Inside the Issue: The Emerging Role of Cereblon E3 Ligase Modulators in Multiple Myeloma

A CME/MOC-Accredited Live Webinar

Wednesday, January 28, 2026
5:00 PM – 6:00 PM ET

Faculty

Natalie S Callander, MD
Paul G Richardson, MD

Moderator

Neil Love, MD

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Faculty

Natalie S Callander, MD
Director, Myeloma Clinical Program
University of Wisconsin Carbone Cancer Center
Madison, Wisconsin

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Paul G Richardson, MD
Clinical Program Leader and Director of Clinical Research
Jerome Lipper Multiple Myeloma Center
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RJ Corman Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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Commercial Support

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Dr Love — Disclosures

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Dr Callander — Disclosures

No relevant conflicts of interest to disclose

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Dr Richardson — Disclosures

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Contracted Research	Oncopeptides

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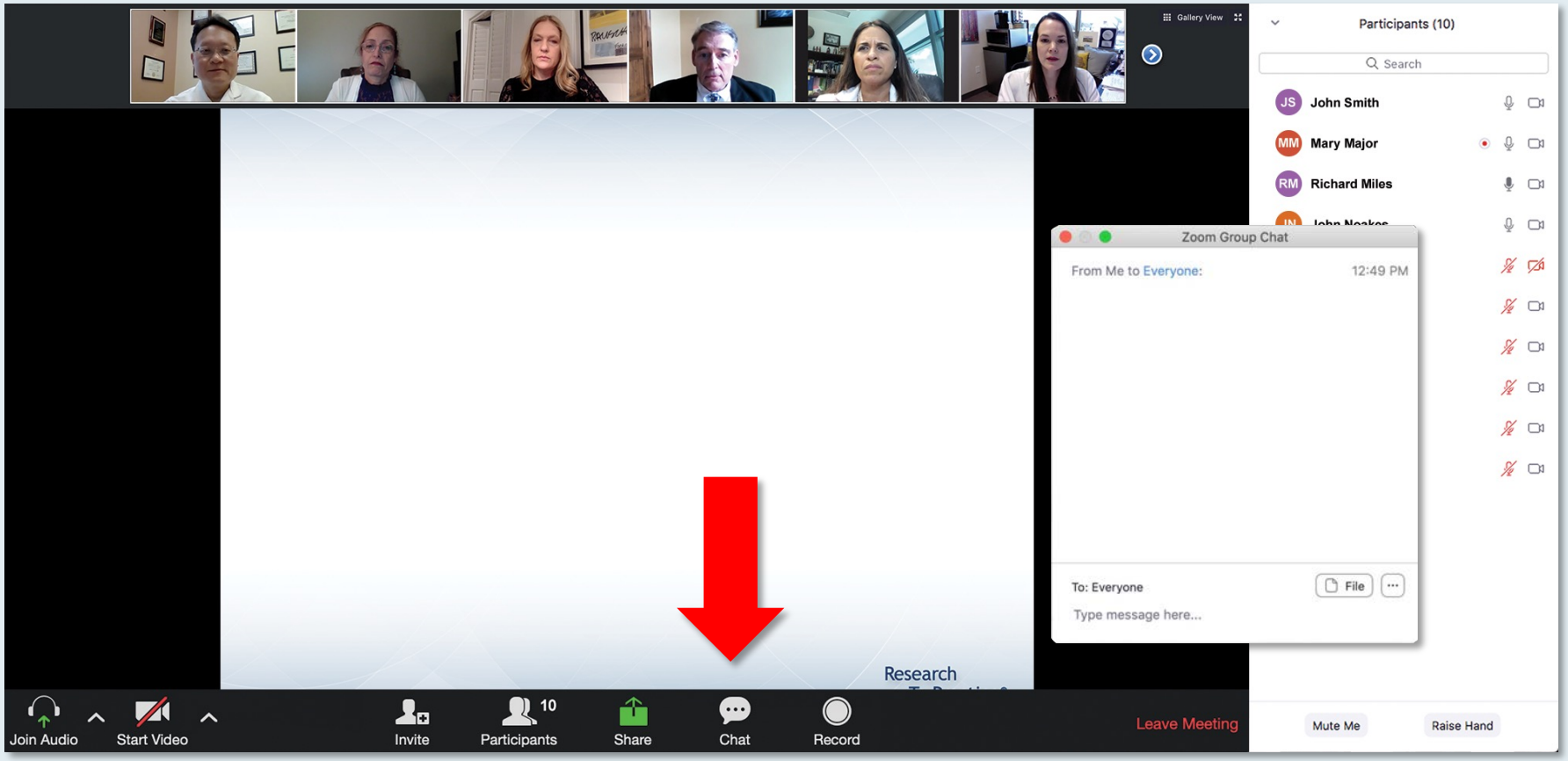

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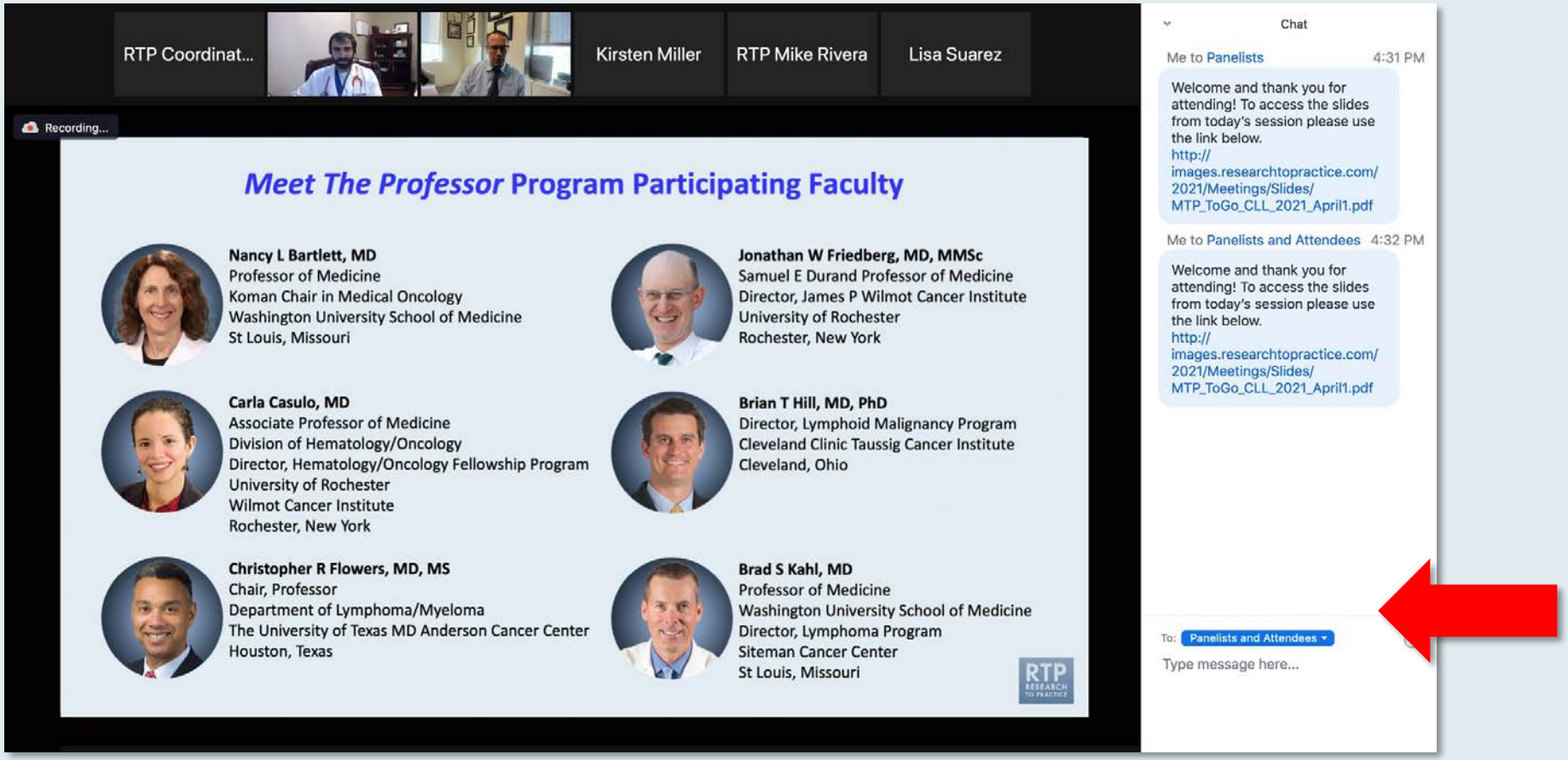

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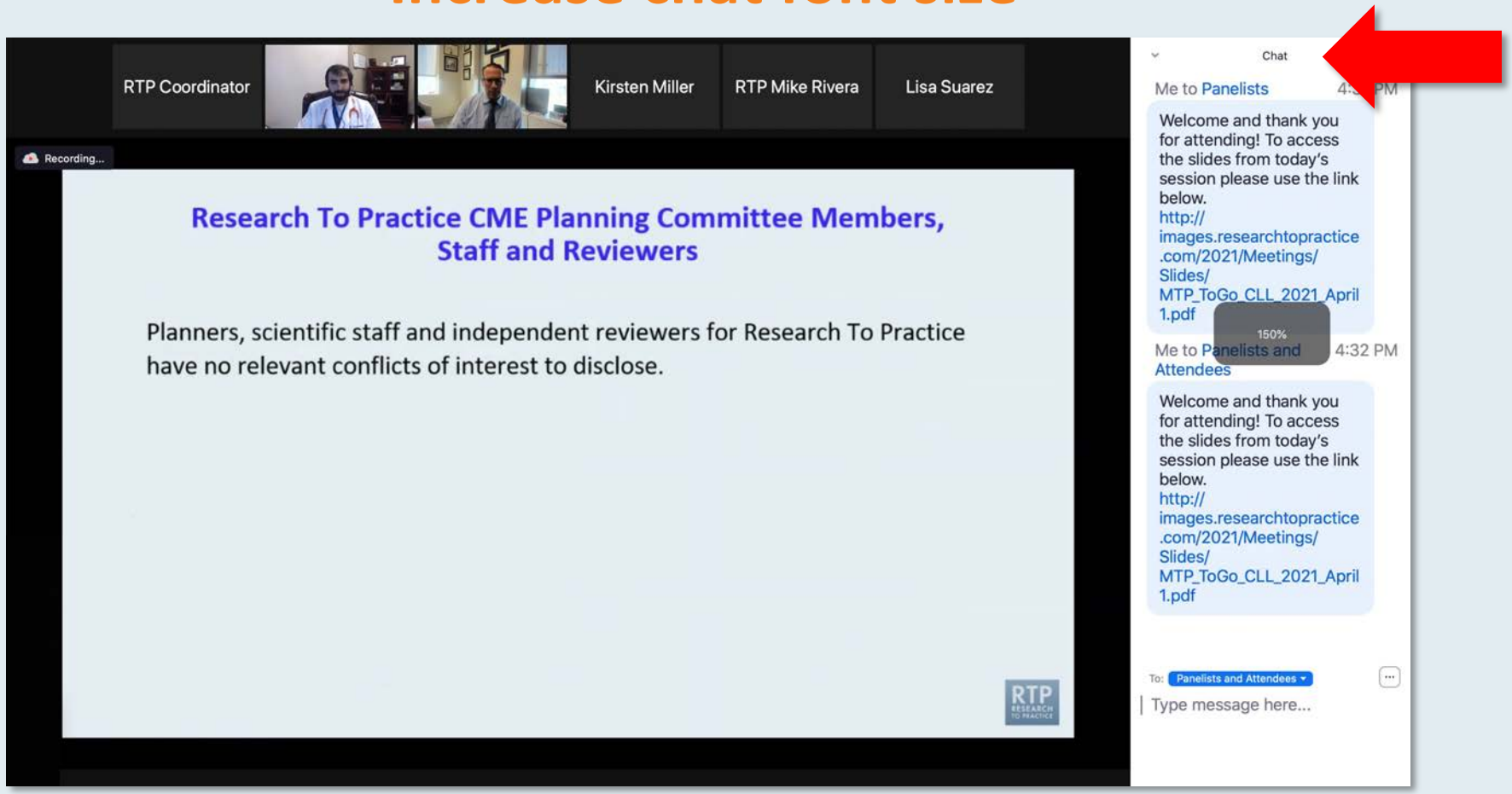

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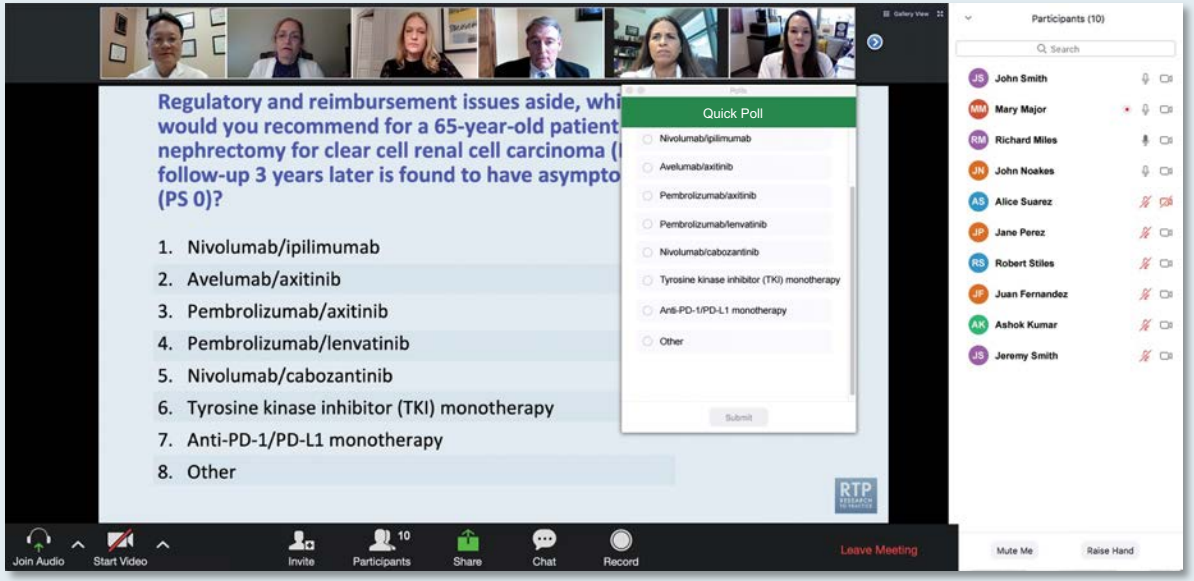

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Relapsed/Refractory Multiple Myeloma — ASH 2025 Review

DR SAGAR LONIAL
WINSHIP CANCER INSTITUTE OF EMORY UNIVERSITY

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Exploring Current Patterns of Care in the Community: Selection of First-Line and Maintenance Therapy for Patients with Extensive-Stage Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 4, 2026
5:00 PM – 6:00 PM ET

Faculty

Hossein Borghaei, DO, MS
Anne Chiang, MD, PhD

Moderator

Neil Love, MD

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Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Antibody-Drug Conjugates for Breast Cancer

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Sara M Tolaney, MD, MPH

Moderator

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RTP Year in Review 2026

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Ovarian Cancer

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Nicoletta Colombo, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP Year in Review 2026

Second Opinion: Clinical Investigators Discuss the Optimal Management of Genitourinary Cancers

A CME Symposium Series Held Adjunct to the 2026 ASCO® Genitourinary Cancers Symposium

Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

Thursday, February 26, 2026
7:00 PM – 9:00 PM PT
(10:00 PM – 12:00 AM ET)

AKT Inhibition in Prostate Cancer

Friday, February 27, 2026
6:00 PM – 7:30 PM PT
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Friday to Sunday, April 24 to 26, 2026

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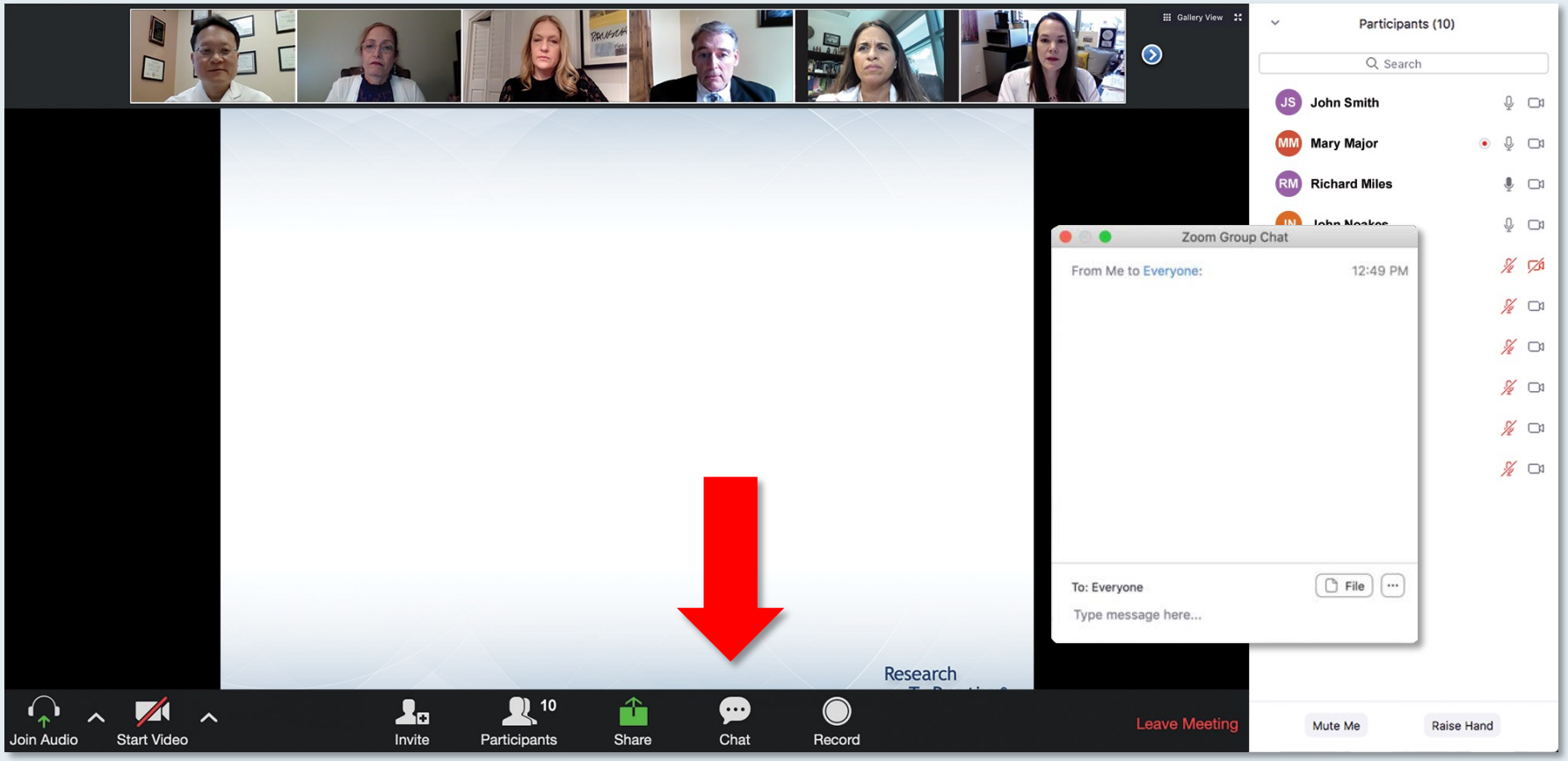

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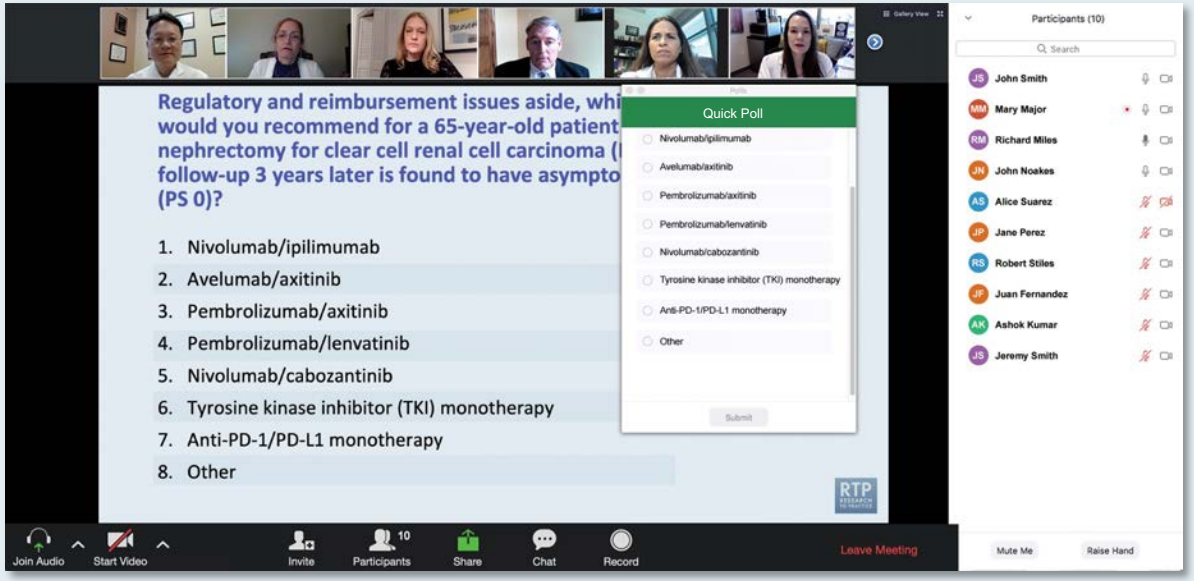

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Dr Callander — Disclosures

No relevant conflicts of interest to disclose

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Agenda

Introduction: Clinical Trials We LOVE to Discuss

Module 1: Mechanism of Action of Cereblon E3 Ligase Modulators (CELMoDs)

Module 2: Available Efficacy Data with CELMoDs in the Management of Relapsed/Refractory Multiple Myeloma (MM)

Module 3: Extramedullary Disease

Module 4: Spectrum and Management of CELMoD-Associated Adverse Events

Module 5: Ongoing Phase II and III Trials Evaluating CELMoDs for MM

Module 6: Other Trials in Progress

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Clinical Trials We LOVE to Discuss!

Trial	Cancer Type	Experimental Arm
EMBARK	Prostate	Enzalutamide/leuprolide
VIALE-A	AML	Azacitidine/venetoclax
SOLO1	Ovarian	Olaparib
ADAURA	Lung	Osimertinib
HERIZON-GEA-01	Gastroesophageal	Zanidatamab/CT ± tislelizumab
ATOMIC	Colon	Atezolizumab/CT
IMvigor011	Urothelial bladder	Atezolizumab
lidERA	Breast	Giredestrant/LHRH

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Clinical Trials We LOVE to Discuss!

