Martínez-López[12], Surbhi Sidana[13], Danielle Trancucci[14], Raluca Verona[15], Suzette Girgis[15], Clarissa Uhlar[15], Tara Stephenson[15], Arnob Banerjee[15], Amrita Krishnan[16]

[1]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [2]University Hospital Hôtel-Dieu, Nantes, France; [3]Memorial Sloan Kettering Cancer Cent NY, USA; [4]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [5]Amsterdam University Medical Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands; [6]University of Navarra, Pamplona, Spain; [7]Hospital Germans Trias I Pu Spain; [8]Mount Sinai School of Medicine, New York, NY, USA; [9]Centre Hospitalier Lyon Sud, France; [10]University Hospital of Salamanca/IBSAL/CIC, Salar [11]University College London Hospitals, NHS Foundation Trust, London, UK; [12]Hematología Hospital 12 de Octubre, Madrid, Spain; [13]Stanford Universit Medicine, Stanford, CA, USA; [14]Janssen Research & Development, Raritan, NJ, USA; [15]Janssen Research & Development, Spring House, PA, USA; [16]City Comprehensive Cancer Center, Duarte, CA, USA

Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL

N Engl J Med 2022 June 5;[Online ahead of print].

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Teclistamab in Relapsed or Refractory Multiple Myeloma

P. Moreau, A.L. Garfall, N.W.C.J. van de Donk, H. Nahi, J.F. San-Miguel, A. Oriol, A.K. Nooka, T. Martin, L. Rosinol, A. Chari, L. Karlin, L. Benboubker, M.-V. Mateos, N. Bahlis, R. Popat, B. Besemer, J. Martínez-López, S. Sidana, M. Delforge, L. Pei, D. Trancucci, R. Verona, S. Girgis, S.X.W. Lin, Y. Olyslager, M. Jaffe, C. Uhlar, T. Stephenson, R. Van Rampelbergh, A. Banerjee, J.D. Goldberg, R. Kobos, A. Krishnan, and S.Z. Usmani

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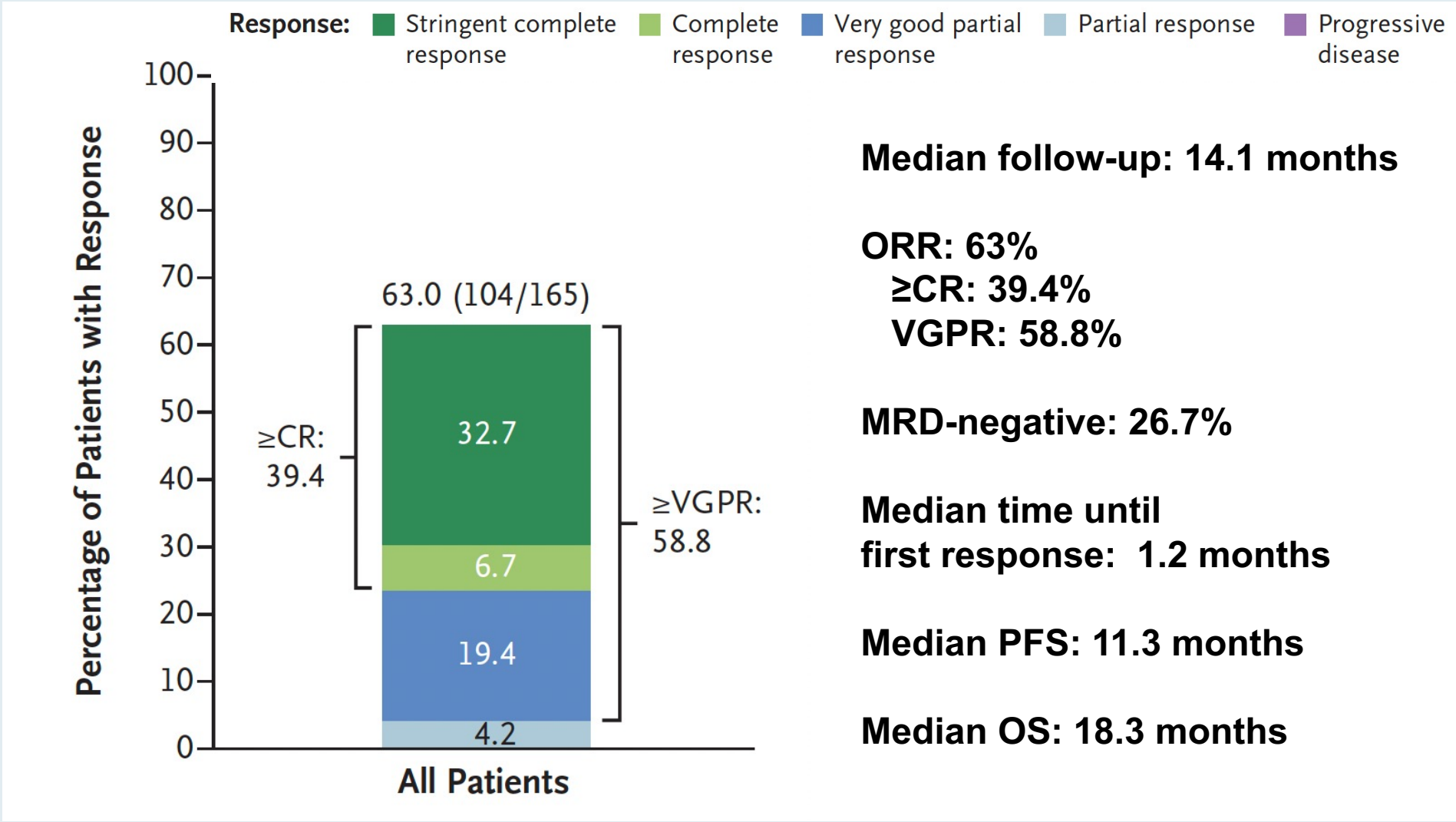
MajesTEC-1: Response and Survival



Median follow-up: 14.1 months

ORR: 63%
≥CR: 39.4%
VGPR: 58.8%

MRD-negative: 26.7%

Median time until first response: 1.2 months

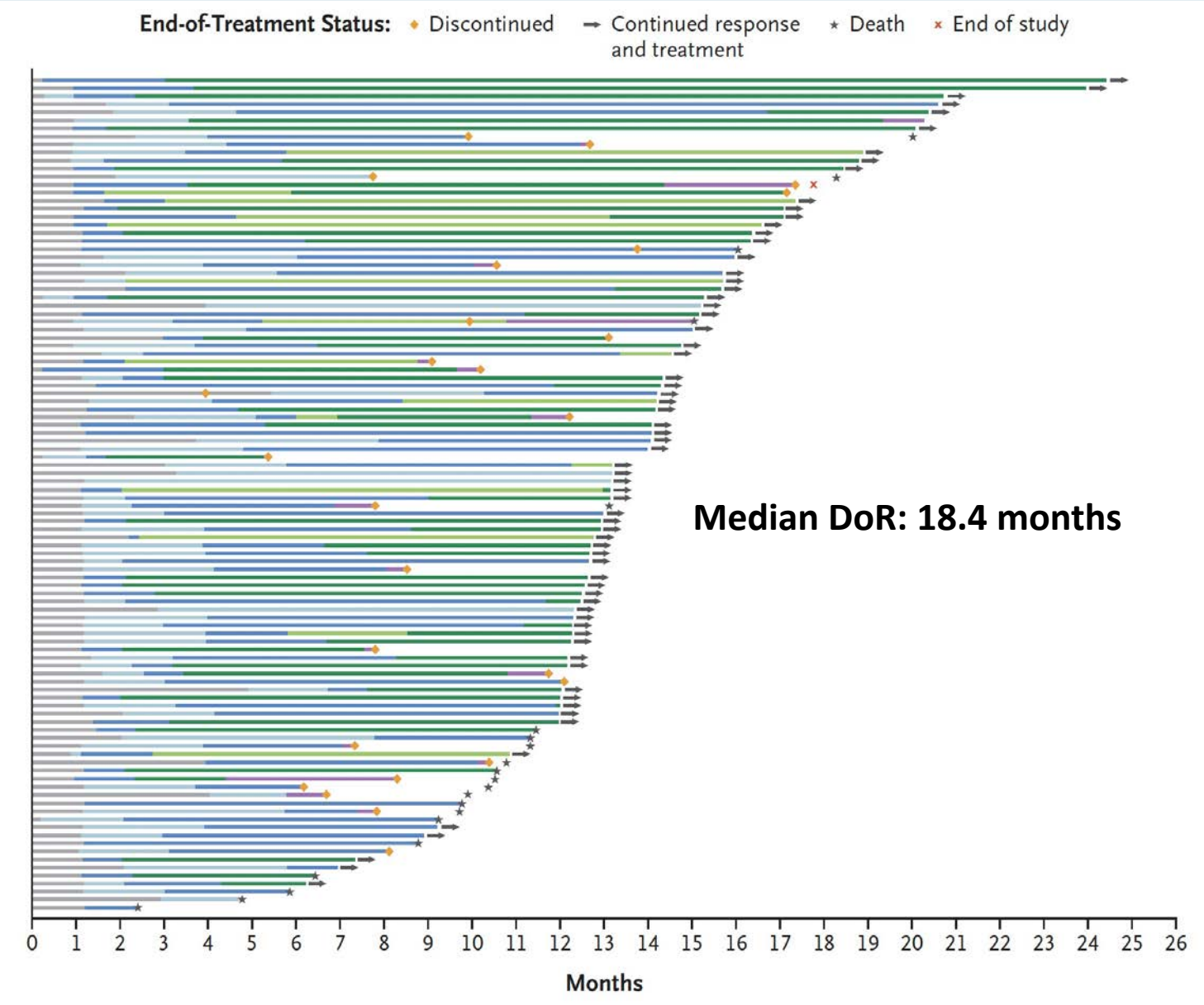
Median PFS: 11.3 months

Median OS: 18.3 months

Moreau P et al. *N Engl J Med* 2022 June 5;[Online ahead of print].

RTP RESEARCH TO PRACTICE

MajesTEC-1: Duration of Response (DoR)



Moreau P et al. *N Engl J Med* 2022 June 5;[Online ahead of print].

MajesTEC-1: Adverse Events

Event	Any Grade	Grade 3 or 4
	no. of patients (%)	
Any adverse event	165 (100)	156 (94.5)
Hematologic		
Neutropenia	117 (70.9)	106 (64.2)
Anemia	86 (52.1)	61 (37.0)
Thrombocytopenia	66 (40.0)	35 (21.2)
Lymphopenia	57 (34.5)	54 (32.7)
Leukopenia	29 (17.6)	12 (7.3)
Nonhematologic		
Diarrhea	47 (28.5)	6 (3.6)
Fatigue	46 (27.9)	4 (2.4)
Nausea	45 (27.3)	1 (0.6)
Injection-site erythema	43 (26.1)	0

Event	Any Grade	Grade 3 or 4
	no. of patients (%)	
Nonhematologic		
Pyrexia	45 (27.3)	1 (0.6)
Headache	39 (23.6)	1 (0.6)
Arthralgia	36 (21.8)	1 (0.6)
Constipation	34 (20.6)	0
Cough	33 (20.0)	0
Pneumonia	30 (18.2)	21 (12.7)
Covid-19	29 (17.6)	20 (12.1)
Bone pain	29 (17.6)	6 (3.6)
Back pain	27 (16.4)	4 (2.4)
Cytokine release syndrome†	119 (72.1)	1 (0.6)
Neurotoxic event	24 (14.5)	1 (0.6)

Moreau P et al. *N Engl J Med* 2022 June 5;[Online ahead of print].

RTP RESEARCH TO PRACTICE

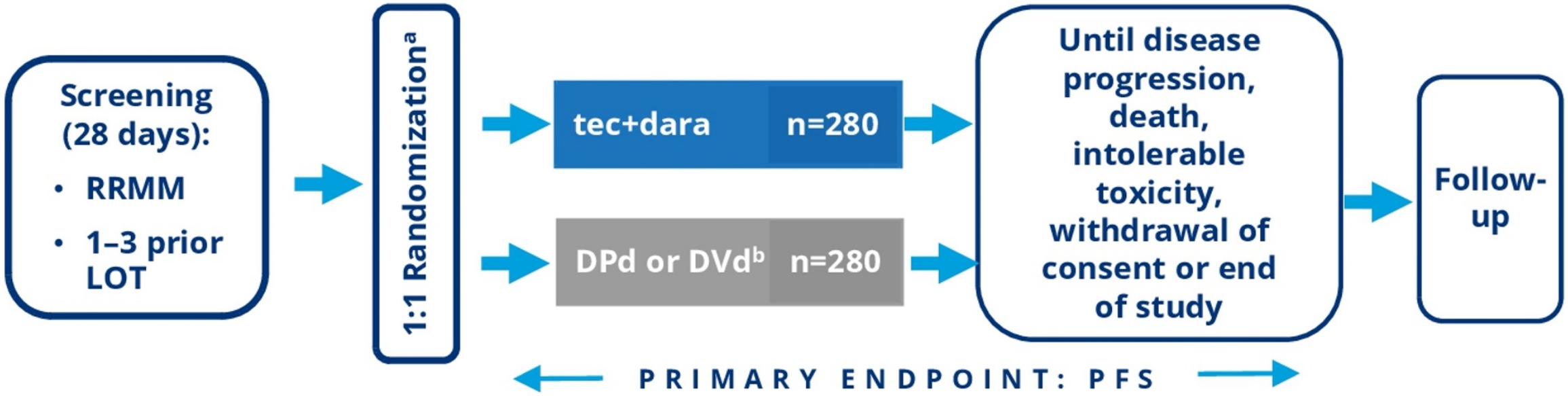
MajesTEC-1: Neurotoxic Events

Parameter	N=165
Neurotoxic event[a], n (%)	**24 (14.5)**
Headache	**14 (8.5)**
ICANS[b]	**5 (3.0)**
Dysgeusia	**2 (1.2)**
Lethargy	**2 (1.2)**
Tremor	**2 (1.2)**
Grade ≥3 events, n (%)	**1 (0.6)**
Time to onset, median (range) days	**3.0 (1–13)**
Duration, median (range) days	**7.0 (1–291)**
Received supportive measures for neurotoxic events[c], n (%)	**14 (8.5)**
Tocilizumab	**3 (1.8)**
Dexamethasone	**3 (1.8)**
Levetiracetam	**2 (1.2)**
Gabapentin	**1 (0.6)**

- The overall incidence of neurotoxic events was low
- All neurotoxic events were grade 1/2, except for 1 grade 4 seizure (in the context of bacterial meningitis during cycle 7)
- 5 patients (3.0%) had a total of 9 ICANS events
  - 7 events were concurrent with CRS
  - All ICANS events were grade 1/2 and fully resolved
- There were no treatment discontinuations or dose reductions due to neurotoxic events, including ICANS

Nooka AK et al. ASCO 2022;Abstract 8007.

MajesTEC-3 Ongoing Phase III Study Design



Key Eligibility Criteria:

- Received 1-3 prior lines of therapy, including PI and lenalidomide
  - Patients with only 1 prior line of therpay must be lenalidomide-refractory
- No prior BCMA-directed therapy and/or not refractory to anti-CD38 mAb

Mateos MV et al. ASCO 2022;Abstract TPS8072.

Initial Safety Results for MagnetisMM-3: A Phase 2 Trial of Elranatamab, a B-Cell Maturation Antigen (BCMA)-CD3 Bispecific Antibody, in Patients (pts) with Relapsed/Refractory (R/R) Multiple Myeloma (MM)

Lesokhin AM et al.

ASCO 2022;Abstract 8006.

Novel Non-BCMA Bispecific Antibodies: Summary

Therapy	Characteristics	N	Population	Safety	Response
Talquetamab[1]	▪ G protein-coupled receptor family C group 5 member D (GPRC5D) x CD3 bispecific antibody ▪ IV or SC admin	184, 30 at RP2D (405 µg/kg)	▪ Median of 6PL (6PL at RP2D) ▪ 76% triple refractory ▪ 28% penta refractory	▪ Infections in 37% of SC and RP2D patients; G3-4 3% at RP2D ▪ Neurotoxicity in 4 SC patients; 2 (7%) at RP2D ▪ CRS 73%, G3-4 2% at RP2D	At RP2D: 70% ORR with ≥ VGPR 60%
Cevostamab (BFCR4350A)[2]	▪ FcRH5/CD3 bispecific T-cell engager ▪ Q3W IV infusions	53	▪ Median of 6PL ▪ 72% triple refractory ▪ 45% penta refractory	▪ Thrombocytopenia 32%, G3-4 25% ▪ CRS 76%, G3-4 2% ▪ Neurotoxicity 28%, no G3-4	ORR in ≥3.6/20-mg cohorts: 53% (18/34) in all pts 63% (5/8) in pts with prior anti-BCMA

1. Berdeja JG et al. ASCO 2021;Abstract 8008. 2. Cohen A et al. ASH 2020;Abstract 292.

Content courtesy of Noopur Raje, MD

FDA Grants Breakthrough Therapy Designation to Talquetamab for Relapsed/Refractory Multiple Myeloma

Press Release: June 29, 2022

"Talquetamab was granted breakthrough therapy designation by the FDA for the treatment of patients with relapsed/refractory multiple myeloma who were treated with a minimum of 4 previous lines of therapy, including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody.

The designation is supported by findings from the phase 1/2 MonumenTAL-1 trial (NCT03399799; NCT04634552), which assessed the agent in patients with relapsed/refractory disease. Data from the study, which were presented at the 2022 American Society of Clinical Oncology Annual Meeting, indicated that patients who were treated with 405 µg/kg of talquetamab (n = 30) experienced an overall response rate (ORR) of 70.0%, including a very good partial response (VGPR) rate or better of 56.7%. Additionally, the ORR among patients treated at the 800 µg/kg dose was 63.6%, including a VGPR or better of 56.8%. Moreover, the stringent complete response (CR) rates were 23.3% and 9.1%, CR rates were 6.7% and 11.4%, the VGPR rates were 26.7% and 36.4%, and PR rates were 13.3% and 6.8% in each respective arm.

Talquetamab is an off-the-shelf T-cell–redirecting bispecific antibody that targets GPRC5D on myeloma cells and CD3 on T cells."

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-designation-to-talquentamab-for-relapsed-refractory-multiple-myeloma

RTP RESEARCH TO PRACTICE

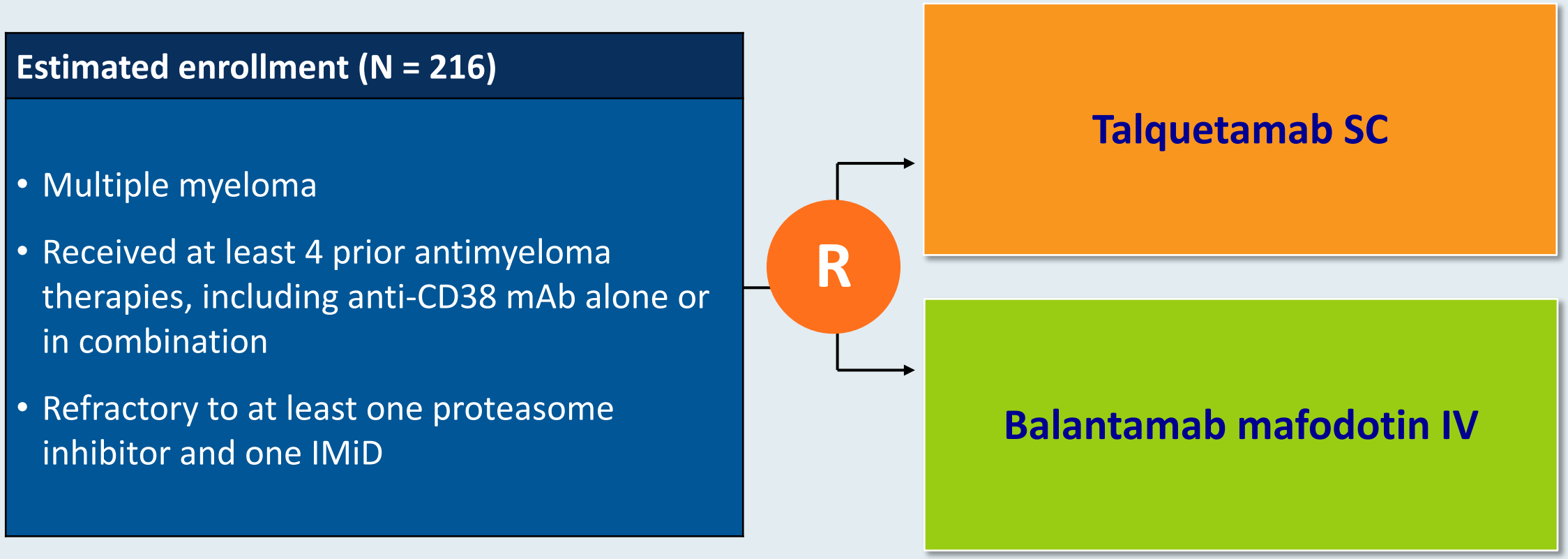
Efficacy and Safety of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D x CD3 Bispecific Antibody, in Patients With Relapsed/ Refractory Multiple Myeloma: Updated Results From MonumenTAL-1

Monique C Minnema[1], Amrita Krishnan[2], Jesus G. Berdeja[3], Albert Oriol[4], Niels WCJ van de Donk[5], Paula Rodríguez-Otero[6], Daniel Morillo[7], María-Victoria Mateos[8], Luciano J. Costa[9], Jo Caers[10], Deeksha Vishwamitra[11], Joanne Ma[11], Shiyi Yang[11], Brandi W Hilder[11], Jaszianne Tolbert[11], Jenna D Goldberg[12], Ajai Chari[13]

ASCO 2022;Abstract 8015.

RTP RESEARCH TO PRACTICE

MonumenTAL-5 Phase III Study Design



Primary endpoint: Overall response rate, progression-free survival

www.clinicaltrials.gov. NCT05461209. Accessed August 2022.

Regulatory and reimbursement issues aside, at what point, if any, would you attempt to access venetoclax for a patient with t(11;14) MM?

 Dr Fonseca	Up front	 Dr Lonial	Second line
 Dr Kumar	Second line	 Dr Mikhael	Third line
 Dr Landgren	Second line	 Dr Richardson	Second line

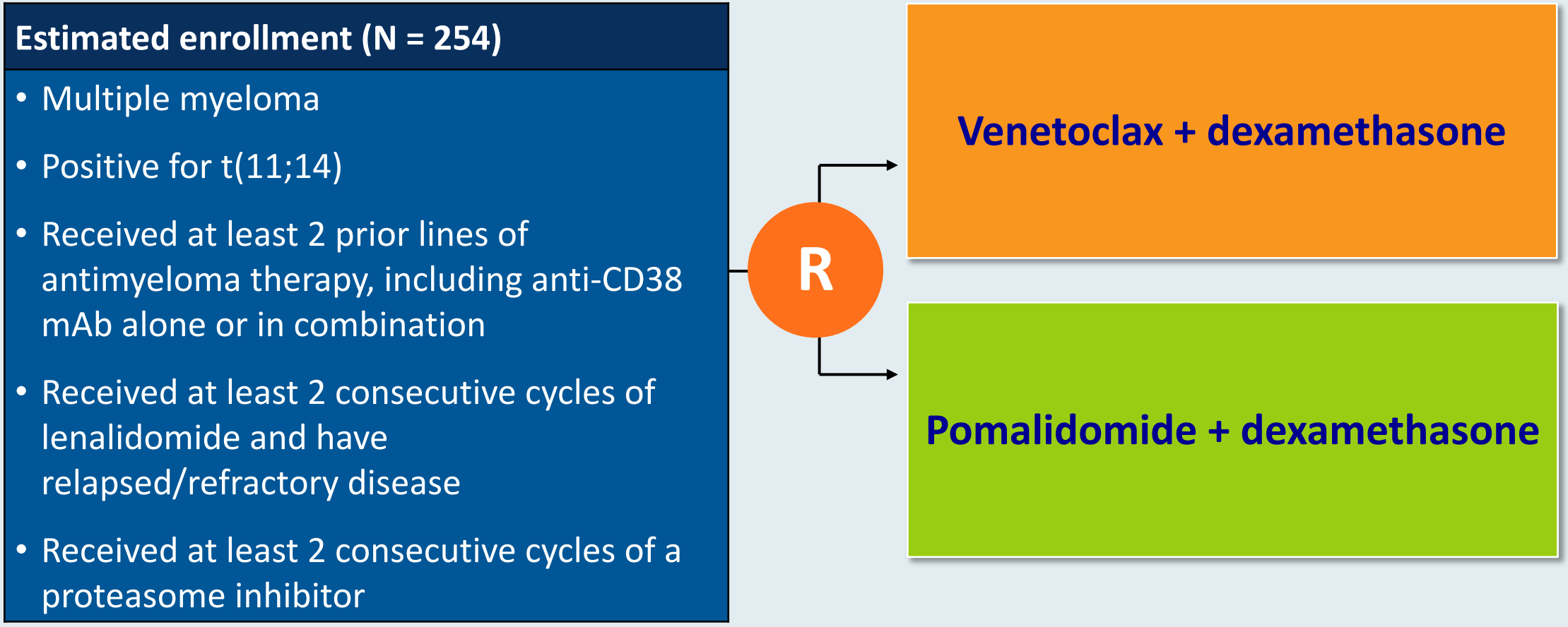
RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which method do you consider optimal for administering venetoclax to a patient with MM?

 Dr Fonseca	In combination	 Dr Lonial	In combination, 400 mg
 Dr Kumar	In combination, 200 mg - 400 mg	 Dr Mikhael	In combination
 Dr Landgren	In combination, escalating dose (200 mg → 800 mg)	 Dr Richardson	In combination, 200 mg - 800 mg

RTP RESEARCH TO PRACTICE

Ongoing Phase III M13-494 Study Design



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. NCT03539744. Accessed August 2022.

For a patient with R/R MM who is ineligible for CAR T-cell therapy because of age or performance status and whose disease is refractory to anti-CD38 antibodies, proteasome inhibitors and immunomodulatory drugs (IMiDs), how do you generally sequence belantamab mafodotin and selinexor?

 Dr Fonseca	Selinexor → belantamab mafodotin	 Dr Lonial	Belantamab mafodotin → selinexor
 Dr Kumar	Belantamab mafodotin → selinexor	 Dr Mikhael	Selinexor → belantamab mafodotin
 Dr Landgren	Selinexor → belantamab mafodotin	 Dr Richardson	Selinexor → belantamab mafodotin

In general, how would you prefer to administer selinexor in the treatment of R/R MM?

 Dr Fonseca	Once a week, usually with carfilzomib	 Dr Lonial	Once a week with bort/dex
 Dr Kumar	Once a week with bort/dex	 Dr Mikhael	Once weekly with carfilzomib/dex
 Dr Landgren	Once a week with bort/dex	 Dr Richardson	Once a week with bort/dex or carfilzomib/dex

Bort/dex = bortezomib/dexamethasone

Efficacy and tolerability of once-weekly selinexor, bortezomib, and dexamethasone in comparison with standard twice-weekly bortezomib and dexamethasone in previously treated multiple myeloma with renal impairment: Subgroup analysis from the BOSTON study

Am J Hematol 2022 March 1;97(3):E83-6.

Sosana Delimpasi[1], Maria Victoria Mateos[2], Holger W. Auner[3], Maria Gavriatopoulou[4], Meletios A. Dimopoulos[5], Hang Quach[6], Halyna Pylypenko[7], Roman Hájek[8], Xavier Leleu[9], Tuphan Kanti Dolai[10], Dinesh Kumar Sinha[11], Christopher P. Venner[12], Reuben Benjamin[13], Mamta Krishnan Garg[14], Vadim Doronin[15], Yair Levy[16], Philippe Moreau[17], Yi Chai[18], Melina Arazy[18], Jatin Shah[18], Sharon Shacham[18], Michael G. Kauffman[18], Paul G. Richardson[19], Sebastian Grosicki[20]

2021 August;14(8):697-706.

Taylor & Francis
Taylor & Francis Group

Expert Review of Hematology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierr20

Selinexor for the treatment of patients with previously treated multiple myeloma

Clifton C. Mo, Sundar Jagannath, Ajai Chari, Ajay K. Nooka, Sagar Lonial, David Siegel, Noa Biran, Cristina Gasparetto, Nizar J. Bahlis & Paul Richardson

BMC Cancer

RESEARCH ARTICLE Open Access

Quality of life analyses in patients with multiple myeloma: results from the Selinexor (KPT-330) Treatment of Refractory Myeloma (STORM) phase 2b study

Gabriel Tremblay[1*], Patrick Daniele[1], Janis Breeze[1], Lingling Li[2], Jatin Shah[2], Sharon Shacham[2], Michael Kauffman[2], Monika Engelhardt[3], Ajaj Chari[4], Ajay Nooka[5], Dan Vogl[6], Maria Gavriatopoulou[7], Meletios-Athanasios Dimopoulos[8], Paul Richardson[9], Noa Biran[10], David Siegel[10], Philip Vlummens[11], Chantal Doyen[12], Thierry Facon[13], Mohamad Mohty[14], Nathalie Meuleman[15], Moshe Levy[16], Luciano Costa[17], James E. Hoffman[18], Michel Delforge[19], David Kaminetzky[20], Katja Weisel[21], Marc Raab[22], David Dingli[23], Sascha Tuchman[24], Frenzel Laurent[25], Ravi Vij[26], Gary Schiller[27], Philippe Moreau[28], Joshua Richter[29], Martin Schreder[30], Klaus Podar[31], Terri Parker[32], Robert Frank Cornell[33], Karlin Lionel[34], Sylvain Choquet[35] and Jagannath Sundar[29]

Meet The Professor with Dr Richardson

INTRODUCTION

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

MODULE 3: Journal Club with Dr Richardson

MODULE 4: Appendix of Key Publications

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ASH 2022 Abstracts

RTP
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TO PRACTICE

Multivariable Analyses of Prognostic Factors for Progression-Free Survival (PFS) and Complete Response (CR) with Lenalidomide, Bortezomib, and Dexamethasone (RVd) Alone versus RVd plus Autologous Stem Cell Transplantation (ASCT) in Patients (Pts) with Newly Diagnosed Multiple Myeloma (NDMM) in the DETERMINATION Phase 3 Trial

Hani Hassoun, MD et al.

ASH 2022;Abstract 2110.

A Phase II Study of Once Weekly Carfilzomib, Lenalidomide, Dexamethasone, and Isatuximab in Newly Diagnosed, Transplant-Eligible Multiple Myeloma (the SKylaRk Trial)

Elizabeth K O'Donnell, MD et al.

ASH 2022;Abstract 3239.

Daratumumab plus Lenalidomide, Bortezomib, and Dexamethasone (D-RVd) in Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM) Patients (Pts): Final Analysis of GRIFFIN Among Clinically Relevant Subgroups

Ajai Chari, MD et al.

ASH 2022;Abstract 3238.

Analysis of Transplant-Eligible Patients (Pts) Who Received Frontline Daratumumab (DARA)-Based Quadruplet Therapy for the Treatment of Newly Diagnosed Multiple Myeloma (NDMM) with High-Risk Cytogenetic Abnormalities (HRCA) in the GRIFFIN and MASTER Studies

Natalie Callander, MD et al.

ASH 2022;Abstract 4557.

Health-Related Quality of Life in Transplant-Eligible Patients with Newly Diagnosed Multiple Myeloma Treated with Daratumumab, Lenalidomide, Bortezomib, and Dexamethasone: Patient Reported Outcomes from GRIFFIN

Rebecca Silbermann, MD et al.
ASH 2022;Abstract 473.

An End-of-Study Subgroup Analysis of Black Patients from the Phase 2 GRIFFIN Study of Daratumumab (DARA) plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients with Transplant-Eligible Newly Diagnosed Multiple Myeloma (NDMM)

Ajay K Nooka, MD et al.
ASH 2022;Abstract 4560.

Isatuximab plus Pomalidomide/Low-Dose Dexamethasone versus Pomalidomide/Low-Dose Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma (ICARIA-MM): Characterization of Subsequent Antimyeloma Therapies

Paul G Richardson, MD et al.
ASH 2022;Abstract 247.

A Phase I/II Study of Twice Weekly Ixazomib plus Pomalidomide and Dexamethasone in Relapsed and Refractory Multiple Myeloma

Omar Nadeem, MD et al.
ASH 2022;Abstract 4570.

Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD), Combined with Dexamethasone (DEX) in Patients (Pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Preliminary Results from the Dose-Expansion Phase of the CC-92480-MM-001 Trial

Paul G Richardson, MD et al.
ASH 2022;Abstract 568.

Single-Agent Belantamab Mafodotin in Patients with Relapsed or Refractory Multiple Myeloma: Final Analysis of the DREAMM-2 Trial

Ajay K Nooka, MD et al.
ASH 2022;Abstract 3246.

Targeting Autophagy to Overcome Resistance to Immunogenic Chemotherapy in High-Risk Multiple Myeloma

Annamaria Gulla, MD et al.

ASH 2022;Abstract 3165.

Clinical Effectiveness and Long-Term Serologic Responses of COVID-19 Vaccination in Patients with Multiple Myeloma and Waldenström Macroglobulinemia

Andrew R Branagan, MD et al.

ASH 2022;Abstract 4535.

Drugs of Today 2022, 58(8): 407-423

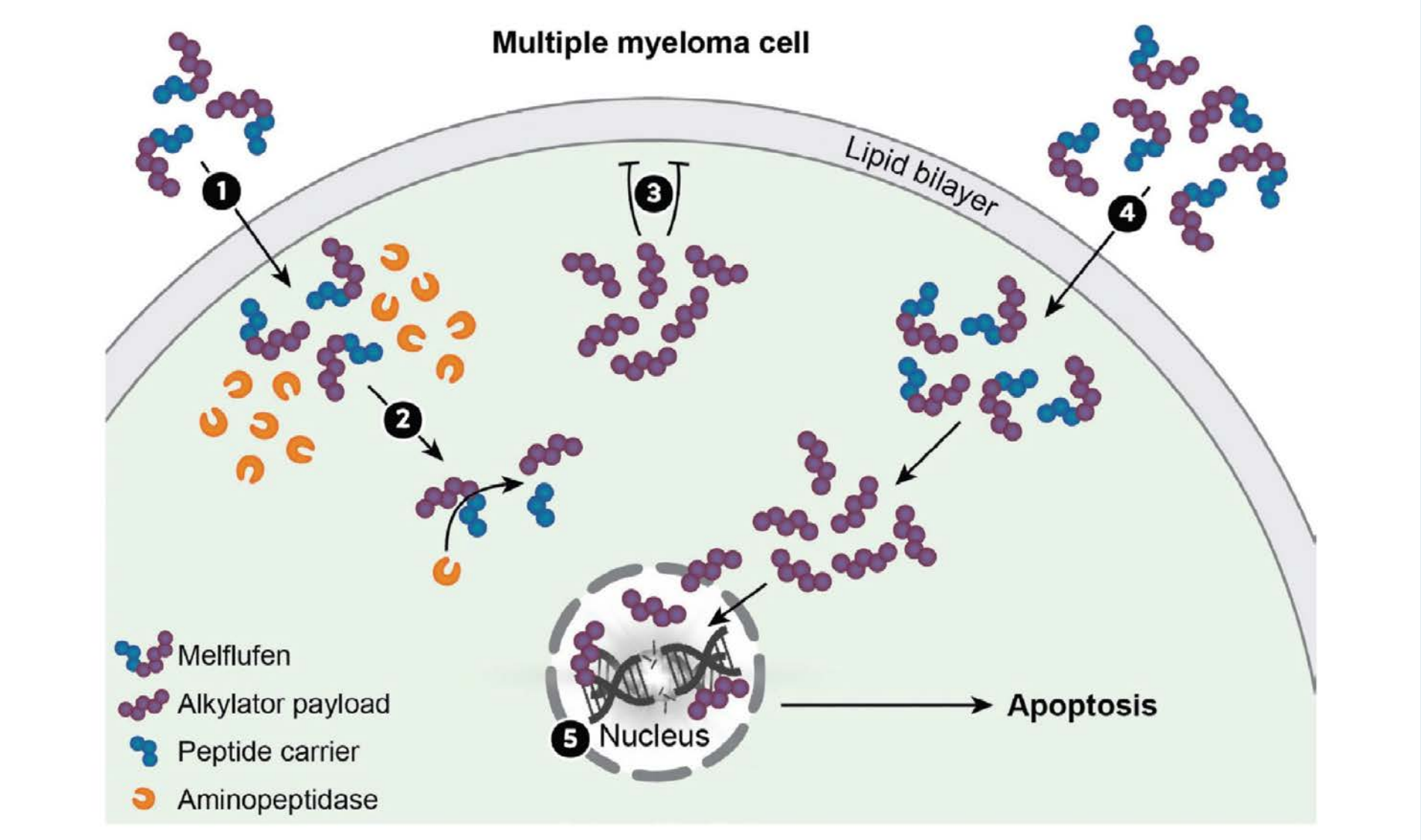
Clarivate™

Monograph

Melphalan flufenamide for relapsed/refractory multiple myeloma

Omar Nadeem[1], Maria-Victoria Mateos[2], Yvonne A. Efebera[3], Agne Paner[4], Alessandra Larocca[5], Paula Rodríguez-Otero[6], Xavier Leleu[7] and Paul G. Richardson[1]

Mechanism of Action of Melflufen



Nadeem O et al. *Drugs of Today* 2022;58(8):407-23.

2022 April;15(4):371-82.

Taylor & Francis
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Expert Review of Clinical Pharmacology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierj20

Melflufen for the treatment of multiple myeloma

Enrique M. Ocio, Omar Nadeem, Fredrik Schjesvold, Francesca Gay, Cyrille Touzeau, Meletios A. Dimopoulos, Paul G. Richardson & Maria-Victoria Mateos

Blood Cancer Journal 2022 March 21;12(3):45. www.nature.com/bcj

REVIEW ARTICLE OPEN

Check for updates

Extramedullary disease in multiple myeloma: a systematic literature review

Joan Bladé[1]✉, Meral Beksac[2], Jo Caers[3], Artur Jurczyszyn[4], Marie von Lilienfeld-Toal[5], Philippe Moreau[6], Leo Rasche[7], Laura Rosiñol[1], Saad Z. Usmani[8], Elena Zamagni[9] and Paul Richardson[10]

Definitions of Plasma Cell Neoplasms

Plasma cell neoplasm	Definition
Extramedullary disease	An aggressive form of multiple myeloma characterized by the presence of soft-tissue plasmacytomas that result from hematogenous spread
Paraskeletal plasmacytoma	A form of multiple myeloma characterized by the presence of soft-tissue plasmacytomas that occur due to direct growth from skeletal tumors following cortical bone disruption
Solitary plasmacytoma	A single mass of clonal plasma cells (bone or extramedullary) with no or minimal BM plasmacytosis and with no other symptoms than those derived from the primary lesion
Plasma cell leukemia	A rare and aggressive variant of myeloma characterized by the presence of circulating plasma cells; diagnosis is based upon the percentage (≥20%) and absolute number (≥2 × 10^9/L) of plasma cells in peripheral blood

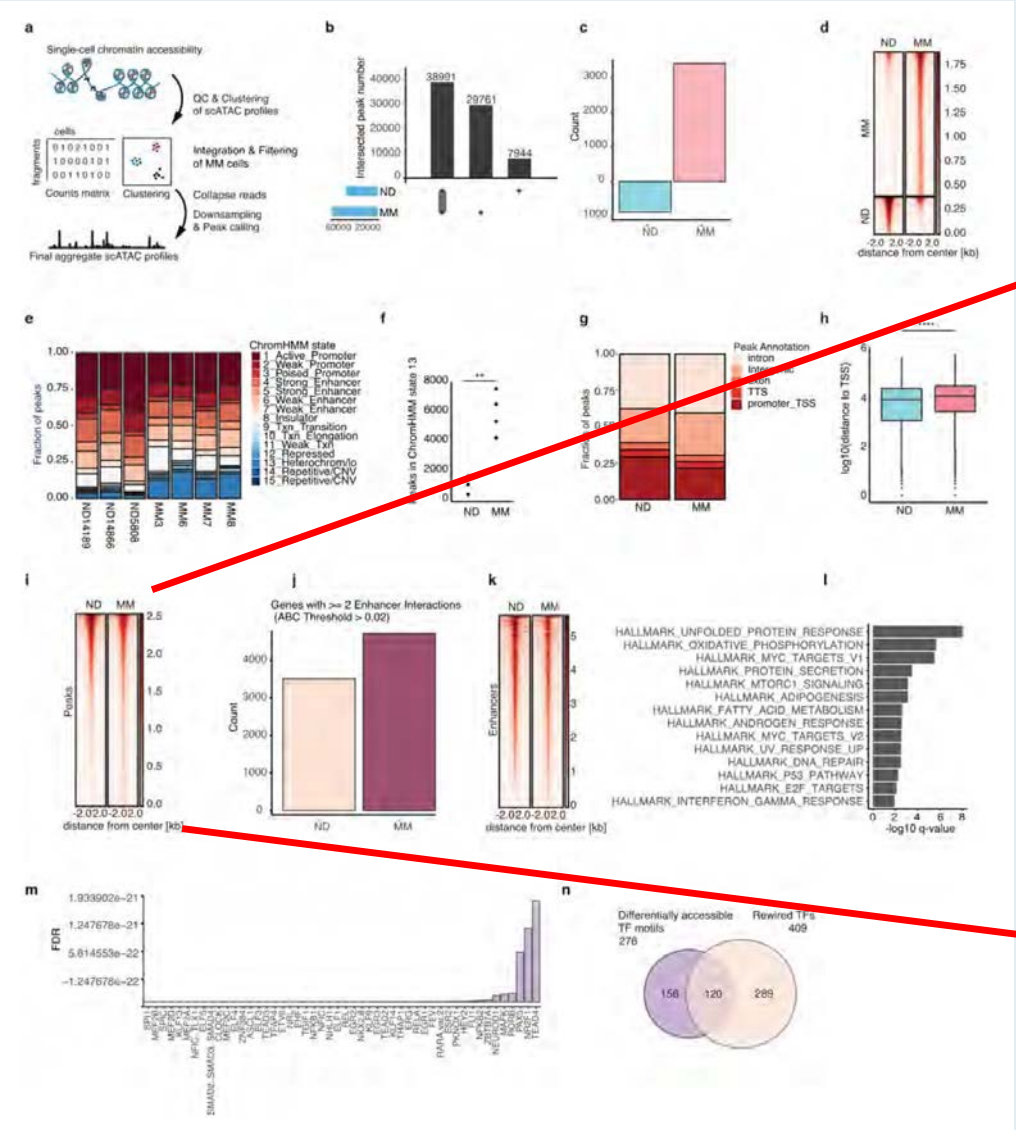
Bladé J et al. *Blood Cancer J* 2022 March 21;12(3):45.

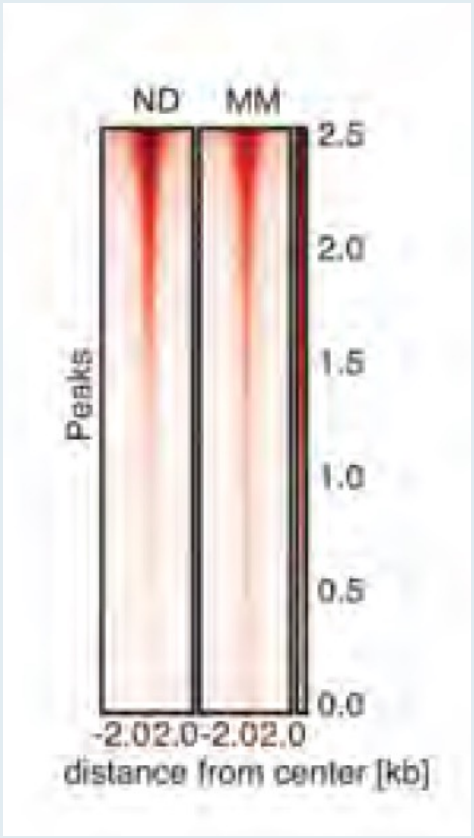
Nat Cell Biol. 2021 November ; 23(11): 1199–1211.

Dynamic transcriptional reprogramming leads to immunotherapeutic vulnerabilities in myeloma

Julia Frede[1,2,3], Praveen Anand[1,2,3], Noori Sotudeh[1,2,3], Ricardo A. Pinto[3,4,5], Monica S. Nair[1], Hannah Stuart[1], Andrew J. Yee[2,6], Tushara Vijaykumar[1], Johannes M. Waldschmidt[1,2,3], Sayalee Potdar[7], Jake A. Kloeber[1], Antonis Kokkalis[1,2,3], Valeriya Dimitrova[2,3,7], Mason Mann[6], Jacob P. Laubach[1,2], Paul G. Richardson[1,2], Kenneth C. Anderson[1,2], Noopur S. Raje[2,6], Birgit Knoechel[2,3,7,8,*], Jens G. Lohr[1,2,3,8,*]

Annotation of Peaks from Aggregated Single-Cell ATAC Data





Heatmap showing accessibility of enhancers (n = 15,748) associated with the top multi-enhancer genes, sorted by the normal donor (ND) sample

Frede J et al. *Nat Cell Biol* 2021;23(11):1199-211.

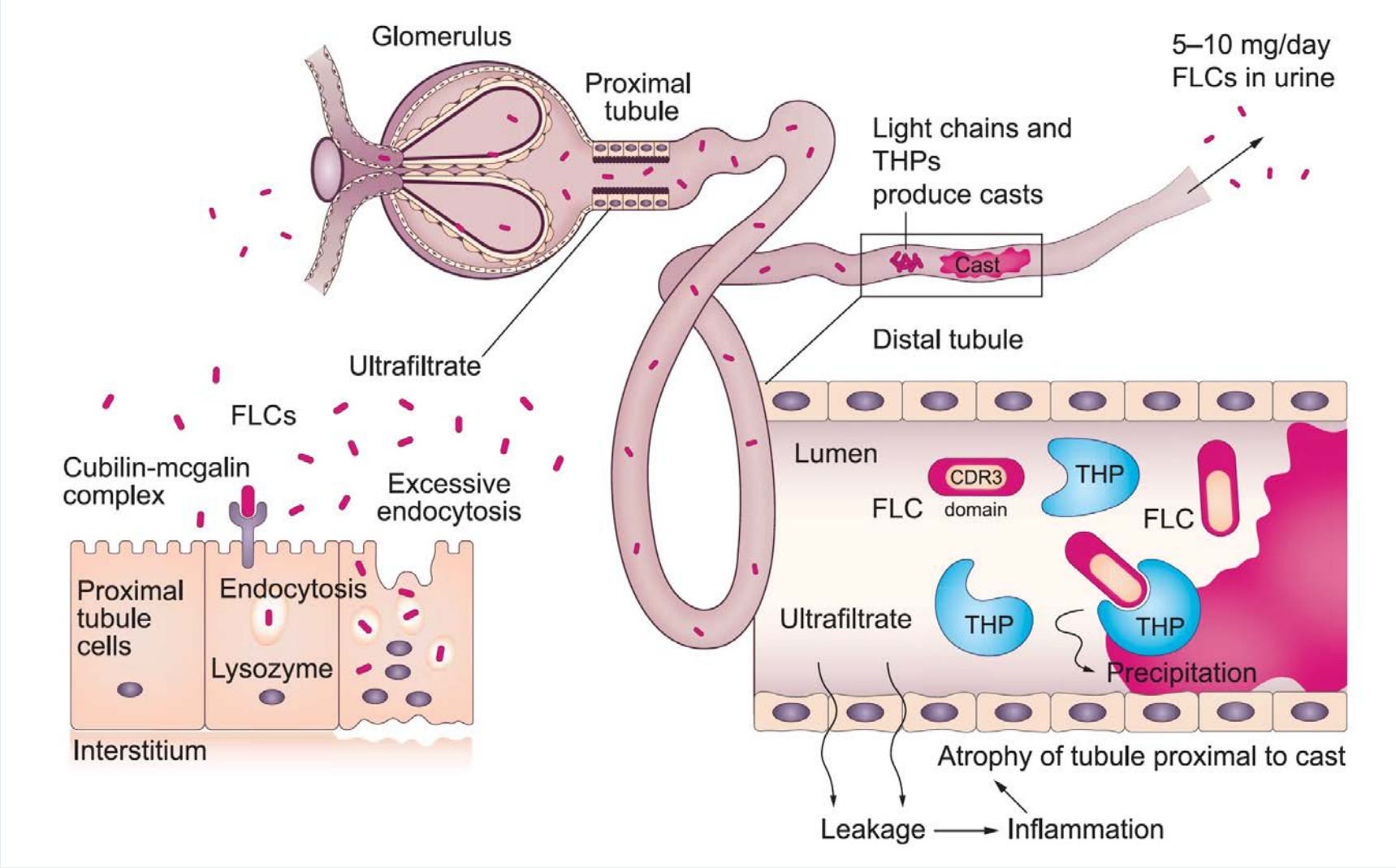
Therapeutic Advances in Hematology *Review*

An overview of treatment options for patients with relapsed/refractory multiple myeloma and renal impairment

Ther Adv Hematol
2022, Vol. 13: 1–18

Meletios A. Dimopoulos, Joseph Mikhael, Evangelos Terpos, Xavier Leleu, Philippe Moreau, Joan Bladé, Jin Seok Kim, Keith Stockerl-Goldstein and Paul G. Richardson

Pathology of Monoclonal Free Light Chain-Mediated Proximal Tubule Damage and Cast Nephropathy



Dimopoulos MA et al. *Ther Adv Hematol* 2022;13;1-18.

Tuazon et al. *Blood Cancer Journal* (2021)11:23

Blood Cancer Journal

CURRENT TREATMENT ALGORITHM Open Access

A clinical perspective on plasma cell leukemia; current status and future directions

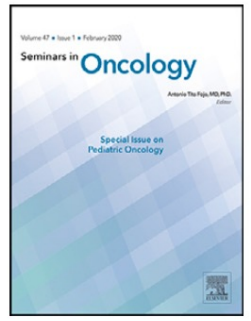
Sherilyn A. Tuazon[1,2], Leona A. Holmberg[1,2], Omar Nadeem[3,4] and Paul G. Richardson[3,4]

Seminars in Oncology 49 (2022) 19–26

Contents lists available at ScienceDirect

Seminars in Oncology

journal homepage: www.elsevier.com/locate/seminoncol



The emerging importance and evolving understanding of clonal hematopoiesis in multiple myeloma

Christin B. DeStefano[a,b,*], Steven J. Gibson[c], Adam S. Sperling[d], Paul G. Richardson[d], Irene Ghobrial[d], Clifton C. Mo[d,*]

Clonal Hematopoiesis

- Over time normal cells accumulate somatic mutations
- Most of these mutations do not confer an advantage and consequently confer no selection advantage
- Rarely an acquired mutation confers an inherent growth advantage and if acquired in a stem cell, the stem cell with the mutation and its progeny expands over time
- That this can occur in diverse tissues has become apparent
- If this acquired mutation with its growth advantage occurs in a hematopoietic stem cell, "clonal hematopoiesis" may occur, and one may find that a substantial fraction of mature blood cells harbors this mutation
- Genes involved in epigenetic regulation (DNMT3A, TET2, ASXL1) are found in most cases of mutation-driven clonal hematopoiesis
- That they represent mutations acquired over time is supported by the fact that these mutations are rare in younger individuals but can be found in as many as 10-20% of individuals $\geq$70 years old
- Unlike established cancers where many mutations can be found in one cell, the cells harboring the mutations "driving" clonal hematopoiesis have only a single driver gene mutated
- The term clonal hematopoiesis of indeterminate potential (CHIP) has been coined to describe a clinical entity characterized by the presence of cancer-associated clonal mutation in at least 4% of nucleated blood cells of individuals without an obvious cancer
- Risk factors for CHIP in healthy adults and patients with non-hematologic cancers include age, smoking, and receipt of chemotherapy, radiotherapy, or radioactive iodine
- Studies have shown that CHIP is associated with an increased risk of developing blood cancer confirming CHIP as a pre-malignant state
- The rate of progression to malignancy for individuals with CHIP is 0.5 to 1% per year with size of clone, number of mutations and number of genes mutated having an impact
- CHIP has also been associated with an increase in the risk of all-cause mortality, with amplification of innate immunity implicated as a possible factor
- Progression to cancer also likely occurs in other mitotically active tissues if their stem cells acquire such mutations
- In analyzing a blood sample, the cells harboring the mutation are mixed in with other cells that do not have the abnormal sequence ("variant allele"). By dividing the fraction of sequences with the variant (abnormal) sequence by the total number of variant and wild type sequences one can generate a value referred to as the variant allele frequency (VAF) that gives a crude estimate of the percent of cells in circulation that have arisen from the single clone that acquired the mutation.
- CHIP is characterized by somatic mutations with a VAF $\geq$0.02 in genes related to hematologic malignancies in patients with absence of cytopenia. The limit of 0.02 has been arbitratily selected

DeStefano CB et al. *Seminars Oncol* 2022;49:19-26.

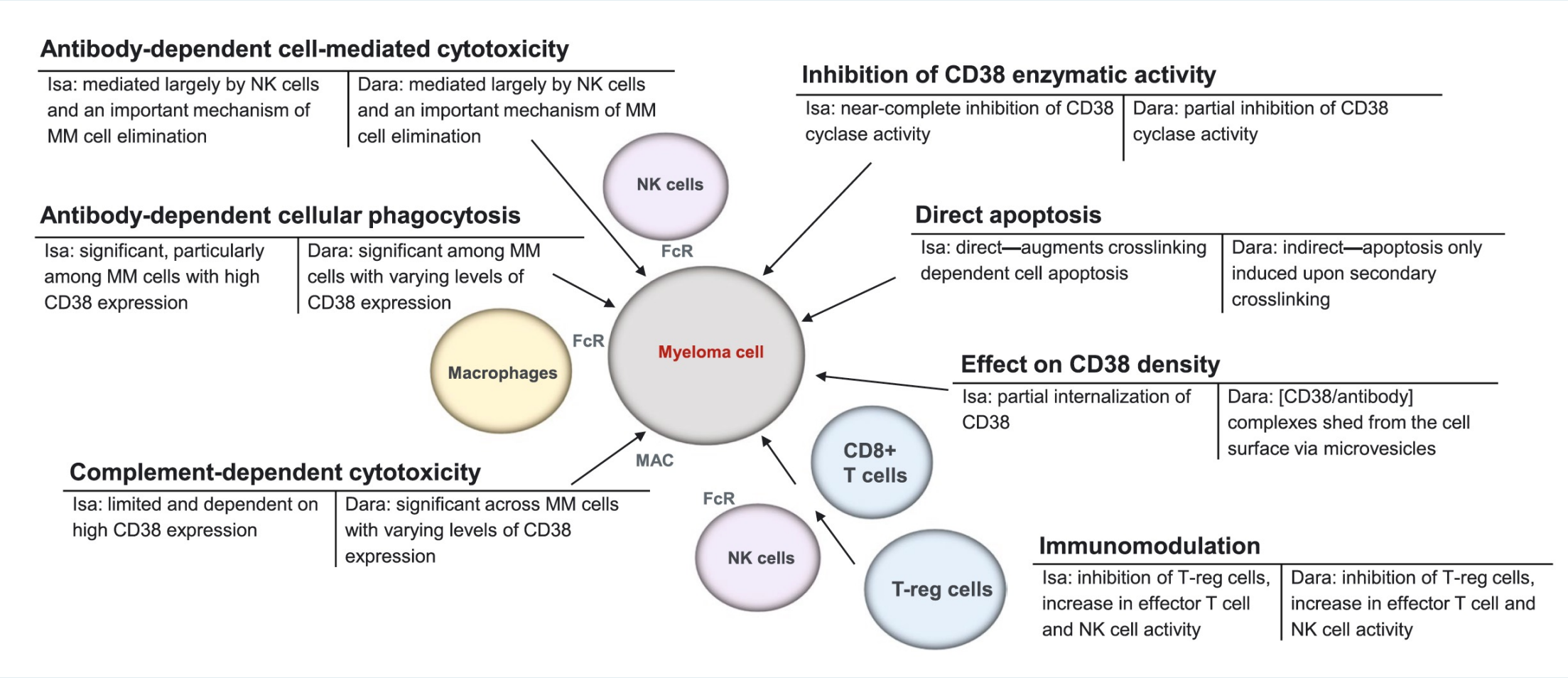
Annals of Hematology (2022) 101:2123–2137

REVIEW ARTICLE

Anti-CD38 antibody therapy for patients with relapsed/refractory multiple myeloma: differential mechanisms of action and recent clinical trial outcomes

Xavier Leleu[1] · Thomas Martin[2] · Katja Weisel[3] · Fredrik Schjesvold[4] · Shinsuke Iida[5] · Fabio Malavasi[6] · Salomon Manier[7] · Chang-Ki Min[8] · Enrique M. Ocio[9] · Charlotte Pawlyn[10] · Aurore Perrot[11] · Hang Quach[12] · Joshua Richter[13] · Ivan Spicka[14] · Kwee Yong[15] · Paul G. Richardson[16]

Mechanisms of Action of the Anti-CD38 Monoclonal Antibodies Isatuximab and Daratumumab



Leleu X et al. *Ann Hematol* 2022;101:2123-37.

ASCO 2022;Abstract 8011.

Daratumumab (DARA) + Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): A Post Hoc Analysis of Sustained Minimal Residual Disease (MRD) Negativity From GRIFFIN

Cesar Rodriguez,[1] Jonathan L. Kaufman,[2] Jacob Laubach,[3] Douglas W. Sborov,[4] Brandi Reeves,[5] Ajai Chari,[1] Rebecca Silbermann,[6] Luciano J. Costa,[7] Larry D. Anderson Jr,[8] Nitya Nathwani,[9] Nina Shah,[10] Naresh Bumma,[11] Andrzej Jakubowiak,[12] Robert Z. Orlowski,[13] Huiling Pei,[14] Annelore Cortoos,[15] Sharmila Patel,[15] Thomas S. Lin,[15] Paul G. Richardson,[3] Peter M. Voorhees[16]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [5]University of North Carolina – Chapel Hill, Chapel Hill, NC, USA; [6]Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA; [7]University of Alabama at Birmingham, Birmingham, AL, USA; [8]Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [9]Judy and Bernard Briskin Center for Multiple Myeloma Research, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [10]Department of Medicine, University of California San Francisco, San Francisco, CA, USA; [11]Division of Hematology, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [12]University of Chicago Medical Center, Chicago, IL, USA; [13]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [14]Janssen Research & Development, LLC, Titusville, NJ, USA; [15]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [16]Levine Cancer Institute, Atrium Health, Charlotte, NC, USA.

Br J Haematol 2022 October;199(2):190-204.

REVIEW

Lenalidomide, bortezomib and dexamethasone induction therapy for the treatment of newly diagnosed multiple myeloma: a practical review

Georgia J. McCaughan[1,2] | Sara Gandolfi[3,4] | John J. Moore[1,2] | Paul G. Richardson[5]

Modified Bortezomib, Lenalidomide, Dexamethasone (RVD) Protocols

Protocol name	Cycle length, days	Bortezomib	Lenalidomide	Dexamethasone
RVD classic	21	SC 1.3 mg/m^2 Day 1, 4, 8, 11	25 mg Day 1–14	Day 1, 2, 4, 5, 8, 9, 11, 12
RVD lite	35	SC 1.3 mg/m^2 Day 1, 8, 15, 22	15 mg Day 1–21	Day 1, 2, 8, 9, 15, 16, 22, 23
RVD premium lite	28	SC 1.3 mg/m^2 Day 1, 8, 15, 22[a]	15–25 mg Day 1–21[b]	Day 1, 2, 8, 9, 15, 16, 22, 23
RVD ultra lite	28–35	SC 1.3 mg/m^2 Day 1, 8, 15	15 mg Day 1–21[b]	Day 1, 2, 8, 8, 15 and 16

McCaughan GJ et al. *Br J Haematol* 2022 October;199(2):190-204.

original reports

Elotuzumab Plus Pomalidomide and Dexamethasone for Relapsed/Refractory Multiple Myeloma: Final Overall Survival Analysis From the Randomized Phase II ELOQUENT-3 Trial

Meletios A. Dimopoulos, MD[1]; Dominik Dytfeld, MD, PhD[2]; Sebastian Grosicki, MD, PhD[3]; Philippe Moreau, MD[4]; Naoki Takezako, MD, PhD[5]; Mitsuo Hori, MD, PhD[6]; Xavier Leleu, MD, PhD[7]; Richard LeBlanc, MD[8]; Kenshi Suzuki, MD[9]; Marc S. Raab, MD, PhD[10]; Paul G. Richardson, MD[11]; Mihaela Popa McKiver, MD, PhD[12]; Ying-Ming Jou, PhD[12]; David Yao, MD, PhD[12]; Prianka Das, PharmD[12]; and Jesús San-Miguel, MD, PhD[13]

J Clin Oncol 2022 August 12;[Online ahead of print].

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Richardson

INTRODUCTION

MODULE 1: Case Presentations

MODULE 2: Faculty Survey

MODULE 3: Journal Club with Dr Richardson

MODULE 4: Appendix of Key Publications

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Selection of Front-Line Therapy for Multiple Myeloma (MM)

IMS 2022;Abstract OAB-057.