Trial	Cancer Type	Experimental Arm
AMPLIFY	CLL	Acalabrutinib/venetoclax
ZUMA-7	DLBCL	Axicabtagene ciloleucel
GO29781	Follicular Lymphoma	Mosunetuzumab
ASC4FIRST	CML	Asciminib
VAYHIT2	ITP	Ianalumab
DeFi	Desmoid	Nirogacestat
TRIANGLE	MCL	ASCT

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2022 ASCO® ANNUAL MEETING

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

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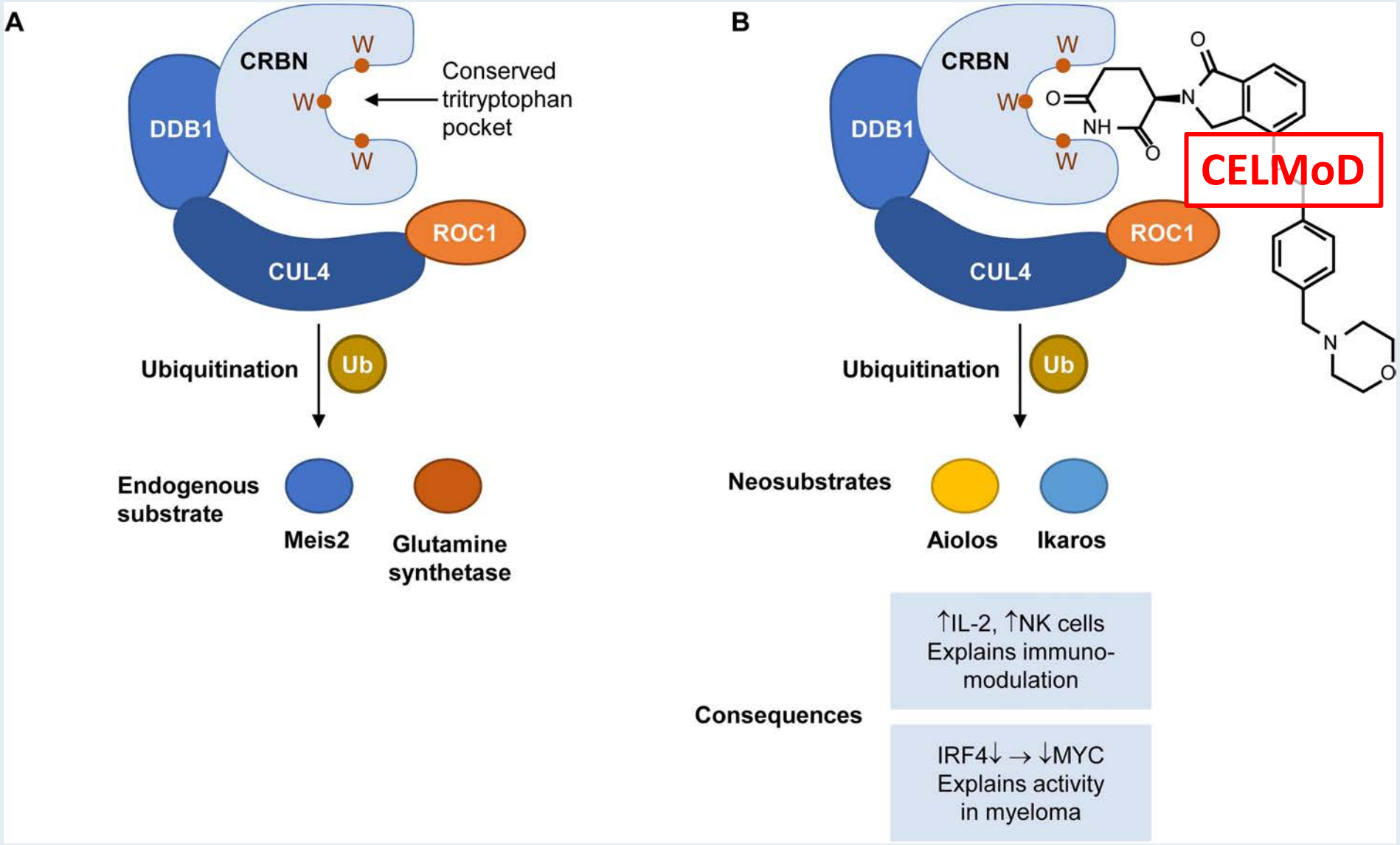
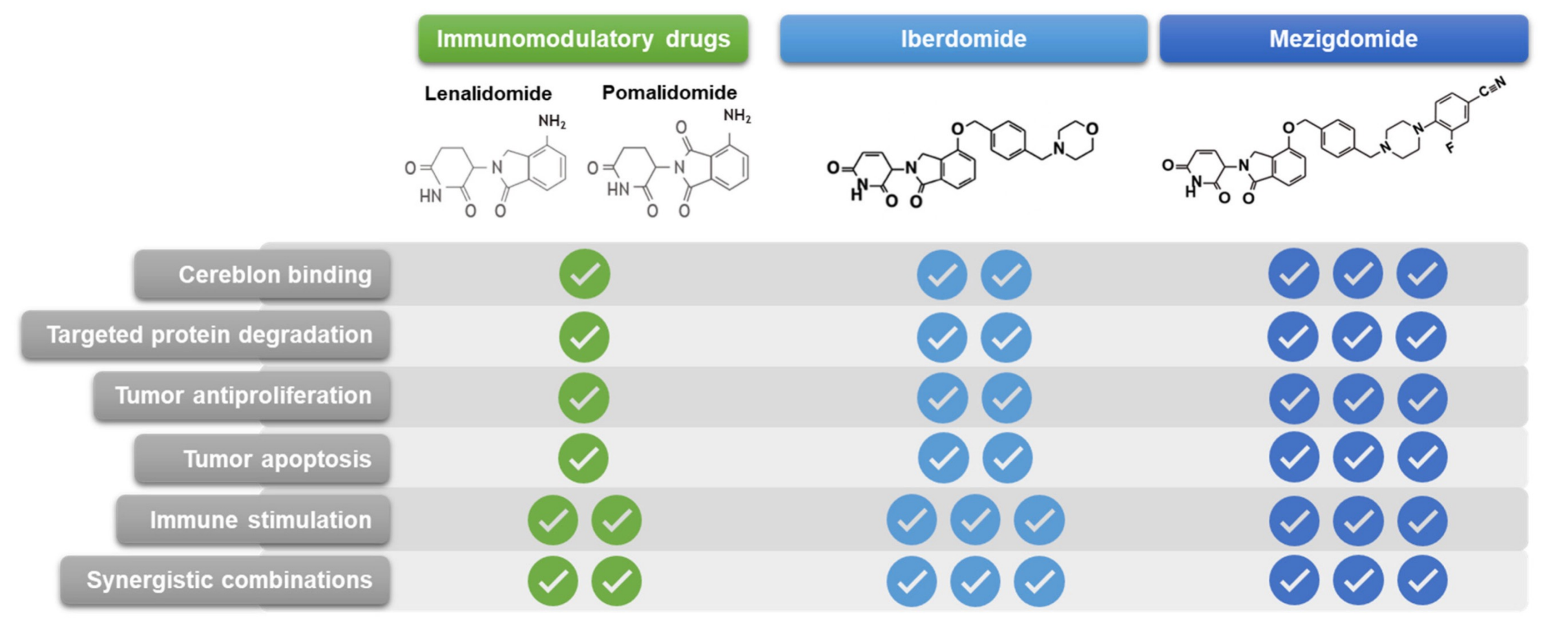
CELMoDs Overview: The Cereblon (CRBN) Pathway



van de donk NWCJ et al. *Onco Targets Ther* 2025;18:921-33.

IMiDs and CELMoDs



van de donk NWCJ et al. *Onco Targets Ther* 2025;18:921-33.
Hartley-Brown MA et al. *Cancers* (Basel) 2024 ;16(6):1166.

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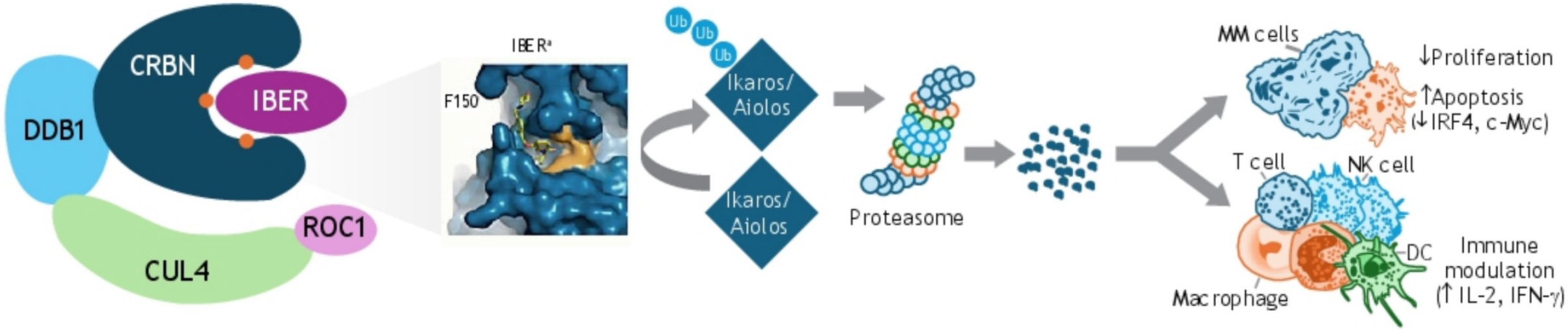
Rationale for Iberdomide in MM

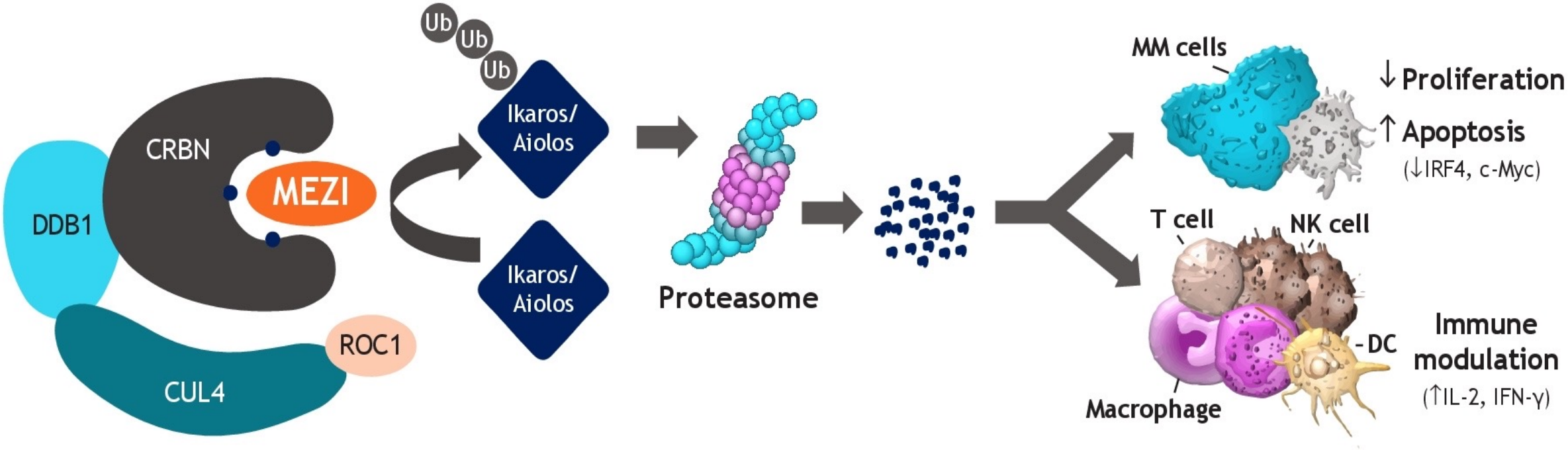


[a]Adapted with permission from Matyskiela ME, et al. *J Med Chem* 2018;61:535-542 © 2018 American Chemical Society.

c-Myc, cellular Myc; CUL4, cullin 4; DC, dendritic cell; DDB1, DNA damage-binding protein 1; IFN-γ, interferon-gamma; IL-2, interleukin-2; IRF4, interferon regulatory factor 4; NK, natural killer; ROC1, regulator of cullins-1; Ub, ubiquitin.

White D et al. ASCO 2025;Abstract 7532

Rationale for Mezigdomide in MM



c-Myc, cellular Myc; CUL4, cullin 4; DC, dendritic cell; DDB1, DNA damage-binding protein 1; IFN, interferon; IL, interleukin; IRF4, interferon regulatory factor 4; MEZI, mezigdomide; NK, natural killer; ROC1, regulator of cullins-1; Ub, ubiquitin.

Richardson PG et al. ASCO 2023;Abstract TPS8070

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Iberdomide Key Datasets

- Landgren O et al. A **phase 2** trial of **iberdomide, carfilzomib, daratumumab and dexamethasone** quadruplet therapy for **relapsed/refractory multiple myeloma**: **The ReKinDLE study**. ASH 2025;Abstract 251.
- Suvannasankha A et al. **Safety and efficacy** of **elranatamab in combination with iberdomide** in patients with **relapsed or refractory multiple myeloma: Results from the phase 1b MagnetisMM-30 trial**. ASH 2025;Abstract 100.
- Korst CLBM et al. **Iberdomide plus low-dose cyclophosphamide and dexamethasone in patients with relapsed and refractory multiple myeloma (the ICON study):** A multicentre, single-arm, phase 2 trial. *Lancet Haematol* 2026 January;13(1):e30-40.
- White D et al. **Iberdomide, bortezomib, and dexamethasone (IberVd) in transplant-ineligible (TNE) newly diagnosed multiple myeloma (NDMM): Updated results** from the **CC-220-MM-001 trial**. ASCO 2025;Abstract 7532.

ASH 2025;Abstract 251

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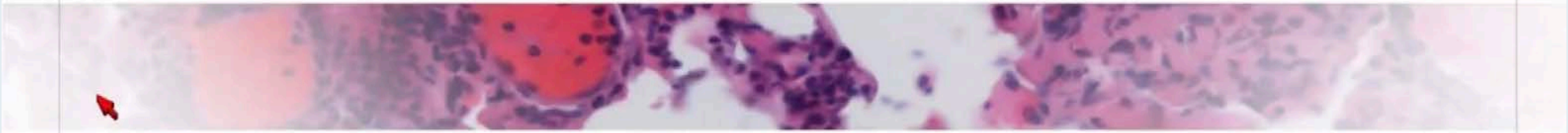

A phase 2 trial of iberdomide, carfilzomib, daratumumab and dexamethasone quadruplet therapy for relapsed/refractory multiple myeloma: The **ReKInDLE** study

Ola Landgren, James Hoffman, Abhishek Pandey, Andrew Kowalski, Michael Durante, David Coffey, Marcella Kaddoura, Brian Walker, Leslie Gallardo, Elizabeth Lyubchenko, Massiel Lopez, Fiorela Flores, Liettel Ortega, Rabia Bukhari, Kellye Koubek, Caterine Diaz, Stephanie Mompoint, Sindy Gutierrez, Faika Shah, Stephanie Fernandes, Michelle Armogan, Dickran Kazandjian, **Benjamin Diamond**

bxd500@miami.edu; @BenDiamondMD

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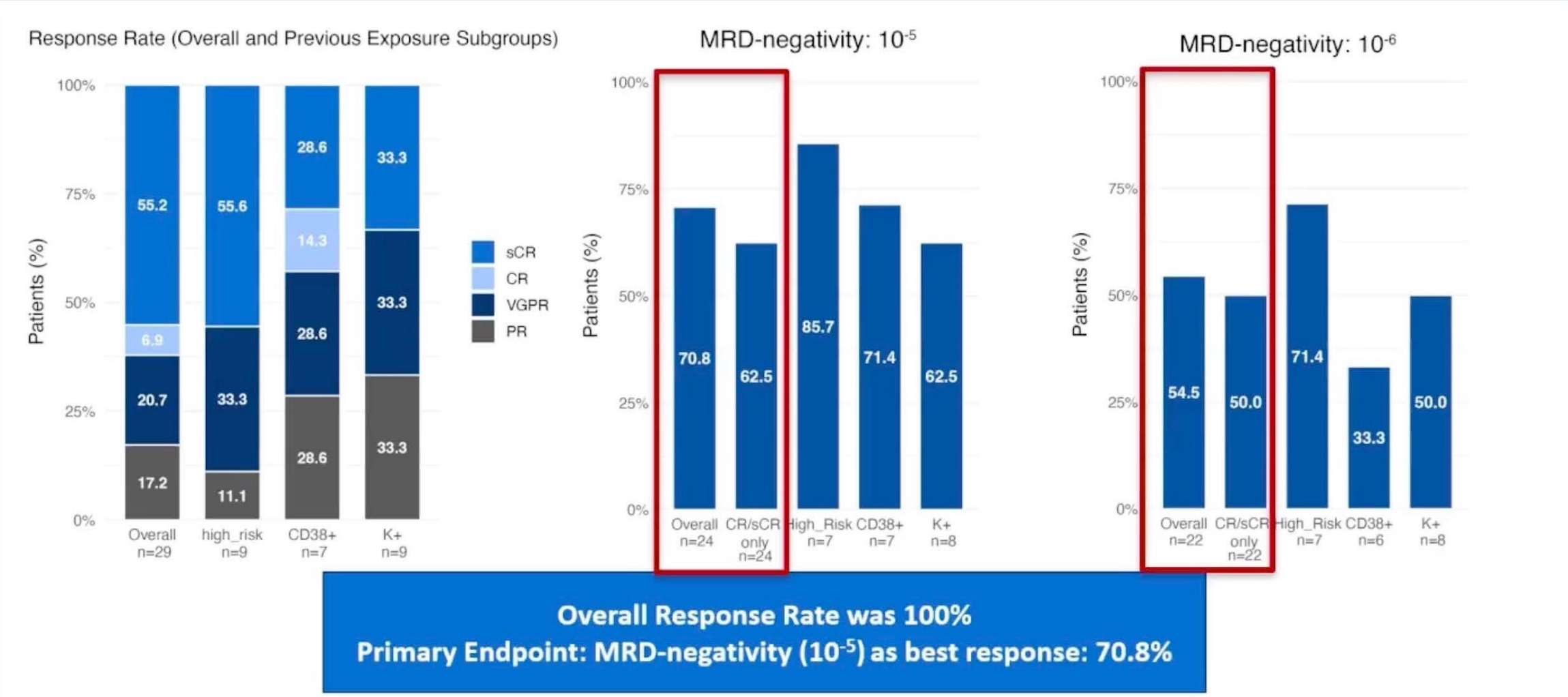
Phase II ReKInDLE: Response Rates, Minimal Residual Disease (MRD) Analysis



sCR = stringent complete response; CR = complete response; VGPR = very good partial response; PR = partial response

Landgren O et al. ASH 2025;Abstract 251.

Phase II ReKInDLE: Authors' Conclusions

- Iber-DKd appears to be a potent regimen in lenalidomide-refractory multiple myeloma.
- MRD-negativity rate (10^{-5}) of 70.8% (62.5% in ≥CR only)
  - DKd (CANDOR: MRD-negative CR; 21.8%, Lenalidomide-Refractory; 32%)
  - DPd (APOLLO: MRD-negativity; 9%, Lenalidomide Refractory; 79%)
  - Activity despite prior exposures to K and anti-CD38 therapy.
- Favorable safety profile with predominantly [expected] hematologic toxicity.
  - Further strategies could leverage early growth factor support to further improve dose intensity.
- Deep responses permit time-limited combination therapy and de-escalation to monotherapy.
  - All [n=18] patients in response at time of de-escalation to monotherapy remain in response.
- With the current reality of triple-class exposure and lenalidomide-refractoriness at first relapse, time-limited or response-adapted iberdomide-based combination therapy is worthy of further investigation.
  - EXCALIBER-RRMM (phase III) to report Iber-Dara-Dex (vs Dara-Bor-Dex) in the early relapse setting

Landgren O et al. ASH 2025;Abstract 251.

ASH 2025;Abstract 100

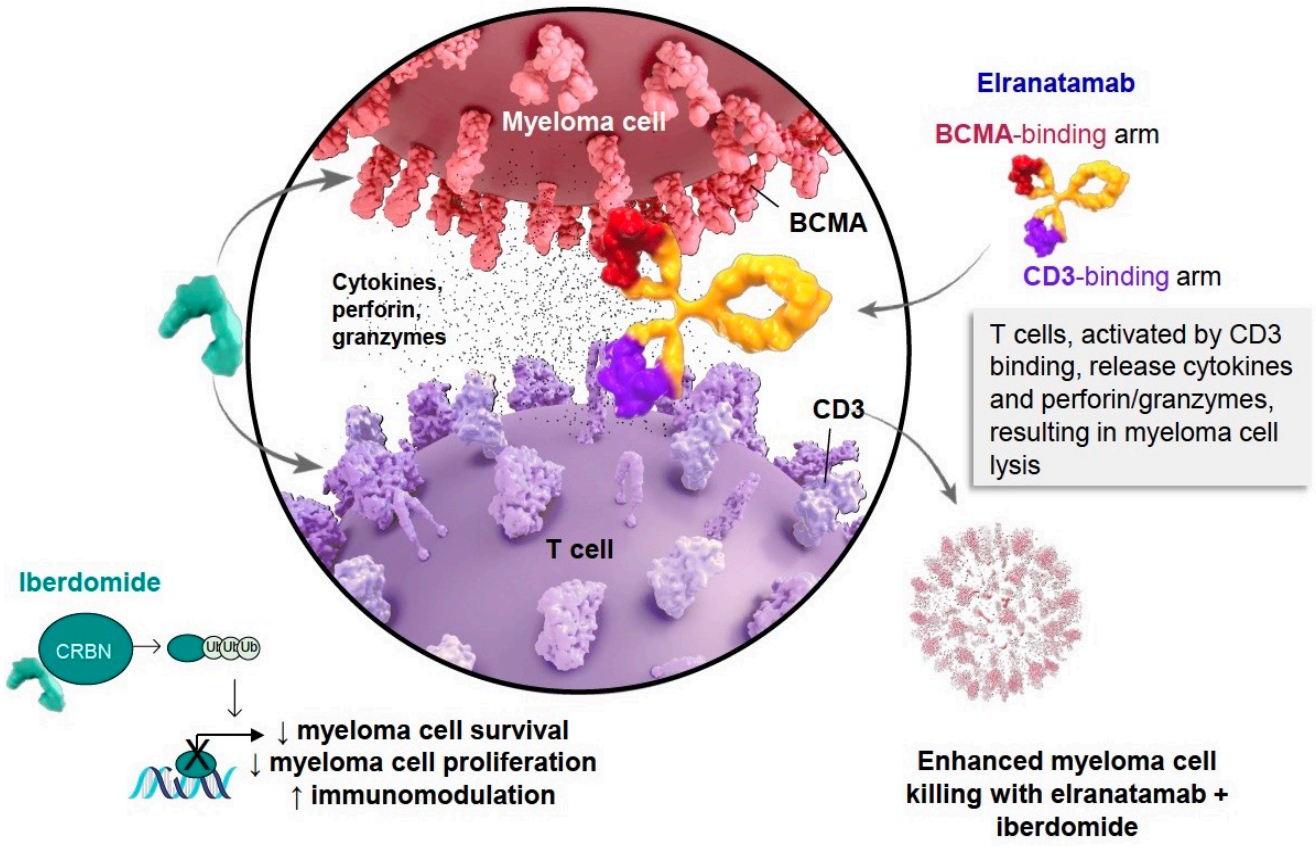
Safety and Efficacy of Elranatamab in Combination With Iberdomide in Patients With Relapsed or Refractory Multiple Myeloma: Results from the Phase 1b MagnetisMM-30 Trial

Attaya Suvannasankha,[1] Jonathan L. Kaufman,[2] Ashraf Badros,[3] Michel Pavic,[4] Hock-Choong Lai,[5] Muhammad S Raza,[6] Parth S Shah,[7] Patrick Y. Muller,[8] Jorge Acosta,[8] Margaret Hoyle,[9] Erik R Vandendries,[10] Jay Cheng,[11] Alexander Lesokhin[12]

[1]Melvin and Bren Simon Comprehensive Cancer Center, Indiana University, Indianapolis, IN, USA; [2]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [3]Greenebaum Comprehensive Cancer Center, University of Maryland, Baltimore, MD, USA; [4]Centre Intégré Universitaire de Santé et de Services Sociaux de l'Estrie - Centre Hospitalier Universitaire de Sherbrooke, Quebec, QC, Canada; [5]Icon Cancer Centre Townsville, Queensland, AU; [6]Dr. Everett Chalmers Hospital, Halifax, NS, Canada; [7]Dartmouth Hitchcock Medical Center, Hanover, NH, USA; [8]Bristol Myers Squibb, Boudry, Switzerland; [9]Pfizer Inc, Milan, Italy; [10]Pfizer Inc, Cambridge, MA, USA; [11]Pfizer Inc, Bothell, WA, USA; [12]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Rationale for Elranatamab/Iberdomide Combination Therapy

- **Elranatamab** is a BCMA-CD3 bispecific antibody approved as a monotherapy for patients with RRMM who have received ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 mAb[1-2]
  - Based on MagnetisMM-3 (NCT04649359), ORR was 61.0%, ≥CR rate was 37.4%, mPFS was 17.2 months, and mOS was 24.6 months[3,4]
- **Iberdomide** is an oral CELMoD™ with superior preclinical features than IMiDs, that:
  - Exhibits greater antiproliferative and proapoptotic activity in myeloma cells and immunomodulatory activity than the IMiDs class
  - Promotes activation and proliferation of T-cells, enhances T-cell engager function and prevents T-cell exhaustion in vitro and in vivo[5-7]



Elranatamab in combination with **iberdomide** may provide additional benefit to patients with RRMM based on the complementary mechanisms of action of this combination

1. Elrexfio (elranatamab-bcmm). Prescribing information. Pfizer Inc; 2025. **2.** Elrexfio (elranatamab-bcmm). Summary of product characteristics. Pfizer Europe MA EEIG; 2024. **3.** Lesokhin AM, et al. Nat Med 2023;29:2259-2267. **4.** Tomasson MH, et al. Hemasphere 2024;8:e136 **5.** Lonial S, et al. Lancet Haematol 2022;9:e822-e832. **6.** Bjorklund CC, et al. Leukemia 2020;34:1197-1201. **7.** Paiva B, et al. Hemasphere 2023;7(suppl 3):P799.