Daratumumab (DARA) + Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients With Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): Final Analysis of GRIFFIN

Douglas W. Sborov,[1] Jacob Laubach,[2] Jonathan L. Kaufman,[3] Brandi Reeves,[4] Cesar Rodriguez,[5] Ajai Chari,[5] Rebecca Silbermann,[6] Luciano J. Costa,[7] Larry D. Anderson Jr.,[8] Nitya Nathwani,[9] Nina Shah,[10] Naresh Bumma,[11] Sarah A. Holstein,[12] Caitlin Costello,[13] Andrzej Jakubowiak,[14] Robert Z. Orlowski,[15] Kenneth H. Shain,[16] Andrew J. Cowan,[17] Huiling Pei,[18] Annelore Cortoos,[19] Sharmila Patel,[19] Thomas S. Lin,[19] Paul Richardson,[2] Saad Z. Usmani,[20] Peter M. Voorhees[21]

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Presented at the 19th International Myeloma Society (IMS) Annual Meeting; August 25-27, 2022; Los Angeles, CA, USA.

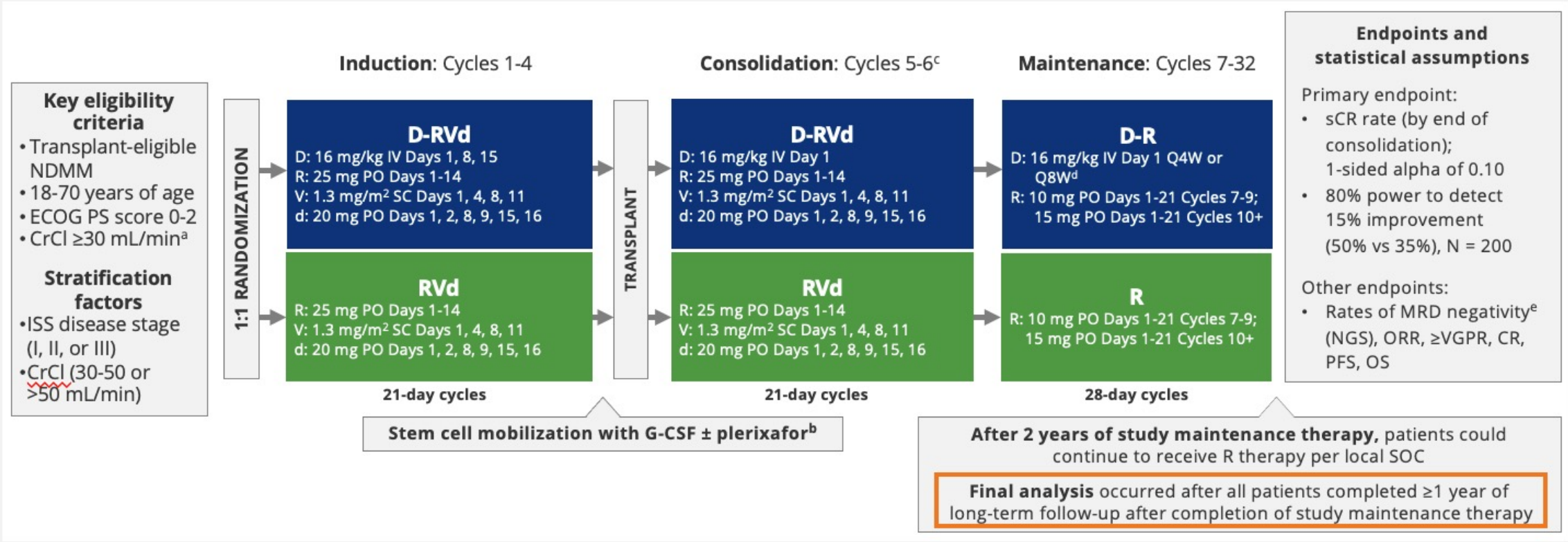
Scan the QR code.

https://www.congresshub.com/Oncology/IMS2022/Daratumumab/Sborov

RTP RESEARCH TO PRACTICE

GRIFFIN Phase II Study Design

- 35 sites in the United States with enrollment between December 2016 and April 2018

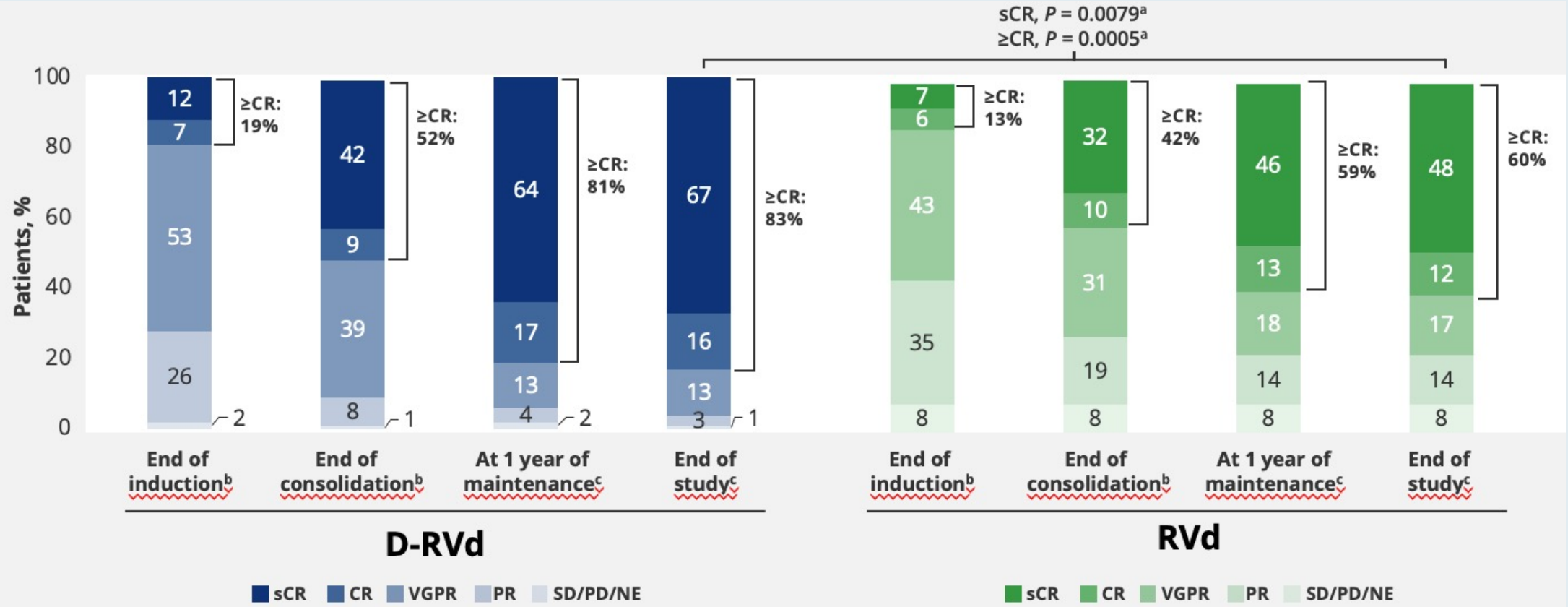


ECOG PS, Eastern Cooperative Oncology Group performance status; CrCl, creatinine clearance; IV, intravenous; PO, oral; SC, subcutaneous; G-CSF, granulocyte colony-stimulating factor; D-R, daratumumab plus lenalidomide; Q4W, every 4 weeks; Q8W, every 8 weeks; NGS, next-generation sequencing; ORR, overall response rate; VGPR, very good partial response; CR, complete response; PFS, progression-free survival; PFS2, PFS on next subsequent line of therapy; OS, overall survival. [a]Lenalidomide dose adjustments were made for patients with CrCl ≤50 mL/min. [b]Cyclophosphamide-based mobilization was permitted if unsuccessful. [c]Consolidation was initiated 60 to 100 days post-transplant. [d]Protocol amendment 2 allowed for the option to dose DARA Q4W based on pharmacokinetic results from study SMM2001 (ClinicalTrials.gov Identifier: NCT02316106). [e]To measure MRD negativity at a minimum threshold of 10^{-5}, bone marrow aspirates were collected at first evidence of suspected CR or sCR (including patients with ≥VGPR and suspected DARA interference), after induction but before stem cell collection, at the post-transplant consolidation disease evaluation, and at 12 months and 24 months (±3 weeks) of maintenance therapy.

CrCl,

Sborov DB et al. IMS 2022;Abstract OAB-057.

GRIFFIN Final Analysis: Response Rates over Time



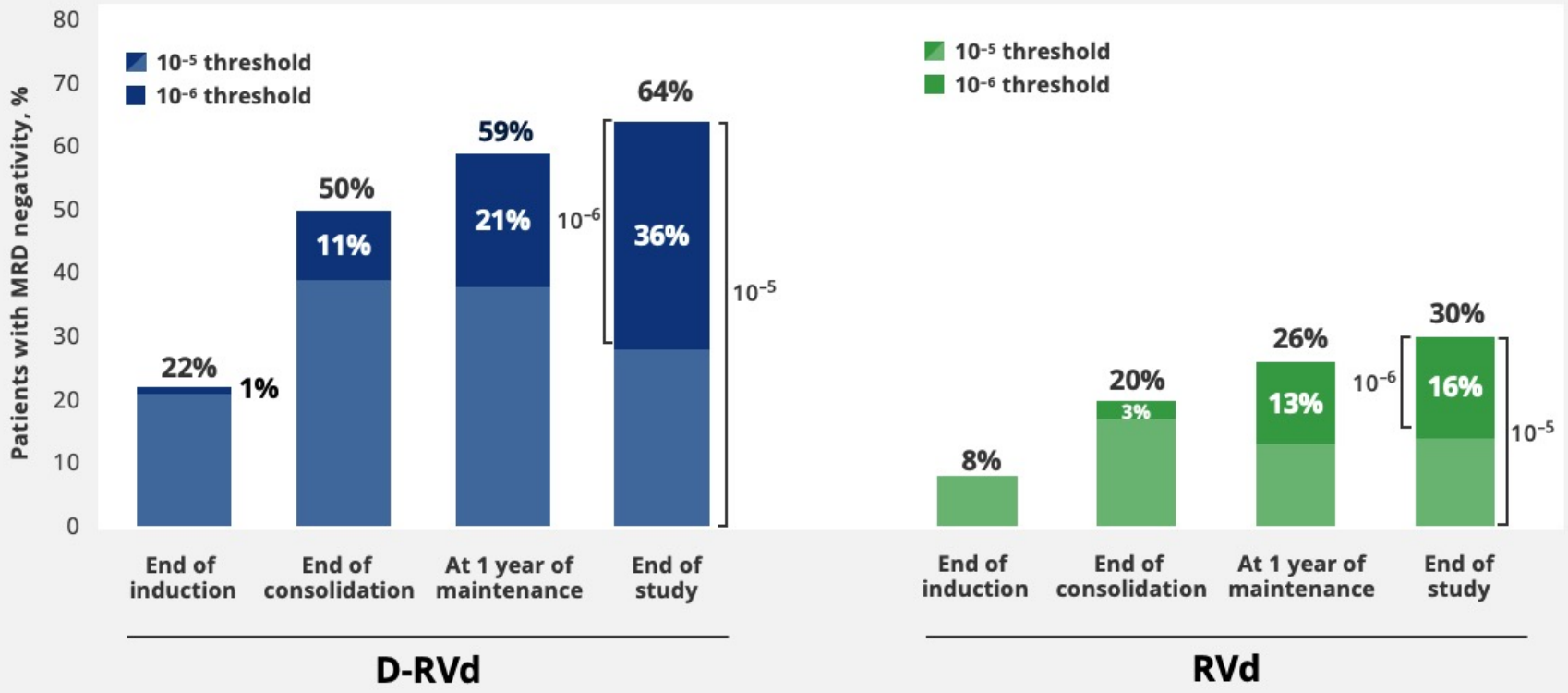
- Rates of ≥CR improved over time and the deepest responses occurred at the end of study maintenance
- At all timepoints, response rates for D-RVd were consistently higher versus RVd

PR, partial response; SD/PD/NE, stable disease/progressive disease/not evaluable. [a] *P* value was calculated using the Cochran–Mantel–Haenszel chi-squre test. [b]Response rates are from the primary analysis cutoff (median follow-up: 13.5 months), and the response-evaluable population included 196 patients (D-RVd, n = 99; RVd, n = 97). [c]Response rates for the maintenance phase were evaluated at the time of final analysis (median follow-up: 49.6 months), and the response-evaluable population included 198 patients (D-RVd, n = 100; RVd, n = 98).

Sborov DB et al. IMS 2022;Abstract OAB-057.

RTP RESEARCH TO PRACTICE

GRIFFIN Final Analysis: Minimum Residual Disease (MRD) Negativity Rates over Time



MRD-negative (10^{-5}) conversion rate

- 14% (15/104) of D-RVd and 10% (10/103) of RVd patients converted from MRD positive at the end of consolidation to MRD negative by the end of 2 years of study maintenance therapy

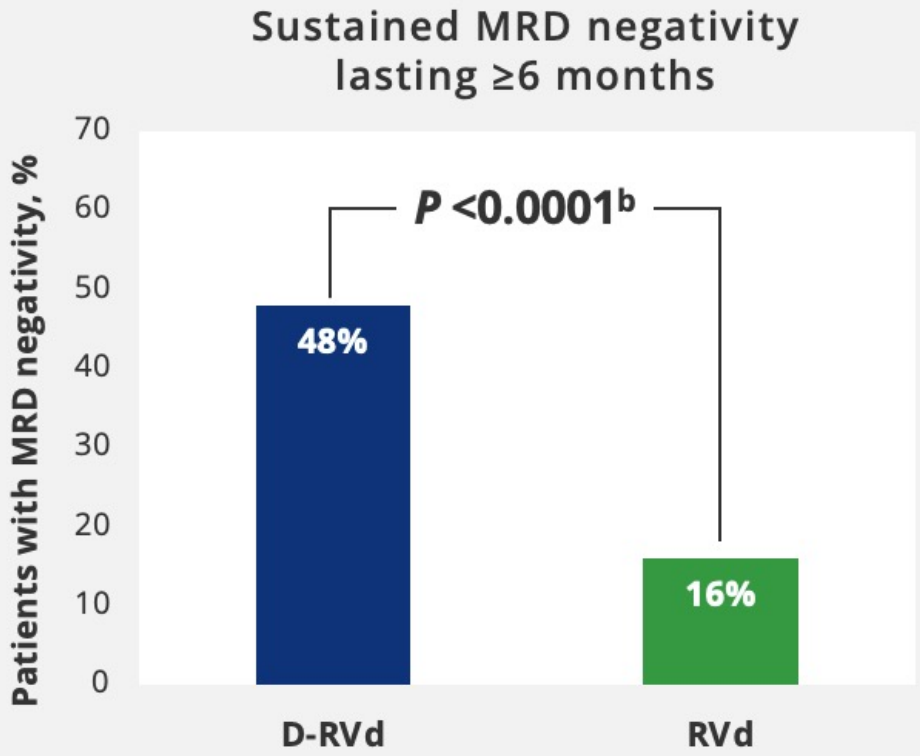
- MRD-negativity rates improved over time and were consistently higher for D-RVd versus RVd
- Rates of MRD negativity continued to deepen throughout the study maintenance period

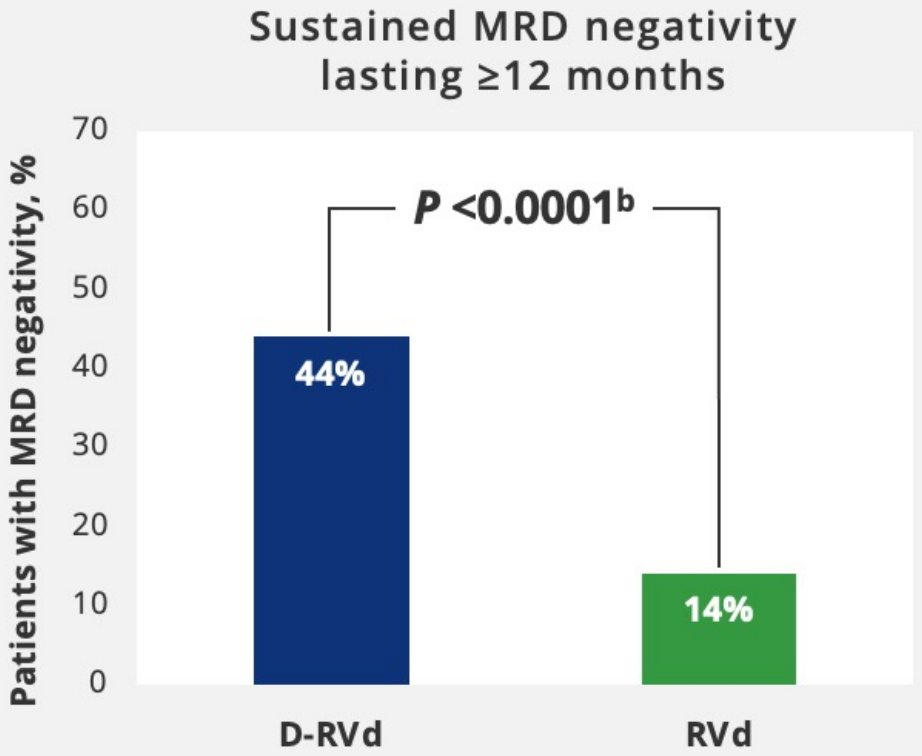
[a]MRD status is based on the assessment of bone marrow aspirates by NGS in accordance with International Myeloma Working Group criteria. Bone marrow aspirates were assessed at baseline, at first evidence of suspected CR or sCR (including patients with VGPR or better and suspected DARA interference), at the end of induction and consolidation, and after 1 and 2 years of maintenance, regardless of response. MRD-negativity rates for all time points were evaluated at the time of final analysis (median follow-up: 49.6 months), and MRD-negativity rates were among the ITT population (D-RVd, n = 104; RVd, n = 103).

Sborov DB et al. IMS 2022;Abstract OAB-057.

RTP RESEARCH TO PRACTICE

GRIFFIN Final Analysis: Rates of Sustained MRD Negativity (10^{-5})

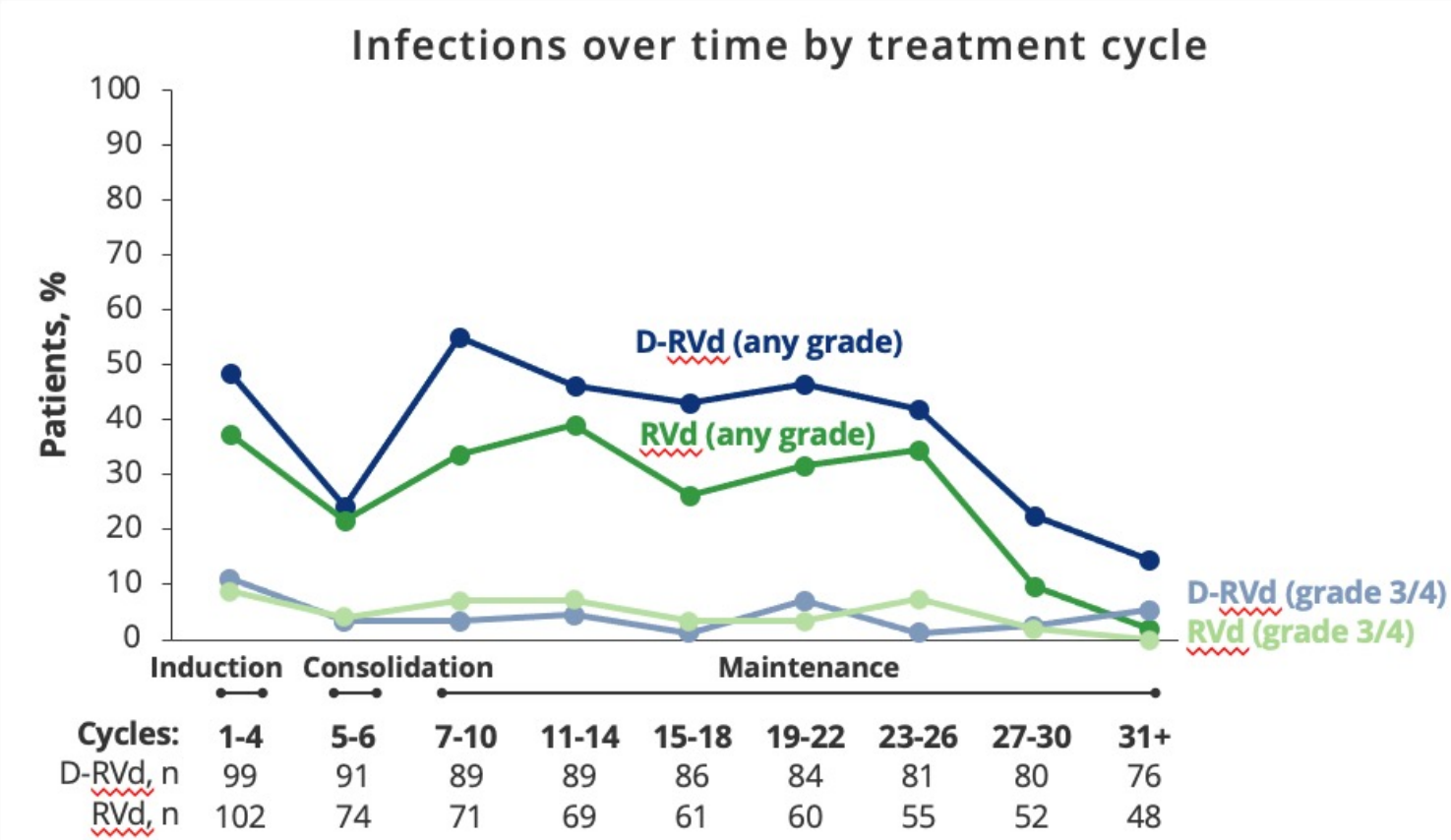




[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status is based on the assessment of bone marrow aspirates by NGS in accordance with International Myeloma Working Group criteria. Median follow-up was 49.6 months, and MRD-negativity rates are among the ITT population (D-RVd, n = 104; RVd, n = 103). Bone marrow aspirates were assessed at baseline, at first evidence of suspected CR or sCR (including patients with VGPR or better and suspected DARA interference), at the end of induction and consolidation, and after 1 and 2 years of maintenance, regardless of response. [b]*P* values were calculated using the Fisher's exact test.

Sborov DB et al. IMS 2022;Abstract OAB-057.

GRIFFIN Final Analysis: Summary of Infections



- The highest incidence of infections occurred in earlier cycles of treatment and maintenance therapy
- The most common infection was upper respiratory tract infection in both groups
- COVID-19 infections occurred in 5 and 2 patients in the D-RVd and RVd groups, respectively
- Rate of infections leading to treatment discontinuation were similar between groups (D-RVd, 2%; RVd, 3%)

Sborov DB et al. IMS 2022;Abstract OAB-057.

RTP RESEARCH TO PRACTICE

ORIGINAL PAPER

Br J Haematol 2022 November;199(3):355-65.

BJHaem BRITISH JOURNAL OF HAEMATOLOGY

Daratumumab plus lenalidomide, bortezomib and dexamethasone in newly diagnosed multiple myeloma: Analysis of vascular thrombotic events in the GRIFFIN study

Douglas W. Sborov[1,*] | Muhamed Baljevic[2,*] | Brandi Reeves[3] | Jacob Laubach[4] | Yvonne A. Efebera[5] | Cesar Rodriguez[6] | Luciano J. Costa[7] | Ajai Chari[8] | Rebecca Silbermann[9] | Sarah A. Holstein[10] | Larry D. Anderson Jr[11] | Jonathan L. Kaufman[12] | Nina Shah[13] | Huiling Pei[14] | Sharmila Patel[15] | Annelore Cortoos[15] | J. Blake Bartlett[16] | Jessica Vermeulen[17] | Thomas S. Lin[15] | Peter M. Voorhees[18] | Paul G. Richardson[4]

2022 ASCO® ANNUAL MEETING

Abstract 8002

Daratumumab Carfilzomib Lenalidomide and Dexamethasone as induction therapy in high-risk transplant eligible newly diagnosed myeloma patients: results of the phase 2 study IFM 2018-04

Cyrille Touzeau[1], Aurore Perrot[2], Cyrille Hulin[3], Salomon Manier[4], Margaret Macro[5], Marie-Lorraine Chretien[6], Lionel Karlin[7], Martine Escoffre[8], Caroline Jacquet[9], Mourad Tiab[10], Xavier Leleu[11], Lucie Planche[12], Hervé Avet-Loiseau[2], Philippe Moreau[1]

RTP RESEARCH TO PRACTICE

IFM 2018-04: Phase II Study Design

Key inclusion criteria:

- Age < 66
- **Newly diagnosed multiple myeloma**
- **Transplant-eligible**
- **High-risk FISH :** t(4;14), 17p del, t(14;16)
- ECOG 0-2

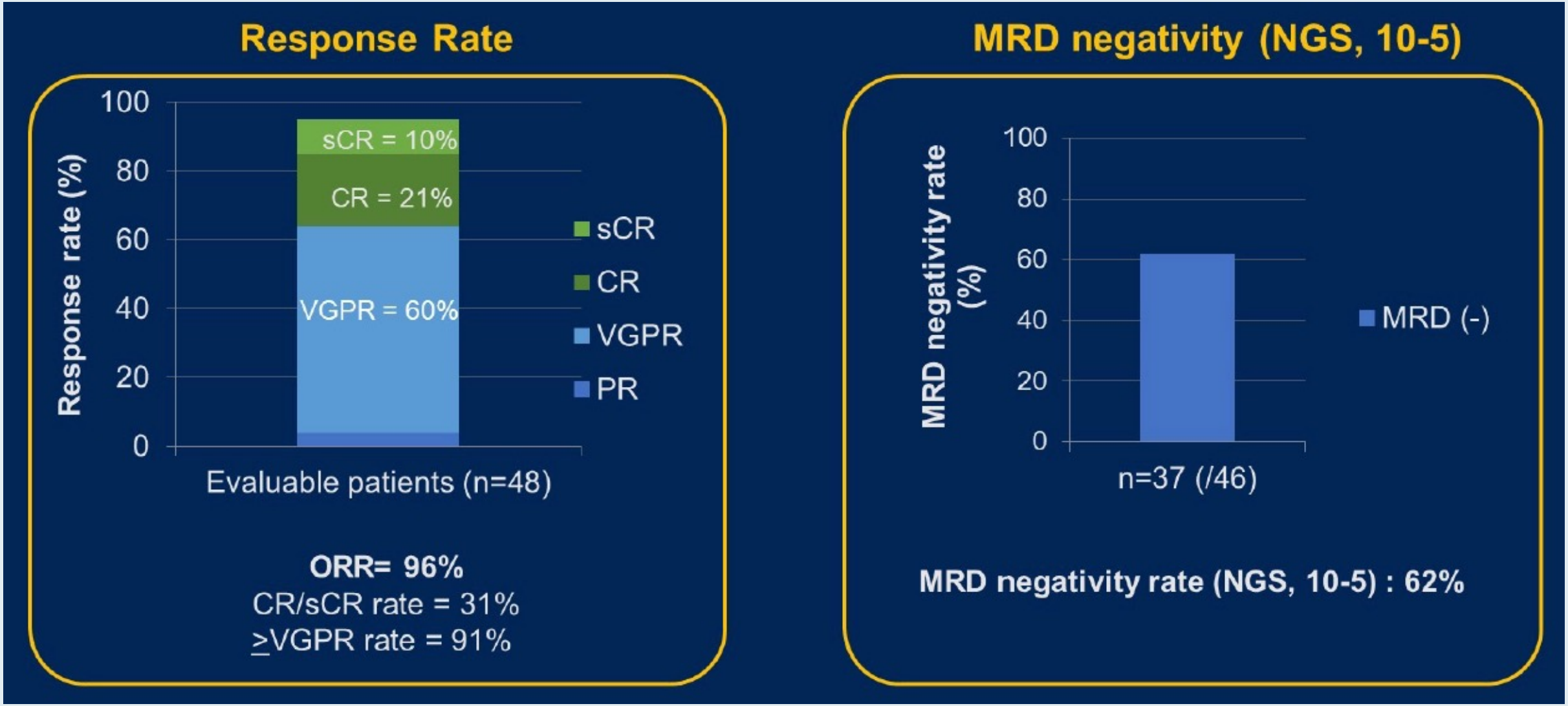
Objectives:

- **Primary Objective :**
  Feasibility (endpoint : >70% patients completed 2nd transplant)
- **Secondary Objectives:**
  Safety, ORR, PFS, OS, stem-cell collection

Induction Dara-KRd x 6	Stem cell collection	ASCT #1	Consolidation Dara KRd x 4	ASCT #2	Maintenance Dara Len 2 years
Dara : 16 mg/kg IV D1,8,15,22 (cycle 1 - 2) D1 D15 (Cycle 3 to 6) **K : (20)36 mg/m2 IV** D1-2, 8-9, 15-16 **Len : 25 mg** D1-21 **Dex : 20 mg** D1-2,8-9,15-16,22-23 **28-day cycles**	Cyclo GCSF +/- Plerix	**Mel 200**	**Dara : 16 mg/kg IV** D1 D15 **K : 56 mg/m2 IV** D1, 8, 15 **Len : 15 mg** D1-21 **Dex : 40 mg** D1, 8, 15, 22 **28-day cycles**	**Mel 200**	**Dara** : 16 mg/kg IV every 8 weeks **Len** : 10 mg 21/28

Touzeau C et al. ASCO 2022;Abstract 8002.

IFM 2018-04: Response Rates and MRD with Dara-KRd Induction



Touzeau C et al. ASCO 2022;Abstract 8002.

RTP RESEARCH TO PRACTICE

IFM 2018-04: Safety of Dara-KRd Induction

Hematologic treatment related AE:

	Any grade N (%)	Grade 3/4 N (%)
Neutropenia	22 (44%)	20 (40%)
Anemia	14 (28%)	7 (14%)
Thrombocytopenia	13 (26%)	4 (8%)

AE leading to treatment discontinuation (n=2)
- COVID-19 infection (n=1)
- tumor lysis syndrome (n=1)

Grade 3/4 infection (n=3)
- COVID 19 infection (n=1)
- CMV infection (n=1)
- Pseudomonas aeruginosa bacteriemia (n=1)

Most common non hematologic treatment related AE:

	Any grade N (%)	Grade 3/4 N (%)
GI disorders	23 (46%)	2(4%)
Infection	20 (40%)	3 (6%)
Skin rash	8 (16%)	0
Deep-vein thrombosis	7 (14%)	3 (6%)
Peripheral neuropathy	6 (12%)	0
Hepatic cytolysis	4 (8%)	2 (4%)
Renal failure	3 (6%)	3 (6%)
Cardiac event	1 (2%)	0

AE = adverse event

Touzeau C et al. ASCO 2022;Abstract 8002.