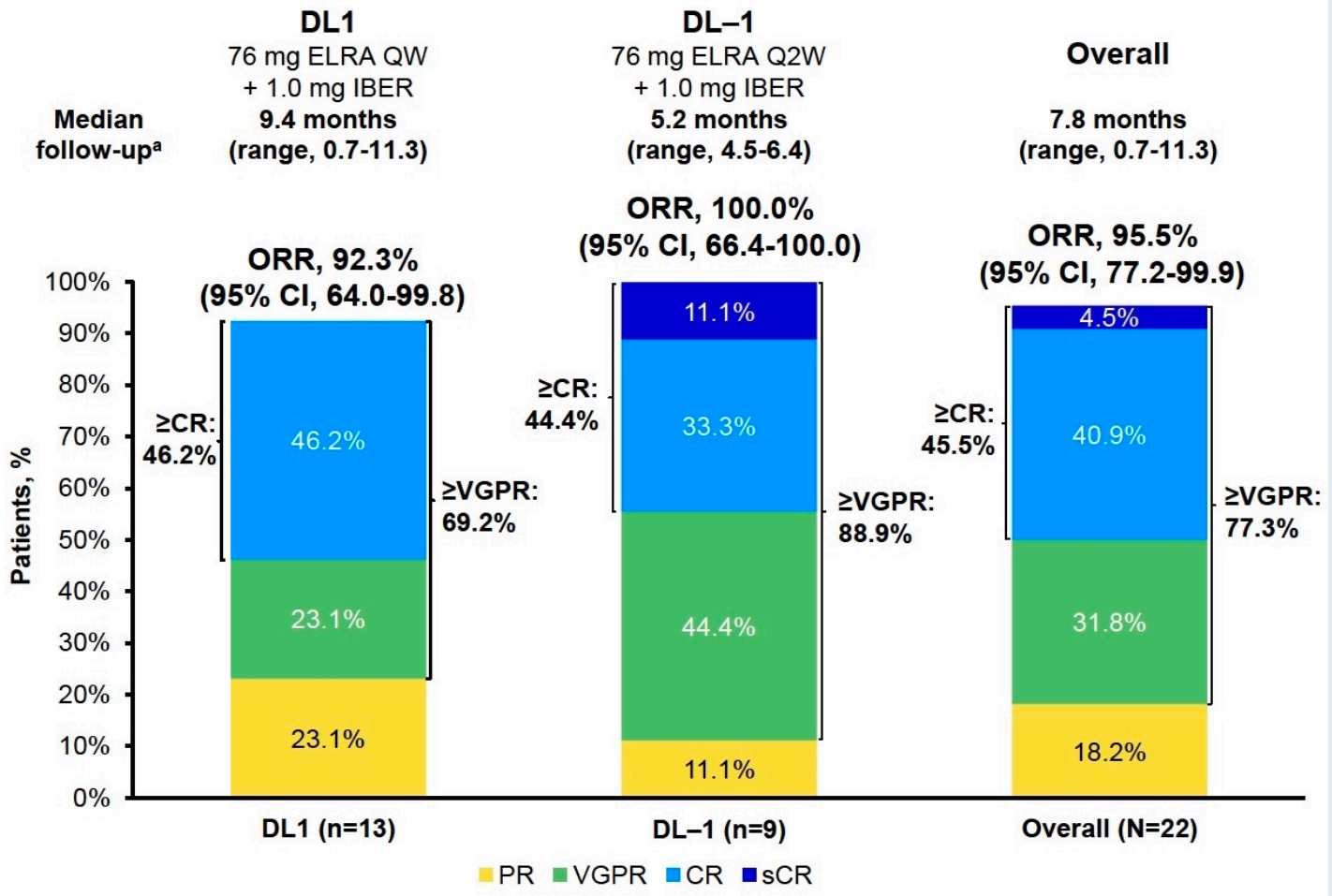
BCMA=B-cell maturation antigen; CR=complete response; CELMoD=cereblon E3 ligase modulatory drug; IMiD=immunomodulatory drug; mAb=monoclonal antibody; mOS=median overall survival; mPFS=median progression-free survival; ORR=objective response rate; PI=proteasome inhibitor; RRMM=relapsed or refractory multiple myeloma

Suvannasankha A et al. ASH 2025;Abstract 100.

Phase Ib MagnetisMM-30: Objective Response Rate

ORR

- Overall, the confirmed ORR by investigator was 95.5% (95% CI, 77.2-99.9)
- Responses occurred early
  - Median time to response was 1.4 months (range, 0.5-2.7)



[a] Simple median of observation times.
CR=complete response; DL=dose level; ELRA=elranatamab; IBER=iberdomide; ORR=objective response rate; PR=partial response; QW=once weekly; Q2W=every 2 weeks; sCR=stringent complete response; VGPR=very good partial response

Suvannasankha A et al. ASH 2025;Abstract 100.

Phase Ib MagnetisMM-30: Authors' Conclusions

- Initial data from MagnetisMM-30 Part 1 demonstrate that the combination of elranatamab + iberdomide is effective and manageable in BCMA-naive patients with RRMM
  - Early and encouraging efficacy
    - With a median follow-up of 7.8 months the ORR was 95.5% and ≥CR rate was 45.5%
    - Responses occurred early and are expected to deepen further with longer follow-up
- Safety profile was consistent with known toxicities of individual components
    - The most frequent TEAEs were hematologic adverse events, infections, and CRS
    - The majority of infections were grade ≤2 and there were no infections grade >3
    - All CRS and ICANS events were grade ≤2
- This study is ongoing and actively recruiting patients for Part 2, which randomizes a larger group of patients with RRMM to two dosing schedules of elranatamab + iberdomide

BCMA=B-Cell maturation antigen; CR=complete response; CRS=cytokine release syndrome; DL=dose level; ICANS=immune effector cell–associated neurotoxicity syndrome; ORR=objective response rate; QD=once daily; Q2W=every 2 weeks; RRMM=relapsed or refractory multiple myeloma; TEAE=treatment-emergent adverse event

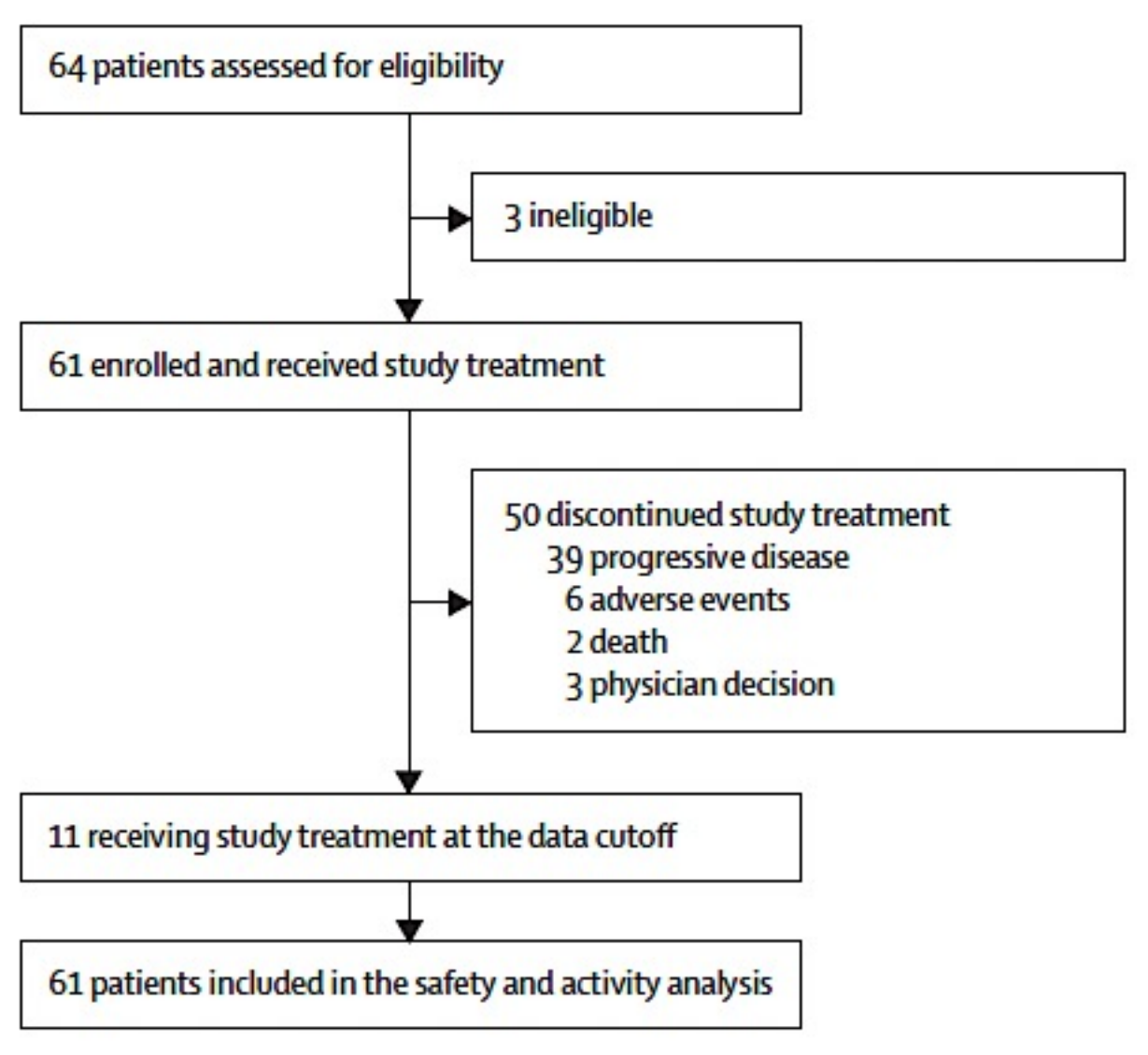
Suvannasankha A et al. ASH 2025;Abstract 100.

Lancet Haematol 2026; 13:e30-40

Iberdomide plus low-dose cyclophosphamide and dexamethasone in patients with relapsed and refractory multiple myeloma (the ICON study): a multicentre, single-arm, phase 2 trial

Charlotte L B M Korst, Wouter Plattel, Elizabeth A de Kort, Febe Smits, Alexandra J Croockewit, Mark-David Levin, Matthijs Westerman, Okke de Weerdt, Inger S Nijhof, Jurgen Wegman, Nina Smit, Christie P M Verkleij, Tuna Mutis, Kazem Nasserinejad, Ramses Kerstiens, Marjolein van der Klift, Laurens E Franssen, Maaike E M de Ruijter, Kaz Groen, Ellen van der Spek, Wilfried W H Roeloffzen, Sonja Zweegman, Niels W C J van de Donk

Phase II ICON Trial Profile

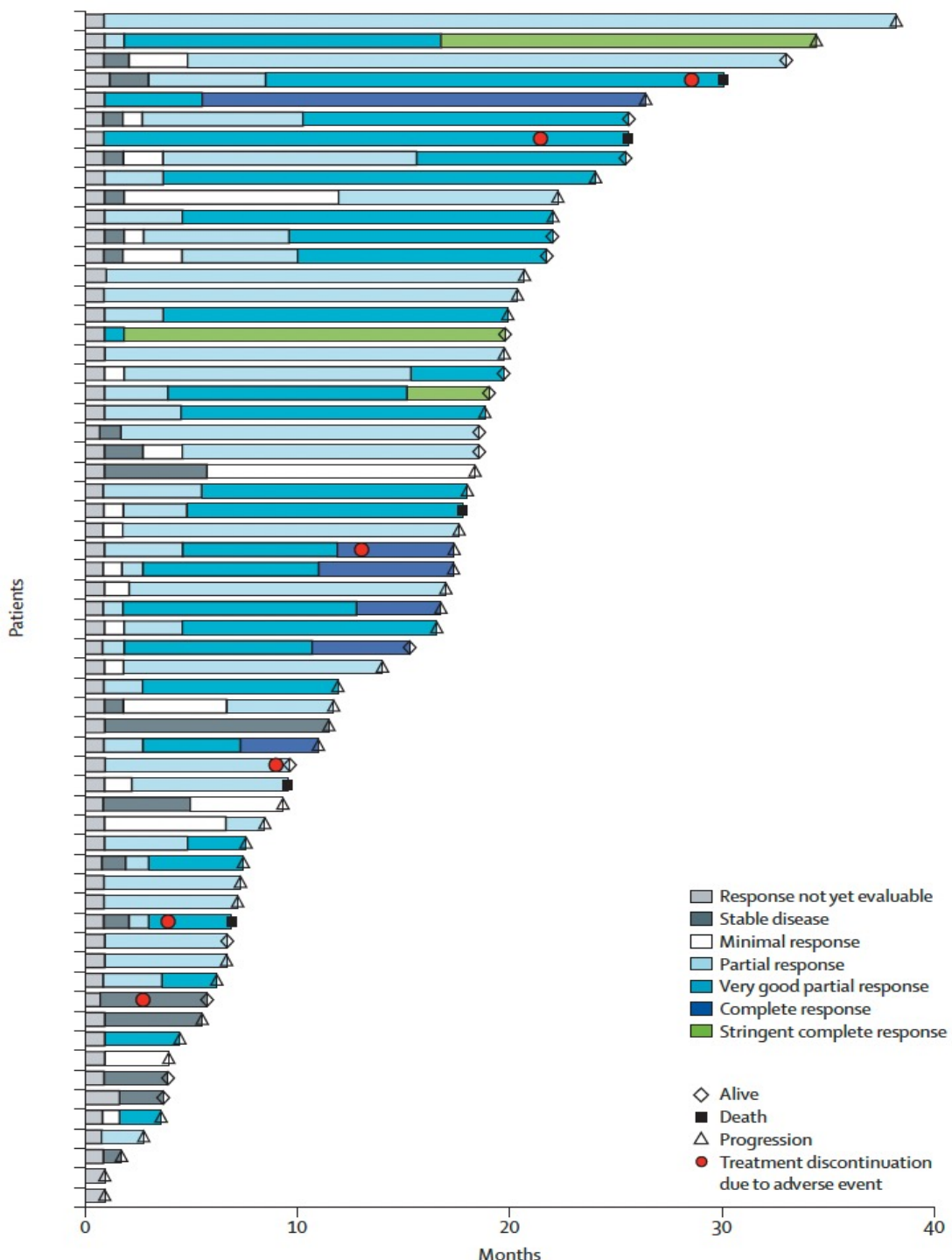


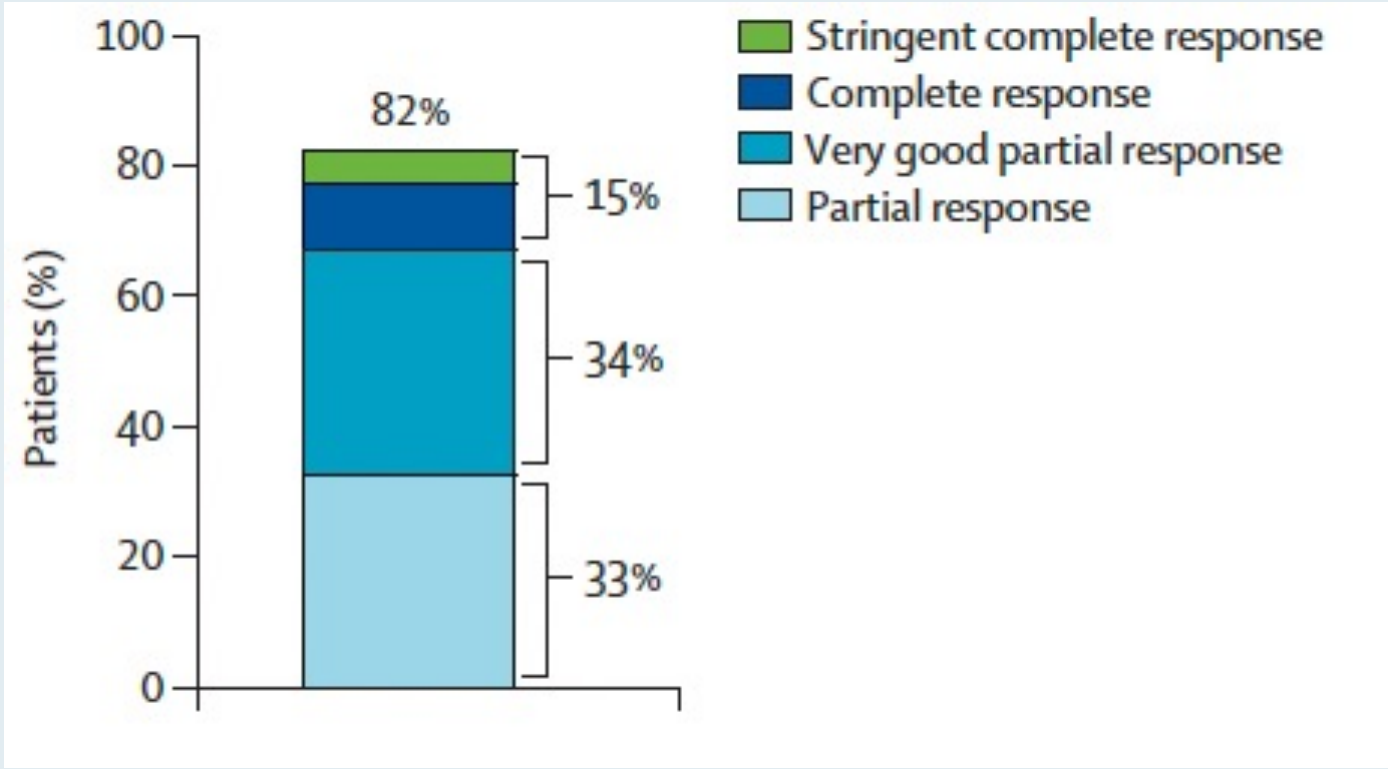
Primary endpoint:
PFS

Secondary endpoints:
ORR, Safety, OS, TTR, DoR, PFS2, TTNT

Korst CLBM et al. *Lancet Haematol* 2026 January;13(1):e30-40.

Phase II ICON: Responses with IberCd





Korst CLBM et al. *Lancet Haematol* 2026 January;13(1):e30-40.

RTP RESEARCH TO PRACTICE

Phase II ICON: Authors' Conclusions

- IberCd induced a high response rate and durable responses in patients with relapsed and refractory multiple myeloma who had received 2 to 4 previous lines of therapy and had lenalidomide-refractory disease.
- The main nonhematologic adverse events were infections, mostly respiratory infections.
- Most patients enrolled were triple-class exposed, representing a population that is challenging to treat. This regimen could be a valuable alternative alongside new T-cell-redirecting therapies, particularly for patients who are ineligible for these treatments because of frailty or comorbidities.

Korst CLBM et al. *Lancet Haematol* 2026 January;13(1):e30-40.

ASCO 2025;Abstract 7532

Iberdomide, bortezomib, and dexamethasone in transplant-ineligible newly diagnosed multiple myeloma: updated results from the CC-220-MM-001 trial

7532

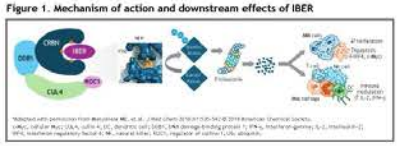
Darrell White,[1] Brea Lipe,[2] Mercedes Gironella Mesa,[3] Ruben Niesvizky,[4] Albert Oriol,[5] Anna Sureda Balari,[6] Manisha Bhutani,[7] Cristina Encinas,[8] Abdullah M. Khan,[9] Michael Amatangelo,[10] Danny Jeyaraju,[10] Kexin Jin,[10] Thomas Solomon,[10] Kevin Hong,[10] Alpesh Amin,[10] Olumoroti Aina,[10] Paulo Maciag,[10] Niels W.C.J. van de Donk,[11] Sagar Lonial[12]

[1]Dalhousie University and Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; [2]The Department of Medicine, University of Rochester Medical Center, Rochester, NY, USA; [3]Hematology Department, Vall d'Hebron Hospital, Barcelona, Spain; [4]Division of Oncology & Hematology, Weill Cornell Medicine, New York, NY, USA; [5]Catalan Institute of Oncology and Josep Carreras Institute, Hospital Germans Trias i Pujol, Badalona, Spain; [6]Hematology Department, Institut Català d'Oncologia - Hospitalet, IDIBELL, University of Barcelona, Barcelona, Spain; [7]Division of Plasma Cell Disorders, Department of Hematologic Oncology & Blood Disorders, Atrium Health Levine Cancer Institute, Wake Forest University School of Medicine, Charlotte, NC, USA; [8]Hospital General Universitario Gregorio Marañón (HGUGM), IISGM, Madrid, Spain; [9]The James Cancer Hospital and Solove Research Institute, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [10]Bristol Myers Squibb, Princeton, NJ, USA; [11]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Department of Hematology, Amsterdam, Netherlands, and Cancer Center Amsterdam, Amsterdam, Netherlands; [12]Winship Cancer Institute, Emory University, Atlanta, GA, USA

Introduction

- Lenalidomide (an immunomodulatory drug [IMiD®]) in combination with dexamethasone (DEX) and bortezomib (BORT) is an approved first-line treatment for patients with newly diagnosed multiple myeloma (NDMM) who are not planned to receive or are ineligible for autologous stem cell transplantation (ASCT)[1]
- CELMoD™ agents provide better therapeutic outcomes than IMiD agents, and they bind with cereblon (CRBN) with higher affinity due to their distinct binding features[2]
- Iberdomide (IBER) is a potent CELMoD agent (**Figure 1**) with stronger tumoricidal activity and immunomodulatory effects than IMiD agents[3-5]
- IBER has shown synergistic antiproliferative activity and apoptosis of MM cell lines in combination with BORT and DEX[3,4]
- IBER in combination with BORT and DEX (IberVd) has shown meaningful efficacy and safety in patients with transplant-ineligible (TNE) NDMM in the ongoing phase 1/2 CC-220-MM-001 trial (NCT02773030)[6]

Figure 1. Mechanism of action and downstream effects of IBER



Objective

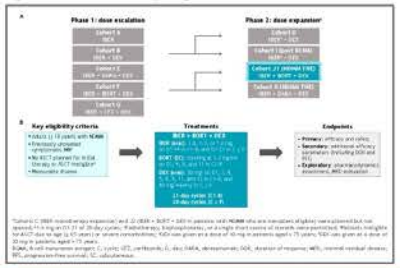
- To report updated results from the dose-expansion cohort of the CC-220-MM-001 trial evaluating IberVd in patients with NDMM who are TNE or are not receiving ASCT as their first therapy

Methods

Study design and treatment

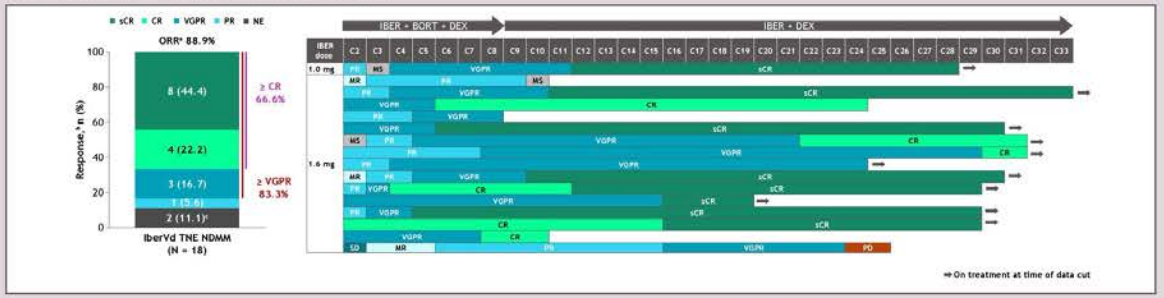
- CC-220-MM-001 is a phase 1/2 study evaluating IBER with different treatment combinations in patients with MM (**Figure 2**)
- In Cohort J1, patients received oral IBER at 1.0 mg or 1.6 mg on D1-14 of each 21-day cycle in C1-8 and on D1-21 of each 28-day cycle in C ≥ 9
- Endpoints included efficacy, safety, pharmacokinetics, and MRD assessment by next-generation flow cytometry
- Bone marrow samples were collected from patients who achieved a response of very good partial response (VGPR) or better at D1C7, and at 12, 18, 24 months, and annually thereafter

Figure 2. CC-220-MM-001 study design



IberVd demonstrates deep and durable responses in patients with TNE NDMM over 2 years of treatment

Figure 3. Efficacy of IberVd in patients with TNE NDMM (ITT population)



[a]Defined as PR or better; [b]Data cutoff: May 29, 2024; [c]Non-evaluable patients discontinued prior to completing 1 treatment cycle due to consent withdrawal or were lost to follow-up. ITT, intent-to-treat; MR, minimal response; MS, missing; SD, stable disease.

Results

Patients

- At data cutoff (May 29, 2024), 18 patients had received IberVd (1 patient at 1.0 mg, 17 patients at 1.6 mg)
- Baseline patient characteristics are shown in **Table 1**
  - Median age was 77.5 years (range, 57-84) and 11 (61.1%) patients had high-risk cytogenetics
  - 11 (61.1%) patients remain on treatment and median follow-up was 25.0 months (range, 0.7-29.5) (**Table 2**)
  - 3 patients discontinued due to withdrawal, 2 due to AEs (peripheral neuropathy and shingles), 1 due to PD, and 1 due to physician decision
  - 1 patient died during follow-up (stroke)

Table 1. Baseline characteristics

Characteristic[a]	IberVd TNE NDMM (N = 18)
Age, median (range), years	77.5 (57-84)
Patients aged ≥ 75 years, n (%)	11 (61.1)
Male sex, n (%)	12 (66.7)
Race, n (%)	
White	17 (94.4)
Not collected or reported	1 (5.6)
Time since diagnosis, median (range), years	0.1 (0-0.4)
ECOG performance status, n (%)	
0	3 (16.7)
1	11 (61.1)
2	4 (22.2)
ISS stage, n (%)	
I	7 (38.9)
II	9 (50.0)
III	2 (11.1)
High-risk cytogenetics,[b] n (%)	11 (61.1)[c]

[a]Data cutoff: May 29, 2024; [b]Defined in the presence of any abnormality for del(17p) and/or translocation (4;14), and for translocation (14;16) and/or amplification 1q21; 10/18 patients' data not available. [c]ECOG, Eastern Cooperative Oncology Group; ISS, International Staging System.

Table 2. Patient disposition

Patient disposition[a]	IberVd TNE NDMM (N = 18)
Follow-up, median (range), months	25.0 (0.7-29.5)
Ongoing treatment, n (%)	11 (61.1)
Discontinued treatment, n (%)	7 (38.9)
Patient withdrawal	3 (16.7)[b]
AE	2 (11.1)[c]
PD	1 (5.6)
Physician decision	1 (5.6)[c]

[a]Data cutoff: May 29, 2024; [b]2 patients withdrew consent and 1 patient stopped attending visits and switched to follow-up, due to peripheral neuropathy and shingles; due to suboptimal response; [c]Due to adverse event; PD, progressive disease.

Treatment received

- Of 17 evaluable patients, all 17 (100%) experienced ≥ 1 IBER dose modification, and 10 patients (58.8%) had ≥ 1 treatment-emergent AE (TEAE) that led to an IBER dose reduction (**Table 3**)
  - Patients received a median of 25.0 (range, 1.0-34.0) cycles, with a median IBER RDI of 74.6% (range, 45.0-100)

Table 3. Dose modifications and treatment exposure

Dose modifications[a]	IberVd TNE NDMM (N = 17)[b]
Patients with ≥ 1 IBER dose modification, n (%)	17 (100)
IBER dose interruptions due to TEAEs, n (%)	14 (82.4)
Patients with ≥ 1 TEAE leading to IBER dose reduction, n (%)	10 (58.8)
TEAEs leading to DEX dose reductions, n (%)	13 (76.5)
TEAEs leading to BORT dose reductions, n (%)	7 (41.2)
Treatment exposure[a]	
Treatment duration, median (range), months	24.9 (0.7-29.5)
Cycles received, median (range), n	25.0 (1.0-34.0)
RDI of IBER, median (range), %	74.6 (45.0-100)

[a]Data cutoff: May 29, 2024; [b]1 patient was enrolled but not included in the safety population due to self-withdrawal (appointment absence).

Safety

- 14 of 17 (82.4%) patients in the safety population had grade 3/4 TEAEs (**Table 4**)

Table 4. Most common (≥ 25% all grade) TEAEs

Most common (≥ 25% all grade) TEAEs and events of interest,[a] n (%)	IberVd TNE NDMM (N = 17)[b]		
	All grade	Grade 3	Grade 4
Hematologic TEAEs			
Neutropenia	7 (41.2)	2 (11.8)	3 (17.6)
Thrombocytopenia	6 (35.3)	2 (11.8)	1 (5.9)
Anemia	6 (35.3)	1 (5.9)	0
Lymphopenia	5 (29.4)	1 (5.9)	0
Non-hematologic TEAEs			
Peripheral edema	12 (70.6)	1 (5.9)	0
Peripheral neuropathy[c]	12 (70.6)	2 (11.8)	0
Constipation	10 (58.8)	1 (5.9)	0
Insomnia	8 (47.1)	1 (5.9)	0
Fatigue	7 (41.2)	2 (11.8)	0
Decreased appetite	7 (41.2)	0	0
Pain in extremity	6 (35.3)	0	0
Rash[c]	6 (35.3)	0	0
Dyspnea	6 (35.3)	1 (5.9)	0
Abdominal pain	5 (29.4)	0	0
Agitation	5 (29.4)	0	0
Dysgeusia	5 (29.4)	0	0
Infections	14 (82.4)	6 (35.3)	2 (11.8)
Pneumonia[c]	4 (23.5)	3 (17.6)	1 (5.9)
COVID-19[c]	8 (47.1)	2 (11.8)	0

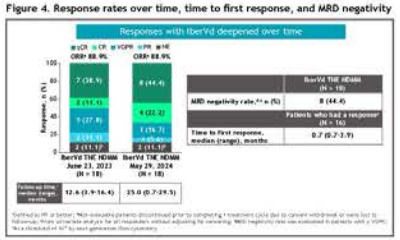
[a]Data cutoff: May 29, 2024; [b]1 patient was enrolled but not included in the safety population due to self-withdrawal (appointment absence); [c]Includes peripheral sensory neuropathy and peripheral motor neuropathy; [c]Includes rash, maculopapular rash, macular rash, follicular rash, and pruritic rash; [c]Includes pneumonia; [c]Includes COVID-19 and COVID-19 pneumonia.

- Grade 3/4 TEAEs were primarily infections (47.1%), including pneumonia (23.5%) and COVID-19 (11.8%)
- The most common hematologic grade 3/4 TEAE was neutropenia (29.4%)
- 2 (11.8%) patients experienced grade 3/4 peripheral neuropathy
- Other grade 3/4 non-hematologic TEAEs, including fatigue, were rare
- No pulmonary embolism events were reported during treatment; 1 patient experienced deep-vein thrombosis
- The most common TEAEs leading to dose reductions were peripheral neuropathy (23.5%), neutropenia (11.8%), and thrombocytopenia (11.8%)
- TEAEs were manageable with dose modifications or interruptions and granulocyte colony-stimulating factor use

Efficacy

- The overall response rate (ORR) was 88.9%: 8 patients achieved stringent complete response (sCR), 4 complete response (CR), 3 VGPR, and 1 partial response (PR); 2 patients were not evaluable (NE) for response (**Figure 3**)
- The ORR in the efficacy-evaluable population was 100%, with 93.8% of patients achieving VGPR or better, and 75.0% of patients achieving CR or better (not shown)
- Median time to response was 0.7 months (0.7-3.9) while median DOR was not reached (not shown), and 5 patients experienced deepening of response post 1 year of treatment (**Figure 4**)
- MRD negativity at 10^{-5} was reported in 8 (44.4%) patients, all of which had CR or better

Figure 4. Response rates over time, time to first response, and MRD negativity



[a]Defined as PR or better; [b]Non-evaluable patients discontinued prior to completing 1 treatment cycle due to consent withdrawal or were lost to follow-up. Prior achievable analysis for all responders without adjusting for censoring. [c]MRD negativity rate was evaluated in patients with a VGPR or better and MRD negativity at a threshold of 10^{-5} by next-generation flow cytometry.

Conclusions

- In this cohort of mostly older patients (median age 77.5 years) with TNE NDMM, longer follow-up confirmed that treatment with IberVd is associated with deep, durable responses
  - The ORR in the ITT population was 88.9% with 12 (66.6%) patients achieving CR or better
  - The ORR in the efficacy-evaluable population was 100%, with 93.8% of patients achieving VGPR or better, and 75.0% of patients achieving CR or better
  - MRD negativity at 10^{-5} was reported in 8 (44.4%) patients, and all had CR or better; 1 (5.6%) patient has converted to MRD negative status after an additional 1 year of follow-up
- IberVd was safe and well-tolerated, with no new safety signals during continued IBER treatment
  - Most grade 3/4 TEAEs were hematologic and the occurrence of grade 3/4 non-hematologic TEAEs was low
  - Only 2 patients discontinued treatment due to an AE (1 due to peripheral neuropathy and 1 due to shingles)
- These data support further evaluation of IBER combinations, including IberVd, in the frontline setting

References

1. Mertz M, et al. *Ann Hematol* 2020;99:1709-1725.
2. Watson ER, et al. *Science* 2022;378:549-553.
3. Amatangelo M, et al. *Blood* 2018;132(suppl 1). Abstract 1935.
4. Amatangelo M, et al. *Blood* 2020;136(suppl 1). Abstract 1359.
5. Lonial S, et al. *Lancet Haematol* 2022;9:e822-e832.
6. White D, et al. *Clin Lymphoma Myeloma Leuk* 2024;24(suppl 1). Abstract S239.

Acknowledgments

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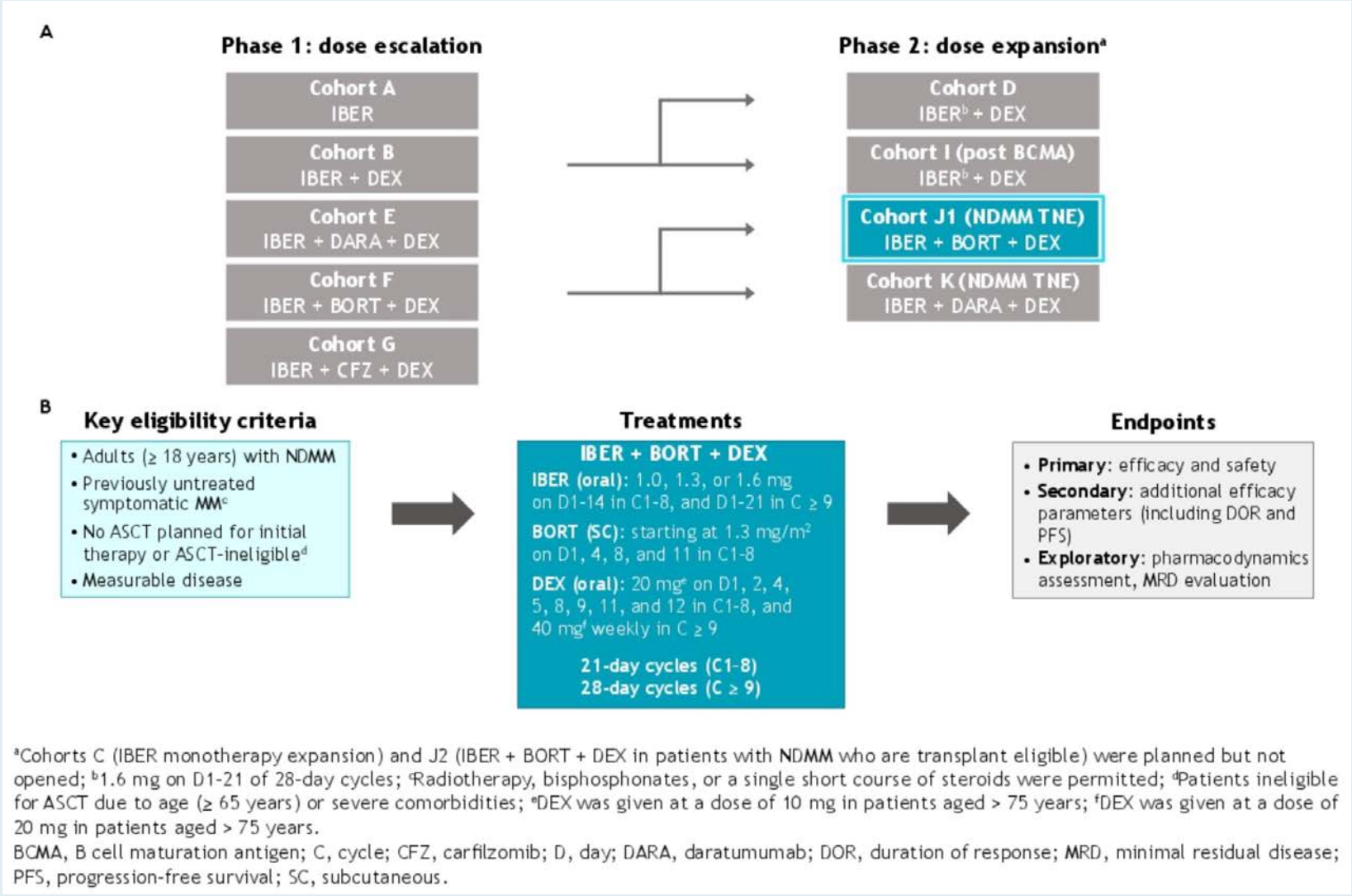
- The clinical study teams who participated
- The investigators of the CC-220-MM-001 study
- The study was supported by Celgene, a Bristol-Myers Squibb Company
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Maura Locati, PhD, of Excerpta Medica, funded by Bristol Myers Squibb

Phase I/II CC-220-MM-001 Study Design

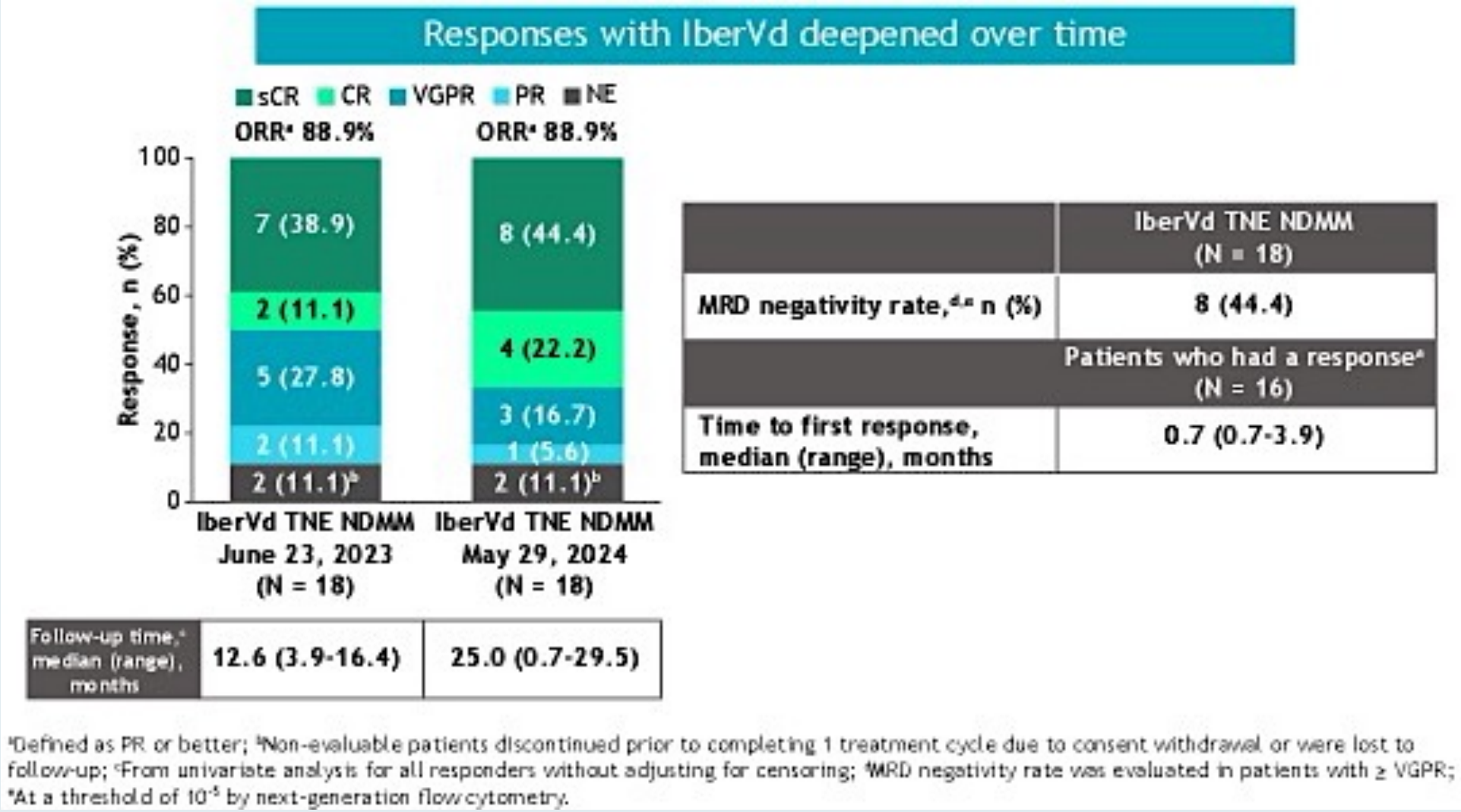


[a]Cohorts C (IBER monotherapy expansion) and J2 (IBER + BORT + DEX in patients with NDMM who are transplant eligible) were planned but not opened; [b]1.6 mg on D1-21 of 28-day cycles; [c]Radiotherapy, bisphosphonates, or a single short course of steroids were permitted; [d]Patients ineligible for ASCT due to age (≥ 65 years) or severe comorbidities; [e]DEX was given at a dose of 10 mg in patients aged > 75 years; [f]DEX was given at a dose of 20 mg in patients aged > 75 years.
BCMA, B cell maturation antigen; C, cycle; CFZ, carfilzomib; D, day; DARA, daratumumab; DOR, duration of response; MRD, minimal residual disease; PFS, progression-free survival; SC, subcutaneous.

NDMM = newly diagnosed MM; TNE = transplant ineligible

White D et al. ASCO 2025;Abstract 7532.

Phase I/II CC-220-MM-001: Responses over Time



Follow-up time,[c] median (range), months	12.6 (3.9-16.4) / 25.0 (0.7-29.5)

	IberVd TNE NDMM (N = 18)
MRD negativity rate,[d,e] n (%)	8 (44.4)
	Patients who had a response[a] (N = 16)
Time to first response, median (range), months	0.7 (0.7-3.9)

[a]Defined as PR or better; [b]Non-evaluable patients discontinued prior to completing 1 treatment cycle due to consent withdrawal or were lost to follow-up; [c]From univariate analysis for all responders without adjusting for censoring; [d]MRD negativity rate was evaluated in patients with ≥ VGPR; [e]At a threshold of 10^{-5} by next-generation flow cytometry.

ORR = overall response rate

White D et al. ASCO 2025;Abstract 7532.

Phase I/II CC-220-MM-001: Authors' Conclusions

- In this cohort of mostly older patients (median age 77.5 years) with TNE NDMM, longer follow-up confirmed that treatment with IberVd is associated with deep, durable responses
  - The ORR in the ITT population was 88.9% with 12 (66.6%) patients achieving CR or better
  - The ORR in the efficacy-evaluable population was 100%, with 93.8% of patients achieving VGPR or better, and 75.0% of patients achieving CR or better
  - MRD negativity at 10^{-5} was reported in 8 (44.4%) patients, and all had CR or better; 1 (5.6%) patient has converted to MRD negative status after an additional 1 year of follow-up
- IberVd was safe and well-tolerated, with no new safety signals during continued IBER treatment
  - Most grade 3/4 TEAEs were hematologic and the occurrence of grade 3/4 non-hematologic TEAEs was low
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- These data support further evaluation of IBER combinations, including IberVd, in the frontline setting

White D et al. ASCO 2025;Abstract 7532.

Mezigdomide Key Datasets

- Richardson PG et al. **Mezigdomide plus dexamethasone** in **relapsed and refractory multiple myeloma**. *N Engl J Med* 2023 September 14;389(11):1009-22.
- Richardson PG et al. **Mezigdomide (MEZI) plus dexamethasone (DEX) and daratumumab (DARA) or elotuzumab** (ELO) in patients (pts) with **relapsed/refractory multiple myeloma (RRMM): Results from the CC-92480-MM-002 trial**. ASH 2023;Abstract 1013.
- Byun JM et al. **Phase I/II study of mezigdomide and elranatamab** for **relapsed/refractory multiple myeloma** patients **(MELT-MM): Initial results from part 1**. ASH 2025;Abstract 5835.
- Mo C et al. **Selinexor, mezigdomide, and dexamethasone** in patients with **relapsed/refractory multiple myeloma** who **relapsed or are ineligible for T-cell–redirecting therapy**: **STOMP Phase 1 results**. ASH 2025;Abstract 4010.

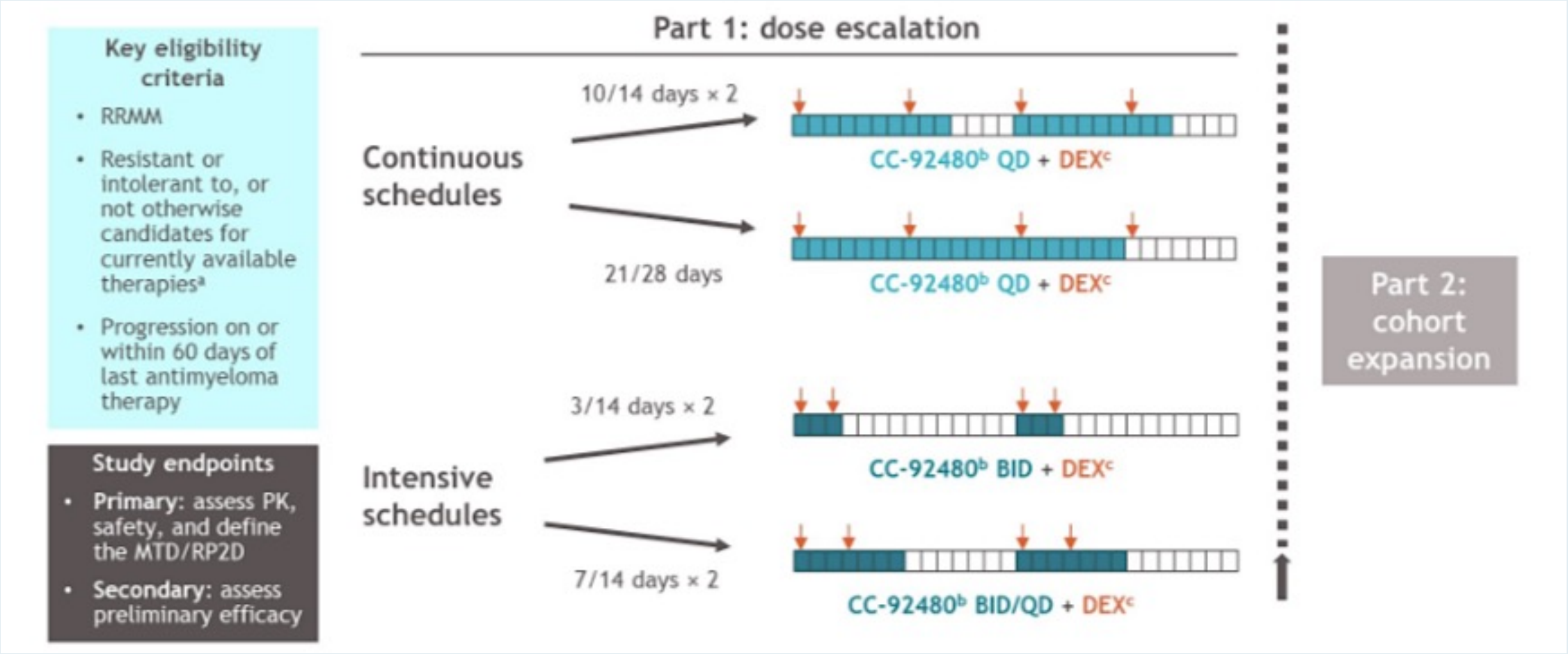
ORIGINAL ARTICLE

Mezigdomide plus Dexamethasone in Relapsed and Refractory Multiple Myeloma

P.G. Richardson, S. Trudel, R. Popat, M.-V. Mateos, A.J. Vangsted, K. Ramasamy, J. Martinez-Lopez, H. Quach, R.Z. Orlowski, M. Arnao, S. Lonial, C. Karanes, C. Pawlyn, K. Kim, A. Oriol, J.G. Berdeja, P. Rodríguez Otero, I. Casas-Avilés, A. Spirli, J. Poon, S. Li, J. Gong, L. Wong, M. Lamba, D.W. Pierce, M. Amatangelo, T. Peluso, P. Maciag, J. Katz, M. Pourdehnad, and N.J. Bahlis, for the CC-92480-MM-001 Study Investigators*

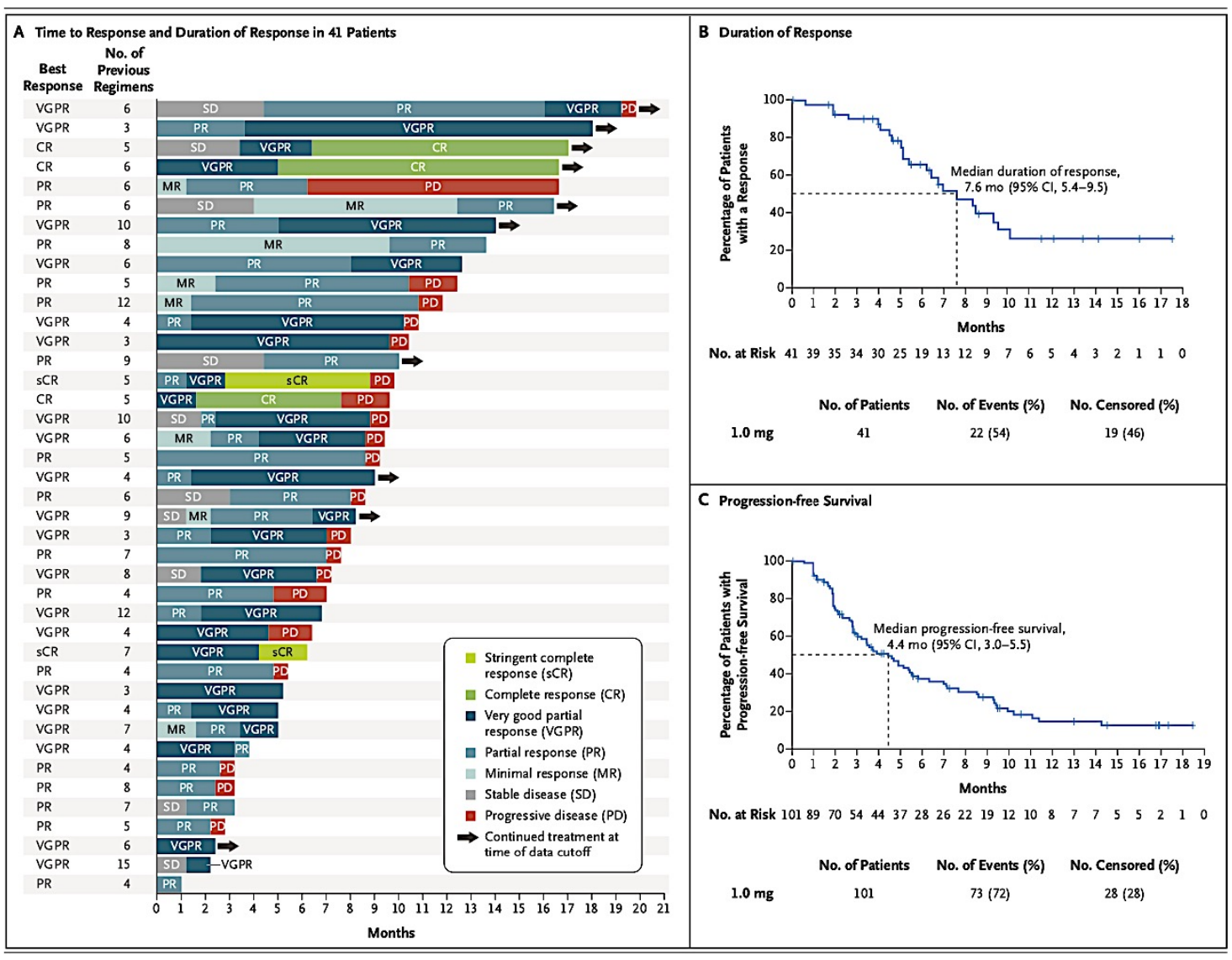
***N Engl J Med* 2023 September 14;389(11):1009-22.**

Phase I/II CC-92480-MM-001 Study Design



Richardson PG et al. *N Engl J Med* 2023 September 14;389(11):1009-22.