2022 ASCO ANNUAL MEETING

Abstract LBA4

RVd ± ASCT and Lenalidomide Maintenance to Progression for NDMM

The Phase 3 DETERMINATION Trial

Paul G. Richardson, MD, RJ Corman Professor of Medicine, Harvard Medical School
Clinical Program Leader, Director of Clinical Research,
Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston, MA

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2022 July 14;387(2):132-47.

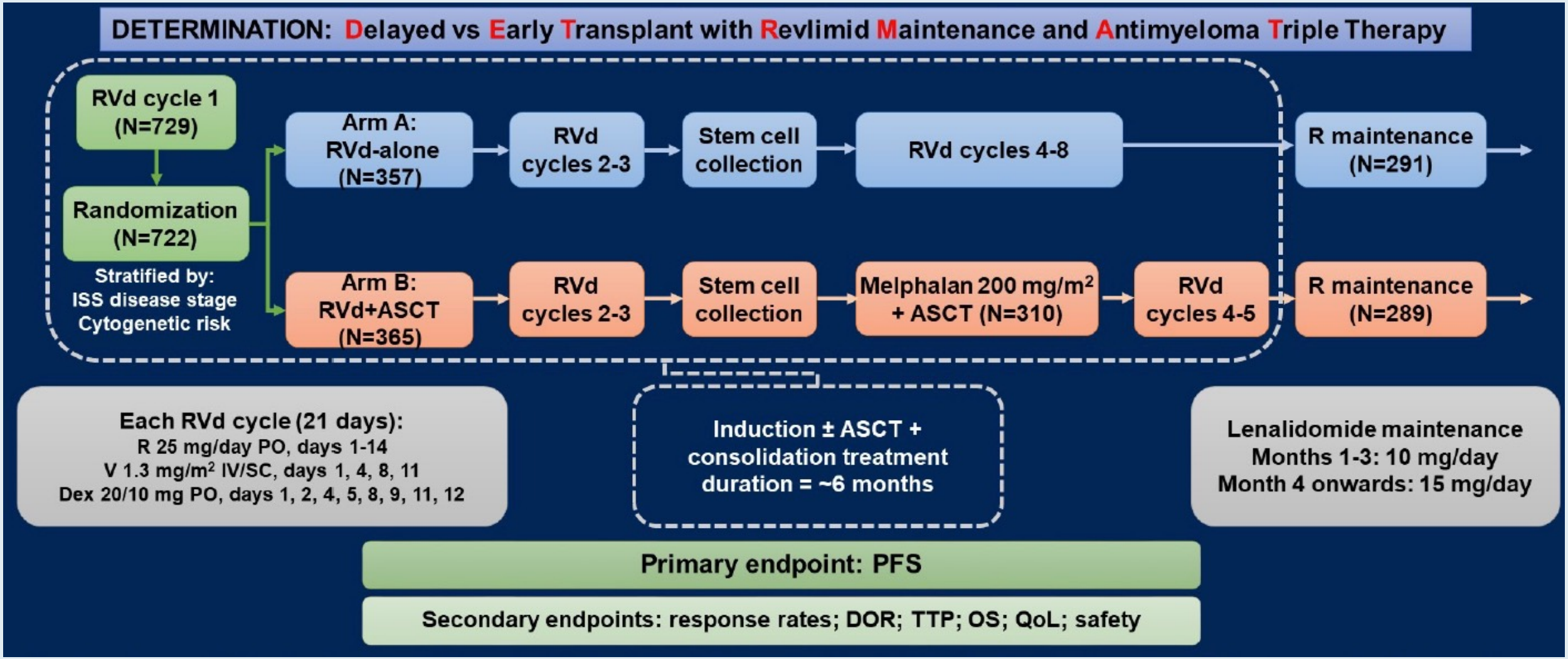
ORIGINAL ARTICLE

Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma

P.G. Richardson, S.J. Jacobus, E.A. Weller, H. Hassoun, S. Lonial, N.S. Raje, E. Medvedova, P.L. McCarthy, E.N. Libby, P.M. Voorhees, R.Z. Orlowski, L.D. Anderson, Jr., J.A. Zonder, C.P. Milner, C. Gasparetto, M.E. Agha, A.M. Khan, D.D. Hurd, K. Gowin, R.T. Kamble, S. Jagannath, N. Nathwani, M. Alsina, R.F. Cornell, H. Hashmi, E.L. Campagnaro, A.C. Andreescu, T. Gentile, M. Liedtke, K.N. Godby, A.D. Cohen, T.H. Openshaw, M.C. Pasquini, S.A. Giralt, J.L. Kaufman, A.J. Yee, E. Scott, P. Torka, A. Foley, M. Fulciniti, K. Hebert, M.K. Samur, K. Masone, M.E. Maglio, A.A. Zeytoonjian, O. Nadeem, R.L. Schlossman, J.P. Laubach, C. Paba-Prada, I.M. Ghobrial, A. Perrot, P. Moreau, H. Avet-Loiseau, M. Attal, K.C. Anderson, and N.C. Munshi, for the DETERMINATION Investigators*

RTP RESEARCH TO PRACTICE

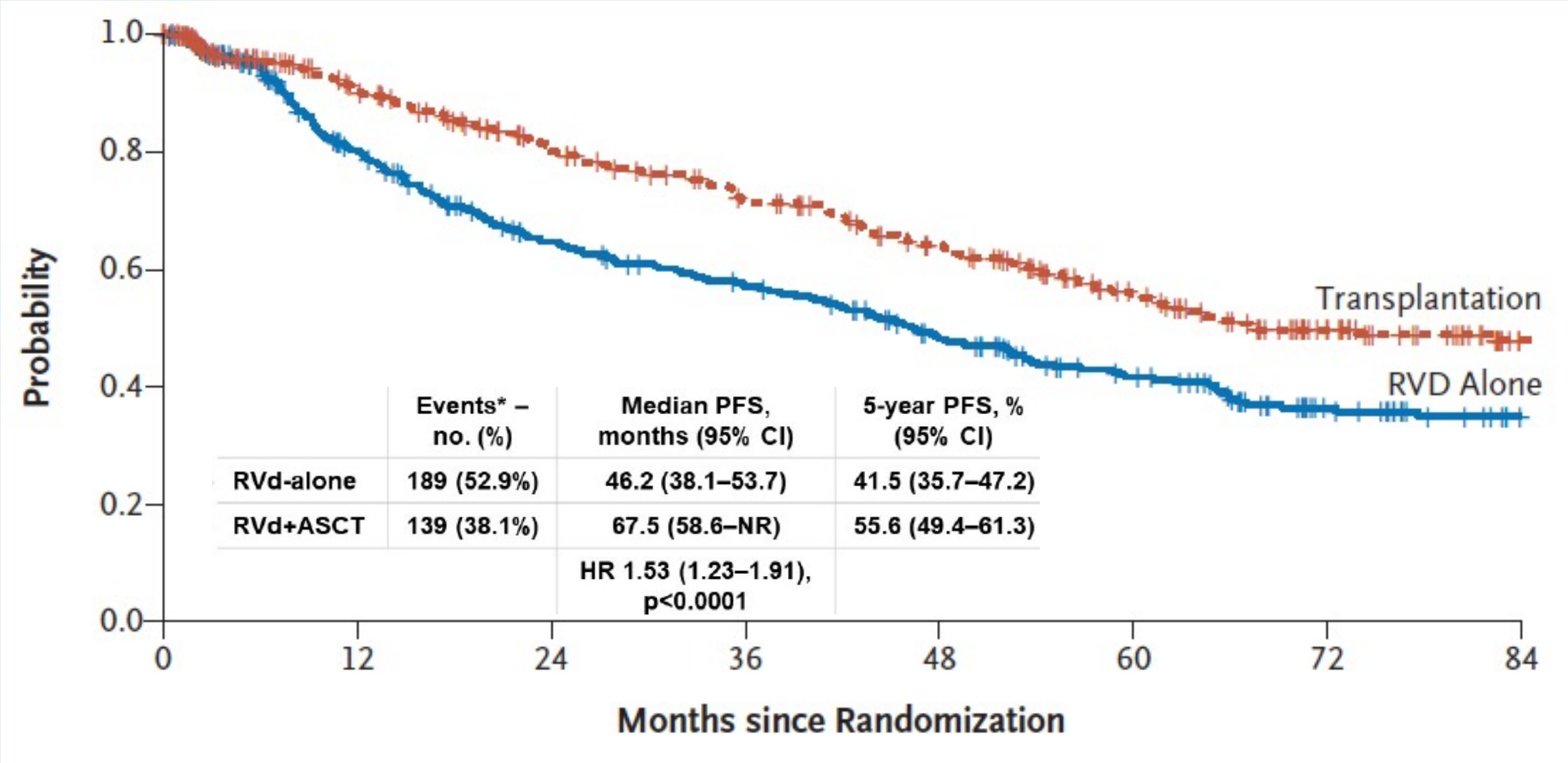
DETERMINATION: Phase III Study Design and Patient Disposition



PFS = progression-free survival; DOR = duration of response; TTP = time to progression; OS = overall survival; QoL = quality of life

Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Progression-Free Survival (Primary Endpoint)

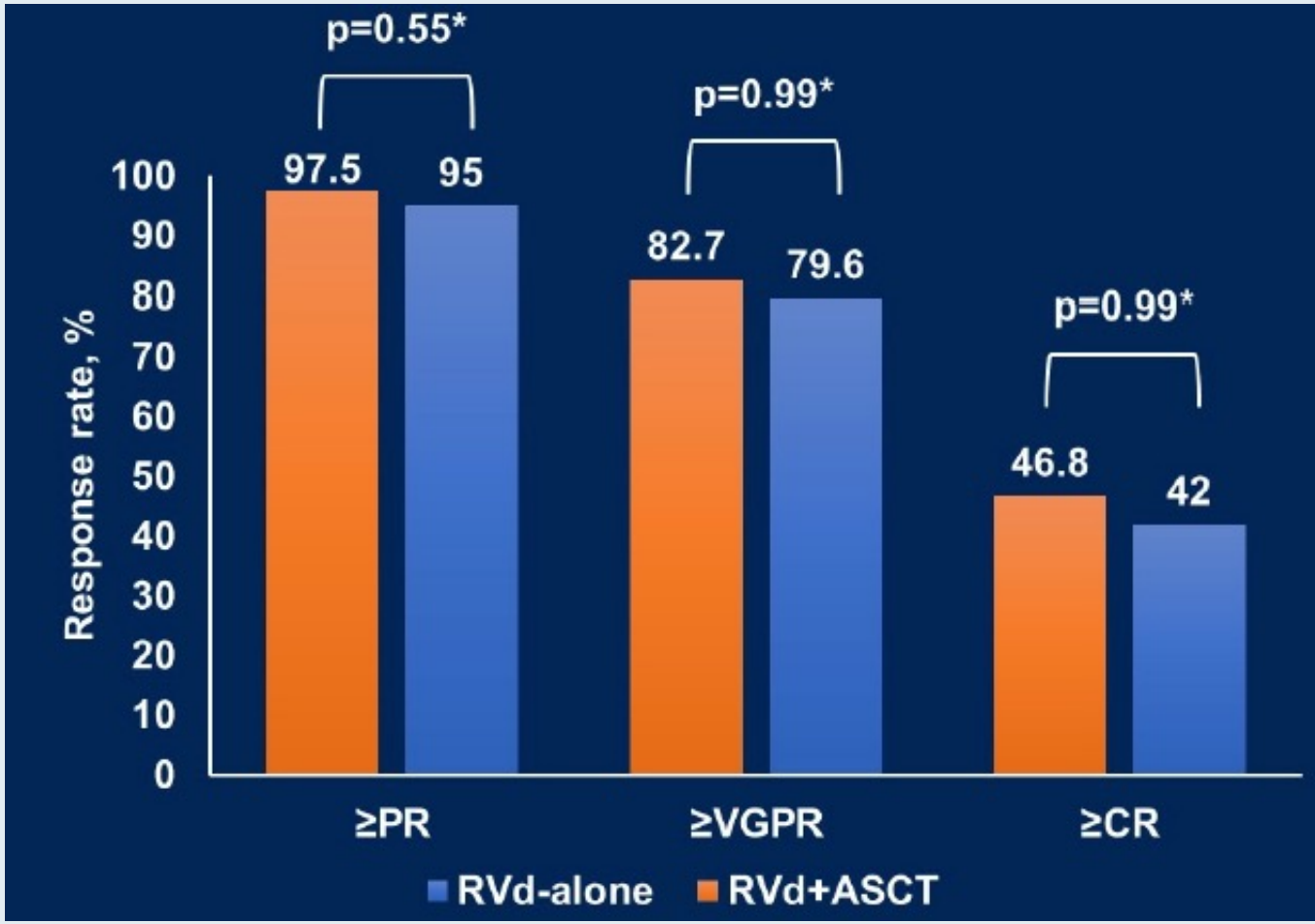


	Events* – no. (%)	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	189 (52.9%)	46.2 (38.1–53.7)	41.5 (35.7–47.2)
RVd+ASCT	139 (38.1%)	67.5 (58.6–NR)	55.6 (49.4–61.3)
		HR 1.53 (1.23–1.91), p<0.0001	

Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47; ASCO 2022;Abstract LBA4.

RTP RESEARCH TO PRACTICE

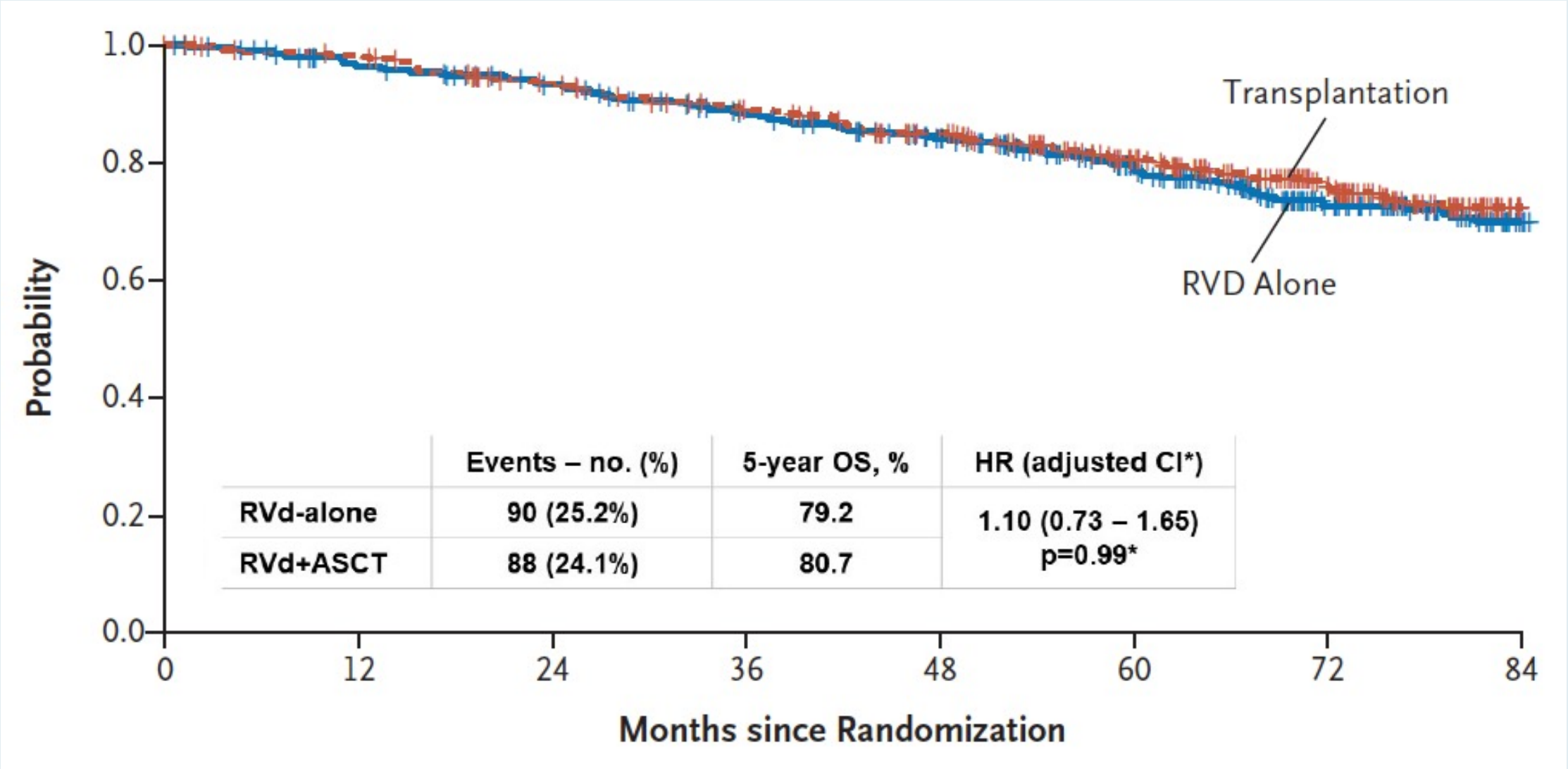
DETERMINATION: Best Response to Treatment and Duration of Response



Duration of response	RVd-alone	RVd+ASCT
Median duration of ≥PR, months	38.9	56.4
	HR 1.45 (Adjusted CI* 1.09–1.93), p=0.003*	
5-year duration of ≥CR, %	52.9	60.6
	HR 1.35 (Adjusted CI* 0.83–2.22), p=0.698*	

Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Overall Survival (Key Secondary Endpoint)



	Events – no. (%)	5-year OS, %	HR (adjusted CI*)
RVd-alone	90 (25.2%)	79.2	1.10 (0.73 – 1.65) p=0.99*
RVd+ASCT	88 (24.1%)	80.7	

Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47; ASCO 2022;Abstract LBA4.

DETERMINATION: Grade ≥3 Treatment-Related Adverse Events (AEs)

AE, %	RVd-alone (N=357)	RVd+ASCT (N=365)
Any	78.2	94.2
Any hematologic	60.5	89.9
Any grade 5 (fatal) AE	0.3	1.6 *
Neutropenia	42.6	86.3
Thrombocytopenia	19.9	82.7
Leukopenia	19.6	39.7
Anemia	18.2	29.6
Lymphopenia	9.0	10.1
Febrile neutropenia	4.2	9.0
Diarrhea	3.9	4.9
Nausea	0.6	6.6
Mucositis oral	0	5.2
Fatigue	2.8	6.0
Fever	2.0	5.2
Pneumonia	5.0	9.0
Hypophosphatemia	9.5	8.2
Neuropathy	5.6	7.1

- Rates of all grade ≥3 and of hematologic grade ≥3 treatment-related AEs during all treatment significantly higher with RVd + ASCT (both p<0.001)
  - Rates hematologic grade ≥3 treatment-related AEs during maintenance: 26.1% vs 41.9%
- Related SAEs:
  - Prior to maintenance: 40.3% vs 47.1%
  - During maintenance: 11.3% vs 16.6%

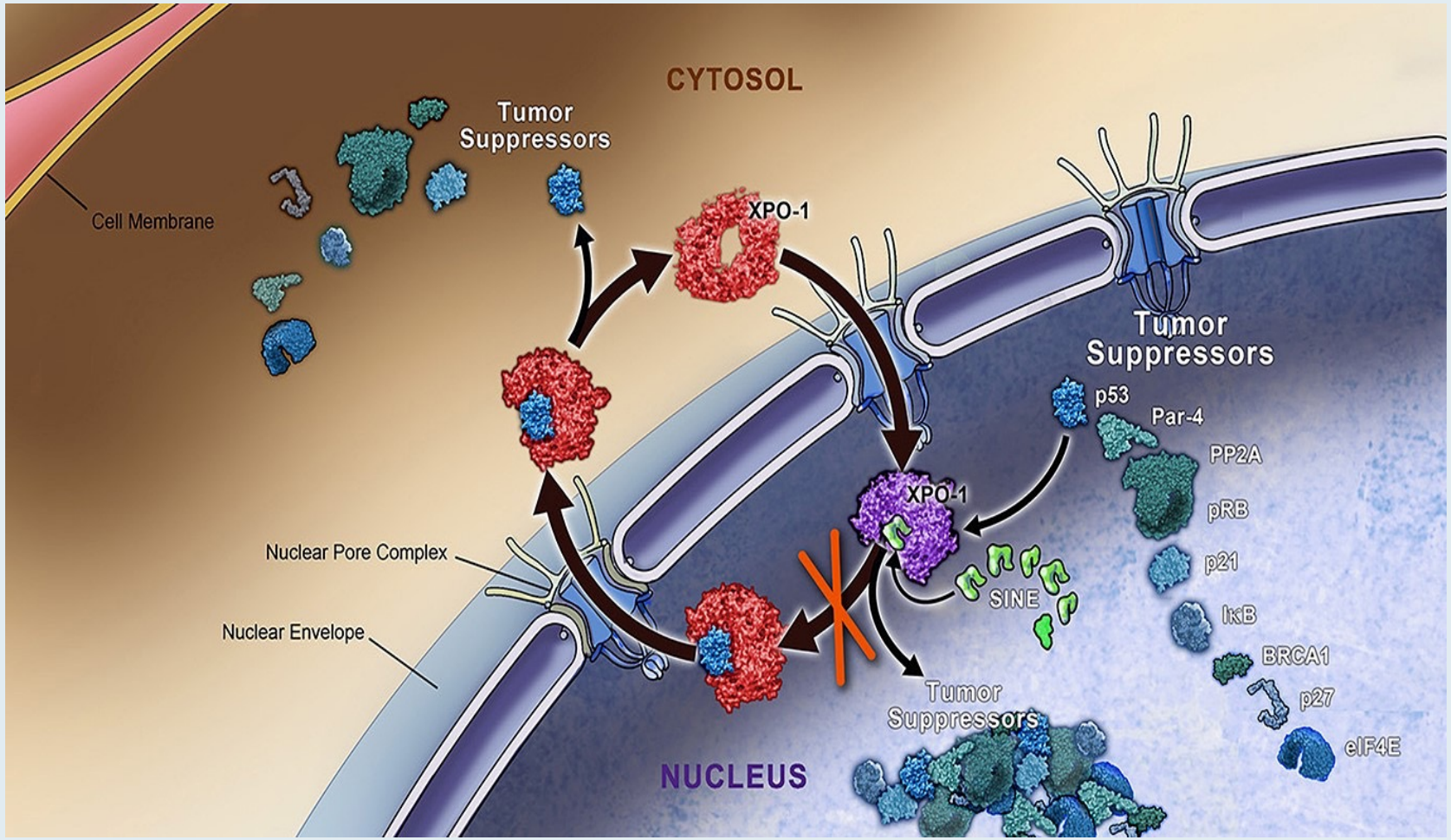
SAE = serious AE

Richardson PG et al. *N Engl J Med* 2022 July 14;387(2):132-47; ASCO 2022;Abstract LBA4.

RTP RESEARCH TO PRACTICE

Integration of Novel Therapies into the Management of Relapsed/Refractory (R/R) MM

Selinexor Mechanism of Action



- Exportin 1 (XPO1) is the major nuclear export protein for tumor suppressor proteins (TSPs), the glucocorticoid receptor (GR) and eIF4E-bound oncoprotein mRNAs (c-myc, Bcl-2, Bcl-xL and cyclins)
- XPO1 is overexpressed in MM and its levels often correlate with poor prognosis
- Selinexor is a first-in-class XPO1 inhibitor that induces nuclear retention and activation of TSPs and the GR in the presence of steroids and suppresses oncoprotein expression

Bahlis N et al. EHA 2016;Abstract P277.

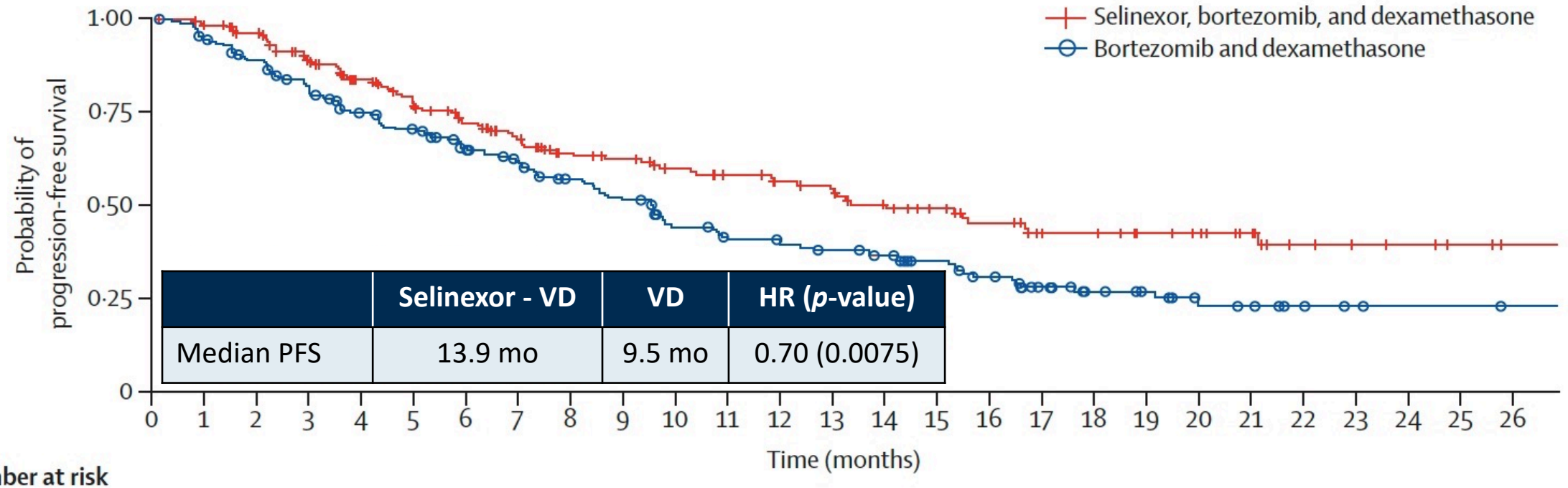
RTP RESEARCH TO PRACTICE

Lancet 2020;396(10262):1563-73.

Once-per-week selinexor, bortezomib, and dexamethasone versus twice-per-week bortezomib and dexamethasone in patients with multiple myeloma (BOSTON): a randomised, open-label, phase 3 trial

Sebastian Grosicki, Maryana Simonova, Ivan Spicka, Ludek Pour, Iryrna Kriachok, Maria Gavriatopoulou, Halyna Pylypenko, Holger W Auner, Xavier Leleu, Vadim Doronin, Ganna Usenko, Nizar J Bahlis, Roman Hajek, Reuben Benjamin, Tuphan K Dolai, Dinesh K Sinha, Christopher P Venner, Mamta Garg, Mercedes Gironella, Artur Jurczyszyn, Pawel Robak, Monica Galli, Craig Wallington-Beddoe, Atanas Radinoff, Galina Salogub, Don A Stevens, Supratik Basu, Anna M Liberati, Hang Quach, Vesselina S Goranova-Marinova, Jelena Bila, Eirini Katodritou, Hanna Oliynyk, Sybiryna Korenkova, Jeevan Kumar, Sundar Jagannath, Phillipe Moreau, Moshe Levy, Darrell White, Moshe E Gatt, Thierry Facon, Maria V Mateos, Michele Cavo, Donna Reece, Larry D Anderson Jr, Jean-Richard Saint-Martin, Jacqueline Jeha, Anita A Joshi, Yi Chai, Lingling Li, Vishnuvardhan Peddagali, Melina Arazy, Jatin Shah, Sharon Shacham, Michael G Kauffman, Meletios A Dimopoulos, Paul G Richardson, Sosana Delimpasi**

BOSTON: Progression-Free Survival (ITT)



	Selinexor - VD	VD	HR (*p*-value)
Median PFS	13.9 mo	9.5 mo	0.70 (0.0075)

Number at risk (number censored)

Selinexor, bortezomib, and dexamethasone	195 (0)	187 (5)	175 (12)	152 (21)	135 (31)	117 (37)	106 (42)	89 (50)	79 (57)	76 (59)	69 (63)	64 (66)	57 (71)	51 (73)	45 (76)	41 (80)	35 (83)	27 (89)	26 (90)	22 (94)	19 (97)	14 (102)	9 (106)	7 (108)	6 (109)	4 (111)	2 (113)
Bortezomib and dexamethasone	207 (0)	187 (8)	175 (10)	152 (15)	138 (20)	127 (22)	111 (29)	100 (32)	90 (37)	81 (37)	66 (41)	59 (43)	56 (44)	53 (45)	49 (47)	42 (52)	35 (55)	26 (60)	20 (65)	16 (69)	10 (73)	8 (75)	5 (78)	4 (79)	3 (80)	3 (80)	2 (81)

VD = bortezomib and low-dose dexamethasone

Grosicki S et al. *Lancet* 2020;396(10262):1563-73.

RTP RESEARCH TO PRACTICE

BOSTON: Response

Response	Selinexor + VD (n = 195)	VD (n = 207)
Overall response rate	76.4%	62.3%
Best overall response		
Stringent complete response	10%	6%
Complete response	7%	4%
Very good partial response	28%	22%
Partial response	32%	30%
Minimal response	8%	10%
Stable disease	13%	19%
Progressive disease	1%	5%
Nonevaluable	2%	4%
Minimal residual disease-negative	5%	4%

Grosicki S et al. *Lancet* 2020;396(10262):1563-73.

BOSTON: Select Adverse Events

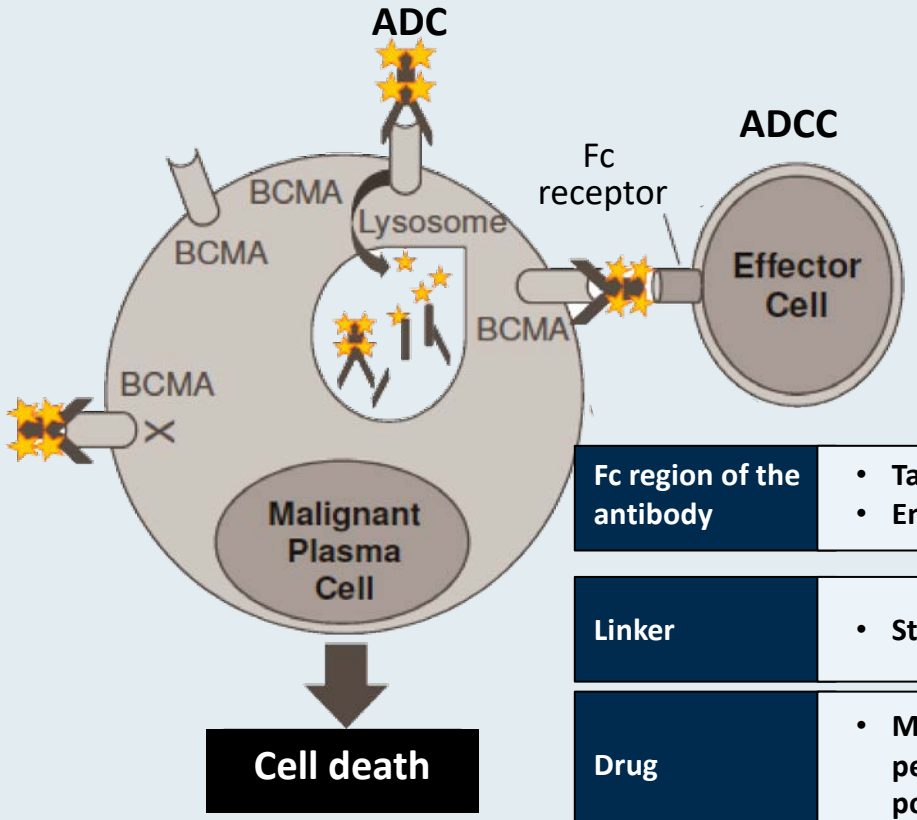
Adverse event	Selinexor + bort/dex (n = 195)		Bort/dex (n = 204)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Thrombocytopenia	60%	39%	27%	17%
Fatigue	42%	13%	18%	1%
Anemia	36%	16%	23%	10%
Peripheral neuropathy	32%	5%	47%	9%
Neutropenia	15%	9%	6%	3%
Treatment discontinuation due to TEAEs	21%		16%	

TEAEs = treatment emergent adverse events

Grosicki S et al. *Lancet* 2020;396(10262):1563-73.