Phase I/II CC-92480-MM-001: Responses, PFS



Richardson PG et al. *N Engl J Med* 2023 September 14;389(11):1009-22.

Phase I/II CC-92480-MM-001: Authors' Conclusions

The all-oral combination of mezigdomide and dexamethasone showed promising efficacy in patients with heavily pretreated multiple myeloma, with treatment-related adverse events consisting mainly of myelotoxic effects.

Richardson PG et al. *N Engl J Med* 2023 September 14;389(11):1009-22.

Oral Abstracts

653.Multiple Myeloma: Prospective Therapeutic Trials

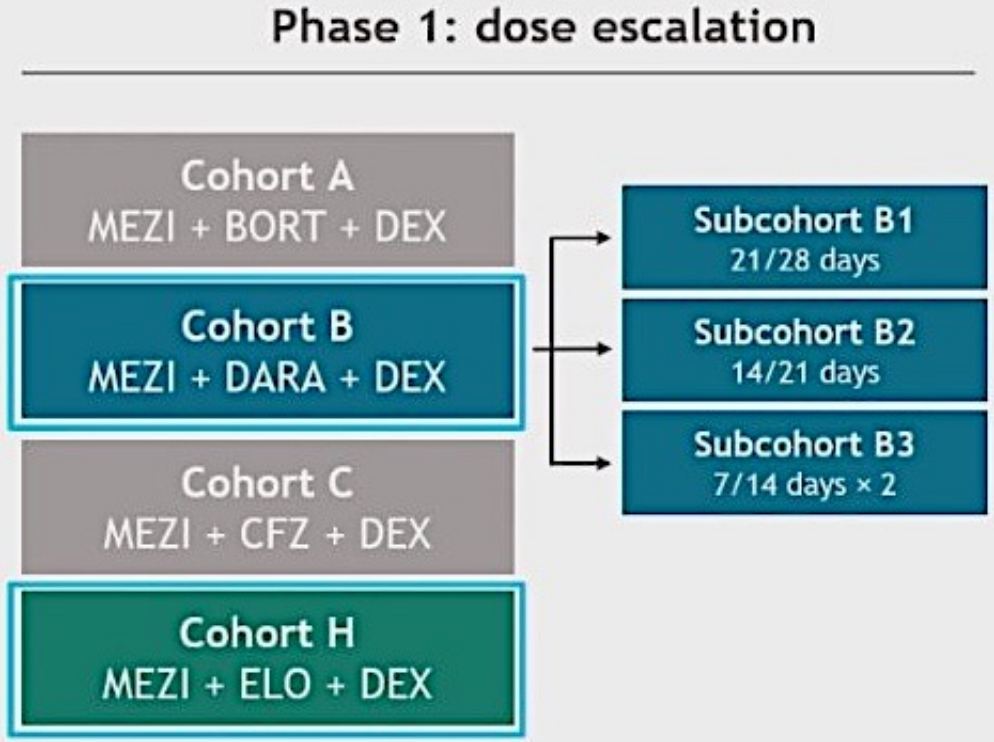
Mezigdomide (MEZI) Plus Dexamethasone (DEX) and Daratumumab (DARA) or Elotuzumab (ELO) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Results from the CC-92480-MM-002 Trial

Paul G. Richardson MD [1], Irwindeep Sandhu [2], Craig C. Hofmeister MD [3], Robert Z. Orlowski MD PhD [4], Darrell White [5], Angelo Belotti MD [6], Charlotte Toftmann Hansen [7], Noopur S. Raje [8], Tracy T. Chow [9], Zehua Zhou [9], Tiziana Civardi [10], Phillip Koo [9], Yue Zhu [9], Jessica Katz [9], Albert Oriol [11]

ASH 2023:Abstract 1013.

Phase I/II CC-92480-MM-002 Study Design

- Phase 1/2 study evaluating MEZI with different treatment combinations in MM[1,2]
- MEZI + BORT + DEX (MeziVd) was shown to be safe and effective in patients with RRMM[3]
- Promising results were also achieved with MEZI + CFZ + DEX (MeziKd)[3]
- **Objective:** to report the first results from the cohorts evaluating the dose and schedule of MEZI + DARA + DEX (MeziDd) and MEZI + ELO + DEX (MeziEd)

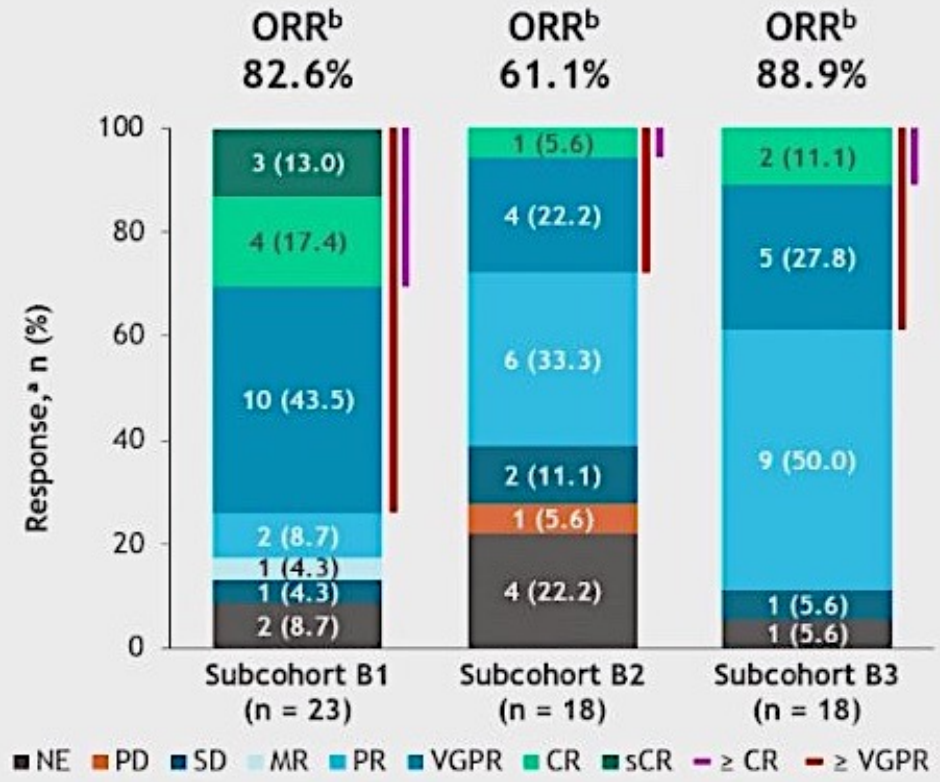


BORT, bortezomib; CFZ, carfilzomib; DARA, daratumumab; ELO, elotuzumab.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT03989414 NCT03989414. Accessed Nov 28, 2023; 2. EudraCT. https://www.clinicaltrialsregister.eu/ctr-search/search?query=2018-004767-31. Accessed Nov 28, 2023; 3. Oriol A, et al. *Clin Lymphoma Myeloma Leuk* 2023;23(suppl 2). Abstract OA-49.

Richardson PG et al. ASH 2023;Abstract 1013.

Phase I/II CC-92480-MM-002: Efficacy in Cohort B – MeziDd



ORR = overall response rate

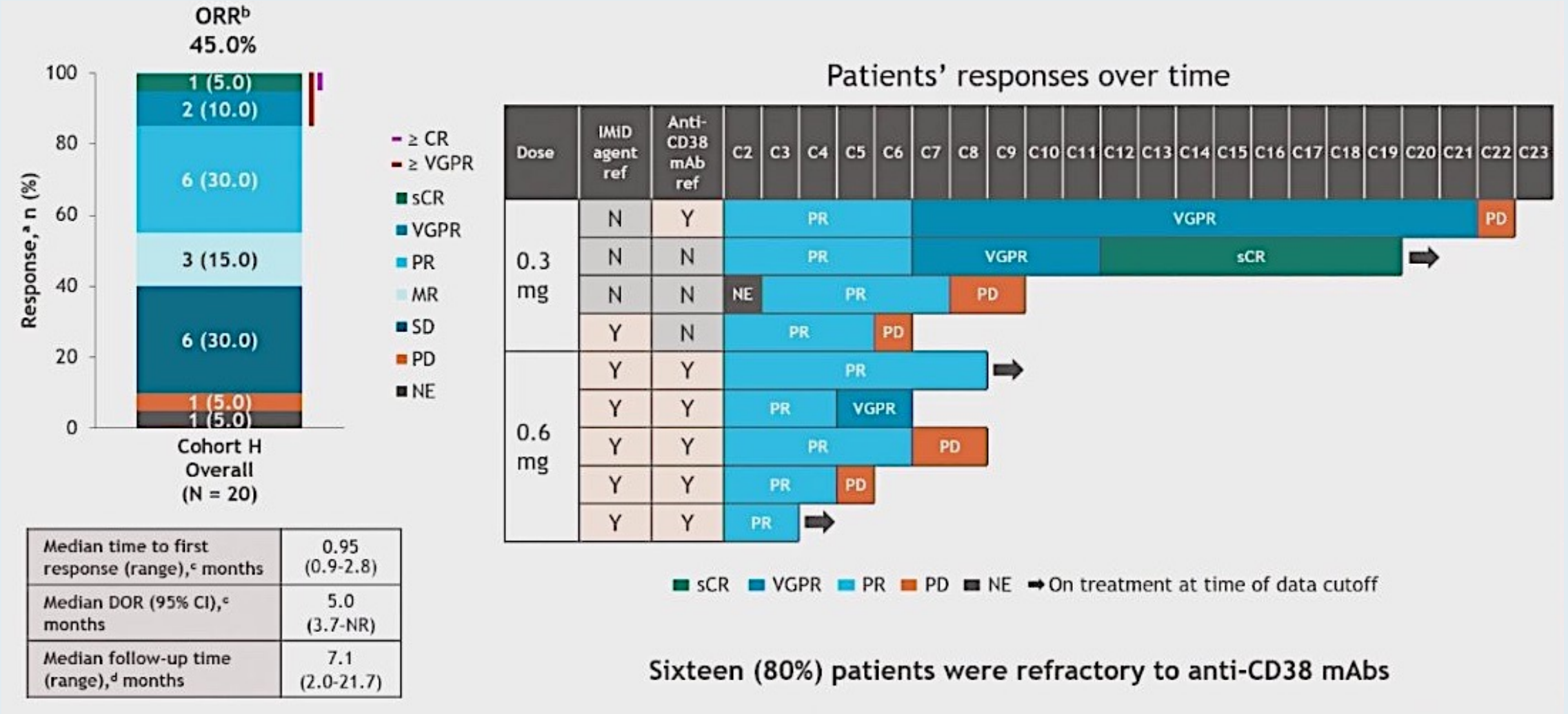
	Subcohort B1 21/28 days (n = 23)	Subcohort B2 14/21 days (n = 18)	Subcohort B3 7/14 days × 2 (n = 18)
Median time to first response (range),[c] months	1.18 (0.9-4.6)	0.89 (0.7-2.8)	1.61 (0.9-4.6)
Median DOR (95% CI),[c] months	NR (23.3-NR)	NR (4.6-NR)	9.5 (9.5-NR)
Median follow-up time (range),[d] months	22.6 (0.7-39.6)	3.1 (0.5-15.2)	6.6 (2.8-14.1)

- **Combined ORR for cohort B (B1+B2+B3) was 78%**
- Lower response rates to date in Subcohort B2 might be explained by the median follow-up time of only 3 months
- Among the efficacy-evaluable population in Subcohort B2, only 1 instance of disease progression was observed
- Importantly, dose exposure per cycle was highest in patients receiving MEZI in 3 out of 4 weeks and lowest in patients receiving MEZI in 1 out of 2 weeks, suggesting that Subcohort B2 is not yet mature for ORR

Richardson PG et al. ASH 2023;Abstract 1013.

RTP RESEARCH TO PRACTICE

Phase I/II CC-92480-MM-002: Efficacy in Cohort H – MeziEd



Median time to first response (range),[c] months	0.95 (0.9-2.8)
Median DOR (95% CI),[c] months	5.0 (3.7-NR)
Median follow-up time (range),[d] months	7.1 (2.0-21.7)

ORR = overall response rate; DOR = duration of response; mAbs = monoclonal antibodies

Richardson PG et al. ASH 2023;Abstract 1013.

RTP RESEARCH TO PRACTICE

Phase I/II CC-92480-MM-002: Authors' Conclusions

- MEZI in combination with mAbs (DARA or ELO) showed promising efficacy in patients with RRMM
  - ORR with MeziDd was 82.6% (Subcohort B1), 61.1% (Subcohort B2), and 88.9% (Subcohort B3); ORR with MeziEd was 45.0% (overall)
  - Patients treated with MeziDd achieved a response regardless of dose and schedule
  - MeziEd was active in patients who were refractory to prior anti-CD38 mAb therapy
- The safety profile of MEZI plus mAbs was manageable, consistent with prior reports[1,2]
  - Most grade 3/4 TEAEs following MeziDd or MeziEd were hematologic; neutropenia was the most common grade 3/4 TEAE and was managed with G-CSF and dosing schedule adjustments
  - The occurrence of grade 3/4 non-hematologic TEAEs was relatively low with either combination
- MEZI was immune-stimulatory in combination with DARA and ELO at all schedules and dose levels tested
  - Translational data from the MeziDd cohorts was presented in the Chow T, et al. ASH poster on Sunday, December 10, 2023 (poster 3318)
- These data support further evaluation of MEZI in combination with immunotherapies (including CD38, SLAMF7, BCMA, and GPRC5D-targeting approaches) at flexible doses and schedules in RRMM

Richardson PG et al. ASH 2023;Abstract 1013.

Phase I/II study of Mezigdomide and Elranatamab for Relapsed/ Refractory Multiple Myeloma Patients (MELT-MM): Initial Results from Part 1

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1. Seoul National University College of Medicine, Seoul National University Hospital, Seoul, Korea; 2. Seoul St Mary's Hospital, The Catholic University of Korea, Seoul, Korea ; 3. Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea; 4. Asan Medical Center, University of Ulan College of Medicine, Seoul, Korea; 5. Chonnam National University Hwasun Hospital, Chonnam National University Medical School, Hwasun, Korea; 6. Cancer Science Institute of Singapore, National University of Singapore, Singapore ; 7. Singapore General Hospital, Singapore

BACKGROUND

- Despite significant advances, multiple myeloma (MM) remains incurable and new therapies are needed to improve outcomes.
- Mezigdomide (MEZI) is a high potent CELMOD™ agent with enhanced tumoricidal and immune-modulatory effects by inducing rapid degradation of Ikaros/Aiolos.
- Elranatamab (ELRA) is a BCMA-CD3 bispecific antibody, approved for use in many parts of the world based on its durable response with a manageable safety profiles in patients with R/R MM.
- Considering (1) the cell autonomous and immunomodulatory effects of MEZI; (2) that MEZI may reverse and prevent T-cell exhaustion/ dysfunction when used with T-cell engagers; and (3) the fact that BCMA expression persists through disease relapses, we expect the combination of MEZI plus ELRA will yield promising results in R/R setting based on NK-cell / T-cell modulation, anti-proliferation and tumor apoptosis.

OBJECTIVES

- Part 1: To evaluate the tolerability and safety of elranatamab in combination with mezigdomide and dexamethasone and define RP2D.
- Part 2: To evaluate the efficacy of elranatamab in combination with mezigdomide based on ORR per IMWG 2016.

METHODS

STUDY DESIGN (NCT06645678)

- Open-label, single arm, multinational phase I/II study
- Conducted in 2 parts (Figure 1) This is a report of **Part 1** (Figure 2) results.

Figure 1. Study Design

Figure 2. Part 1 schema (3+3 design with target MEZI dose of 1mg)

*C0 is 14 days; C1~ is 28 days. ELRA Weekly up to C6, if PR or better response after C6 then q 2 weeks → if CR or better response after C12 then q 4 weeks

Table 1. Key eligibility criteria

- Relapsed or refractory after failure of 2 or more lines of systemic treatments.
- All patients must have received at least one proteasome inhibitor and lenalidomide.
- Measurable disease per IMWG criteria
- ECOG performance status 0-2
- Adequate liver, renal, and bone marrow function

IMWG, International Myeloma Working Group; ECOG, Eastern Cooperation Oncology Group

Table 2. Primary & secondary endpoints

Primary endpoints

ORR per IMWG criteria
Timeframe: from baseline and every 28 days through disease progression/death up to 24 months

Secondary endpoints

- Recommended mezigdomide dose
- Safety
- Progression free survival (PFS)
- Overall survival (OS)
- Complete response rate or better
- Very good partial response rate or better
- Time to response (TTR)
- Duration of response (DOR)
- Time to next treatment (TTNT)
- Minimal residual disease negativity rate

RESULTS-I

BASELINE CHARACTERISTICS

	N=15
Age, years (median, range)	69 (52-76)
Sex, male (N, %)	9 (60)
Prior lines (median, range)	4 (2-7)
High risk (N,%)	
del17p	3 (20.0)
t(4;14)	3 (20.0)
t(14;16)	0
EMD at enrollment (N,%)	5 (33.3)
Prior treatment (N, %)	
ASCT	10 (66.7)
Daratumumab	8 (53.3)
non-BCMA TCE	4 (26.7)
Triple refractory	8 (53.3)
Penta-refractory	7 (46.7)
MEZI dose*	
0.3mg (N=8)	DLT evaluable in 6
0.6mg (N=7)	DLT evaluable in 6

EMD, extramedullary disease; ASCT, autologous stem cell transplantation; TCE, t-cell engager

*Replacements due to 1) traumatic hip fracture, leading to inadequate drug dose intensity (0.3mg); 2) progression after C0 ELRA (0.3mg); and 3) patient's consent withdrawal due to religious reasons (0.6mg).

RESULTS-II

DOSE LIMITING TOXICITIES (DLT) & SAFETY SIGNALS

Table 3. Safety (N=12)

	N, %
Cytokine release syndrome (CRS)	8 (66.7%)
Grade ≥ 3 CRS	0
ICANS	0
Infection during DLT period	1 (8.3%)
clinically significant CMV	1
Neutropenia during DLT period	1 (8.3%)
Grade 3	1
Thrombocytopenia during DLT period	2 (16.7%)
Grade 3	2

ICANS, immune effector cell-associated neurotoxicity syndrome; CMV, cytomegalovirus

- The protocol mandates the use of pegteograstim or pegfilgrastim for the first 6 cycles prior to D15 (Recommendation: D1 or D8). The use of pegteograstim did not aggravate CRS.
- 2 DLT events occurred in 0.6mg cohort
  1. 75/F, IMWG-FS 2, 4 prior lines of therapy
     - C1D15 DLT d/t grade 4 thrombocytopenia lasting 6 days
     - Resolved → currently ongoing, on 0.3mg MEZI
  2. 76/F, IMWG-FS 2, 4 prior lines of therapy
     - C1D13 DLT d/t grade 3 AKI related to infection (parainfluenza pneumonia)
     - Resolved → currently onngoing, on 0.3mg MEZI

PRELIMINARY EFFICACY DATA

- Available from 11 / 15 patients, with median FU duration 213 days (59-311 days)
- Median time to first response (PR): 17 days (14-40 days)

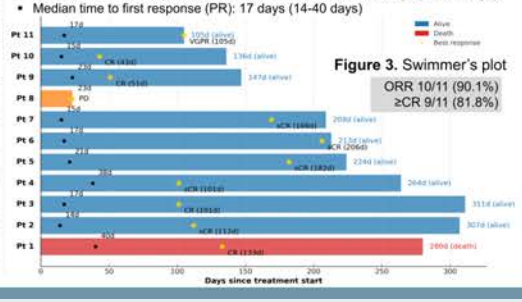

Figure 3. Swimmer's plot

ORR 10/11 (90.1%)
≥CR 9/11 (81.8%)

CONCLUSIONS

In patients with R/R MM, initial results suggest that the combination of MEZI + ELRA is clinically feasible and show therapeutic potential.

CONTACT INFORMATION

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ACKNOWLEDGMENTS

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ASH 2025;Abstract 5835.

Phase I/II MELT-MM Study Design

Figure 1. Study Design

Figure 2. Part 1 schema (3+3 design with target MEZI dose of 1mg)

[Cohort 1]
Elranatamab 76mg sc weekly* + Mezigdomide 0.3mg D1-21 + dexamethasone

[Cohort 2]
Elranatamab 76mg sc weekly* + Mezigdomide 0.6mg D1-21 + dexamethasone

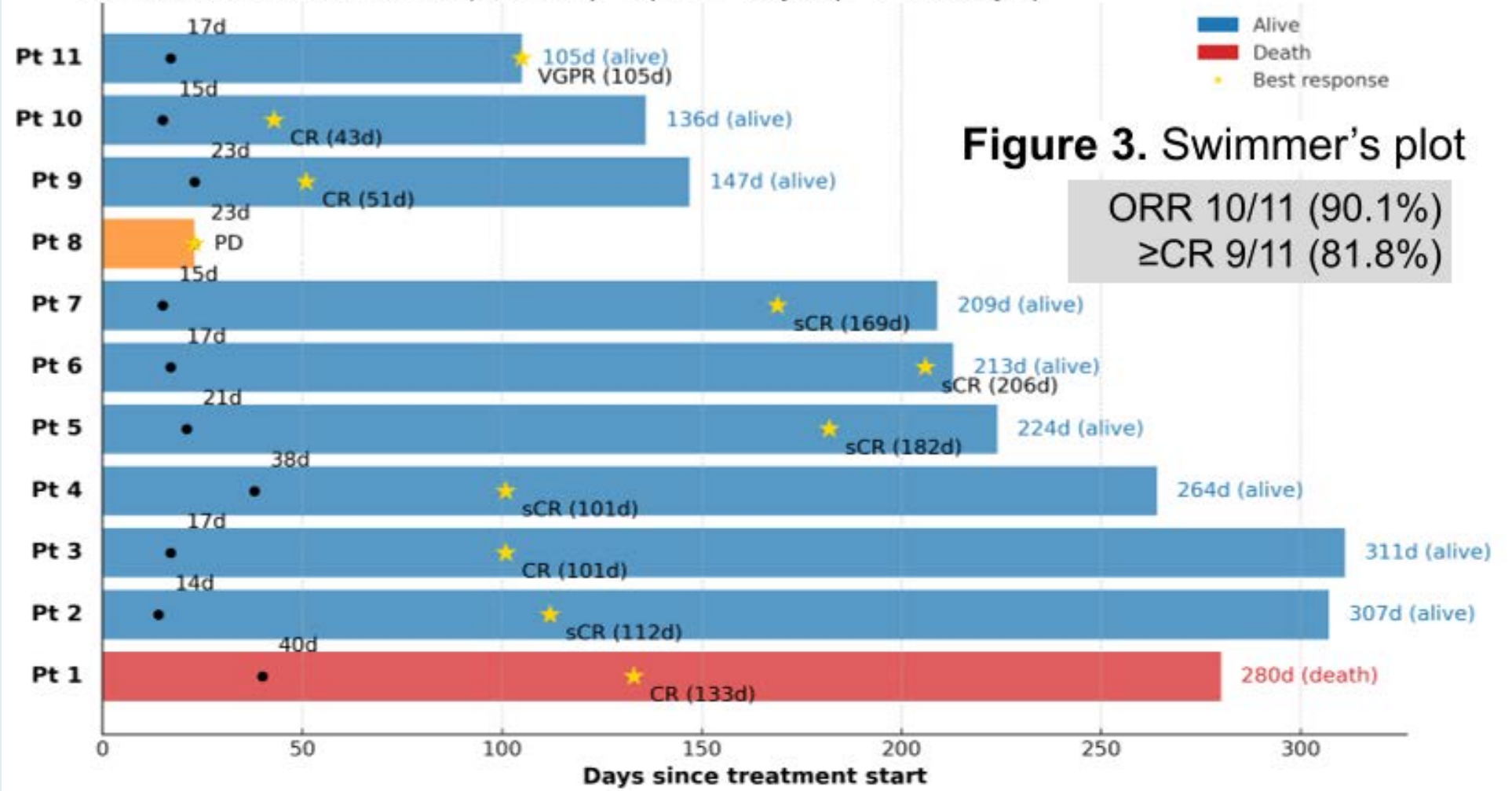
[Cohort 3]
Elranatamab 76mg sc weekly* + Mezigdomide 1mg D1-21 + dexamethasone

*C0 is 14 days; C1~ is 28 days. ELRA Weekly up to C6, if PR or better response after C6 then q 2 weeks → if CR or better response after C12 then q 4 weeks

Byun JM et al. ASH 2025;Abstract 5835.

Phase I/II MELT-MM: Preliminary Efficacy Data

- Available from 11 / 15 patients, with median FU duration 213 days (59-311 days)
- Median time to first response (PR): 17 days (14-40 days)



ORR = overall response rate

Byun JM et al. ASH 2025;Abstract 5835.

Phase I/II MELT-MM: Authors' Conclusions

In patients with R/R MM, initial results suggest that the combination of MEZI + ELRA is clinically feasible and shows therapeutic potential.

Byun JM et al. ASH 2025;Abstract 5835.

Poster# 4010

Selinexor, mezigdomide, and dexamethasone in patients with relapsed/refractory multiple myeloma who relapsed or are ineligible for T-cell redirecting therapy: STOMP Phase 1 preliminary results

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[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Duke Cancer Institute, Durham, NC, USA; [3]University of Washington, Seattle, WA, USA; [4]Karyopharm Therapeutics, Newton, MA, USA; [5]Bristol Myers Squibb, Princeton, NJ, USA

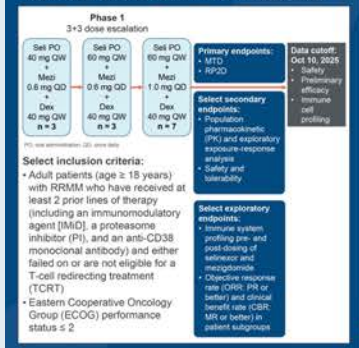
Introduction

- CAR T-cell therapy and anti-B-cell maturation antigen (BCMA) bispecific antibody treatments for relapsed/refractory multiple myeloma (RRMM) show excellent clinical activity, but nearly all patients relapse within 24 months[1]
- Some anti-myeloma therapies such as alkylating chemotherapy may promote T-cell exhaustion and inferior T-cell therapy outcomes[1], leaving an unmet need to identify agents that could be used to either optimize a future CAR-T or bispecific antibody therapy, and/or salvage T-cell redirecting treatment failures
- Both selinexor (seli), an oral exportin 1 (XPO1) inhibitor and mezigdomide (mezi), a novel cereblon E3 ubiquitin ligase modulator (CELMoD), have been shown to have T-cell stimulatory activity in preclinical and clinical studies
  - Selinexor is approved in combination with dexamethasone (dex) in penta-refractory multiple myeloma (MM) and with dexamethasone and bortezomib in RRMM after ≥1 prior therapy[2]
  - Selinexor shown to have anti-inflammatory and T-cell activating properties that may facilitate a favorable immune microenvironment for effector T cells[3–5]
  - Mezigdomide has been shown to reverse T-cell exhaustion and reinvigorate cytokine production pathways, as well as be active and well tolerated in RRMM, including anti-BCMA-exposed and refractory patients[6,7]
- STOMP Arm 12 is investigating whether the all-oral combination of selinexor, mezigdomide, and dexamethasone (SMd) could produce additive or synergistic effects superior to either agent alone in RRMM that has either progressed after or is otherwise ineligible for T-cell redirecting therapy. The Phase 1 results for Arm 12 are presented herein

Methods

STOMP Arm 12: A Phase 1/2 Study of SMd for RRMM (NCT02343042)

- STOMP Arm 12 is multicenter, open-label, clinical study with a 3+3 dose escalation (Phase 1) and expansion (Phase 2) to independently assess the maximum tolerated dose (MTD), efficacy, and safety of SMd in patients with RRMM that has either progressed after or is otherwise ineligible to be treated with a T-cell redirecting therapy
- During the Phase 1 dose escalation phase, selinexor was escalated from 40 mg once weekly (QW) to 60 mg on days 1, 8, 15 (3 weeks on 1 week off), in combination with mezigdomide 0.6 to 1.0 mg daily (QD) on days 1-21 and dexamethasone 40 mg on days 1, 8, 15, and 22 of a 28-day cycle to establish the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D)



Select inclusion criteria:

- Adult patients (age ≥ 18 years) with RRMM who have received at least 2 prior lines of therapy (including an immunomodulatory agent [IMiD], a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody) and either failed on or are not eligible for a T-cell redirecting treatment (TCRT)
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2

Results

Patient Demographics and Baseline Characteristics

- As of Oct 10, 2025, a total of 13 patients have been enrolled
  - 3 in **Cohort 1** seli 40 mg QW/mezi 0.6 mg QD/dex 40 mg QW
  - 3 in **Cohort 2** seli 60 mg QW/mezi 0.6 mg QD/dex 40 mg QW
  - 7 in **Cohort 3** seli 60 mg QW/mezi 1.0 mg QD/dex 40 mg QW

Characteristics	Total (N = 13)
Age (years), median (range)	66 (42–83)
≥ 75 years, n (%)	2 (15)
Sex (male), n (%)	9 (69)
Race, n (%)	
African American	3 (23)
Native Hawaiian or Pacific Islander	1 (8)
White	9 (69)
ECOG performance status, n (%)	
0	8 (62)
1	5 (39)
ISS disease stage, %	
I	9
II	2
III	2
Time since diagnosis (years), median (range)	7.5 (2.7–22.0)
Extramedullary lesions, n (%)	3 (23)
Number of prior lines of therapy, median (range)	5 (2–12)
Exposure to at least one IMiD, n (%)	13 (100)
Exposure to at least one PI, n (%)	13 (100)
Exposure to at least one anti-CD38 antibody, n (%)	13 (100)
Exposure/refractory to T-cell redirecting treatment,[1] n (%)	3 (23)
Exposure/refractory to belantamab mafodotin, n (%)	3 (23)
Exposure/refractory to to iberdomide, (%)	1 (7)
Autologous stem cell transplant, n (%)	9 (69)
Refractory to at least one IMiD, n (%)	12 (92)
Refractory to at least one PI, n (%)	10 (77)
Refractory to at least one anti-CD38 antibody, n (%)	13 (100)
Refractory to last line of treatment, n (%)	12* (92)

*Data pending. [1]TCRTs include: CAR T-cell therapy, IgM3N4 (CE3xCD3 bispecific), belantamab (GPRC5DxCD3 bispecific). ISS, International Staging System.

Patient Disposition

*11 patients were enrolled into the Phase 1 study, and 2 patients from the compassionate use program received at least one dose of selinexor

TEAEs

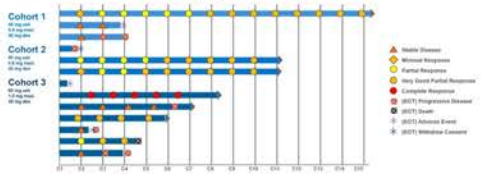
- As of data cutoff (Oct 10, 2025), median duration of treatment was 117 days (range 15–392)
- The most common treatment-emergent adverse events (TEAEs) in the total population:
  - neutropenia (85%)
  - thrombocytopenia (62%)
  - constipation (54%)
  - leukopenia (54%)
- The most common serious TEAE (Grade 3/4) was neutropenia (54%)
- Dose-limiting toxicities (DLTs)
  - None in cohorts 1 and 2
  - Two DLTs occurred in cohort 3
    - One patient experienced Grade 2 constipation and proctitis (pre-existing) and despite medical intervention withdrew consent prior to completion of Cycle 1, thus being assessed as a DLT per protocol
    - One patient experienced a Grade 4 neutropenia on Cycle 1 Day 15 that did not resolve within 7 days of supportive care and holding all study medication

Recommended Phase 2 Dose

- Seli 60 mg QW + mezi 0.6 mg QD + dex 40 mg QW was selected as the RP2D

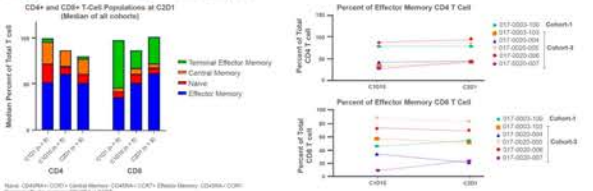
TEAE, n (%)	Cohort 1 (n = 3)	Cohort 2 (n = 3)	Cohort 3 (n = 7)	Total (N = 13)
Any Grade	3 (100)	3 (100)	7 (100)	13 (100)
Grade 3/4	3 (100)	1 (33)	4 (57)	8 (62)
Serious TEAE	1 (33)	0 (0)	3 (43)	4 (31)
Leading to dose modification	2 (67)	2 (67)	3 (43)	7 (54)
Leading to dose interruption	2 (67)	1 (33)	2 (29)	5 (39)
Leading to treatment discontinuation	1 (33)	0 (0)	0 (0)	1 (8)
Leading to death	0 (0)	0 (0)	1 (14)	1 (8)
Most common TEAE (≥ 25%), n (%)				
Neutropenia	3 (100)	2 (67)	6 (86)	11 (85)
Thrombocytopenia	2 (67)	2 (67)	4 (57)	8 (62)
Constipation	2 (67)	2 (67)	3 (43)	7 (54)
Leukopenia	1 (33)	2 (67)	4 (57)	7 (54)
Hypocalcemia	1 (33)	2 (67)	4 (57)	7 (54)
Decreased appetite	2 (67)	1 (33)	3 (43)	6 (46)
Anemia	2 (67)	2 (67)	1 (14)	5 (39)
Diarrhea	1 (33)	1 (33)	3 (43)	5 (39)
Fatigue	1 (33)	1 (33)	3 (43)	5 (39)
Nausea	2 (67)	1 (33)	2 (29)	5 (39)
Chills	2 (67)	2 (67)	0 (0)	4 (31)
Dyspnea	0 (0)	1 (33)	3 (43)	4 (31)
Hyperglycemia	1 (33)	1 (33)	2 (29)	4 (31)
Insomnia	0 (0)	3 (100)	1 (14)	4 (31)
Sinus bradycardia	1 (33)	1 (33)	2 (29)	4 (31)
Grade 3/4 TEAE (≥ 25%), n (%)				
Neutropenia	3 (100)	1 (33)	3 (43)	7 (54)

SMd Demonstrated Preliminary Signs of Efficacy



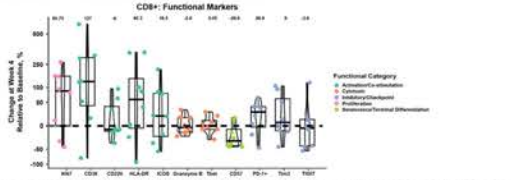
- As of Oct 10, 2025, 12 patients have had a response assessment
- The objective response rate (ORR) by investigator was 50% (6/12)
  - Six had a very good partial response (VGPR) or better (50%)
- The clinical benefit rate (CBR) (≥ MR) was 50% (6/12)

SMd Induces a Sustained Effector Phenotype in CD4 and CD8 T-Cell Populations Following Drug Holiday in Primary Patient Samples



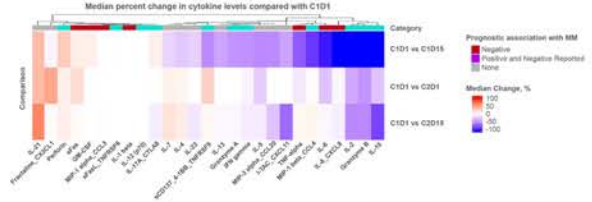
- Median increase in the total number of effector memory CD4 and CD8 T cells were seen after SMd treatment
- The percentage of effector cells was persistent even during dose holiday

SMd Results in CD8+ T-Cell Proliferation and Activation



- Increase in median expression of markers related to CD8 expansion (Ki67, CD38) and MHC-II expression (HLA-DR) and decrease in marker of senescence (CD57) were observed across all dose cohorts
- There were mixed results for change in immune checkpoints and granzyme B

SMd Upregulates T-cell Activation Related Cytokines and Suppresses Pro-inflammatory Cytokines Inversely Associated With Poor MM Prognosis



- Cytokine panel testing in primary patient samples indicated increased T-cell activation signaling (IL-21, Perforin) during on- (C1D15, C2D15) and off-treatment (C2D1) periods
- Pro-inflammatory cytokines and IL-8, IL-6, and TNF-alpha decreased modestly with SMd treatment. These cytokines have also been shown to negatively correlate with MM prognosis[8-10]

Conclusions and Future Directions

- The RP2D of SMd in RRMM is selinexor 60 mg on D1, 8, 15; mezigdomide 0.6 mg on D1-21, and dexamethasone 40mg weekly in a 28-day cycle. Dose limiting toxicities were Grade 2 proctitis and extended Grade 4 neutropenia
- TEAEs were consistent with known selinexor and mezigdomide toxicities, and no new safety signals were detected
- Initial data for this all-oral combination of SMd at dose level 2 demonstrated preliminary signs of efficacy with an overall response rate of 50% in a heavily-pretreated RRMM population that had either failed or was otherwise ineligible to receive a T-cell redirecting therapy. At data cutoff, 5/13 enrolled subjects remained on treatment, with three patients exceeding 11 months of treatment
- Preliminary correlative testing indicated increased T-cell activation and decreases in pro-inflammatory cytokines while on SMd treatment
- Ongoing results support the continued investigation of SMd in patients with RRMM with selinexor 60 mg QW + mezigdomide 0.6 mg QD + dexamethasone 40 mg QW as the RP2D
- Further exploration of 1-mg mezigdomide dosing in combination with selinexor and dexamethasone is anticipated given the DLT based on the Grade 2 proctitis that was pre-existing

References: 1. Sinder AF, et al. Front Immunol. 2023;14:1270320. 2. Xpovio [package insert]. Newton, MA: Karyopharm Therapeutics, Inc; 2022. 3. Mehta PH, et al. Front Immunol. 2023;12:780442. 4. Kashyap T, et al. Antiviral Res. 2021;192:105103. 5. Kang Y, et al. Blood Immunol Cell Ther. 2025;1(3):100008. 6. Jelinek DV, et al. Blood. 2022;140(suppl 1):7070–7071. 7. Richardson PG, et al. N Engl J Med. 2023;389:1509–1522. 8. Zhang XG, et al. Blood. 1998;74:11–13. 9. Hamieh AG, et al. Am J Path. 2016;190:2171–2182. 10. Joachim M, et al. Eur Cytokine Netw. 1999;10:63–70.

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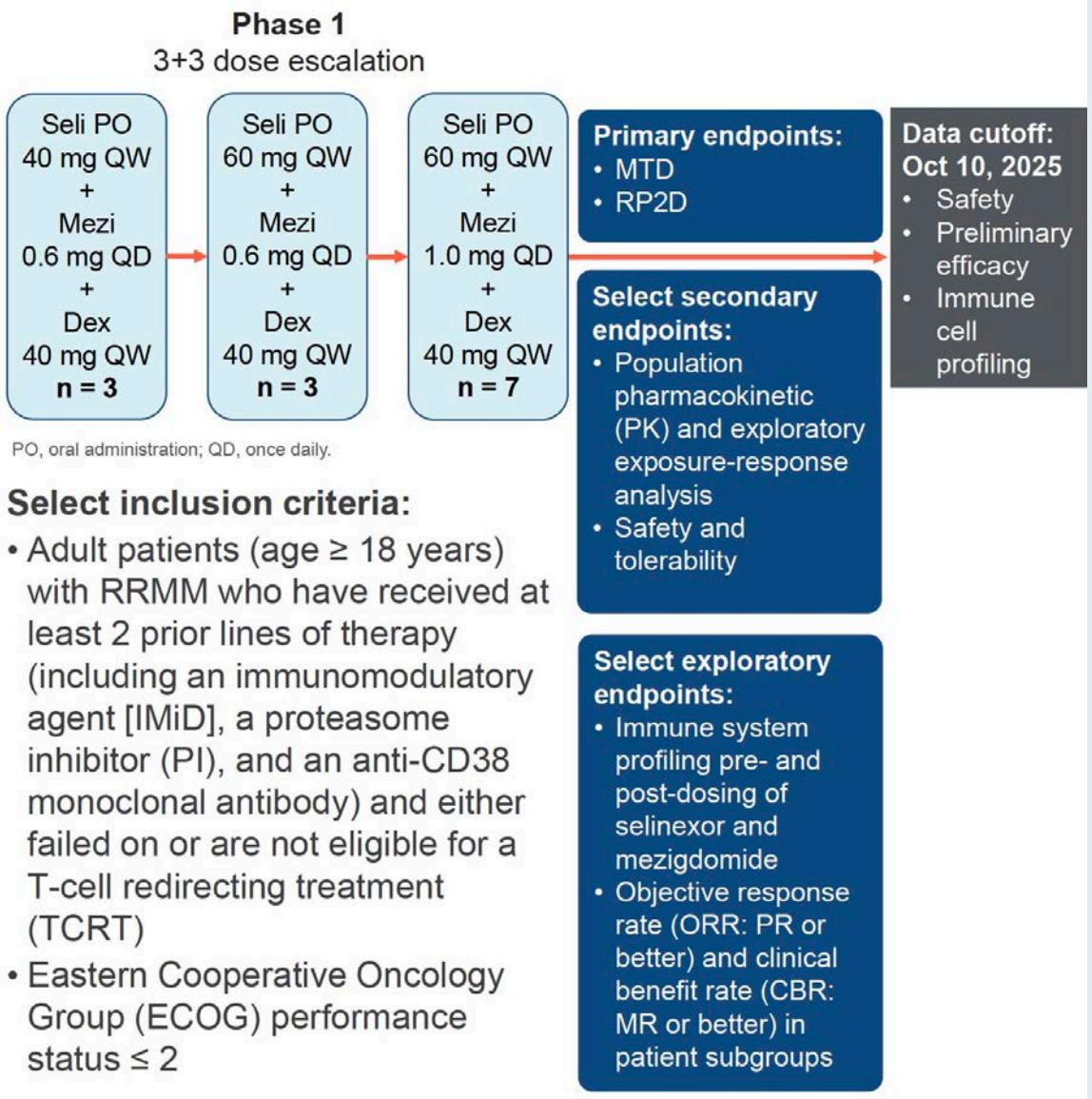
Dana-Farber Cancer Institute | HARVARD MEDICAL SCHOOL | Duke Cancer Institute | UW Medicine

67th American Society of Hematology Annual Meeting and Exhibition, December 6-9, 2025, Orlando, Florida

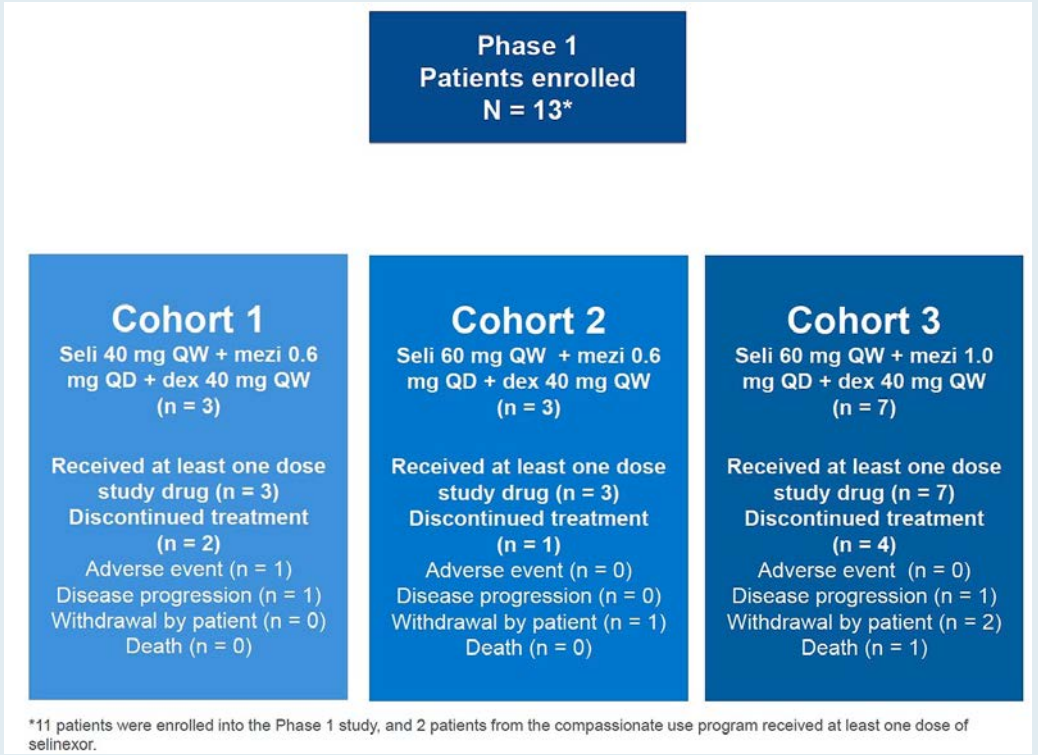
ASH 2025;Abstract 4010.