Belantamab Mafodotin: Anti-BCMA Antibody-Drug Conjugate

- B-cell maturation factor (BCMA) expression is restricted to B cells at later stages of differentiation and is required for survival of plasma cells
- BCMA is broadly expressed at variable levels on malignant plasma cells
- Belantamab mafodotin is a humanized, afucosylated IgG1 anti-BCMA antibody conjugated to microtubule disrupting agent MMAF via a stable, protease-resistant maleimidocaproyl linker



Fc region of the antibody	• **Target specific** • **Enhanced ADCC**
Linker	• **Stable in circulation**
Drug	• **MMAF (non cell permeable, highly potent auristatin)**

Mechanisms of action:
- ADC mechanism
- ADCC mechanism
- Immunogenic cell death
- BCMA receptor signaling inhibition

ADC = antibody-drug conjugate; ADCC = antibody-dependent cell-mediated cytotoxicity

Tai YT et al. *Blood* 2014;123(20):3128-38.

Longer Term Outcomes With Single-Agent Belantamab Mafodotin in Patients With Relapsed or Refractory Multiple Myeloma: 13-Month Follow-Up From the Pivotal DREAMM-2 Study

Sagar Lonial, MD [1]; Hans C. Lee, MD[2]; Ashraf Badros, MD [3]; Suzanne Trudel, MD[4]; Ajay K. Nooka, MD [1]; Ajai Chari, MD [5]; Al-Ola Abdallah, MD[6]; Natalie Callander, MD[7]; Douglas Sborov, MD[8]; Attaya Suvannasankha, MD[9]; Katja Weisel, MD[10]; Peter M. Voorhees, MD[11]; Lynsey Womersley, MSc[12]; January Baron, MS[13]; Trisha Piontek, BSN[13]; Eric Lewis, MD[14]; Joanna Opalinska, MD[13]; Ira Gupta, MD[13]; and Adam D. Cohen, MD[15]

Cancer 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

DREAMM-2: Single-Agent Belantamab Mafodotin Efficacy Outcomes

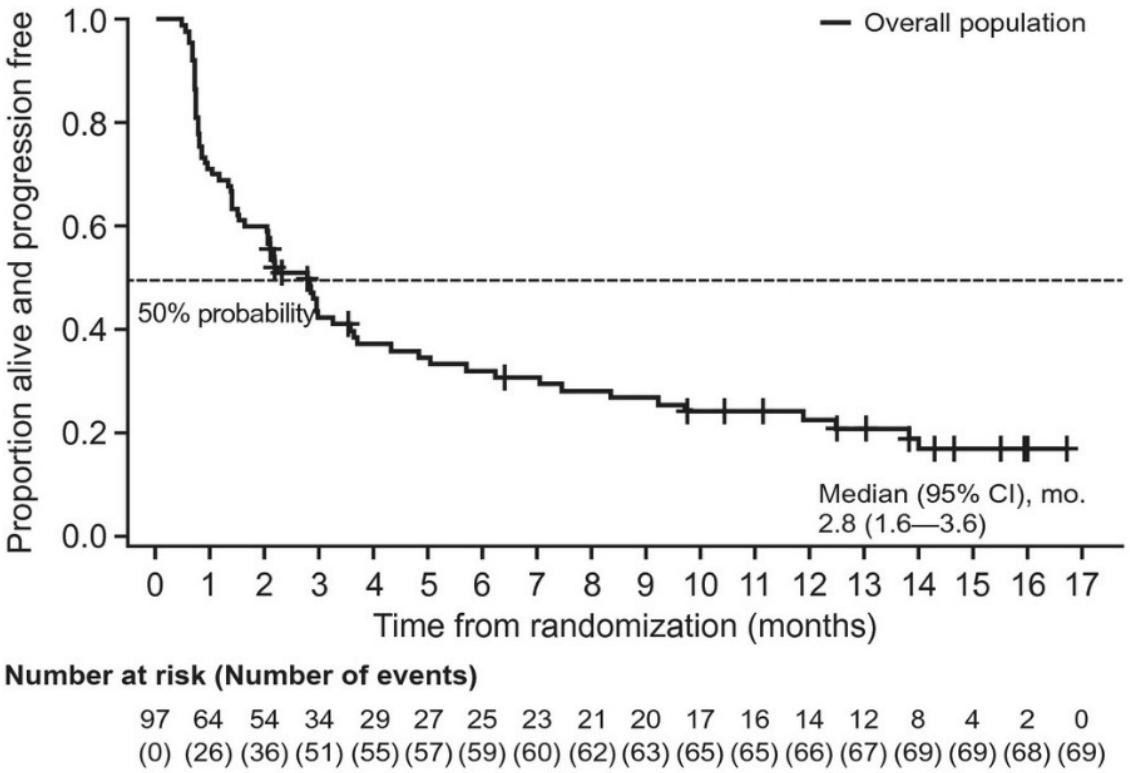
	Patients with 3-6 prior therapies (n = 47)	Patients with ≥7 prior therapies (n = 50)
ORR, % (97.5% CI)	32 (21.7-43.6)	30 (16.5-46.6)
Median DoR (95% CI estimates), months	11.0 (4.2-NR)	13.1 (4.0-NR)
Probability of DoR ≥6 months, % (95% CI estimates)	63 (31-83)	73 (44-89)
Median PFS (95% CI estimates), months	2.8 (1.6-3.6)	2.2 (1.2-3.6)
Probability of PFS at 6 months, % (95% CI estimates)	35 (20-50)	30 (17-43)

ORR = overall response rate; CI = confidence interval; DoR = duration of response; NR = not reached; PFS = progression-free survival

Lonial S et al. *Cancer* 2021;127(22):4198-212; ASH 2020;Abstract 1417.

DREAMM-2: Longitudinal Outcomes

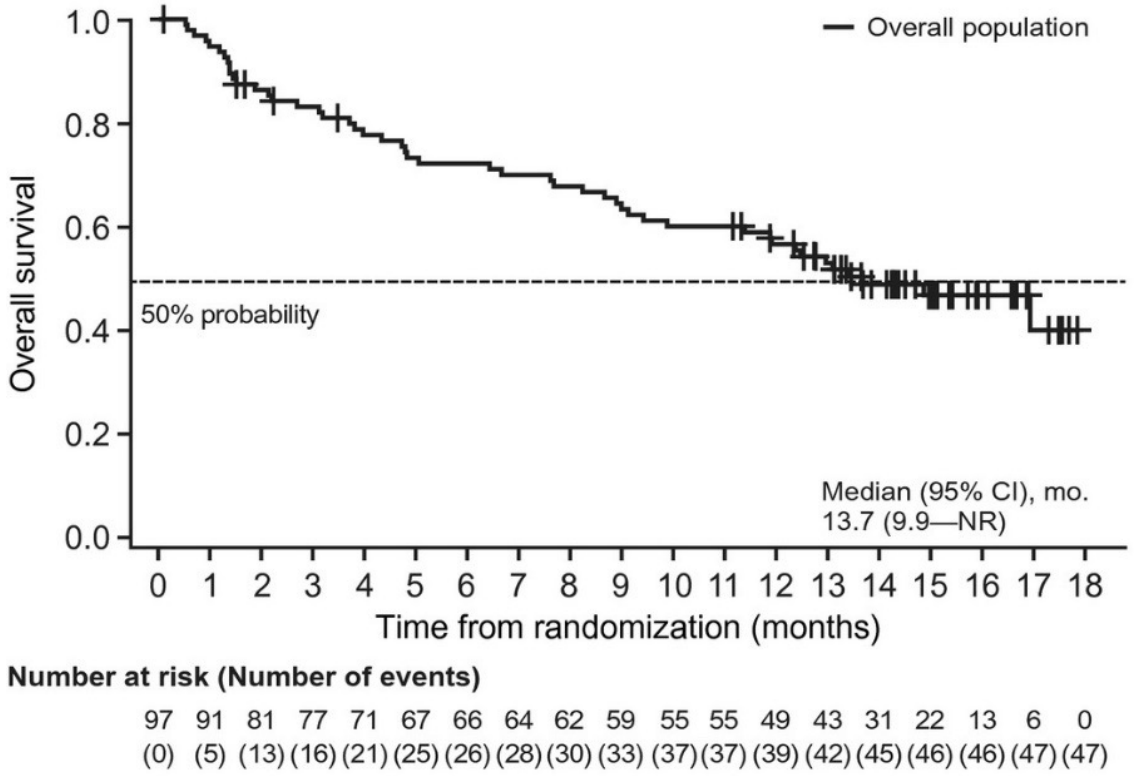
Progression-Free Survival



Number at risk (Number of events)

97	64	54	34	29	27	25	23	21	20	17	16	14	12	8	4	2	0
(0)	(26)	(36)	(51)	(55)	(57)	(59)	(60)	(62)	(63)	(65)	(65)	(66)	(67)	(69)	(69)	(68)	(69)

Overall Survival (OS)



Number at risk (Number of events)

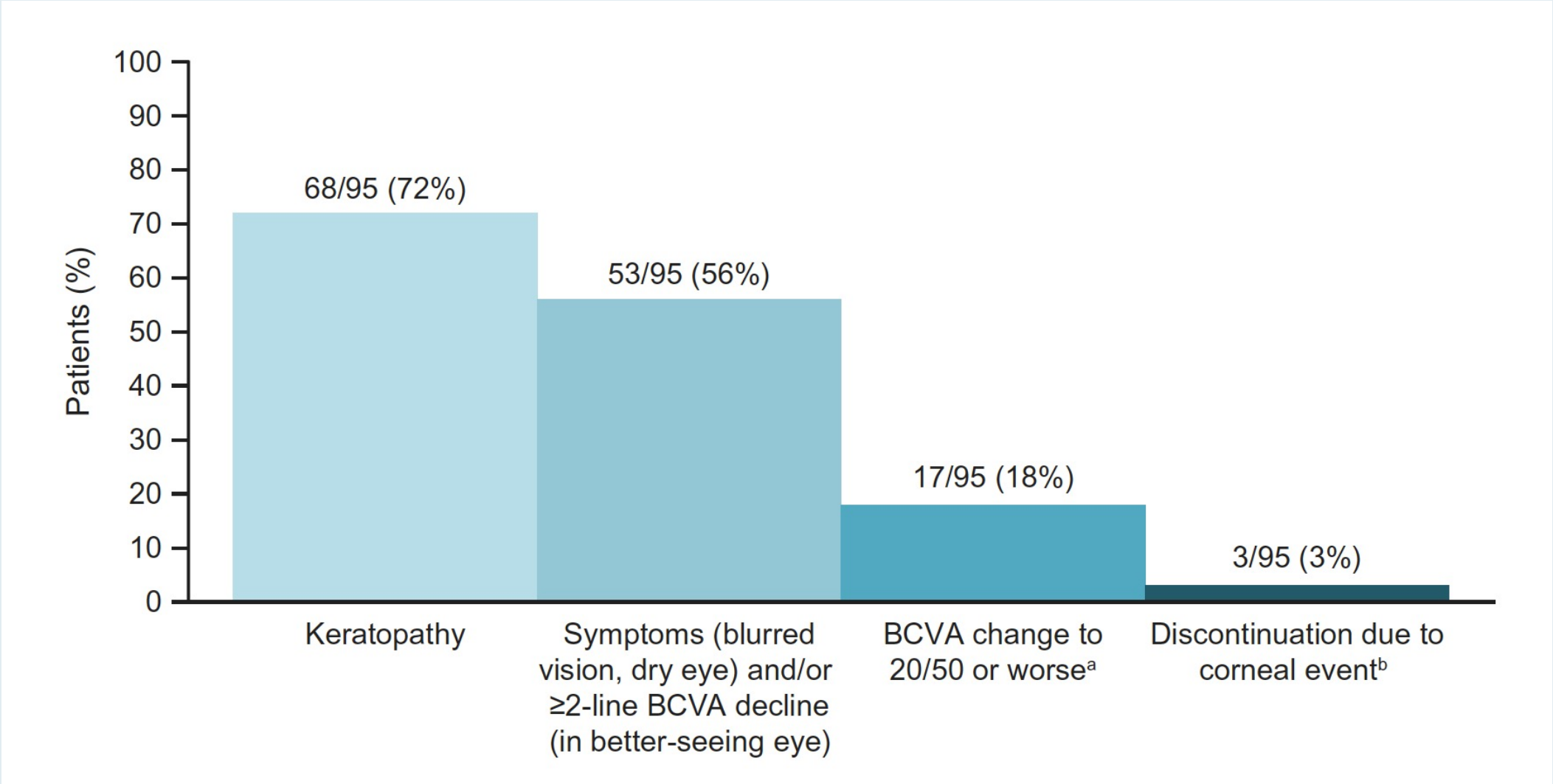
97	91	81	77	71	67	66	64	62	59	55	55	49	43	31	22	13	6	0
(0)	(5)	(13)	(16)	(21)	(25)	(26)	(28)	(30)	(33)	(37)	(37)	(39)	(42)	(45)	(46)	(46)	(47)	(47)

Expected median OS in triple-class refractory myeloma: 8.6 months

Lonial S et al. *Cancer* 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

DREAMM-2: Frequency of Corneal and Vision-Related Events



BCVA = best corrected visual acuity

Lonial S et al. *Cancer* 2021;127(22):4198-212.

RTP RESEARCH TO PRACTICE

Summary of Select Clinical Trials of Belantamab Mafodotin (Belamaf) Combination Approaches for R/R Multiple Myeloma

Trial	Characteristics	ORR	Safety
DREAMM-6 (NCT03544281)	• Phase I/II • Arm A: belamaf + len/dex (n = 45) • Arm B: belamaf +bor/dex (n = 18)	• Arm A: highest ORR of 75% in the 1.9 mg/kg Q4W dose • Arm B: 78%	Arm A Grade ≥3 AEs: • Thrombocytopenia – 3 (7%) • Keratopathy – 15 (33%) Arm B Grade ≥3 AEs: • Thrombocytopenia – 12 (67%) • Keratopathy – 11 (61%)
DREAMM-4 (NCT03848845)	▪ Phase I/II (N = 34) ▪ Belamaf + pembrolizumab ▪ Dose escalation belamaf 2.5 mg/kg and 3.4 mg/kg	• 47% at RP2D of 2.5 mg/kg	All grades: • Thrombocytopenia – 12 (35%) • Keratopathy – 26 (76%)
ALGONQUIN (NCT03715478)	▪ Phase I/II (N = 56) ▪ Belamaf + pom/dex	• ≥PR/VGPR 89%/72% across all dosing cohorts	Grade ≥3 TEAEs: • Thrombocytopenia – 19 (34%) • Keratopathy – 39 (70%)

ORR = overall response rate; AEs = adverse events; PR = partial response; VGPR = very good partial response; TEAEs = treatment-emergent AEs

Popat R et al. ASH 2020;Abstract 1419; Quach H et al. ASCO 2022;Abstract 8017; Lonial S et al. SOHO 2022;Abstract MM-459; Suvannasankha A et al. EHA 2022;Abstract P940; Trudel S et al. ASH 2021;Abstract 2736.

Phase III DREAMM-3 Trial of Belantamab Mafodotin Monotherapy versus Pomalidomide in Combination with Low-Dose Dexamethasone Does Not Meet Its Primary Endpoint

Press Release: November 7, 2022

The DREAMM-3 Phase III open-label, randomized, head-to-head superiority trial of belantamab mafodotin monotherapy versus pomalidomide in combination with low dose dexamethasone (PomDex) for patients with relapsed or refractory multiple myeloma did not meet its primary endpoint of progression-free survival (PFS).

“In the DREAMM-3 trial, the primary endpoint of PFS demonstrated a hazard ratio of 1.03 (95% CI: 0.72, 1.47). The observed median progression-free survival was longer for belantamab mafodotin vs PomDex (11.2 months vs 7 months).”

“Data from DREAMM-3 is in the process of being shared with health authorities. Discussions with health authorities are currently ongoing. Additional trials within the DREAMM (DRiving Excellence in Approaches to Multiple Myeloma) clinical trial programme will continue.”

“Data from the DREAMM-7 and DREAMM-8 phase III trials are anticipated in the first half of 2023.”

https://www.gsk.com/en-gb/media/press-releases/gsk-provides-update-on-dreamm-3-phase-iii-trial-for-blenrep/

BelaRd: Results Summary from a Phase I/II Study of Belantamab Mafodotin with Lenalidomide/Dexamethasone for Newly Diagnosed, Transplant-Ineligible MM

Clinical response, n (%)	All patients	Cohort 1 Belamaf 2.5 mg/kg	Cohort 2 Belamaf 1.9 mg/kg	Cohort 3 Belamaf 1.4 mg/kg
Evaluable patients	28	9	9	10
Overall response rate	27 (96.4%)	9 (100.0%)	9 (100.0%)	9 (90%)
CR	4 (14.3%)	2 (22.2%)	2 (22.2%)	—
VGPR	10 (35.7%)	4 (44.4%)	2 (22.2%)	4 (40%)
Select Grade 3/4 AEs	**N = 36**	**n = 12**	**n = 12**	**n = 12**
Leukopenia	2 (5.6%)	2 (16.7%)	—	—
Neutropenia	2 (5.6%)	1 (8.3%)	—	1 (8.3%)
Keratopathy	—	—	—	—
Ocular symptoms	—	—	—	—
Visual acuity reduced	5 (13.9%)	3 (25%)	1 (8.3%)	—

CR = complete response; VGPR = very good partial response

Terpos E et al. EHA 2022;Abstract S178.

DREAMM-9: Efficacy and Safety Summary with Belantamab Mafodotin and Standard Therapy (VRd) for Newly Diagnosed MM

Clinical response, n (%)	Cohort 1 Belamaf 1.9 mg/kg q3 or 4wk, every cycle of VRd n = 12	Cohort 2 Belamaf 1.4 mg/kg q6 or 8wk, every other cycle of VRd n = 12	Cohort 3 Belamaf 1.9 mg/kg q6 or 8wk, every other cycle of VRd n = 12	Cohort 4 Belamaf 1.0 mg/kg q3 or 4wk, every cycle of VRd n = 15	Cohort 5 Belamaf 1.4 mg/kg q3 or 4wk, every cycle of VRd n = 13
ORR	12 (100%)	11 (92%)	12 (100%)	12 (80%)	12 (92%)
sCR	6 (50%)	1 (8%)	0	3 (20%)	2 (15%)
CR	3 (25%)	0	2 (17%)	2 (13%)	1 (8%)
VGPR	3 (25%)	9 (75%)	7 (58%)	5 (33%)	8 (62%)
Adverse events	**n = 12**	**n = 12**	**n = 12**	**n = 14**	**n = 13**
Grade 3/4 corneal exam findings	9 (75%)	4 (33%)	3 (25%)	7 (50%)	5 (39%)
Grade 3/4 visual acuity changes	10 (83%)	7 (58%)	4 (33%)	3 (21%)	6 (46%)

VRd = bortezomib/lenalidomide/dexamethasone; ORR = overall response rate; CR = complete response; sCR = stringent CR; VGPR = very good partial response

Usmani SZ et al. EHA 2022;Abstract P942.

Clin Lymphoma Myeloma Leuk 2021 November;21(11):752-65.

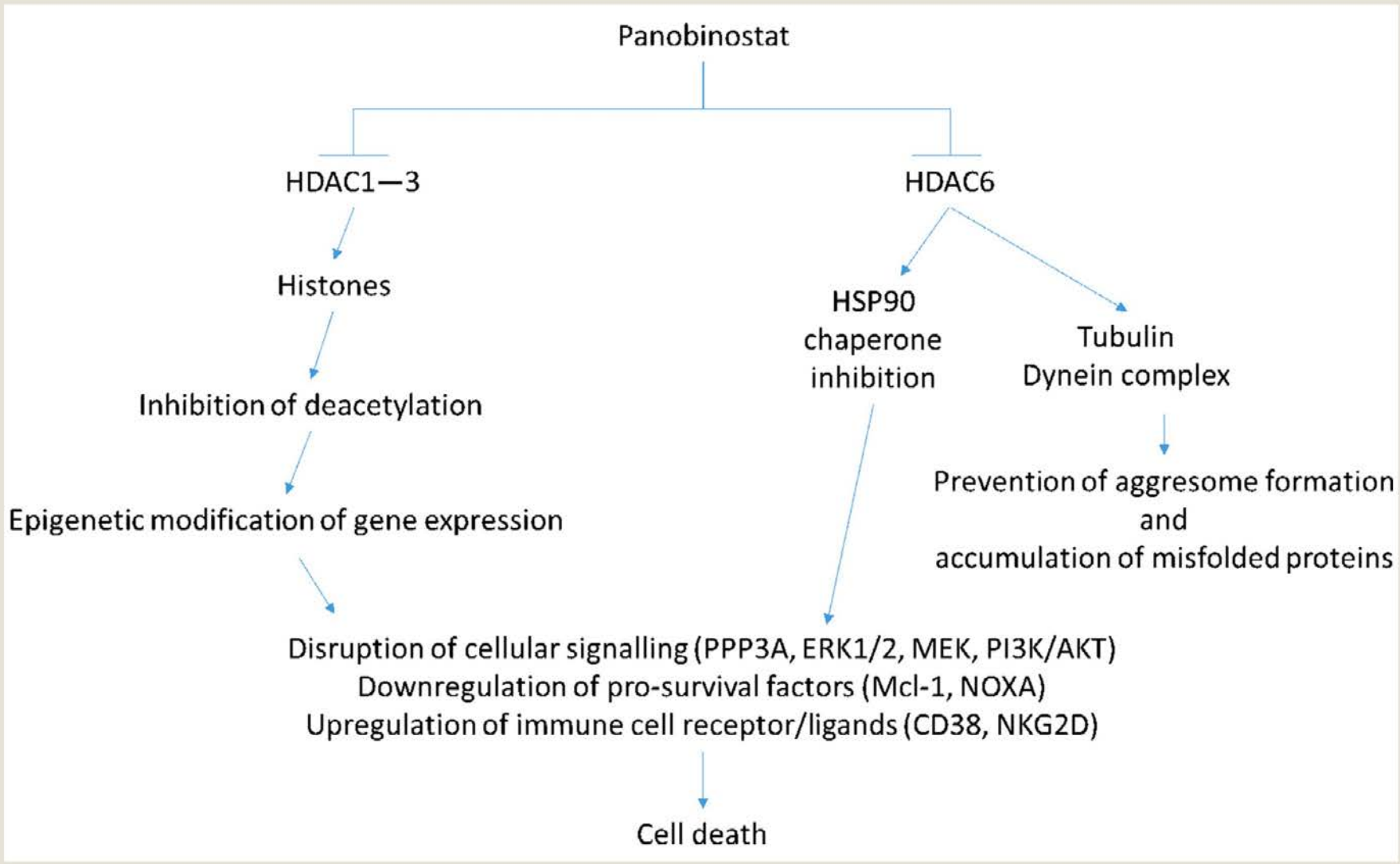
Review Article

Panobinostat From Bench to Bedside: Rethinking the Treatment Paradigm for Multiple Myeloma

Jesus G. Berdeja, MD,[1,2] Jacob P. Laubach, MD, MPP,[3] Joshua Richter, MD,[4] Steve Stricker, PharmD, MS,[5] Andrew Spencer, MBBS,[6] Paul G. Richardson, MD,[3] Ajai Chari, MD[4]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

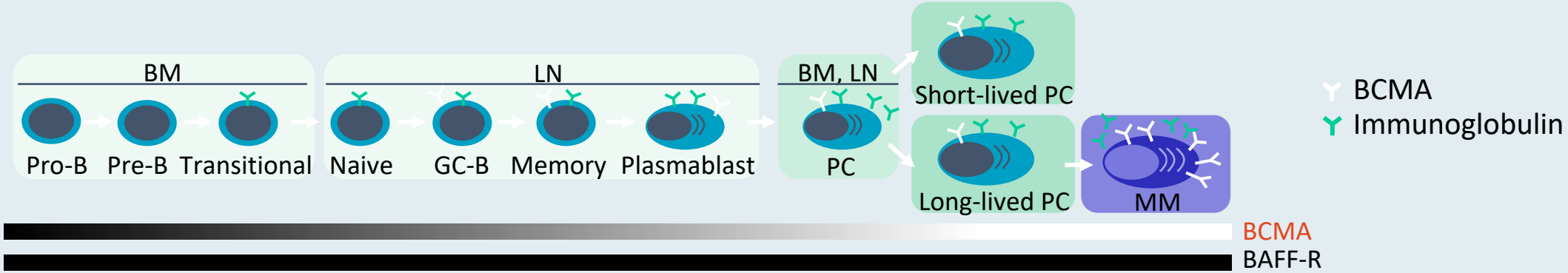
Examples of the Antimyeloma Effects of Panobinostat Treatment

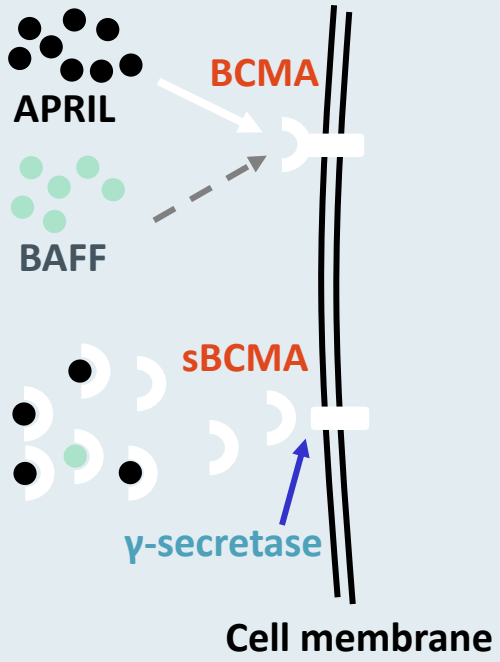


Berdeja JG et al. *Clin Lymphoma Myeloma Leuk* 2021 November;21(11):752-65.

Incorporation of Chimeric Antigen Receptor (CAR) T-Cell Therapy into the Care of Patients with MM

BCMA as a Target in Myeloma Treatment





- **BCMA: antigen expressed specifically on PCs and myeloma cells**
- **Higher expression on myeloma cells than normal PCs**
- **Not expressed in other tissues**

- **Cell-surface receptor in TNF superfamily**
- **Receptor for APRIL and BAFF**
- **Key role in B-cell maturation and differentiation**
- **Promotes myeloma cell growth, chemotherapy resistance, immunosuppression in bone marrow microenvironment**

Cho S-F et al. *Front Immunol* 2018;9:1821. Moreaux J et al. *Blood* 2004;103(8):3148-57. Sanchez E at al. *Br J Haematol* 2012;158(6):727-38.

Content courtesy of Jesús G Berdeja, MD

RTP RESEARCH TO PRACTICE

Select Clinical Trials of BCMA-Directed CAR T-Cell Therapy for Multi-Agent Refractory Multiple Myeloma: Efficacy Summary

	KarMMa (N = 128)	CARTITUDE-1 (N = 97)	CRB-402 (N = 72)
Phase	II	Ib/II	I/II
Product	Ide-cel	Cilta-cel	BB21217
Median prior lines of therapy	6	6	6
Overall response rate	73%	98%	69%
Complete response	33%	sCR: 83%	sCR/CR: 36%
MRD-negative	26%	92%	67%
Median PFS	8.6 months	Not reached	Not applicable
Median OS	24.8 months	Not reached	Not applicable

Anderson LD et al. ASCO 2021;Abstract 8016. Usmani SZ et al ASCO 2022;Abstract 8028. Martin T et al. *J Clin Oncol* 2022 June 4;[Online ahead of print]. Raje N et al. ASH 2021;Abstract 548. Mateos M-V et al. 2022 ASCO Educational Book.

Select Clinical Trials of BCMA-Directed CAR T-Cell Therapy for Multi-Agent Refractory Multiple Myeloma: CRS and Neurotoxicity

	KarMMa (N = 128)	CARTITUDE-1 (N = 97)	CRB-402 (N = 72)
Product	Ide-cel	Cilta-cel	BB21217
Median prior lines of therapy	6	6	6
CRS	Grade 3: 4%	Grade 3/4: 4%	Grade 3/4: 1%
Neurotoxicity	Grade 3: 3%	Grade 3/4: 11%	Grade 3/4: 4%

CRS = cytokine release syndrome

Anderson LD et al. ASCO 2021;Abstract 8016. Usmani SZ et al ASCO 2022;Abstract 8028. Martin T et al. *J Clin Oncol* 2022 June 4;[Online ahead of print]. Raje N et al. ASH 2021;Abstract 548. Mateos M-V et al. 2022 ASCO Educational Book.

Topline Results from the KarMMa-3 Trial Showing Ide-cel Significantly Improves Progression-Free Survival versus Standard Regimens for Relapsed and Refractory Multiple Myeloma

Press Release: August 10, 2022

Positive topline results were announced from KarMMa-3, a Phase III, global, randomized, multicenter, open-label study evaluating idecabtagene vicleucel compared to standard combination regimens for adults with multiple myeloma that is relapsed and refractory after 2 to 4 prior lines of therapy and refractory to the last regimen.