Phase I STOMP Study and Cohort Design



Select inclusion criteria:

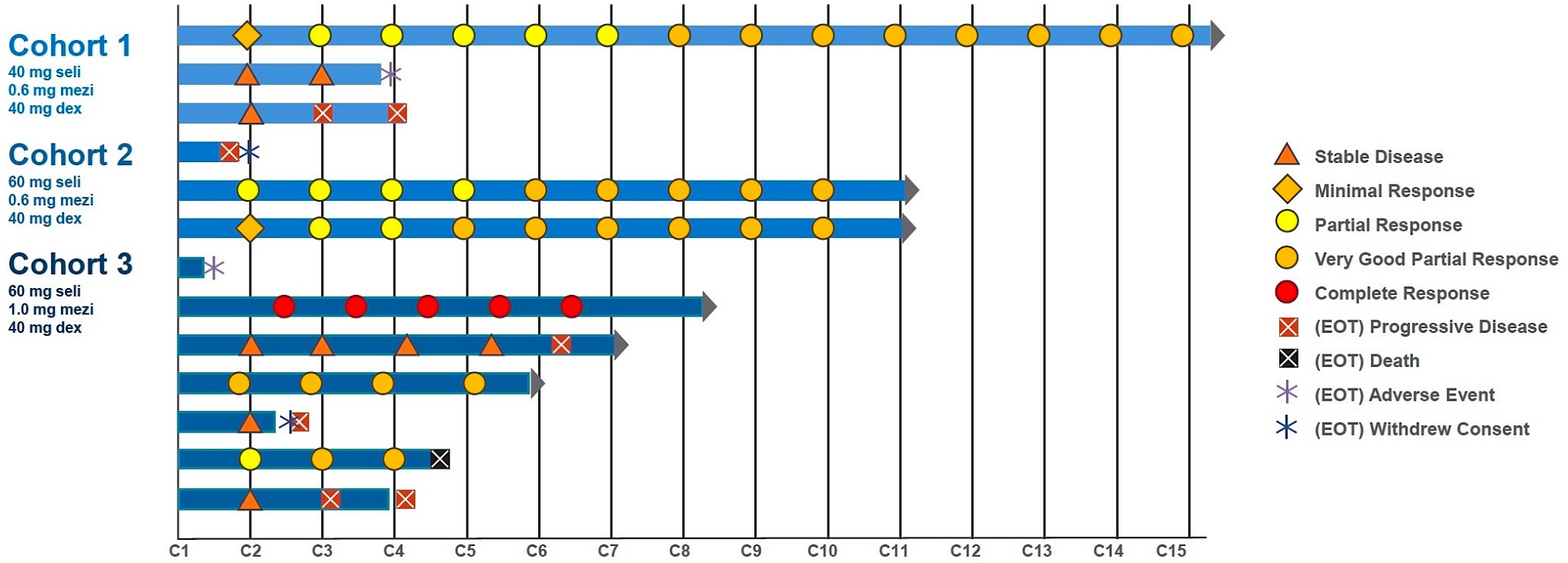
- Adult patients (age ≥ 18 years) with RRMM who have received at least 2 prior lines of therapy (including an immunomodulatory agent [IMiD], a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody) and either failed on or are not eligible for a T-cell redirecting treatment (TCRT)
- Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2



Seli = selinexor

Mo C et al. ASH 2025;Abstract 4010.

Phase I STOMP: Preliminary Efficacy



C, cycle; EOT, end of treatment.

- As of Oct 10, 2025, 12 patients have had a response assessment
- The objective response rate (ORR) by investigator was 50% (6/12)
  - Six had a very good partial response (VGPR) or better (50%)
- The clinical benefit rate (CBR) (≥ MR) was 50% (6/12)

Mo C et al. ASH 2025;Abstract 4010.

Phase I STOMP: Authors' Conclusions

- The recommended Phase II dose of selinexor/mezigdomide/dexamethasone (SMd) for RRMM is selinexor 60 mg on D1, 8, 15; mezigdomide 0.6 mg on D1-21, and dexamethasone 40 mg weekly in a 28-day cycle. Dose-limiting toxicities were Grade 2 proctitis and extended Grade 4 neutropenia
- TEAEs were consistent with known selinexor and mezigdomide toxicities, and no new safety signals were detected
- Initial data for this all-oral combination of SMd at dose level 2 demonstrated preliminary signs of efficacy with an overall response rate of 50% for patients with heavily pretreated RRMM that was refractory to or was otherwise ineligible to receive a T-cell-redirecting therapy. At data cutoff, 5/13 enrolled patients remained on treatment, with 3 exceeding 11 months of treatment
- Further exploration of 1-mg mezigdomide dosing in combination with selinexor and dexamethasone is anticipated given the DLT based on the Grade 2 proctitis that was preexisting

Mo C et al. ASH 2025;Abstract 4010.

Agenda

Introduction: Clinical Trials We LOVE to Discuss

Module 1: Mechanism of Action of Cereblon E3 Ligase Modulators (CELMoDs)

Module 2: Available Efficacy Data with CELMoDs in the Management of Relapsed/Refractory Multiple Myeloma (MM)

Module 3: Extramedullary Disease

Module 4: Spectrum and Management of CELMoD-Associated Adverse Events

Module 5: Ongoing Phase II and III Trials Evaluating CELMoDs for MM

Module 6: Other Trials in Progress

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Module 6: Other Trials in Progress

Key Datasets

Iberdomide

- Landgren O et al. A **phase 2** trial of **iberdomide, carfilzomib, daratumumab and dexamethasone** quadruplet therapy for **relapsed/refractory multiple myeloma**: **The ReKinDLE study**. ASH 2025;Abstract 251.
- Korst CLBM et al. **Iberdomide plus low-dose cyclophosphamide and dexamethasone in patients with relapsed and refractory multiple myeloma (the ICON study):** A multicentre, single-arm, phase 2 trial. *Lancet Haematol* 2026 January;13(1):e30-40.
- Suvannasankha A et al. **Safety and efficacy** of **elranatamab in combination with iberdomide** in patients with **relapsed or refractory multiple myeloma: Results from the phase 1b MagnetisMM-30 trial**. ASH 2025;Abstract 100.
- White D et al. **Iberdomide, bortezomib, and dexamethasone (IberVd) in transplant-ineligible (TNE) newly diagnosed multiple myeloma (NDMM): Updated results** from the **CC-220-MM-001 trial**. ASCO 2025;Abstract 7532.

Phase II ReKInDLE: Hematologic Adverse Events

TEAEs, n (%)*	Combination Therapy (n=29)	
	All grade	Grade 3/4
Anemia	15 (52)	1 (3)
Leukopenia	2 (7)	0 (0)
Lymphopenia	5 (17)	3 (10)
Neutropenia	25 (86)	15 (52)
Thrombocytopenia	10 (34)	2 (7)

Neutropenia was the most common all grade hematologic TEAE.
No patients discontinued therapy for hematologic toxicity.
Growth factor was permitted per investigator discretion.
Only 1 patient with febrile neutropenia, Cycle 1.

*TEAE; Treatment-Emergent Adverse Event, Limited to patients with >2 cycles of therapy, n = 29
Highest Grade Instance of TEAE per patient reported

Landgren O et al. ASH 2025;Abstract 251.

Phase II ReKInDLE: Common and Select Nonhematologic Adverse Events

TEAEs, n (%)*	Combination Therapy (n=29)	
	All grade	Grade 3/4
Fatigue	9 (31)	0
Diarrhea	4 (14)	0
Rash	3 (10)	0
Thromboembolic Events**	0	0
Alanine Aminotransferase Increased	4 (14)	0
Alkaline Phosphatase Increased	6 (21)	0
Amylase Increased	8 (28)	1 (3)
Bone Pain	4 (14)	0
Hyperglycemia	3 (10)	1 (3)
Insomnia	8 (28)	1 (3)

TEAEs, n (%)*	Combination Therapy (n=29)	
	All grade	Grade 3/4
Any Infection	18 (62)	4 (14)
Pneumonia	6 (21)	4 (14)
Sinusitis	2 (7)	0
Upper Respiratory Infection	12 (41)	0
Pulmonary Hypertension**	1 (3)	0
Myocardial Infarction**	0	1 (3)
SPM** (Prostate Adenocarcinoma)	1 (3)	0

*TEAE; Treatment-Emergent Adverse Event, Limited to patients with >2 cycles of therapy, n = 29, Some patients suffered more than one infection; all events are counted in infection details, Any infection is per patient. Highest Grade Instance of TEAE per patient reported, TEAEs shown occurred in ≥10% All Grade

**Selected as AE of special interest for this presentation

1 Patient Discontinued Treatment due to Myocardial Infarction During C4
1 Patient with Asymptomatic Mild Pulmonary Hypertension C7 on Echocardiogram
Carfilzomib held for C7 and C8
No Grade 5 TEAEs

Landgren O et al. ASH 2025;Abstract 251.

Phase II ICON: Safety

	Adverse event severity			
	Grade 2	Grade 3	Grade 4	Grade 5
Haematological adverse event				
Anaemia	14 (23%)	8 (13%)	0	0
Neutropenia	3 (5%)	19 (31%)	15 (25%)	0
Thrombocytopenia	3 (5%)	6 (10%)	1 (2%)	0

	Adverse event severity			
	Grade 2	Grade 3	Grade 4	Grade 5
Non-haematological adverse events				
Infections*	24 (39%)	16 (26%)	4 (7%)	1 (2%)†
Upper respiratory tract	14 (23%)	5 (8%)	0	0
Lower respiratory tract	10 (16%)	6 (10%)	4 (7%)	1 (2%)†
Gastrointestinal	1 (2%)	0	0	0
Urinary tract infection	3 (5%)	2 (3%)	0	0
Skin infection	3 (5%)	0	0	0
Sepsis	0	1 (2%)	0	0
Other‡	6 (10%)	3 (5%)	0	0
Peripheral neuropathy§	16 (26%)	2 (3%)	0	0
Fatigue	10 (16%)	2 (3%)	0	0
Thromboembolic events	3 (5%)	1 (2%)	0	0
Diarrhoea	4 (7%)	2 (3%)	0	0
Rash	1 (2%)	2 (3%)	0	0
Nausea	2 (3%)	0	0	0
Cardiac disorders	1 (2%)	0	0	0
Neurodegenerative disease	0	0	0	1 (2%)
Muscle spasms	1 (2%)	0	0	0
Second primary malignancy				
Haematological	0	0	2 (3%)	0
Invasive solid	0	2 (3%)	0	0
Non-invasive cutaneous	0	0	0	0

Korst CLBM et al. *Lancet Haematol* 2026 January;13(1):e30-40.

RTP RESEARCH TO PRACTICE

Phase Ib MagnetisMM-30: Safety

- The AE profile is consistent with the known individual AE profiles of elranatamab and iberdomide
- In 17 evaluable patients (10 patients in DL1 and 7 in DL–1), 4 DLTs were observed
  - DL1: grade 3 anorexia and grade 4 neutropenia
  - DL–1: grade 3 febrile neutropenia and grade 4 neutropenia
- 59.1% of patients were given GCSF during treatment
- All CRS and ICANS events were grade ≤2
  - CRS: 54.5% grade 1, 13.6% grade 2
  - ICANS: 4.5% grade 1, 4.5% grade 2

	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	22 (100.0)	19 (86.4)
Hematologic		
Neutropenia	17 (77.3)	16 (72.7)
Anemia	7 (31.8)	3 (13.6)
Lymphopenia	4 (18.2)	4 (18.2)
Nonhematologic		
CRS	15 (68.2)	0
Fatigue	14 (63.6)	0
Diarrhea	11 (50.0)	0
Headache	10 (45.5)	0
Cough	10 (45.5)	0
Nausea	9 (40.9)	1 (4.5)
Injection site reaction	9 (40.9)	0
Decreased appetite	8 (36.4)	1 (4.5)

[a] TEAEs presented by preferred term according to the Medical Dictionary for Regulatory Activities v28.1 and Common Terminology Criteria for Adverse Events v5. Any-grade TEAE reported in >35% of patients or grade 3/4 TEAE reported in ≥10% of patients; severity of CRS and ICANS was assessed according to the American Society for Transplantation and Cellular Therapy criteria.
AE=adverse event; CRS=cytokine release syndrome; DL=dose level; DLT=dose-limiting toxicity; GCSF=granulocyte colony-stimulating factor; ICANS=immune effector cell–associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

Suvannasankha A et al. ASH 2025;Abstract 100.

Phase Ib MagnetisMM-30: Infections

- Any-grade infections were reported in 40.9% of patients
- Frequent (any grade >10%) infections included upper respiratory tract infection (27.3%) and candida infection (13.6%)
- All infections were grade ≤2, except for 1 event each of grade 3 gastroenteritis *Escherichia coli* and grade 3 skin infection

Infections occurring in >5% of patients	N=22	
TEAE, n (%)[a]	**Any grade**	**Grade 3**
Infections[b]	9 (40.9)	2 (9.1)
Upper respiratory tract infection	6 (27.3)	0
Candida infection	3 (13.6)	0
Urinary tract infection	2 (9.1)	0

IVIG prophylaxis was administered approximately every 4 weeks to maintain IgG levels above 400 mg/dL

[a] TEAEs according to the Medical Dictionary for Regulatory Activities v28.1 and Common Terminology Criteria for Adverse Events v5; [b] Infections include preferred terms in the system organ class of infections and infestations.
IgG=immunoglobulin G; IVIG=intravenous immunoglobulin; TEAE=treatment-emergent adverse event

Suvannasankha A et al. ASH 2025;Abstract 100.

Phase I/II CC-220-MM-001: Common TEAEs (Any Grade)

Most common (≥ 25% all grade) TEAEs and events of interest,[a] n (%)	IberVd TNE NDMM (N = 17)[b]		
	All grade	Grade 3	Grade 4
Hematologic TEAEs			
Neutropenia	7 (41.2)	2 (11.8)	3 (17.6)
Thrombocytopenia	6 (35.3)	2 (11.8)	1 (5.9)
Anemia	6 (35.3)	1 (5.9)	0
Lymphopenia	5 (29.4)	1 (5.9)	0
Non-hematologic TEAEs			
Peripheral edema	12 (70.6)	1 (5.9)	0
Peripheral neuropathy[c]	12 (70.6)	2 (11.8)	0
Constipation	10 (58.8)	1 (5.9)	0
Insomnia	8 (47.1)	1 (5.9)	0
Fatigue	7 (41.2)	2 (11.8)	0
Decreased appetite	7 (41.2)	0	0
Pain in extremity	6 (35.3)	0	0
Rash[d]	6 (35.3)	0	0
Dyspnea	6 (35.3)	1 (5.9)	0
Abdominal pain	5 (29.4)	0	0
Agitation	5 (29.4)	0	0
Dysgeusia	5 (29.4)	0	0
Infections	14 (82.4)	6 (35.3)	2 (11.8)
Pneumonia[e]	4 (23.5)	3 (17.6)	1 (5.9)
COVID-19[f]	8 (47.1)	2 (11.8)	0

[a]Data cutoff: May 29, 2024; [b]1 patient was enrolled but not included in the safety population due to self-withdrawal (appointment absence); [c]Includes peripheral sensory neuropathy and peripheral motor neuropathy; [d]Includes rash, maculo-popular rash, macular rash, follicular rash, and pruritic rash; [e]Includes pneumonia; [f]Includes COVID-19 and COVID-19 pneumonia.

White D et al. ASCO 2025;Abstract 7532.

Key Datasets

Mezigdomide

- Richardson PG et al. **Mezigdomide plus dexamethasone** in **relapsed and refractory multiple myeloma**. *N Engl J Med* 2023 September 14;389(11):1009-22.
- Byun JM et al. **Phase I/II study of mezigdomide and elranatamab** for **relapsed/refractory multiple myeloma** patients **(MELT-MM): Initial results from part 1**. ASH 2025;Abstract 5835.
- Mo C et al. **Selinexor, mezigdomide, and dexamethasone** in patients with **relapsed/refractory multiple myeloma** who **relapsed or are ineligible for T-cell–redirecting therapy**: **STOMP Phase 1 results**. ASH 2025;Abstract 4010.

Phase I/II CC-92480-MM-001: Common Adverse Events

Table 2. Adverse Events That Occurred in More Than 20% of the Patients and Adverse Events of Interest.*

Adverse Event	Dose-Escalation Cohort (N=77)			Dose-Expansion Cohort (N=101)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Hematologic						
Neutropenia	62 (81)	18 (23)	37 (48)	78 (77)	22 (22)	54 (54)
Anemia	47 (61)	29 (38)	0	53 (52)	35 (35)	1 (1)
Thrombocytopenia	39 (51)	9 (12)	9 (12)	43 (43)	14 (14)	14 (14)
Febrile neutropenia	7 (9)	4 (5)	3 (4)	15 (15)	13 (13)	2 (2)
Nonhematologic						
Infections and infestations	57 (74)	28 (36)	3 (4)	66 (65)	29 (29)	6 (6)
Pneumonia†	19 (25)	16 (21)	0	22 (22)	13 (13)	3 (3)
Covid-19	1 (1)	1 (1)	0	17 (17)	7 (7)	0
Fatigue	31 (40)	8 (10)	0	36 (36)	5 (5)	0
Nausea	21 (27)	1 (1)	0	21 (21)	1 (1)	0
Decreased appetite	20 (26)	1 (1)	0	21 (21)	1 (1)	1 (1)
Diarrhea	20 (26)	2 (3)	0	31 (31)	3 (3)	0
Pyrexia	20 (26)	2 (3)	0	15 (15)	3 (3)	0
Peripheral edema	17 (22)	1 (1)	0	8 (8)	0	0
Arthralgia	12 (16)	2 (3)	0	21 (21)	2 (2)	0
Insomnia	12 (16)	0	0	20 (20)	1 (1)	0
Constipation	11 (14)	0	0	24 (24)	0	0
Dyspnea	11 (14)	3 (4)	0	22 (22)	5 (5)	0
Peripheral neuropathy‡	7 (9)	0	0	7 (7)	1 (1)	0
Deep-vein thrombosis	1 (1)	0	0	3 (3)	1 (1)	0

Richardson PG et al. *N Engl J Med* 2023 September 14;389(11):1009-22.

Phase I/II MELT-MM: Safety

Table 3. Safety (N=12)	
	N, %
Cytokine release syndrome (CRS)	8 (66.7%)
Grade ≥ 3 CRS	0
ICANS	0
Infection during DLT period	1 (8.3%)
clinically significant CMV	1
Neutropenia during DLT period	1 (8.3%)
Grade 3	1
Thrombocytopenia during DLT period	2 (16.7%)
Grade 3	2

ICANS, immune effector cell-associated neurotoxicity syndrome; CMV, cytomegalovirus

Byun JM et al. ASH 2025;Abstract 5835.

Phase I STOMP: Adverse Events

TEAE, n (%)	Cohort 1 (n = 3)	Cohort 2 (n = 3)	Cohort 3 (n = 7)	Total (N = 13)
Any Grade	3 (100)	3 (100)	7 (100)	13 (100)
Grade 3/4	3 (100)	1 (33)	4 (57)	8 (62)
Serious TEAE	1 (33)	0 (0)	3 (43)	4 (31)
Leading to dose modification	2 (67)	2 (67)	3 (43)	7 (54)
Leading to dose interruption	2 (67)	1 (33)	2 (29)	5 (39)
Leading to treatment discontinuation	1 (33)	0 (0)	0 (0)	1 (8)
Leading to death	0 (0)	0 (0)	1 (14)	1 (8)
Most common TEAE (≥ 25%), n (%)				
Neutropenia	3 (100)	2 (67)	6 (86)	11 (85)
Thrombocytopenia	2 (67)	2 (67)	4 (57)	8 (62)
Constipation	2 (67)	2 (67)	3 (43)	7 (54)
Leukopenia	1 (33)	2 (67)	4 (57)	7 (54)
Hypocalcemia	1 (33)	2 (67)	4 (57)	7 (54)
Decreased appetite	2 (67)	1 (33)	3 (43)	6 (46)
Anemia	2 (67)	2 (67)	1 (14)	5 (39)
Diarrhea	1 (33)	1 (33)	3 (43)	5 (39)
Fatigue	1 (33)	1 (33)	3 (43)	5 (39)
Nausea	2 (67)	1 (33)	2 (29)	5 (39)
Chills	2 (67)	2 (67)	0 (0)	4 (31)
Dyspnea	0 (0)	1 (33)	3 (43)	4 (31)
Hyperglycemia	1 (33)	1 (33)	2 (29)	4 (31)
Insomnia	0 (0)	3 (100)	1 (14)	4 (31)
Sinus bradycardia	1 (33)	1 (33)	2 (29)	4 (31)
Grade 3/4 TEAE (≥ 25%), n (%)				
Neutropenia	3 (100)	1 (33)	3 (43)	7 (54)

Mo C et al. ASH 2025;Abstract 4010.

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Module 4: Spectrum and Management of CELMoD-Associated Adverse Events

Module 5: Ongoing Phase II and III Trials Evaluating CELMoDs for MM

Module 6: Other Trials in Progress

Key Datasets

- Lonial S et al. **EXCALIBER-RRMM**: A **phase III trial** of **iberdomide, daratumumab, and dexamethasone** in **relapsed/refractory multiple myeloma**. *Future Oncol* 2025 June;21(14):1761-9.
- Richardson PG et al. A Phase III, Two-Stage, Randomized Study **of Mezigdomide, Bortezomib, and Dexamethasone (MeziVd) Versus Pomalidomide, Bortezomib, and Dexamethasone (PVd)** in **Relapsed/Refractory Multiple Myeloma (RRMM)**: **SUCCESSOR-1**. SOHO 2023;Abstract MM-372.
- Richardson PG et al. A **phase 3**, **two-stage**, randomized study of **mezigdomide, carfilzomib, and dexamethasone (MeziKd) versus carfilzomib and dexamethasone (Kd)** in **relapsed/refractory multiple myeloma (RRMM): SUCCESSOR-2**. ASCO 2023;Abstract TPS8070.
- van de Donk NWCJ et al. **Iberdomide maintenance after autologous stem-cell transplantation** in **newly diagnosed multiple myeloma: An update from the phase 2 EMN26 trial**. ASH 2025;Abstract 101.
- Merz L et al. The **impact of Duffy genotype on progression-free survival (PFS) with lenalidomide, Bortezomib, and dexamethasone (RVd) alone or RVd plus autologous stem cell transplantation (ASCT) and continuous R maintenance in patients** (pts) with newly diagnosed multiple myeloma (NDMM): Updated subgroup analysis of the phase 3 DETERMINATION trial. ASH 2025;Abstract 1033.

Minimal Residual Disease and Complete Response in Multiple Myeloma: Use as Endpoints to Support Accelerated Approval

FDA Guidance for Industry Document

January 20, 2026

"On January 20, 2026, the Food and Drug Administration issued a draft guidance for industry that provides recommendations to sponsors about using minimal residual disease (MRD) and complete response (CR) as primary endpoints in trials evaluating drugs and biologics intended to treat patients with multiple myeloma to support approval under the accelerated approval regulations.

The draft guidance, 'Minimal Residual Disease and Complete Response in Multiple Myeloma: Use as Endpoints to Support Accelerated Approval,' provides specific recommendations for designing clinical trials using MRD as an endpoint for accelerated approval. **These recommendations include general drug development considerations, trial design and statistical considerations, and assay considerations for MRD evaluation. The guidance also includes considerations when proposing CR as an endpoint for accelerated approval as well as other regulatory considerations.**

In multiple myeloma, accelerated approval based on an endpoint of overall response rate (ORR) supported by duration of response has expedited the approval of new therapies. However, the ORRs observed with new therapies have surpassed 60-70% in the relapsed or refractory setting and 90% in the newly diagnosed setting. **With the improved outcomes observed in this disease area demonstrating statistically significant differences in ORRs may require infeasibly large clinical trials. Additionally, more sensitive response assessments will allow for continued expeditious drug development.**"

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/minimal-residual-disease-and-complete-response-multiple-myeloma-use-endpoints-support-accelerated

RTP RESEARCH TO PRACTICE

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Measurable Residual Disease–Guided Therapy in Newly Diagnosed Myeloma

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EDITORIALS

Opening the Door to Tailored Treatment in Newly Diagnosed Multiple Myeloma

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CLINICAL TRIAL PROTOCOL

OPEN ACCESS

EXCALIBER-RRMM: a phase III trial of iberdomide, daratumumab, and dexamethasone in relapsed/refractory multiple myeloma

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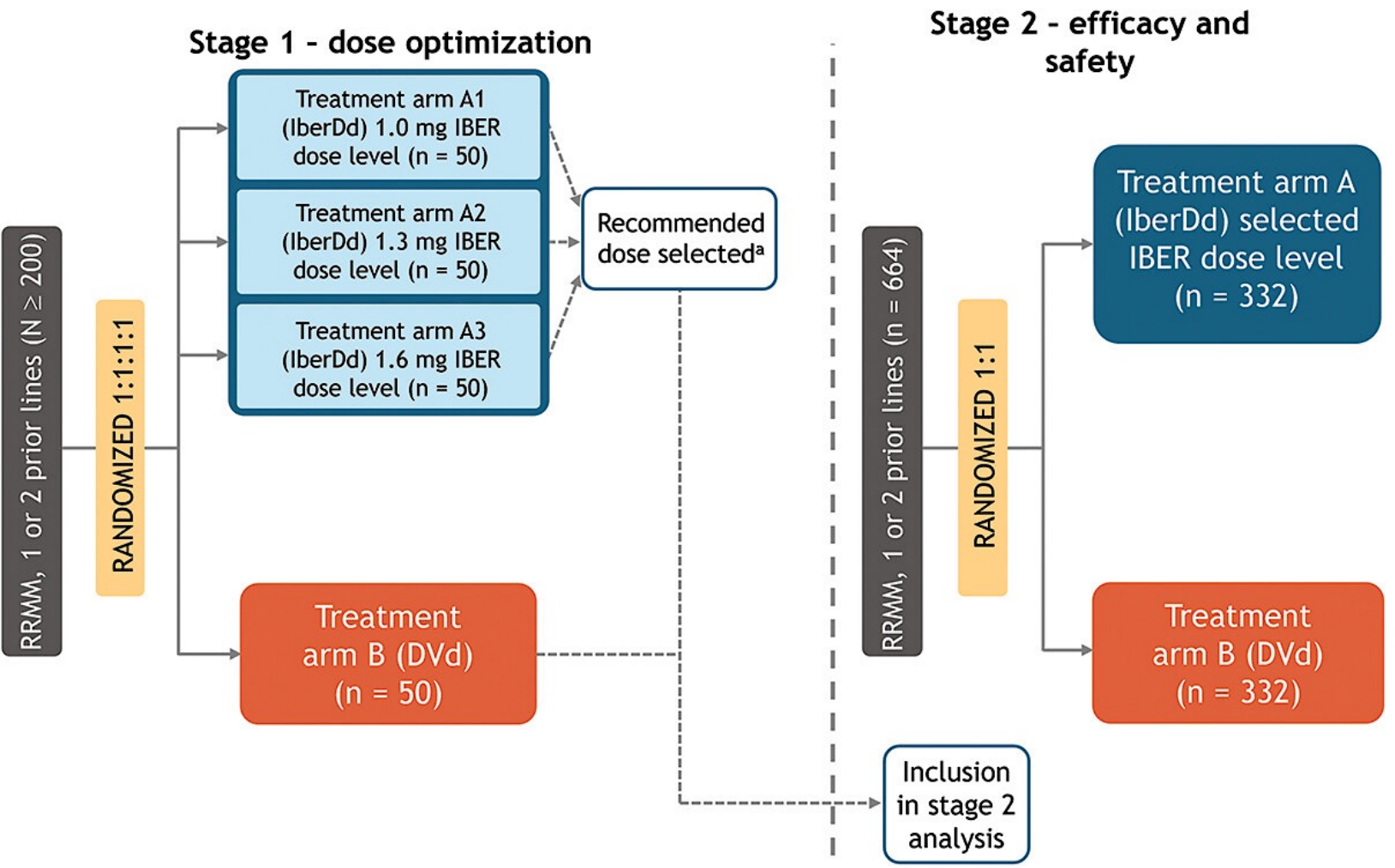
Phase III EXCALIBER-RRMM Study Design, Endpoints



Dual primary endpoint

- PFS: time from randomization to PD or death, whichever occurs first
- MRD-negative CR at any time

Key secondary and exploratory endpoints

- Determination of recommended IBER dose in combination with DARA + DEX (stage 1 only)
- OS
- ORR
- Duration of response
- Time to progression
- Time to response
- PK analyses
- Time to next treatment
- PFS2
- Sustained MRD-negativity rate
- Safety
- Health-related quality of life
- Biomarker analyses (exploratory)

CR: complete response; DARA: daratumumab; DEX: dexamethasone; IBER: iberdomide; MRD: minimal residual disease; ORR: overall response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PFS2: time from randomization to progression on first subsequent therapy; PK: pharmacokinetic.