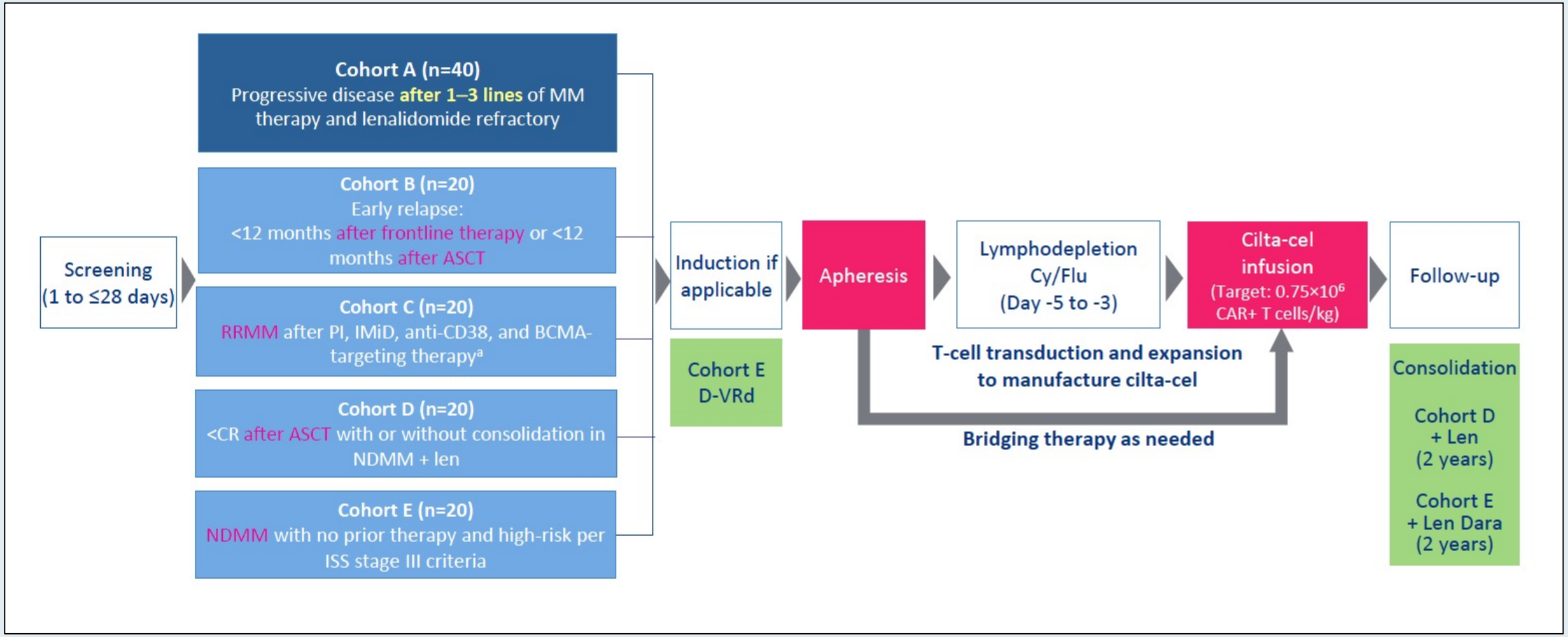
"KarMMa-3 is the first randomized clinical trial to evaluate a CAR T cell therapy in multiple myeloma. Results of a pre-specified interim analysis conducted through an independent review committee showed that KarMMa-3 met its primary endpoint of demonstrating a statistically significant improvement in progression-free survival. Treatment with idecabtagene vicleucel also showed an improvement in the key secondary endpoint of overall response rate compared to standard regimens. Follow-up for overall survival, a key secondary endpoint, remains ongoing.

Safety results in the trial were consistent with the well-established and predictable safety profile of idecabtagene vicleucel previously demonstrated in the pivotal KarMMa trial. No new safety signals were reported in this study."

https://news.bms.com/news/corporate-financial/2022/Bristol-Myers-Squibb-and-2seventy-bio-Announce-Topline-Results-from-KarMMa-3-Trial-Showing-Abecma-idecabtagene-vicleucel-Significantly-Improves-Progression-Free-Survival-Versus-Standard-Regimens-in-Relapsed-and-Refractory-Multiple-Myeloma/default.aspx

RTP RESEARCH TO PRACTICE

CARTITUDE-2 Multicohort Overall Trial Design



Agha M et al. EHA 2021;Abstract S190.

ASCO 2022; Abstract 8020.

Biological Correlative Analyses and Updated Clinical Data of Ciltacabtagene Autoleucel, a BCMA-Directed CAR-T Cell Therapy, in Lenalidomide-Refractory Patients With Progressive Multiple Myeloma After 1–3 Prior Lines of Therapy: CARTITUDE-2, Cohort A

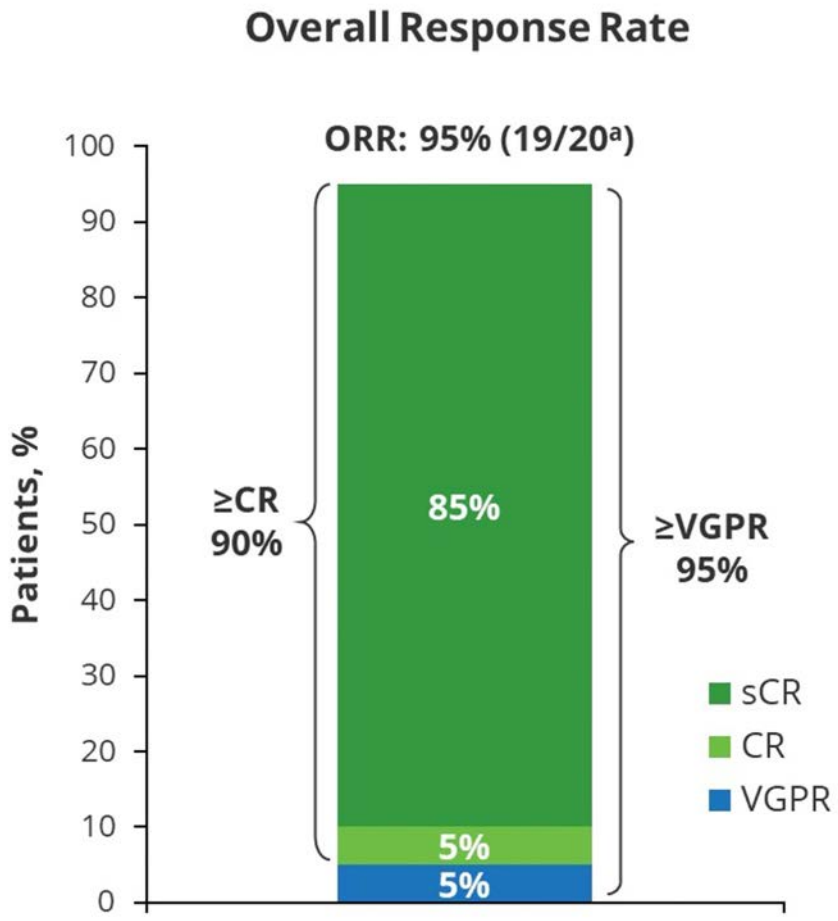
Hermann Einsele[1], Adam Cohen[2], Michel Delforge[3], Jens Hillengass[4], Hartmut Goldschmidt[5], Katja Weisel[6], Marc-Steffen Raab[7], Christoph Scheid[8], Jordan M Schecter[9], Kevin De Braganca[9], Helen Varsos[9], Tzu-Min Yeh[9], Pankaj Mistry[10], Tito Roccia[9], Christina Corsale[9], Muhammad Akram[11], Lida Pacaud[11], Tonia Nesheiwat[11], Mounzer Agha[12], Yael Cohen[13]

[1]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany; [2]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [3]University Hospitals (UZ) Leuven, Leuven, Belgium; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; [5]University Hospital Heidelberg and National Center of Tumor Diseases, Heidelberg, Germany; [6]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [7]University Hospital Heidelberg and Clinical Cooperation Unit Molecular Hematology/Oncology, German Cancer Research Center, Heidelberg, Germany; [8]University of Cologne, Cologne, Germany; [9]Janssen Research & Development, Raritan, NJ, USA; [10]Janssen Research & Development, High Wycombe, UK; [11]Legend Biotech USA, Piscataway, NJ, USA; [12]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [13]Tel-Aviv Sourasky (Ichilov) Medical Center, and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting; June 3-7, 2022; Chicago, IL, USA & Virtual.

RTP RESEARCH TO PRACTICE

CARTITUDE-2 Cohort A: Ciltacabtagene Autoleucel for Lenalidomide-Refractory MM After 1 to 3 Prior Lines of Therapy



AEs ≥20%, n (%)	N=20	
	Any Grade	Grade 3/4
Hematologic		
Neutropenia	19 (95)	19 (95)
Thrombocytopenia	16 (80)	7 (35)
Anaemia	15 (75)	9 (45)
Lymphopenia	14 (70)	14 (70)
Leukopenia	11 (55)	11 (55)
CAR-T–related AEs		
CRS	19 (95)	2 (10)
Neurotoxicity	6 (30)	1 (5)
ICANS	3 (15)	0
Other	3 (15)[a]	1 (5)

Einsele H et al. ASCO 2022;Abstract 8020.

RTP RESEARCH TO PRACTICE

ASCO 2022 | Abstract 8029

Biological Correlative Analyses an Updated Clinical Data of Ciltacabtagene Autoleucel, A BCMA-Directed CAR-T Cell Therapy, in Patients with Multiple Myeloma and Early Relapse After Initial Therapy: CARTITUDE-2, Cohort B

Niels WCJ van de Donk[1] (n.vandedonk@amsterdamumc.nl), Mounzer Agha[2], Adam Cohen[3], Yael Cohen[4], Sébastien Anguille[5], Tessa Kerre[6], Wilfried Roeloffzen[7], Jordan M Schecter[8], Kevin De Braganca[8], Helen Varsos[8], Pankaj Mistry[9], Tito Roccia[8], Enrique Zudaire[10], Christina Corsale[8], Muhammad Akram[11], Dong Geng[11], Tonia Nesheiwat[11], Lida Pacaud[11], Pieter Sonneveld[12], Sonja Zweegman[1]

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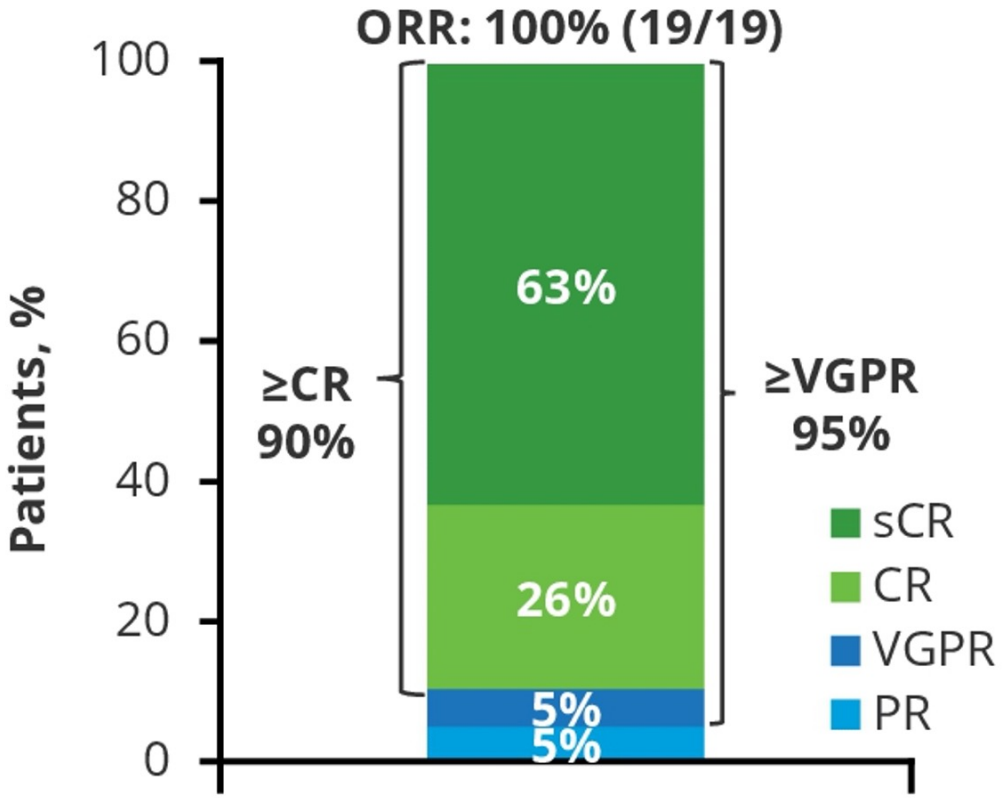
CARTITUDE-2 (Cohort B): Ciltacabtagene Autoleucel for Patients with Multiple Myeloma and Early Relapse After Initial Therapy



AEs ≥20%, n (%)	N=19	
	Any Grade	Grade 3/4
Hematologic		
Neutropenia	18 (95)	17 (90)
Anemia	11 (58)	9 (47)
Thrombocytopenia	11 (58)	5 (26)
Lymphopenia	6 (32)	6 (32)
Leukopenia	5 (26)	5 (26)
CAR-T–related AEs		
CRS	16 (84)	1 (5)
Neurotoxicity	5 (26)	1 (5)
ICANS	1 (5)	0
Other	4 (21)	1 (5)
Parkinsonism	1 (5)	1 (5)

van de Donk N WCJ et al. ASCO 2022;Abstract 8029.

CAR T-Cell-Associated Toxicities: Acute and Late Phase

Acute Phase (Days 0-30)

- Cytokine release syndrome (CRS)
- Immune effector cell-associated neurotoxicity syndrome (ICANS)
- Cytopenias
- B-cell aplasia and hypogammaglobulinemia
- Tumor lysis syndrome (rare and likely varies by disease burden)

Late Phase (Days 30+)

- Persistent cytopenias
- B-cell aplasia and hypogammaglobulinemia
- T-cell deficiency
- Residual effects of acute toxicity
- Delayed CRS and ICANS is rare but can occur
- Impairment to QoL – fatigue, memory issues not yet well described

Content courtesy of Jesús G Berdeja, MD

Cytokine Release Syndrome Associated with CAR T-Cell Therapy for Multiple Myeloma

- Potentially severe or life-threatening reactions, with the most common manifestations being pyrexia, hypotension, tachycardia, chills, hypoxia, fatigue and headache
- Grade 3 or higher events may include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, acute respiratory distress syndrome, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, multiple organ dysfunction syndrome and hemophagocytic lymphohistiocytosis/macrophage activation syndrome
- Occurs in about 85%-95% of patients (Grade ≥3: 5%-9%)
- Time to onset: 1-7 days (range 1-23 days)
- Duration: 4-7 days (range 1-63 days)
- Manage with tocilizumab or tocilizumab and corticosteroids

www.carvyktihcp.com/safety; www.abecmahcp.com/safety/

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ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome) Associated with CAR T-Cell Therapy for MM

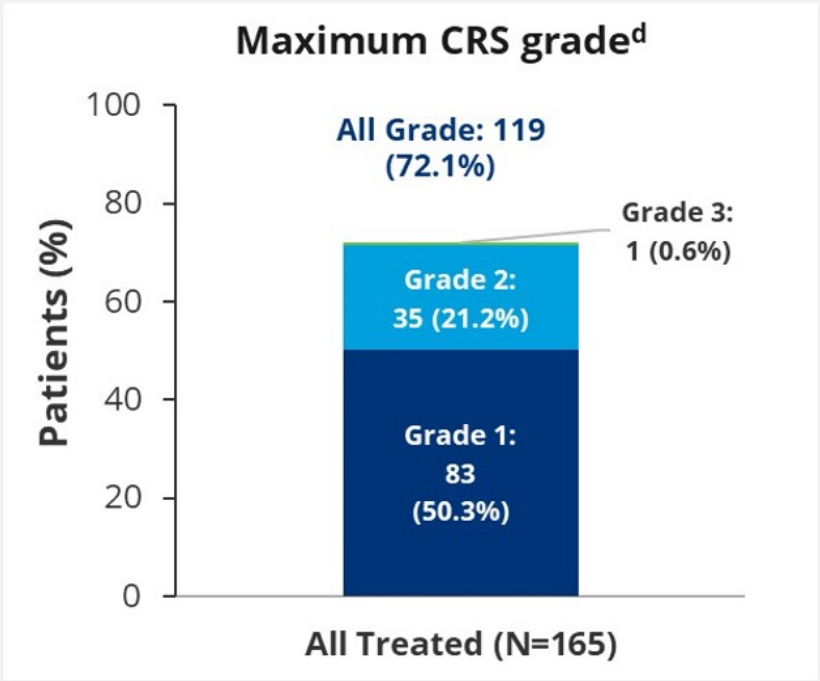
- Potentially severe or life-threatening neurotoxicity, including encephalopathy, tremor, aphasia and delirium.
- Occurs in about 25% of patients (Grade ≥3: 4%-5%)
- Time to onset: 2 to 8 days (range 1-42 days)
- Duration: 6 to 8 days (range 1-578 days)
- Resolved in 77% to 92% of patients
- Manage with supportive care and corticosteroids as needed

www.carvyktihcp.com/safety; www.abecmahcp.com/safety/

Novel Investigational Agents for MM

MajesTEC-1: Cytokine Release Syndrome

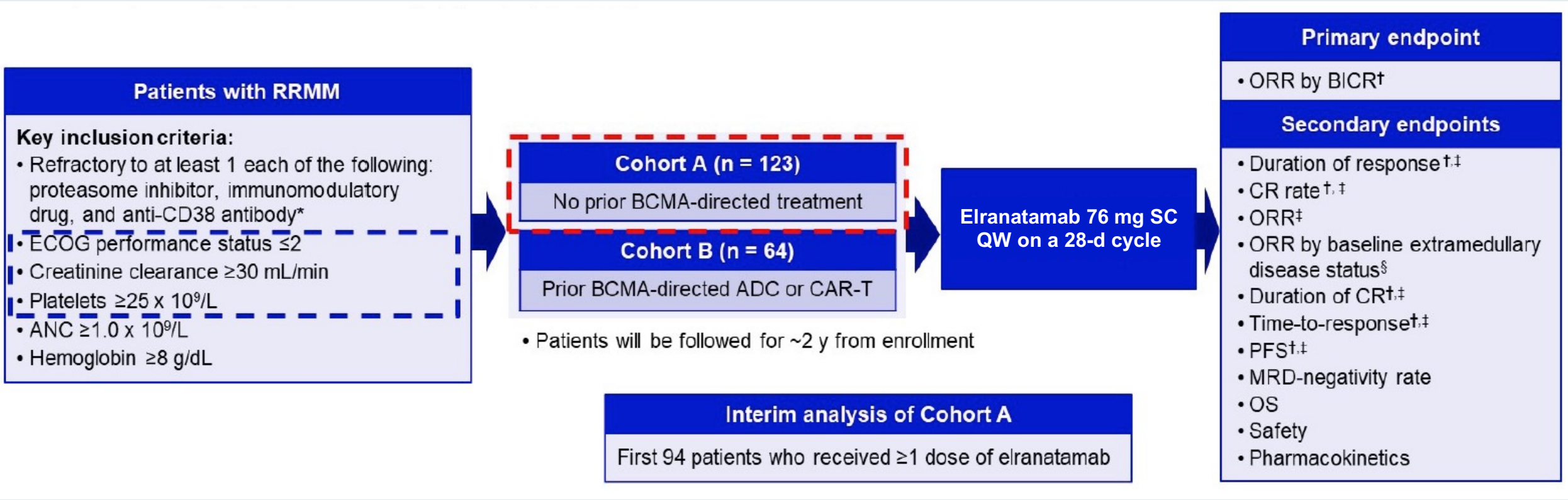
Parameter	N=165
Patients with CRS, n (%)	119 (72.1)
Patients with ≥2 CRS events	55 (33.3)
Time to onset[a] (days), median (range)	2 (1–6)
Duration (days), median (range)	2 (1–9)
Received supportive measures[a] for CRS, n (%)	110 (66.7)
Tocilizumab[b]	60 (36.4)
Low-flow oxygen by nasal cannula[c]	21 (12.7)
Corticosteroids	14 (8.5)
Single vasopressor	1 (0.6)



- Most CRS events were confined to step-up and first full treatment doses
- All CRS events were grade 1/2, except for 1 transient-grade 3 CRS event that occurred in the context of concurrent pneumonia (resolved in 2 days)
- All CRS events fully resolved without treatment discontinuation or dose reduction

Nooka AK et al. ASCO 2022;Abstract 8007.

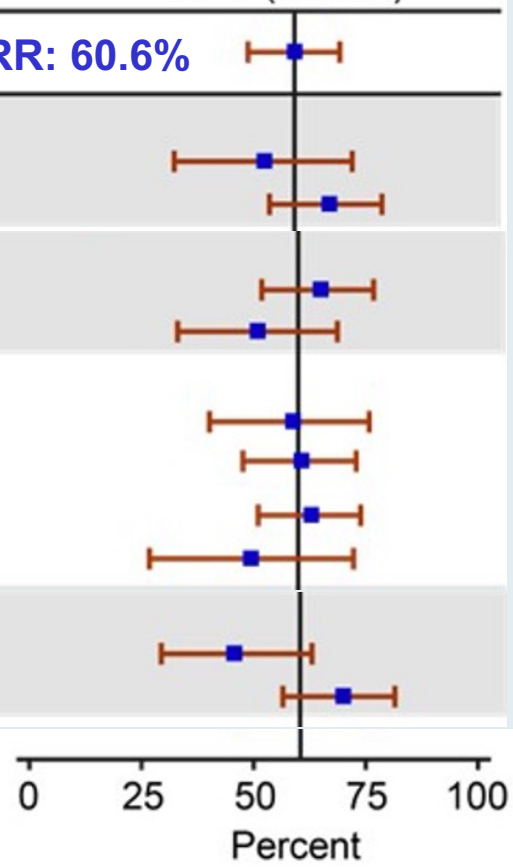
MagnetisMM-3: Phase II Trial Design



Lesokhin AM et al. ASCO 2022;Abstract 8006.

MagnetisMM-3: Overall Response Rate (All and Subgroups)

Subgroup	Patients (N)	ORR (95% CI)
All Patients	94	ORR: 60.6%
Baseline Cytogenetics		
High Risk	26	
Not High-Risk	57	
Number of Prior Lines		
≤5	61	
>5	33	
Age (Years)		
<65	32	
≥65	62	
<75	74	
≥75	20	
Penta Refractory		
Yes	37	
No	57	



Lesokhin AM et al. ASCO 2022;Abstract 8006.

MagnetisMM-3 AEs of Special Interest: Infections

n (%)	Cohort A n = 94	
	Any grade	Grade 3/4
Infection TEAEs in ≥5% of patients		
COVID-related AE	14 (14.9)	8 (8.5)
Upper respiratory tract infection	10 (10.6)	0
Pneumonia	8 (8.5)	4 (4.3)
Urinary tract infection	5 (5.3)	2 (2.1)
TEAEs of interest		
Pneumocystis jirovecii pneumonia	4 (4.3)	3 (3.2)
CMV infection	4 (4.3)	0
CMV infection reactivation	1 (1.1)	0

- Infections reported in 52.1%
  - Grade 3/4: 22.3%
  - Treatment-related: 24.5%
- 1 patient had an infection leading to permanent discontinuation of elranatamab

Lesokhin AM et al. ASCO 2022;Abstract 8006.

MagnetisMM-3 AEs of Special Interest: Peripheral Neuropathy

Peripheral neuropathy, n (%)	Cohort A n = 94	
	Any grade	Grade 3/4
All causality	15 (16.0)	1 (1.1)
Treatment-related	5 (6.4)	1 (1.1)

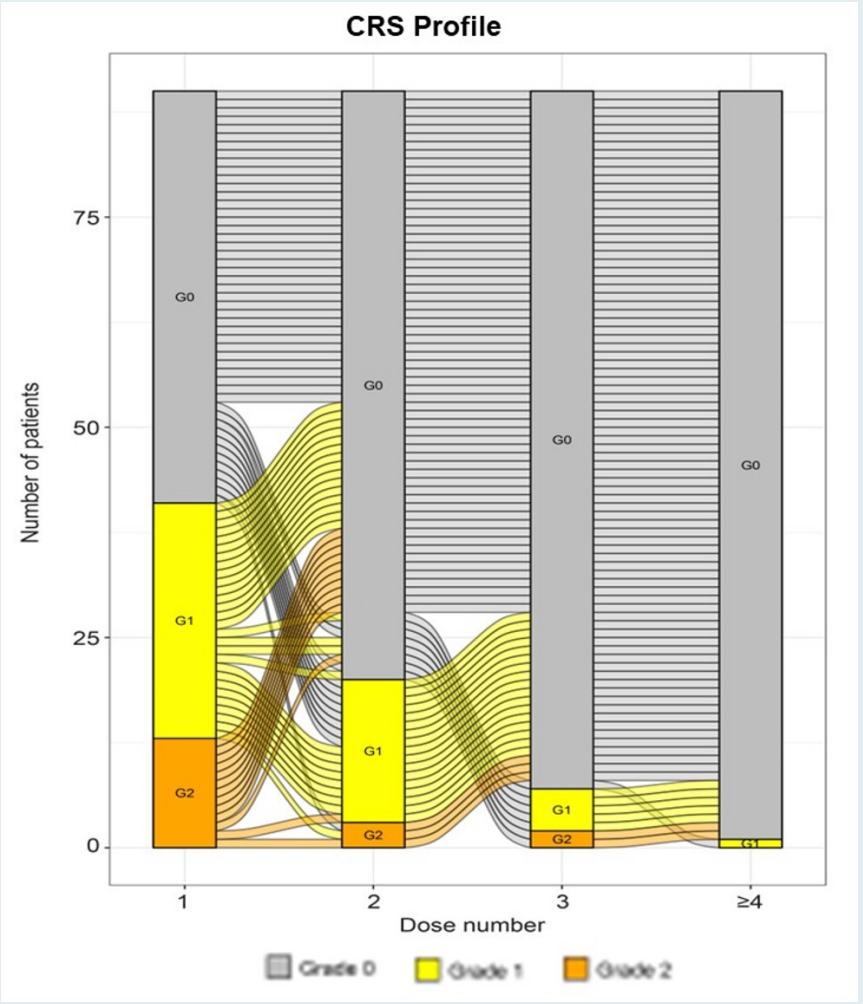
- Most common events (≥2% of patients) were peripheral sensory neuropathy (5.3%) and paresthesia (3.2%). All were grade 1/2, except for 1 patient with grade 3 motor neuropathy
- Two (2.1%) patients had peripheral neuropathy events that led to permanent discontinuation of elranatamab
- A medical history of peripheral neuropathy was reported by 7/15 (46.7%) patients with peripheral neuropathy events

Lesokhin AM et al. ASCO 2022;Abstract 8006.

MagnetisMM-3 AEs of Special Interest: CRS and ICANS

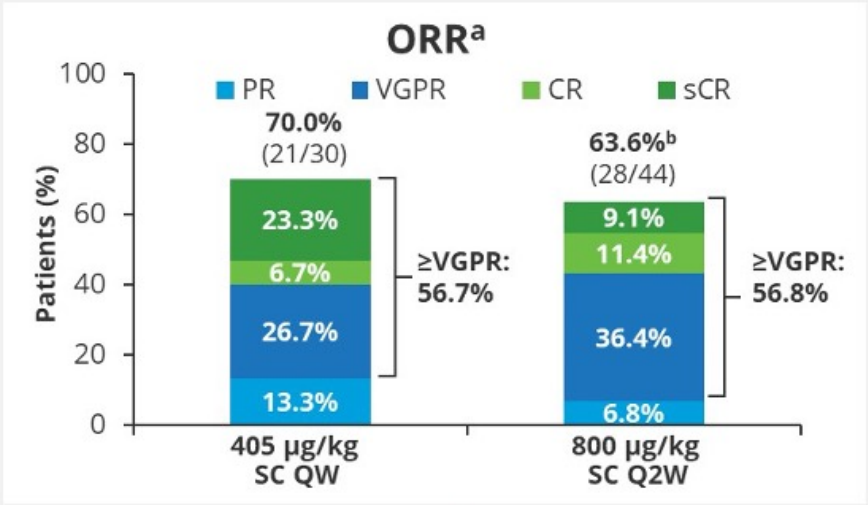
- The 2-step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable with 88.4% of events after the first 2 doses and 98.6% after the first 3 doses

TEAE of special interest	12/32 mg 2-step-up regimen n = 90*	
	CRS	ICANS
Patients with TEAE, n (%)	53 (58.9)	2 (2.2)
Maximum grade 1	36 (40.0)	0
Maximum grade 2	17 (18.9)	2 (2.2)
Patients with >1 TEAE, n (%)	16 (17.8)	1 (1.1)
Median time to onset of TEAE, days (range)	2.0 (1.0–9.0)	2.5 (1.0–4.0)
Median time to resolution of TEAE, days (range)	2.0 (1.0–19.0)	3.0 (2.0–6.0)
Patients with TEAE who received tocilizumab† or steroids, n (%)	26 (49.1)	2 (100)
Tocilizumab	24 (45.3)	2 (100)
Steroids	7 (13.2)	2 (100)
Permanent discontinuation due to AE, n (%)	0	0

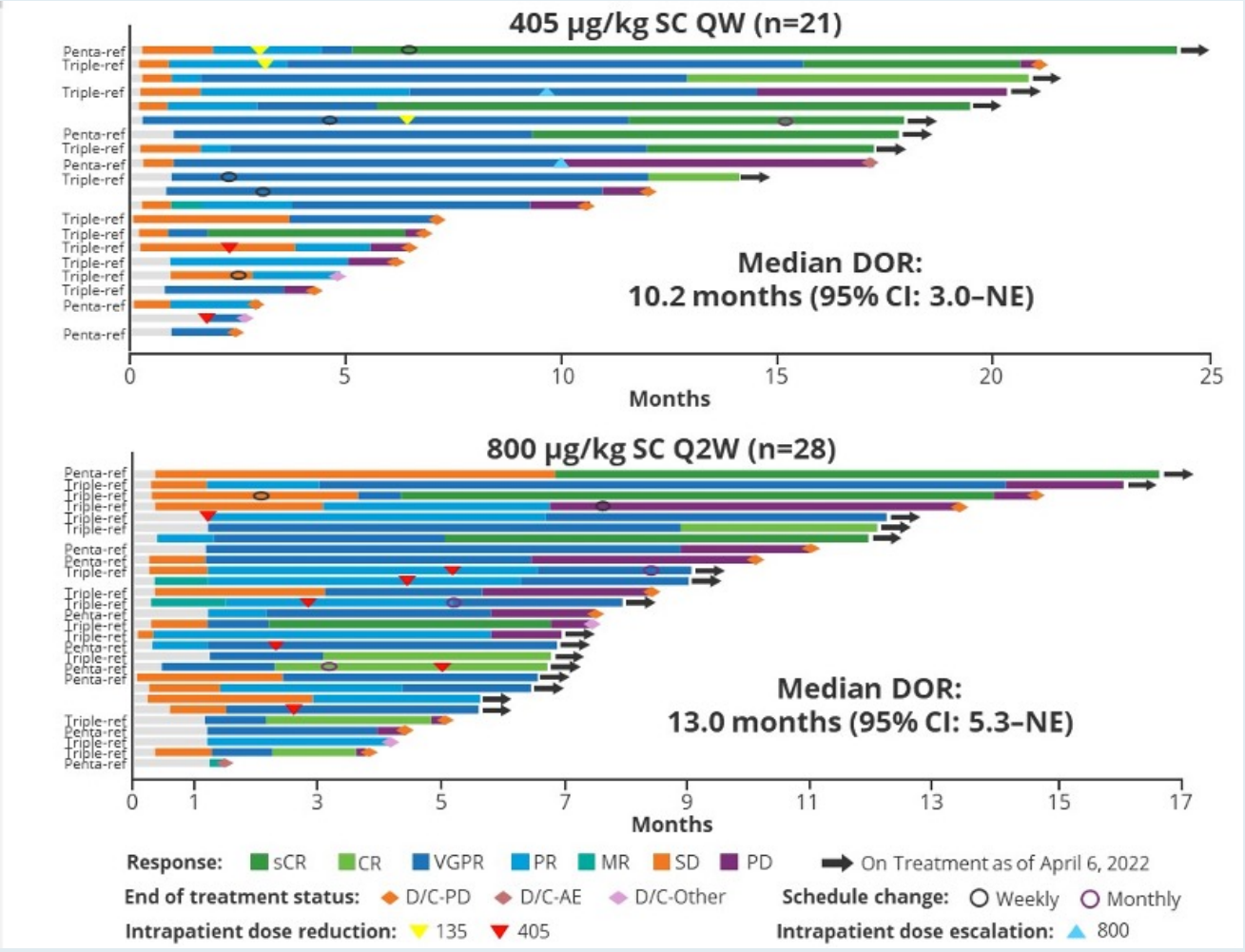


Lesokhin AM et al. ASCO 2022;Abstract 8006.

MonumenTAL-1: Duration of Response with Talquetamab for R/R MM



Response	405 µg/kg SC QW[c] n=30	800 µg/kg SC Q2W[c] n=44
Median follow-up (months), median (range)	13.2 (1.1–24.0)	7.7 (0.7–16.0)
ORR[a], n (%)	21 (70.0)	28 (63.6)
Triple-class–refractory patients, n/N (%)	15/23 (65.2)	23/34 (67.6)
Penta-drug–refractory patients, n/N (%)	5/6 (83.3)	9/12 (75.0)
Median time to first confirmed response (months), median (range)	0.9 (0.2–3.8)	1.2 (0.3–6.8)



Minnema MC et al. ASCO 2022;Abstract 8015.

MonumenTAL-1: Adverse Events with Talquetamab

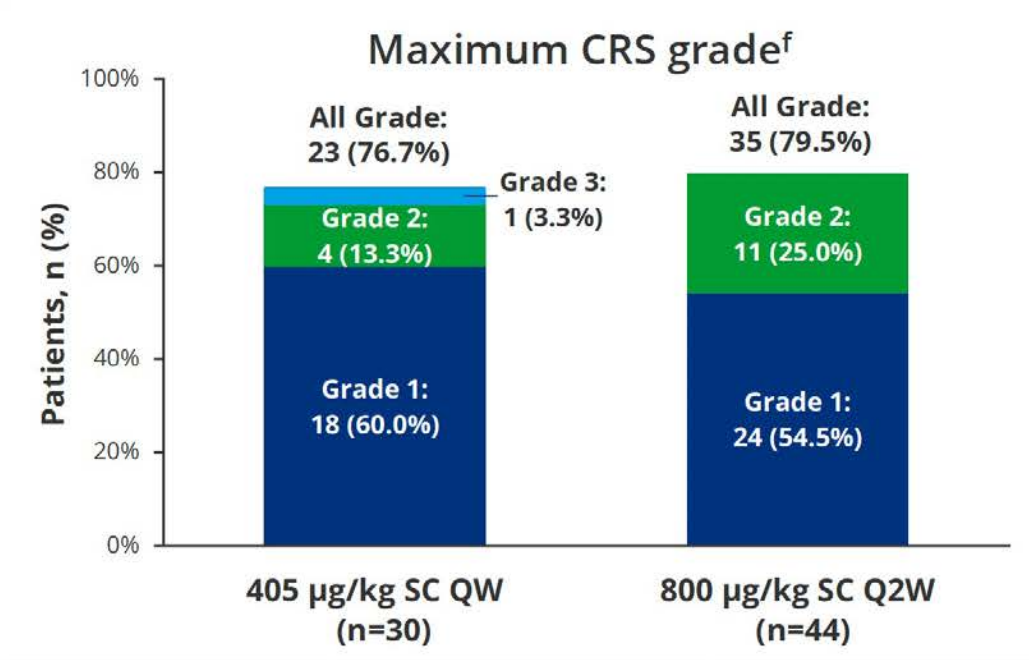
AEs (≥20% of total SC population), n (%)	405 µg/kg SC QW[a] n=30		800 µg/kg SC Q2W[a] n=44	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic				
Neutropenia	20 (66.7)	18 (60.0)	18 (40.9)	15 (34.1)
Anemia	17 (56.7)	9 (30.0)	21 (47.7)	12 (27.3)
Lymphopenia	12 (40.0)	12 (40.0)	18 (40.9)	18 (40.9)
Leukopenia	12 (40.0)	9 (30.0)	10 (22.7)	8 (18.2)
Thrombocytopenia	11 (36.7)	7 (23.3)	10 (22.7)	5 (11.4)
Nonhematologic				
CRS	23 (76.7)	1 (3.3)	35 (79.5)	0
Skin-related AEs[b]	20 (66.7)	0	32 (72.7)	1 (2.3)
Dysgeusia	19 (63.3)	N/A	25 (56.8)	N/A
Nail-related AEs[c]	18 (60.0)	0	15 (34.1)	0
Rash-related AEs[d]	14 (46.7)	1 (3.3)	13 (29.5)	7 (15.9)
Dysphagia	12 (40.0)	0	12 (27.3)	0
Pyrexia	11 (36.7)	0	10 (22.7)	0
Fatigue	10 (33.3)	1 (3.3)	12 (27.3)	0
Dry mouth	9 (30.0)	0	25 (56.8)	0
Weight decreased	9 (30.0)	0	19 (43.2)	1 (2.3)
Nausea	9 (30.0)	0	9 (20.5)	0
Diarrhea	9 (30.0)	0	8 (18.2)	0
ALT increased	6 (20.0)	1 (3.3)	14 (31.8)	3 (6.8)
Decreased appetite	7 (23.3)	1 (3.3)	11 (25.0)	1 (2.3)
Headache	7 (23.3)	0	11 (25.0)	0
AST increased	3 (10.0)	0	14 (31.8)	3 (6.8)

- Overall, the most common adverse events (AEs) were CRS, skin-related events, and dysgeusia
- Cytopenias were mostly confined to step-up and cycle 1–2 doses and generally resolved within 1 week
- Infections occurred in 46.7% of patients at 405 µg/kg QW and 38.6% at 800 µg/kg Q2W (grade 3/4: 6.7%/9.1%)
- CRS events were mostly grade 1/2 and were largely confined to the step-up doses and first full dose
- Dysgeusia was managed with supportive care, and at times with dose adjustments
- No patients died due to drug-related AEs

Minnema MC et al. ASCO 2022;Abstract 8015.

MonumenTAL-1: Cytokine Release Syndrome

Parameter	405 µg/kg SC QW[a] n=30	800 µg/kg SC Q2W[a] n=44
Patients with CRS, n (%)	23 (76.7)	35 (79.5)
Time to onset (days),[b] median (range)	2 (1–22)	2 (1–5)
Duration (days), median (range)	2 (1–3)	2 (1–5)
Patients who received supportive measures,[c] n (%)	23 (76.7)	35 (79.5)
Tocilizumab[d]	19 (63.3)	24 (54.5)
Steroids	1 (3.3)	3 (6.8)
Oxygen	1 (3.3)[e]	2 (4.5)
Single vasopressor	1 (3.3)[e]	0



- All CRS events were grade 1/2, except for one grade 3 event
- CRS was largely confined to the step-up doses and first full dose

Minnema MC et al. ASCO 2022;Abstract 8015.

RTP RESEARCH TO PRACTICE

EHA 2022;Abstract S183.

Novel Combination Immunotherapy for the Treatment of Relapsed/Refractory Multiple Myeloma: Updated Phase 1b Results for Talquetamab (a GPRC5D x CD3 Bispecific Antibody) in Combination With Daratumumab

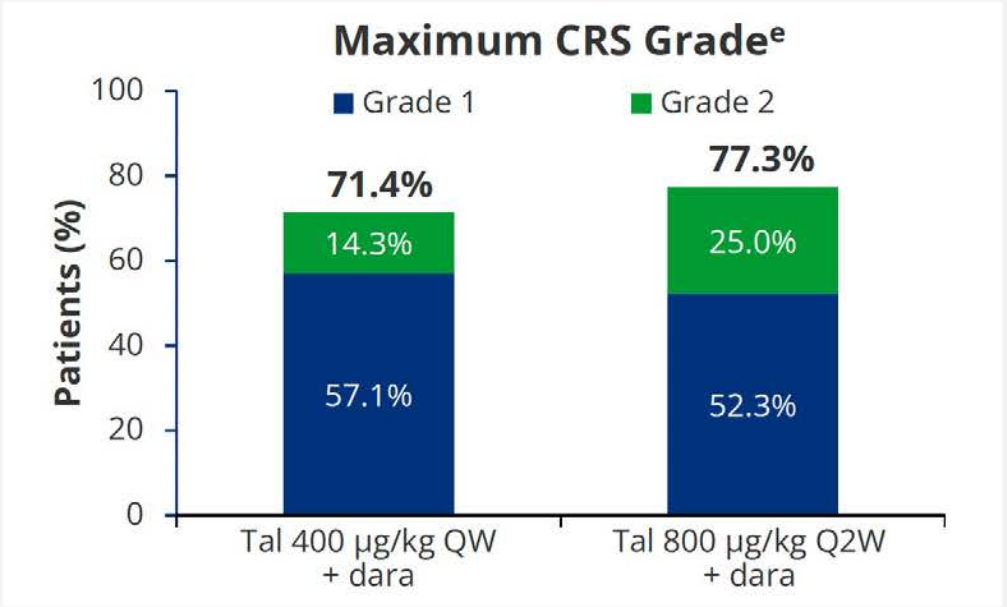
Niels WCJ van de Donk[1], Nizar Bahlis[2], Maria-Victoria Mateos[3], Katja Weisel[4], Bhagirathbhai Dholaria[5], Alfred L Garfall[6], Hartmut Goldschmidt[7], Thomas G Martin[8], Daniel Morillo[9], Donna Reece[10], David Hurd[11], Paula Rodríguez-Otero[12], Manisha Bhutani[13], Anita D'Souza[14], Albert Oriol[15], Elham Askari[9], Jesús F San-Miguel[12], K Martin Kortüm[16], Deeksha Vishwamitra[17], Shun Xin Wang Lin[17], Thomas J Prior[17], Lien Vandenberk[18], Marie-Anne Damiette Smit[19], Jenna D Goldberg[20], Ralph Wäsch[21], Ajai Chari[22]

[1]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Cancer Center Amsterdam, Amsterdam, Netherlands; [2]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, Canada; [3]University Hospital of Salamanca/IBSAL/CIC, Salamanca, Spain; [4]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [5]Vanderbilt University Medical Center, Nashville, TN, USA; [6]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [7]University Hospital Heidelberg and National Center of Tumor Diseases, Heidelberg, Germany; [8]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [9]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [10]Princess Margaret Cancer Centre, Toronto, ON, Canada; [11]Comprehensive Cancer Center of Wake Forest University, Winston-Salem, NC, USA; [12]University of Navarra, Pamplona, Spain; [13]Levine Cancer Institute/Atrium Health, Charlotte, NC, USA; [14]Medical College of Wisconsin, Milwaukee, WI, USA; [15]Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain; [16]University Hospital of Würzburg, Würzburg, Germany, Würzburg, Germany; [17]Janssen Research & Development, Spring House, PA, USA; [18]Janssen Research & Development, Antwerp, Belgium; [19]Janssen Research & Development, Los Angeles, CA, USA; [20]Janssen Research & Development, Raritan, NJ, USA; [21]Freiburg University Medical Center, Freiburg, Germany; [22]Mount Sinai School of Medicine, New York, NY, USA

Presented at the European Hematology Association (EHA) 2022 Hybrid Congress; June 9–12, 2022; Vienna, Austria.

TRIMM-2: Cytokine Release Syndrome

Parameter	Tal 400 µg/kg QW + dara (n=14)	Tal 800 µg/kg Q2W + dara (n=44)
Patients with CRS, n (%)	10 (71.4)	34 (77.3)
Time to onset (days)[a], median (range)	3 (2–4)	2 (1–4)
Duration (days), median (range)	2 (1–10)	2 (1–28)
Received supportive measures[b], n (%)	9 (64.3)	30 (68.2)
Tocilizumab[c]	6 (42.9)	14 (31.8)
Corticosteroids	0	2 (4.5)
Oxygen	0	3 (6.8)
Vasopressor	0	0
Other[d]	7 (50.0)	30 (68.2)



- No grade 3/4 CRS events were observed
- CRS events were mostly confined to step-up doses and the first full treatment dose
- No discontinuations due to CRS
- Two patients had ICANS; both ICANS events were grade 1 and resolved within 1 day

van de Donk N WCJ et al. EHA 2022;Abstract S183.

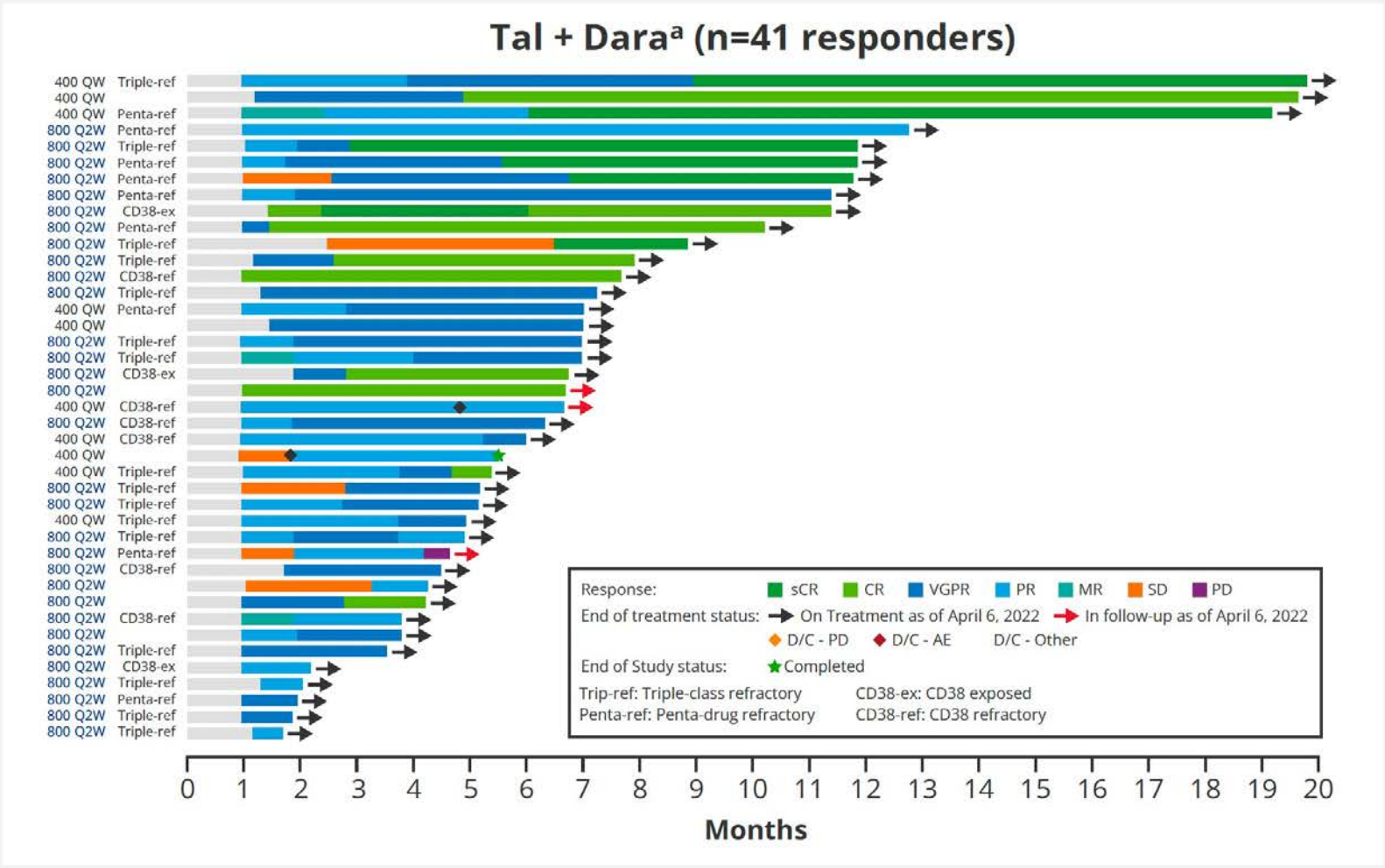
TRIMM-2: Overall Response Rate

Parameter	Evaluable patients[a]	
	Tal 400 µg/kg QW + dara (n=14)	Tal 800 µg/kg Q2W + dara (n=37)
Follow-up, median (range)	**6.7 months** (1.9–19.6)	**4.2 months** (0.2–12.3)
ORR[b], n (%)	**10 (71.4)**	**31 (83.8)**
CR/sCR	4 (28.6)	11 (29.7)
VGPR	4 (28.6)	13 (35.1)
PR	2 (14.3)	7 (18.9)
SD	4 (28.6)	4 (10.8)
PD	0	2 (5.4)
Time to first confirmed response, median (range)	**1.0 month** (0.9–2.4)	**1.0 month** (0.9–6.5)

- With overall median follow-up of 5.1 months, the ORR was **80.4%** (41/51) among all response-evaluable patients
  - VGPR or better: 62.7% (32/51)
  - CR or better: 29.4% (15/51)
- ORR in patients with prior anti-CD38 exposure: 77.3% (34/44)

van de Donk N WCJ et al. EHA 2022;Abstract S183.

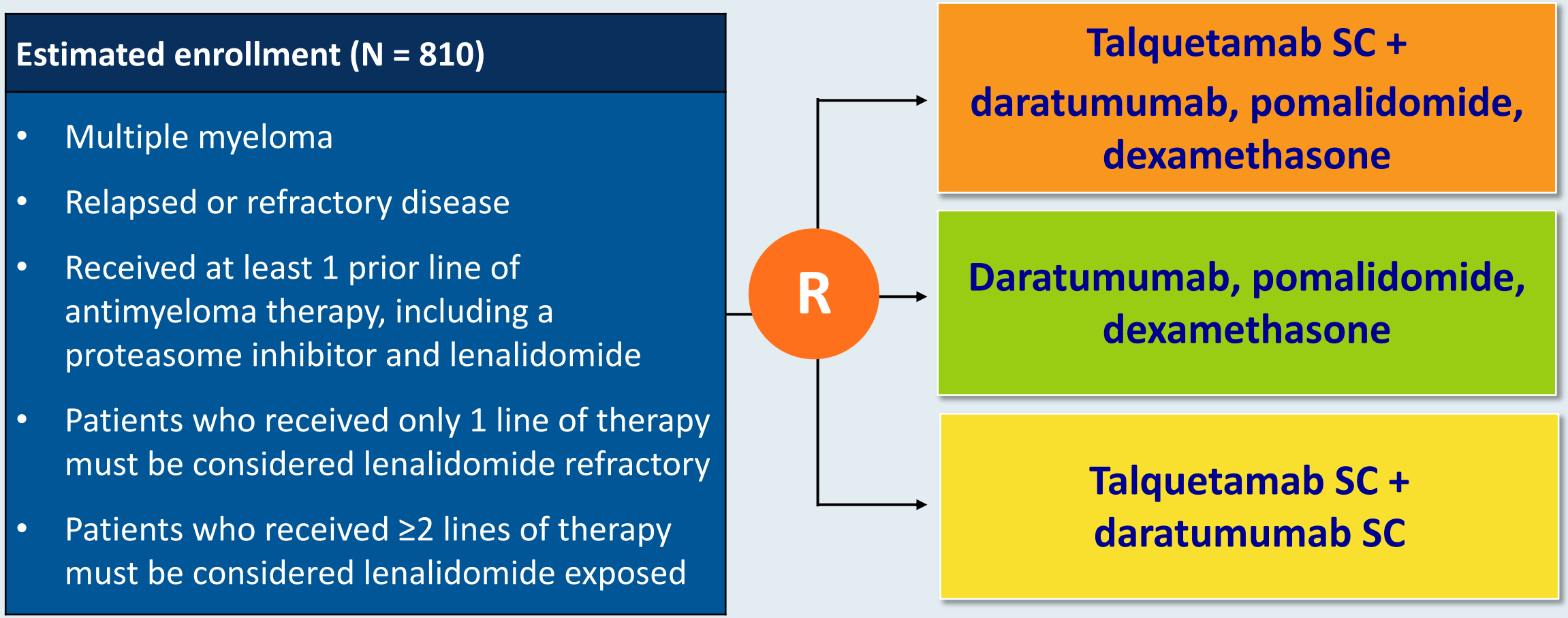
TRIMM-2: Duration of Response



- Responses were observed in heavily pretreated patients, the majority of whom were anti-CD38 refractory
- Responses were durable and deepened over time
- Median duration of response was not reached
- With a median follow-up in responders of 6.5 months (range: 1.6–19.6), 90.2% of responders (37/41) remained on treatment

van de Donk N WCJ et al. EHA 2022;Abstract S183.

MonumenTAL-3 Phase III Study Design



Primary endpoint: Progression-free survival

www.clinicaltrials.gov. NCT05455320. Accessed August 2022.

#84

Final Overall Survival Results from BELLINI, a Phase 3 Study of Venetoclax or Placebo in Combination With Bortezomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma

ASH 2021;Abstract 84.

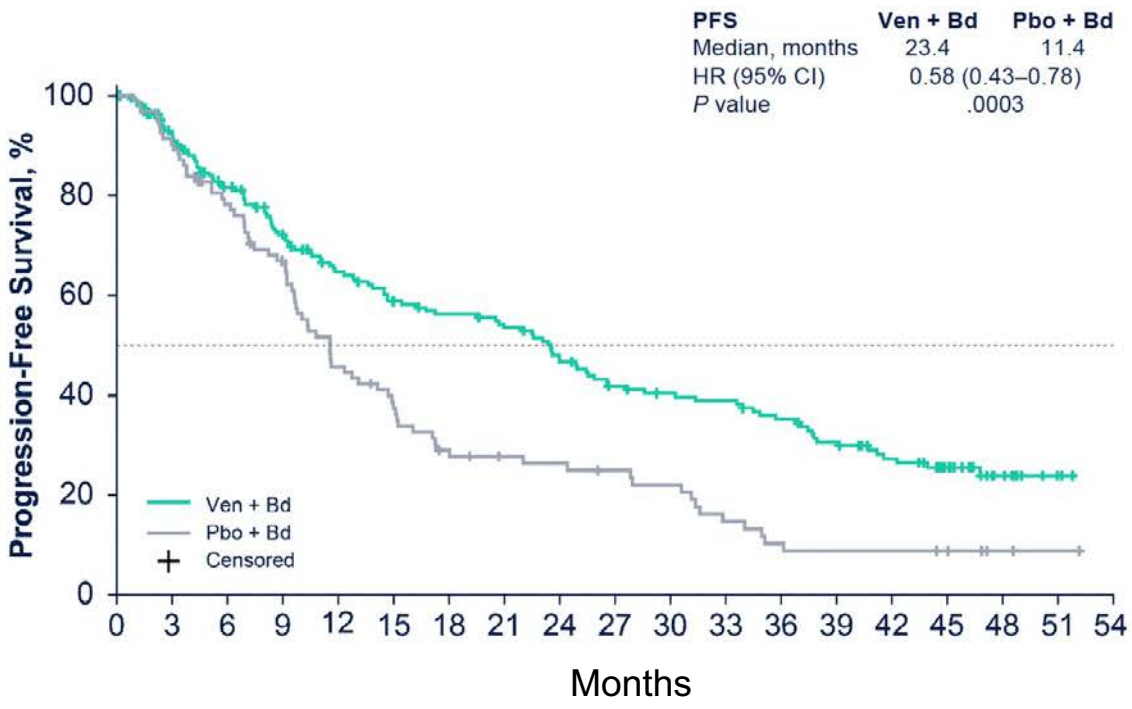
Shaji K. Kumar,[1] Simon J. Harrison,[2] Michele Cavo,[3] Javier de la Rubia,[4] Rakesh Popat,[5] Cristina Gasparetto,[6] Vania Hungria,[7] Hans Salwender,[8] Kenshi Suzuki,[9] Inho Kim,[10] Maika Onishi,[11] Grace Ku,[11] Rajvineeth Pothacamury,[12] Vasudha Sehgal,[12] Abdullah Masud,[12] Jeremy A. Ross,[12] Edyta Dobkowska,[13] and Philippe Moreau[14]

[1]Mayo Clinic, Rochester, MN, USA; [2]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Victoria, Australia; [3]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Seragnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [4]Hematology Service Hospital La Fe and School of Medicine and Dentistry, Catholic University of Valencia, Valencia, Spain; [5]University College Hospitals, London, United Kingdom; [6]Duke University Medical Center, Durham, NC, USA; [7]Clinica São Germano, São Paulo, Brazil; [8]Asklepios Tumorzentrum Hamburg, AK Altona and AK St Georg, Hamburg, Germany; [9]Japanese Red Cross Medical Center, Tokyo, Japan; [10]Seoul National University, Seoul, South Korea; [11]Genentech, Inc, South San Francisco, CA, USA; [12]AbbVie, Inc, North Chicago, IL, USA; [13]Pharmacyclics Switzerland GmbH, An AbbVie Company, Schaffhausen, Switzerland; [14]University Hospital, Nantes, France

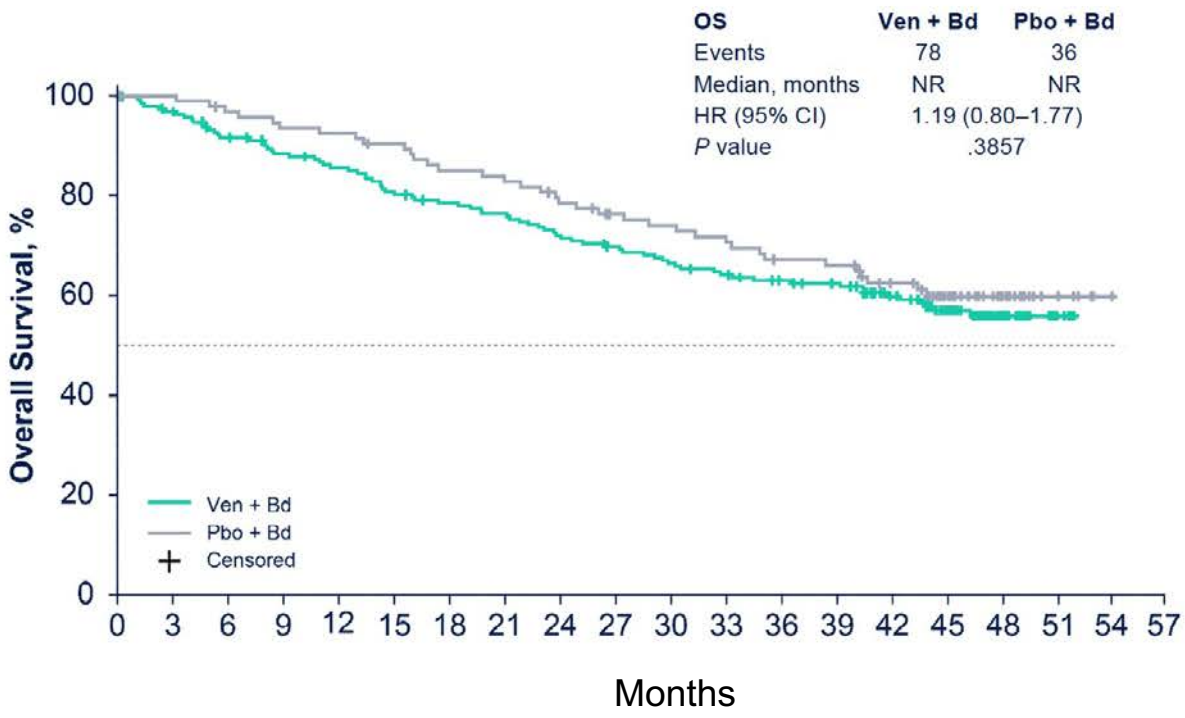
American Society of Hematology Annual Meeting, December 11–14, 2021, Atlanta, Georgia

BELLINI: Investigator-Assessed PFS and OS in All Patients (Median Follow-Up: 45.6 Months)

Investigator-Assessed PFS in All Patients

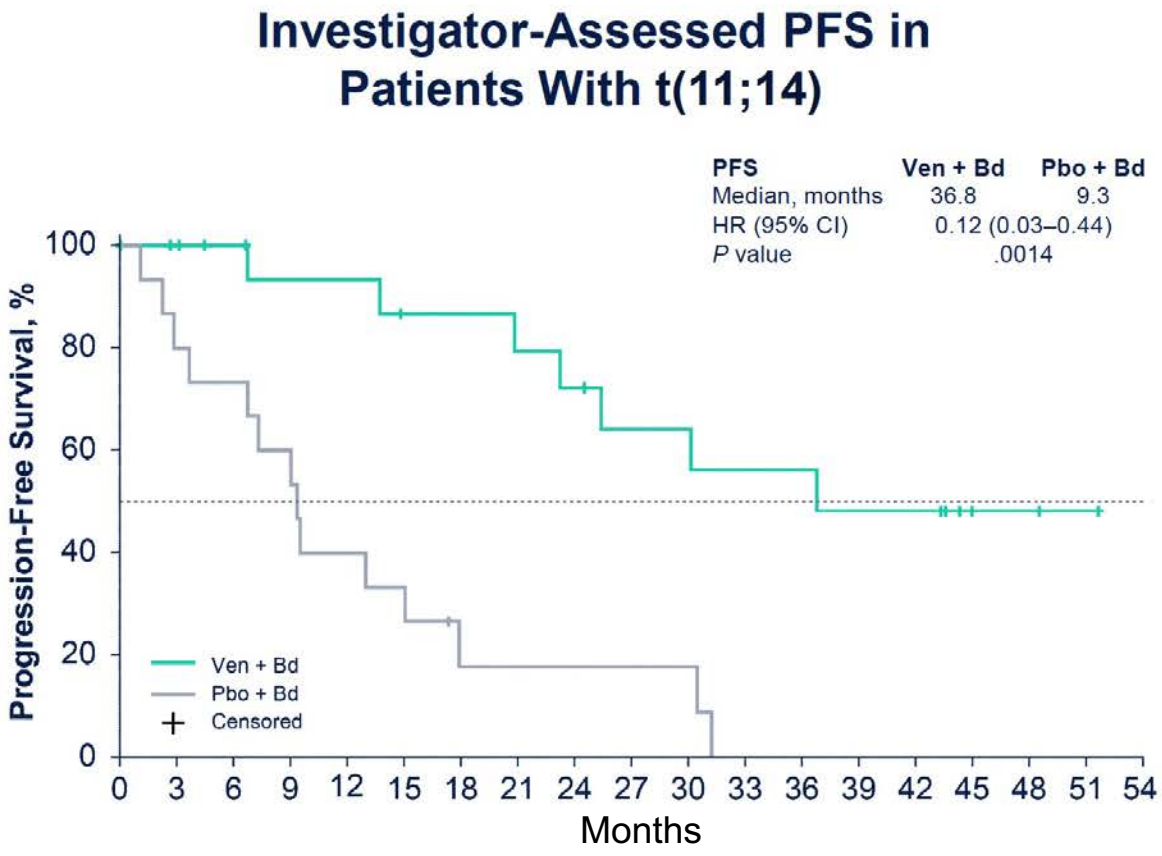


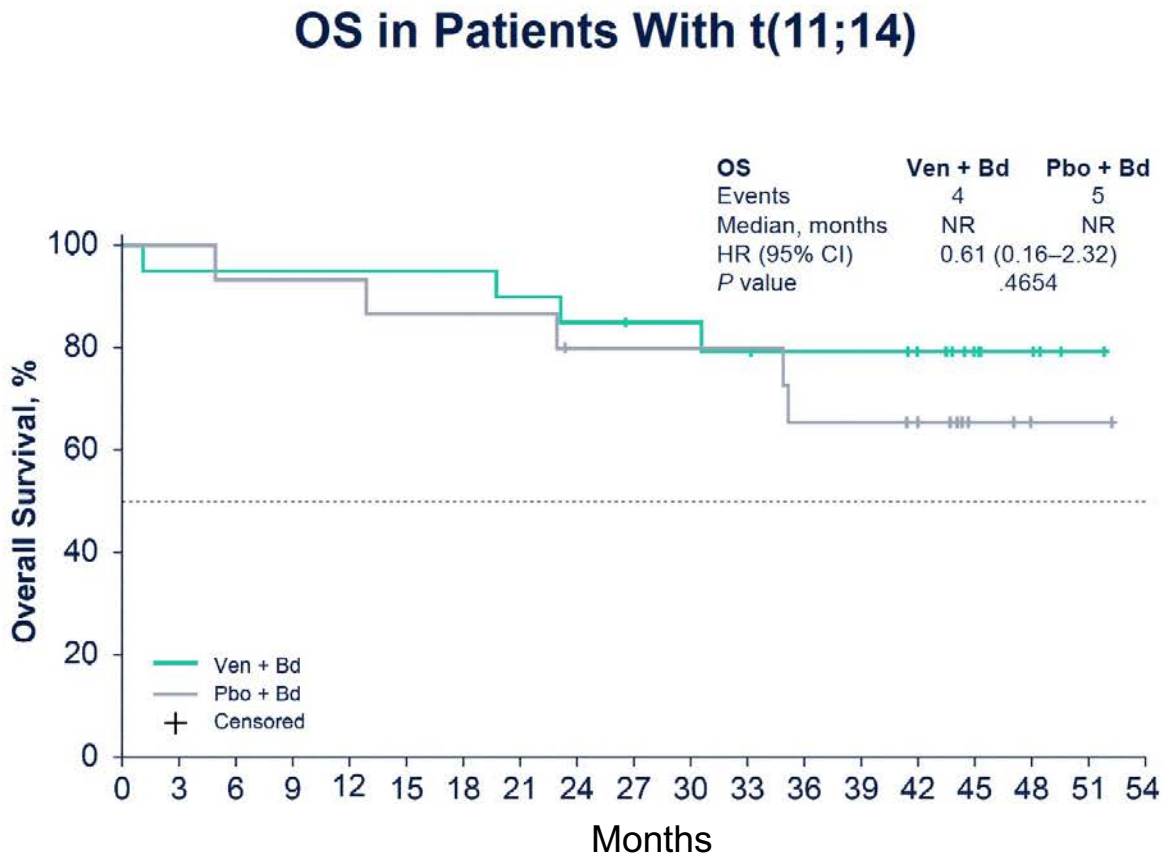
OS in All Patients



Kumar SK et al. ASH 2021;Abstract 84.

BELLINI: Updated PFS and OS in Patients with t(11;14)

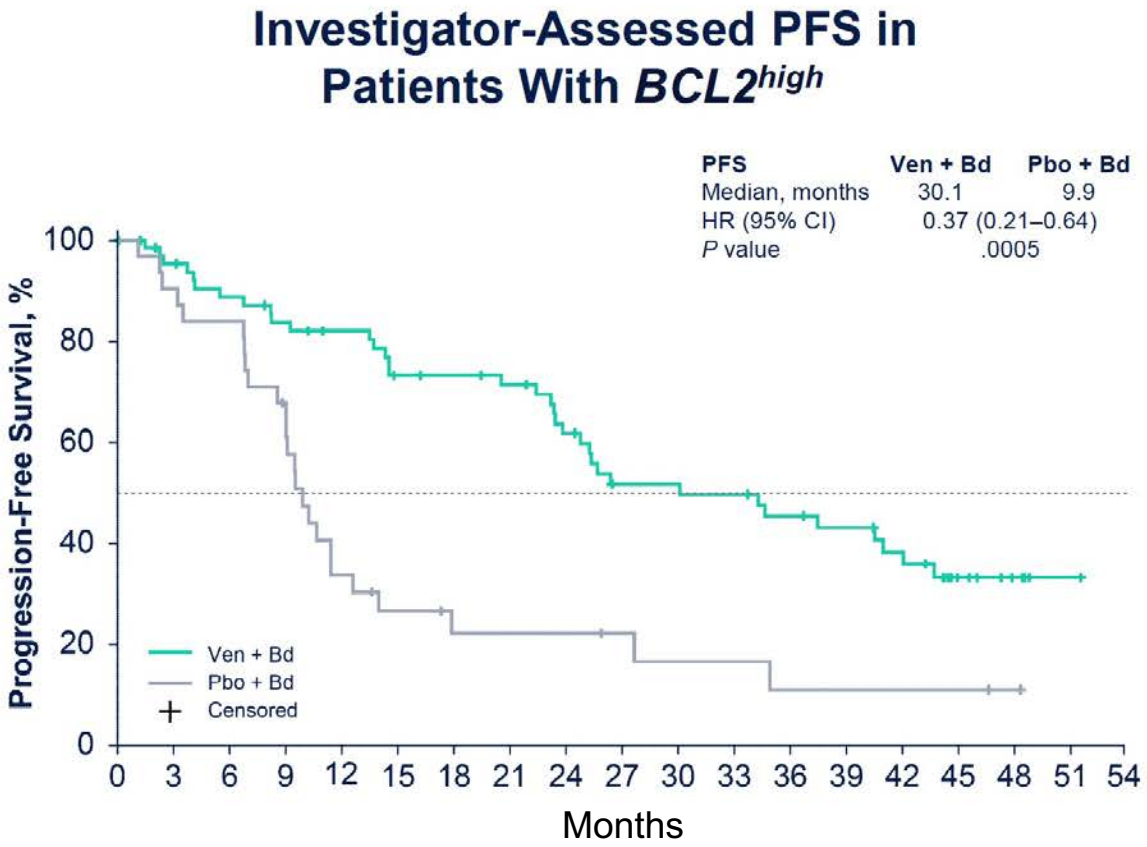


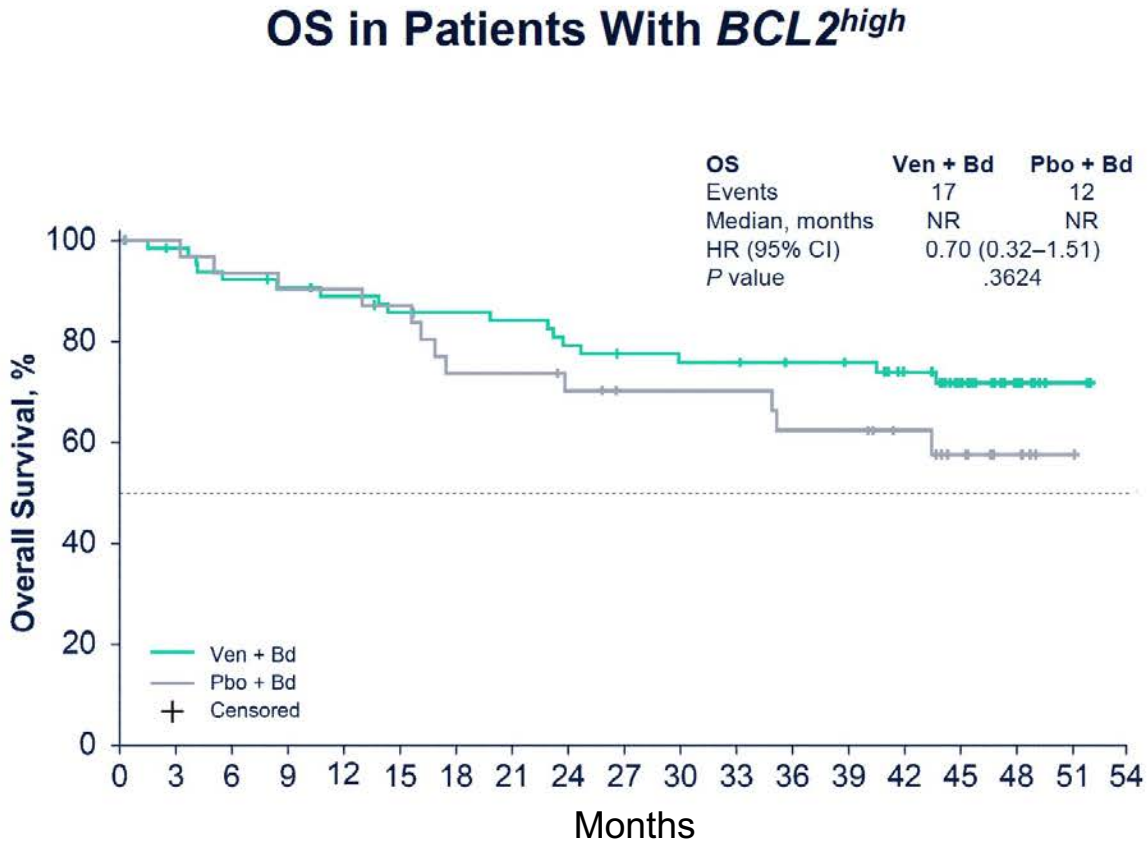


Kumar SK et al. ASH 2021;Abstract 84.

RTP RESEARCH TO PRACTICE

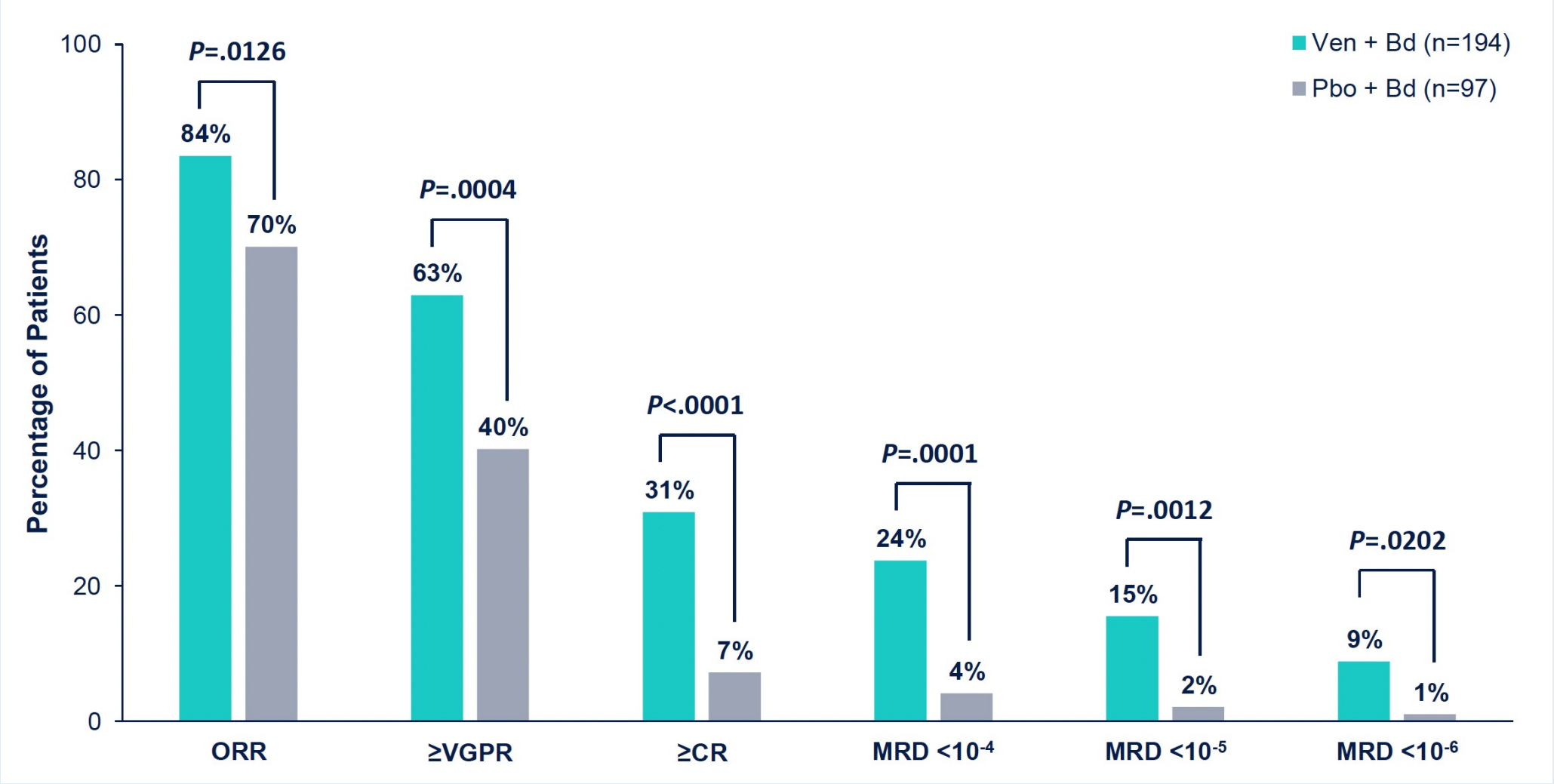
BELLINI: Updated PFS and OS in Patients with High BCL2 Expression





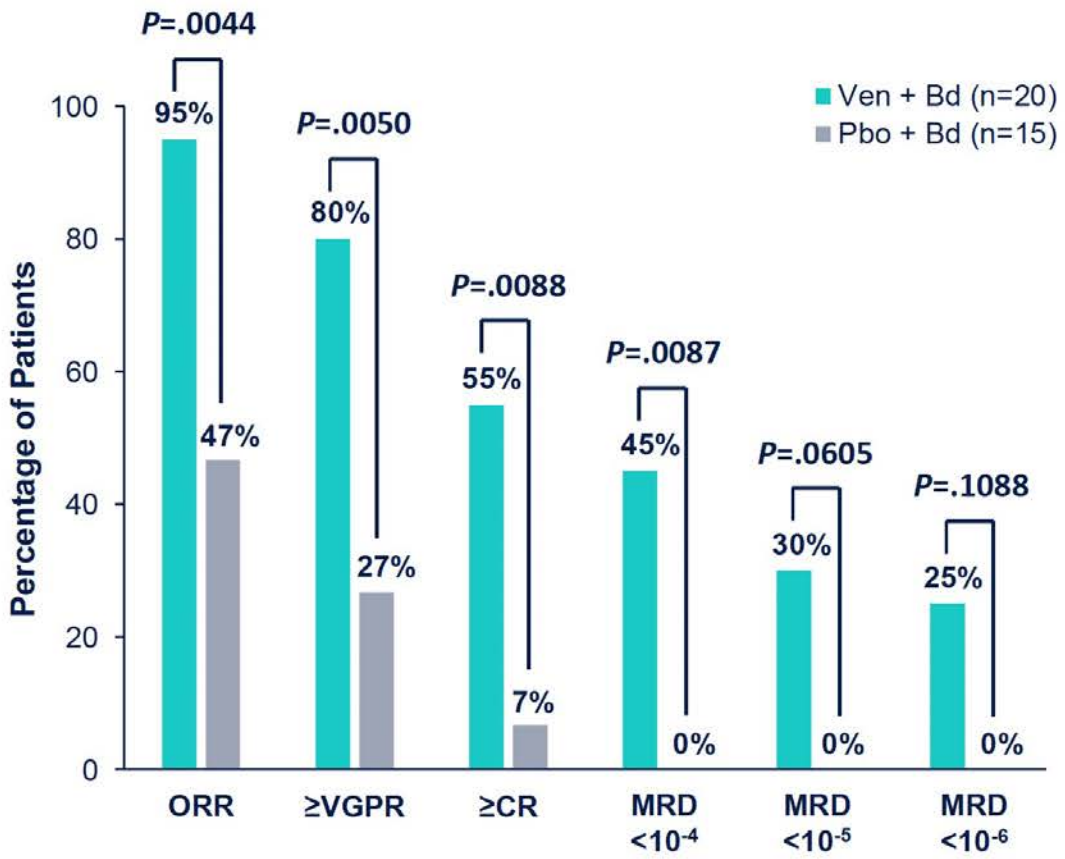
Kumar SK et al. ASH 2021;Abstract 84.

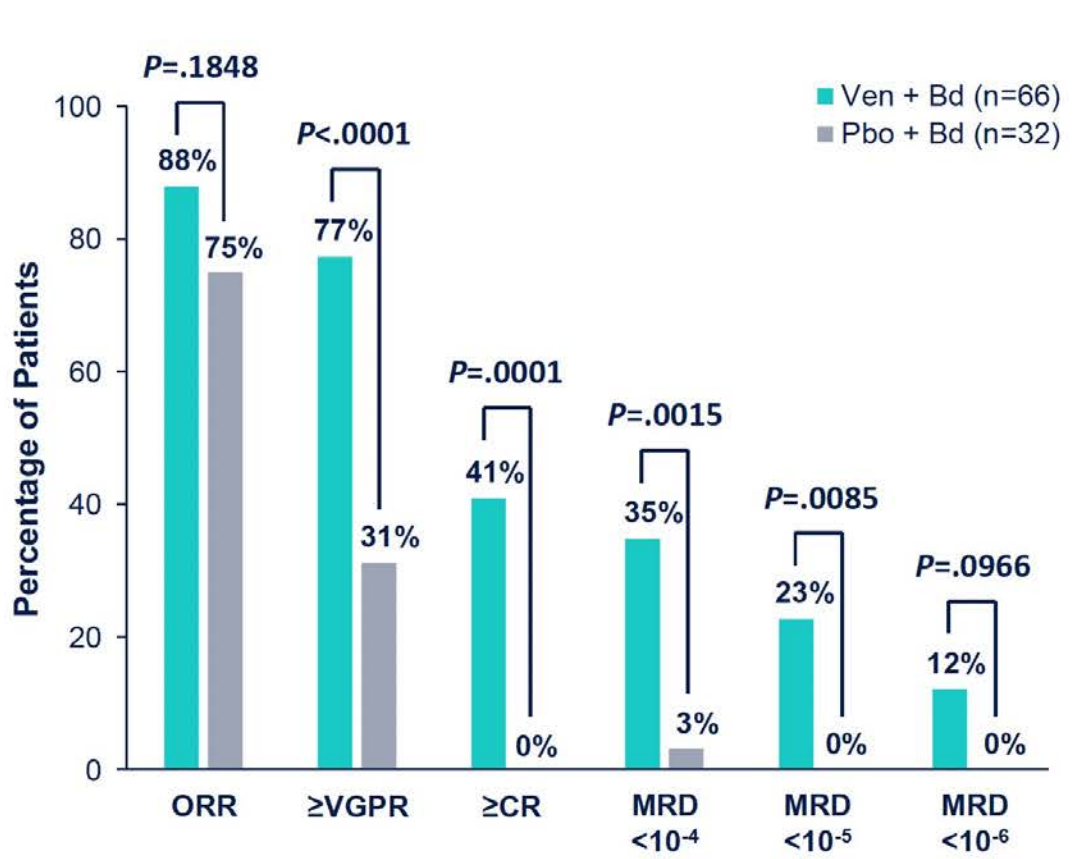
BELLINI: Investigator-Assessed Response Rates and MRD Negativity Rates in All Patients



Kumar SK et al. ASH 2021;Abstract 84.

BELLINI: Response and MRD Negativity Rates in Patients with t(11;14) or High BCL2 Expression





Kumar SK et al. ASH 2021;Abstract 84.

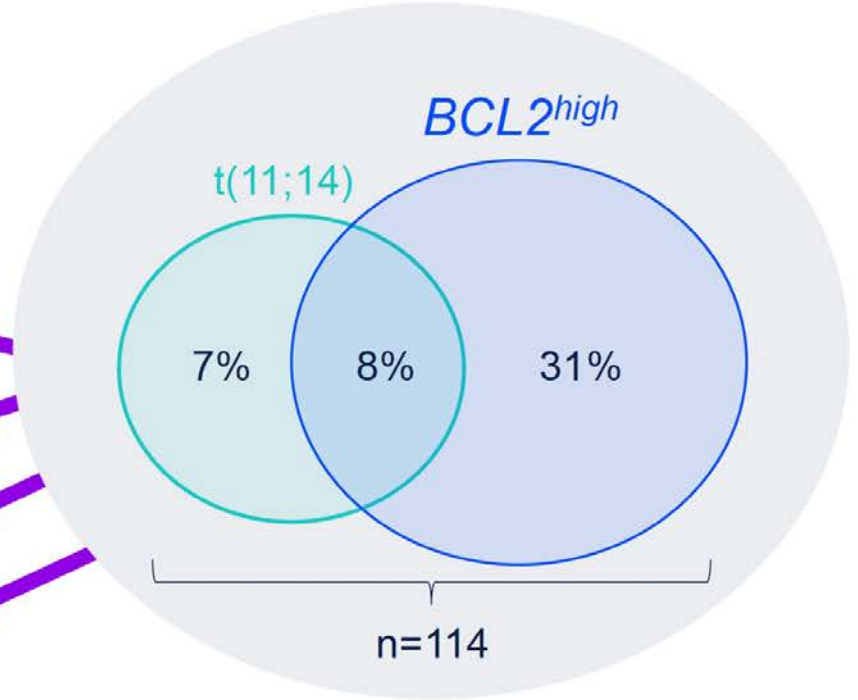
RTP RESEARCH TO PRACTICE

BELLINI: PFS Improvements in Patients with t(11;14) or High BCL2 Expression

Hazard Ratios for PFS and OS by *BCL2* Expression and t(11;14)

	Patients		PFS		OS	
	Ven + Bd (n)	Pbo + Bd (n)	HR (95% CI)	*P* value	HR (95% CI)	*P* value
t(11;14) or *BCL2*^{high}	74	40	0.32 (0.20–0.53)	<.0001	0.82 (0.40–1.70)	NS
t(11;14)	20	15	0.12 (0.03–0.44)	.0014	0.61 (0.16–2.32)	NS
BCL2^{high}	66	32	0.37 (0.21–0.64)	.0005	0.70 (0.32–1.51)	NS
Non-t(11;14) and *BCL2*^{high}	51	24	0.48 (0.26–0.90)	.0215	0.86 (0.35–2.12)	NS

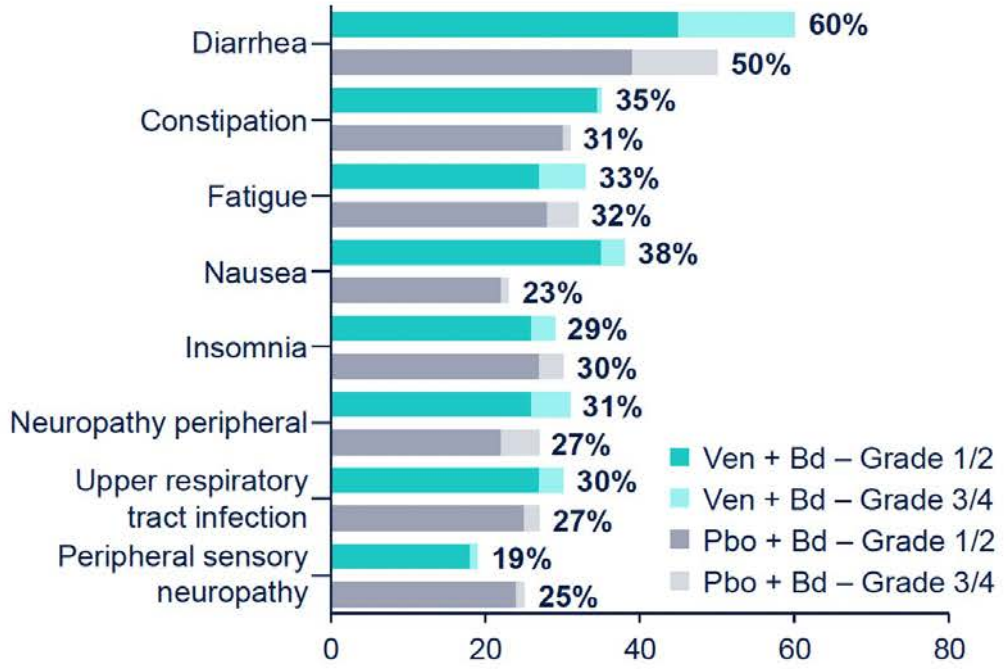
BELLINI Biomarker Subgroups[a] (n=240)



Kumar SK et al. ASH 2021;Abstract 84.

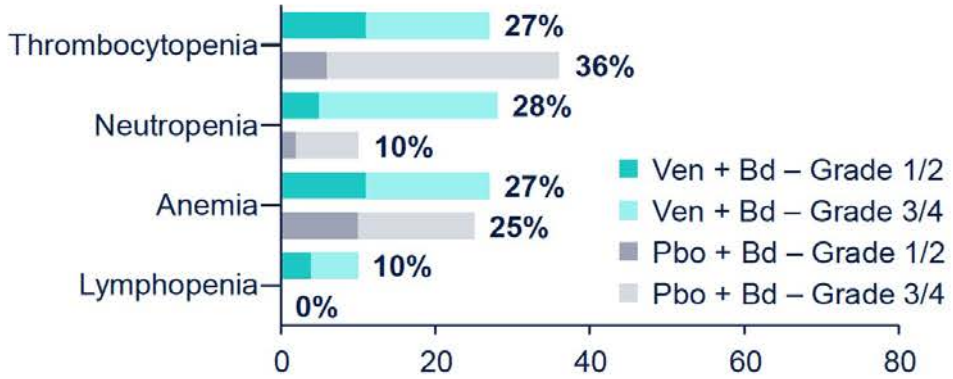
BELLINI: Adverse Event Rates

AEs in ≥25% of Patients in Either Treatment Arm

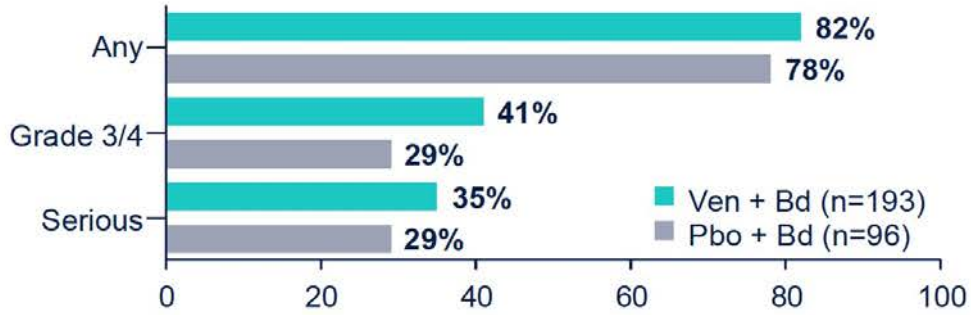


- Overall, 51 patients (26%) in the Ven + Bd arm and 11 patients (11%) in the Pbo + Bd arm discontinued Ven or Pbo due to AEs

Most Common Hematologic AEs



Infections



Kumar SK et al. ASH 2021;Abstract 84.

BELLINI: Treatment-Emergent Deaths

Deaths

n (%)	Ven + Bd (n=193)	Pbo + Bd (n=96)
All deaths	77 (40)	36 (38)
Treatment-emergent deaths[a]	14 (7)[b]	2 (2)
Any AE	12 (6)	1 (1)
Deaths occurring while still receiving study drug	0	0
Infection	9 (5)	0
Progressive disease	2 (1)	1 (1)
Non–treatment-emergent deaths	63 (33)	34 (35)

Kumar SK et al. ASH 2021;Abstract 84.

Faculty Survey

Based on your personal clinical experience and knowledge of available data, how would you compare the efficacy of BCMA-targeted bispecific antibodies (eg, teclistamab) to that of non-BCMA-targeted bispecific antibodies (eg, talquetamab) for patients with R/R MM?

 Dr Fonseca	Efficacy is similar with both	 Dr Lonial	Efficacy is similar with both
 Dr Kumar	Efficacy is similar with both	 Dr Mikhael	Efficacy is similar with both
 Dr Landgren	Efficacy is similar with both	 Dr Richardson	BCMA-targeted bispecific antibodies are more efficacious*

*More experience with BCMA-targeted bispecific antibodies, and non-BCMA approaches may be as efficacious, but my impression is BCMA-targeted is more active.

RTP RESEARCH TO PRACTICE

Based on your personal clinical experience and knowledge of available data, how would you compare the tolerability of BCMA-targeted bispecific antibodies (eg, teclistamab) to that of non-BCMA-targeted bispecific antibodies (eg, talquetamab) for patients with R/R MM?

 Dr Fonseca	Tolerability is similar with both	 Dr Lonial	BCMA-targeted bispecific antibodies are more tolerable
 Dr Kumar	Tolerability is similar with both	 Dr Mikhael	BCMA-targeted bispecific antibodies are more tolerable
 Dr Landgren	Tolerability is similar with both	 Dr Richardson	Tolerability is similar with both

RTP RESEARCH TO PRACTICE

Oncology Today with Dr Neil Love — Novel Agents and Strategies in Acute Myeloid Leukemia

A CME/MOC-Accredited Virtual Event

Thursday, November 17, 2022
5:00 PM – 6:00 PM ET

Faculty

Daniel A Pollyea, MD, MS

Moderator

Neil Love, MD

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Thank you for joining us!

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