Lonial S et al. *Future Oncol* 2025 June;21(14):1761-9.

Phase III EXCALIBER-RRMM: Authors' Conclusions

- EXCALIBER-RRMM is a unique, inferentially seamless, 2-stage, confirmatory, Phase III study supporting dose optimization of iberdomide/daratumumab/dexamethasone (IberDd) and comparing the efficacy and safety of IberDd with daratumumab/bortezomib/dexamethasone for patients with RRMM who had received 1 or 2 prior lines of therapy.
- Enrollment began in June 2022 and is ongoing.
- The clinical implications of this study are significant, as the need for convenient, accessible and safe drugs remains critical for MM, especially with the advantage of an orally bioavailable agent that facilitates a successful translational process into real-world practice.
- Iberdomide is a highly attractive agent for use as a backbone in combination therapies for MM. Therefore, the outcomes of EXCALIBER-RRMM may establish IberDd as a transformative treatment in early-line RRMM and potentially broaden its role in combination regimens across the disease spectrum.

Lonial S et al. *Future Oncol* 2025 June;21(14):1761-9.

Phase III EXCALIBER-RRMM Study Evaluating Iberdomide with Standard Therapies Demonstrated a Significant Improvement in MRD Negativity Rates for RRMM

Press Release: September 23, 2025

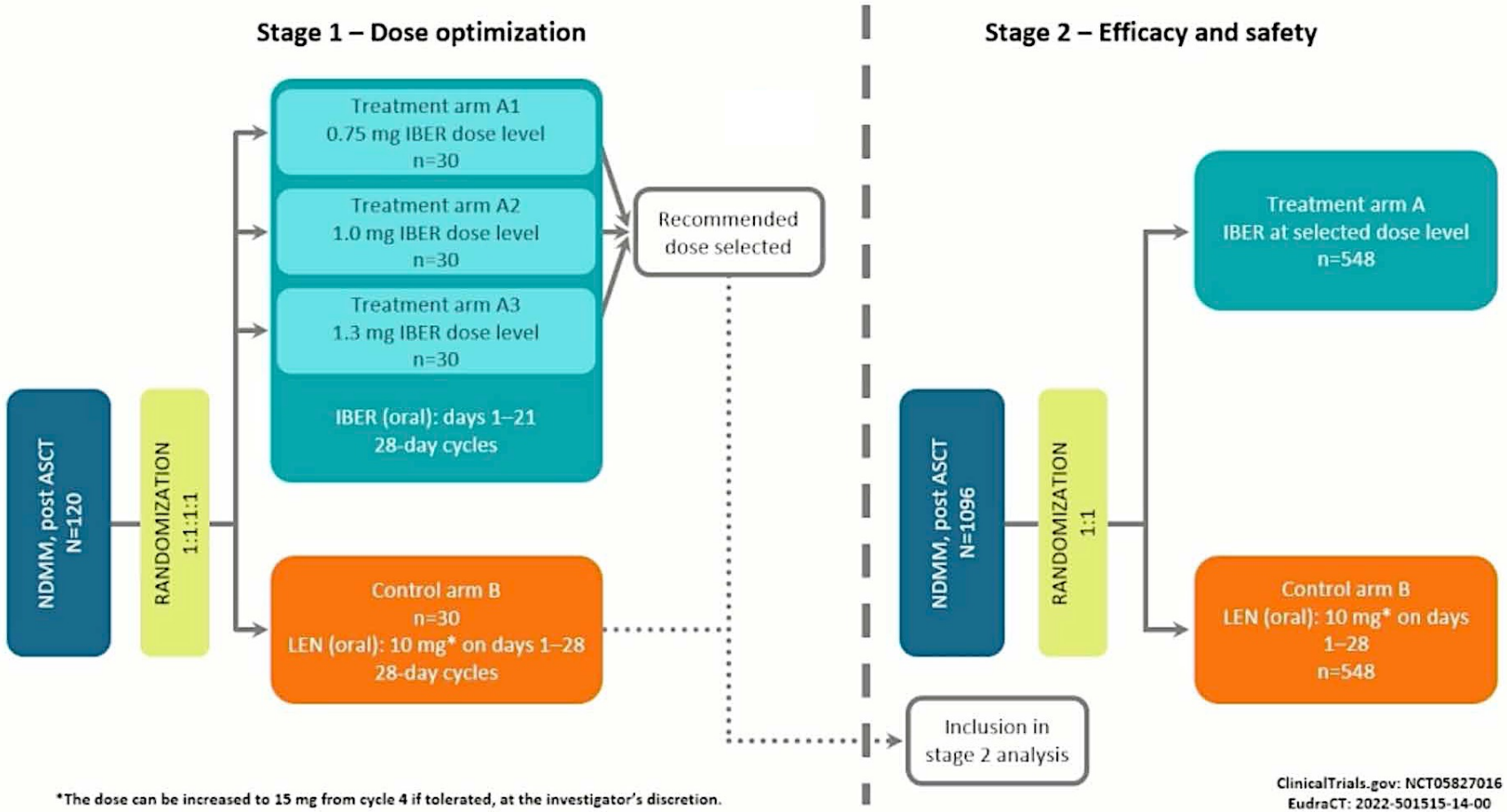
"[The manufacturer] announced that the Phase 3 EXCALIBER-RRMM study evaluating iberdomide, an investigational cereblon E3 ligase modulator, combined with standard therapies (daratumumab + dexamethasone) in patients with relapsed or refractory multiple myeloma (RRMM) demonstrated a statistically significant improvement in minimal residual disease (MRD) negativity rates, compared with the control arm, in a planned interim analysis of the MRD endpoint."

The company plans to discuss these results with health authorities.

https://news.bms.com/news/corporate-financial/2025/Bristol-Myers-Squibb-Announces-Phase-3-EXCALIBER-RRMM-Study-Evaluating-Iberdomide-in-Combination-with-Standard-Therapies-Demonstrated-a-Significant-Improvement-in-Minimal-Residual-Disease-Negativity-Rates-in-Relapsed-or-Refractory-Multiple-Myeloma/default.aspx

RTP RESEARCH TO PRACTICE

EXCALIBER Maintenance Trial



Primary endpoint: PFS

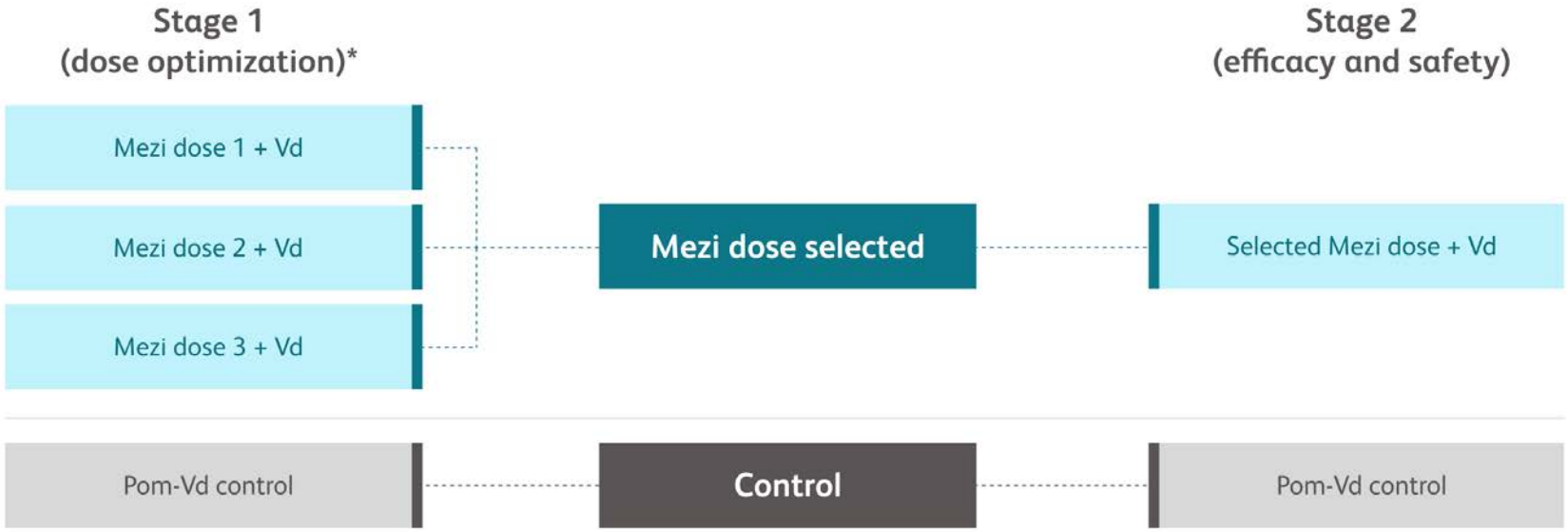
Secondary endpoints:

- MRD;
- OS;
- recommended iberdomide dose for Stage 2;
- safety;
- PFS2;
- MRD conversion rate;
- TTP;
- QoL.

Gay F et al. Clinical Lymphoma Myeloma and Leukemia 2023, 23 (S2), S111 [Abstract #P-137, IMS 2023 20th Annual Meeting]. doi: 10.1016/S2152-2650(23)01755-X. Figure redrawn.

van de Donk NWCJ et al. ASH 2025;Abstract 101.

Phase III SUCCESSOR-1 Study Design



*Patients enrolled in stage 1 on a dose of Mezi that is not chosen for stage 2 will have the possibility to move to that dose if some criteria are met.

Primary Endpoint:

Progression-free survival (PFS)[1]

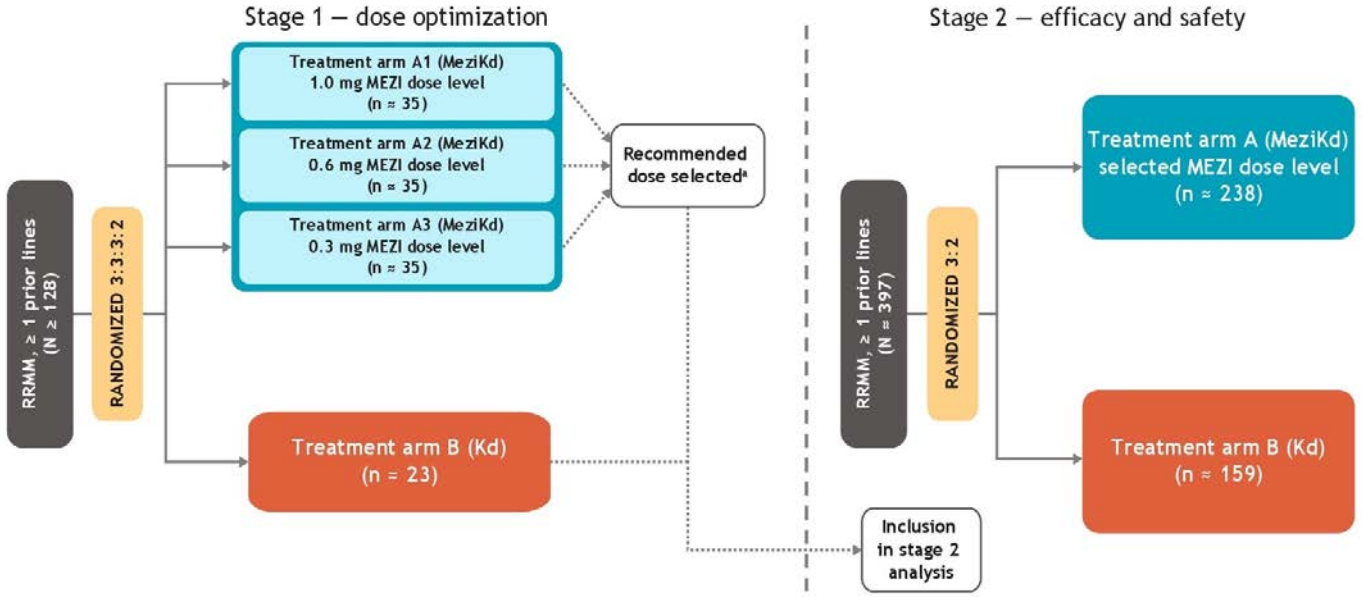
Select Secondary Endpoints:

- Overall response rate (ORR)[1]
- Overall survival (OS)[1]
- Safety[1]
- Complete response rate (CRR)[2]
- Minimal residual disease (MRD) negativity rate[1]
- Health-related quality of life (HRQoL)[1]

Vd = bortezomib/dexamethsone; Pom = pomalidomide

https://www.bmsclinicaltrials.com/celmodmmtrials/successor-1

Phase III SUCCESSOR-2 Study Design



Arm A MeziKd (weekly CFZ)	Arm B Kd (twice-weekly CFZ)
MEZI (oral): 0.3 mg (A3)/0.6 mg (A2)/1.0 mg (A1) on D1–21 CFZ (IV): 20 mg/m^2 on D1 of C1, then 56 mg/m^2 on D8 and 15 of C1, D1, 8, and 15 of C2–12, and D1 and 15 of C ≥ 13 DEX (oral or IV): 40 mg on D1, 8, 15, and 22[b]	CFZ (IV): 20 mg/m^2 on D1 and 2 of C1, then 56 mg/m^2 on D8, 9, 15, and 16 of C1, and on D1, 2, 8, 9, 15, and 16 of C ≥ 2 DEX (oral or IV): 20 mg on D1, 2, 8, 9, 15, 16, 22 and 23[c]
28-day cycles	28-day cycles

ClinicalTrials.gov: NCT05552976; EudraCT: 2022-500861-29-00

[a]The recommended dose for Stage 2 will be determined by an independent data monitoring committee; [b]For pts > 75 years of age, who are underweight (BMI < 18.5), have poorly controlled diabetes, or have prior intolerance/AE to steroid therapy, DEX may be administered at a dose of 20 mg/day on D1, 8, 15, and 22; [c]For pts > 75 years of age, who are underweight (BMI < 18.5), have poorly controlled diabetes, or have prior intolerance to steroid therapy, DEX may be administered at a dose of 10 mg on D1, 2, 8, 9, 15, 16, 22, and 23.
AE, adverse event; BMI, body mass index; C, cycle; D, day; IV, intravenous.

Primary endpoint	
• Progression free survival: time from randomization to PD or death, whichever occurs first	
Key secondary and exploratory endpoints	
• Determination of recommended MEZI dose in combination with Kd (Stage 1 only)	
• Overall survival	• Time to next treatment
• Overall response rate	• PFS2
• Duration of response	• MRD negativity rate
• Time to progression	• Safety
• Time to response	• Health-related quality of life (Stage 2 only)
• PK analyses	• Biomarker analyses (exploratory)

MRD, minimal residual disease; PFS, progression-free survival; PFS2, time from randomization to progression on first subsequent therapy; PK, pharmacokinetics.

Estimated Primary Completion: February 2026

Richardson PG et al. ASCO 2023;Abstract TPS8070.

RTP RESEARCH TO PRACTICE

ASH 2025;Abstract 101

Oral presentation 101. 67th ASH Annual Meeting and Exposition, December 6, 2025, Orlando, US-FL.

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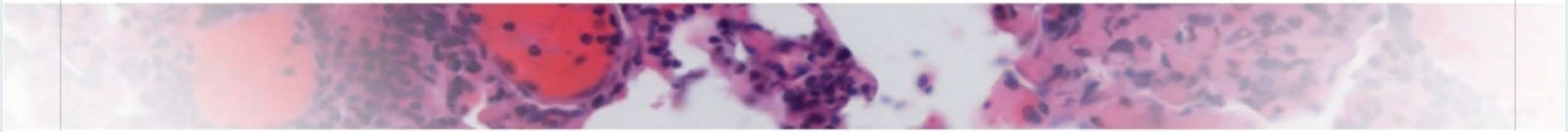
EMN



IBERDOMIDE MAINTENANCE AFTER AUTOLOGOUS STEM-CELL TRANSPLANTATION IN NEWLY DIAGNOSED MULTIPLE MYELOMA: AN UPDATE FROM THE PHASE 2 EMN26 TRIAL

Niels W.C.J. van de Donk, MD, PhD[1]; Cyrille Touzeau, MD[2]; Evangelos Terpos, MD, PhD[3]; Aurore Perrot, MD, PhD[4]; Roberto Mina, MD[5]; Maaike de Ruijter, MANP,MSc[6]; Elisabetta Antonioli, MD[7]; Eirini Katodritou, MD, PhD[8]; Norbert Pescosta, MD[9]; Paulus A.F. Geerts, MD, PhD[10]; Cecile Sonntag, MD[11]; Ruth Wester, MD[12]; Angelo Belotti, MD[13]; Silvia Mangiacavalli, MD[14]; Massimo Offidani, MD[15]; Mattia D'Agostino MD[5]; Mark van Duin PhD[12]; Paola Tacchetti MD, PhD[16]; Sara Aquino, MD[17]; Alessandra Lombardo, MD[18]; Mark-David Levin, MD, PhD[19]; Cyrille Hulin, MD[20]; Mario Boccadoro, MD[21]; Pieter Sonneveld, MD, PhD[12,22]; Francesca Gay, MD, PhD[5]

1) Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Hematology, Cancer Center Amsterdam, Amsterdam, Netherlands; 2) Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; 3) Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; 4) Université de Toulouse, CHU de Toulouse Hématologie, IUCT-Oncopole, Toulouse, France; 5) Division of Hematology, AOU Città della Salute e della Scienza di Torino, University of Torino and Department of Molecular Biotechnology and Health Sciences, University of Torino, Torino, Italy; 6) Amsterdam UMC, VUmc, Department of Hematology, Amsterdam, Netherlands; 7) Hematology Unit, AOU Careggi, Florence, Italy; 8) Department of Hematology, Theagenion Cancer Hospital, Thessaloniki, Greece; 9) Reparto Ematologia e TMNO, Ospedale Provinciale Bolzano, Bolzano, Italy; 10) Isala Klinieken, Zwolle, Netherlands; 11) University Hospital, Hôpital Hautepierre, Strasbourg, France; 12) Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 13) Department of Hematology, ASST Spedali Civili di Brescia, Brescia, Italy; 14) Division of Hematology, IRCCS Fondazione Policlinico San Matteo, Pavia, Italy; 15) AOU delle Marche, Università Politecnica delle Marche, Ancona, Italy,16) IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy; 17) Ematologia e Terapie cellulari, IRCCS Ospedale Policlinico San Martino, Genova, Italy; 18) S.C. di Oncoematologia, A.O. Santa Maria di Terni, Terni, Italy; 19) Albert Schweitzer hospitals, Department of Internal Medicine, Dordrecht, Netherlands; 20) Centre Hospitalier Universitaire Bordeaux, Bordeaux, France; 21) European Myeloma Network, EMN, Italy; 22) European Myeloma Network, EMN, Netherlands.

RTP RESEARCH TO PRACTICE

Phase II EMN26 Study Design

Key eligibility criteria

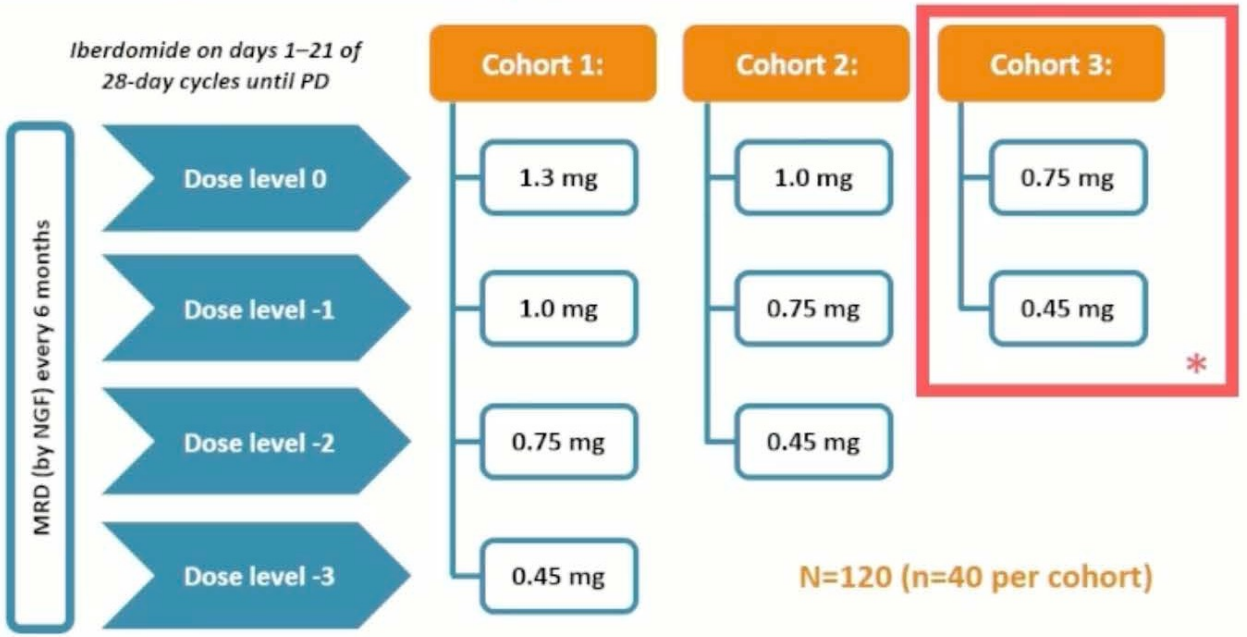
- NDMM patients, ≥PR after ASCT.
- Patients treated with proteasome inhibitor plus immunomodulatory drug-based induction (3-6 cycles), followed by single or double autologous stem-cell transplant (ASCT) with melphalan as conditioning regimen +/- consolidation.
- Patients within 15 months from diagnosis and 120 days after last ASCT or consolidation treatment, if performed.

Primary endpoint

- Efficacy (response improvement within 6 months: PR to ≥VGPR; VGPR to ≥CR; CR to sCR) of the 3 different dose levels of iberdomide maintenance post-ASCT.#

Key secondary endpoints

- Rate of next-generation flow (NGF) minimal residual disease (MRD; 10-5) conversion from positive to negative status
- Rate of adverse events
- PFS, PFS2, OS, TTP, TTNT

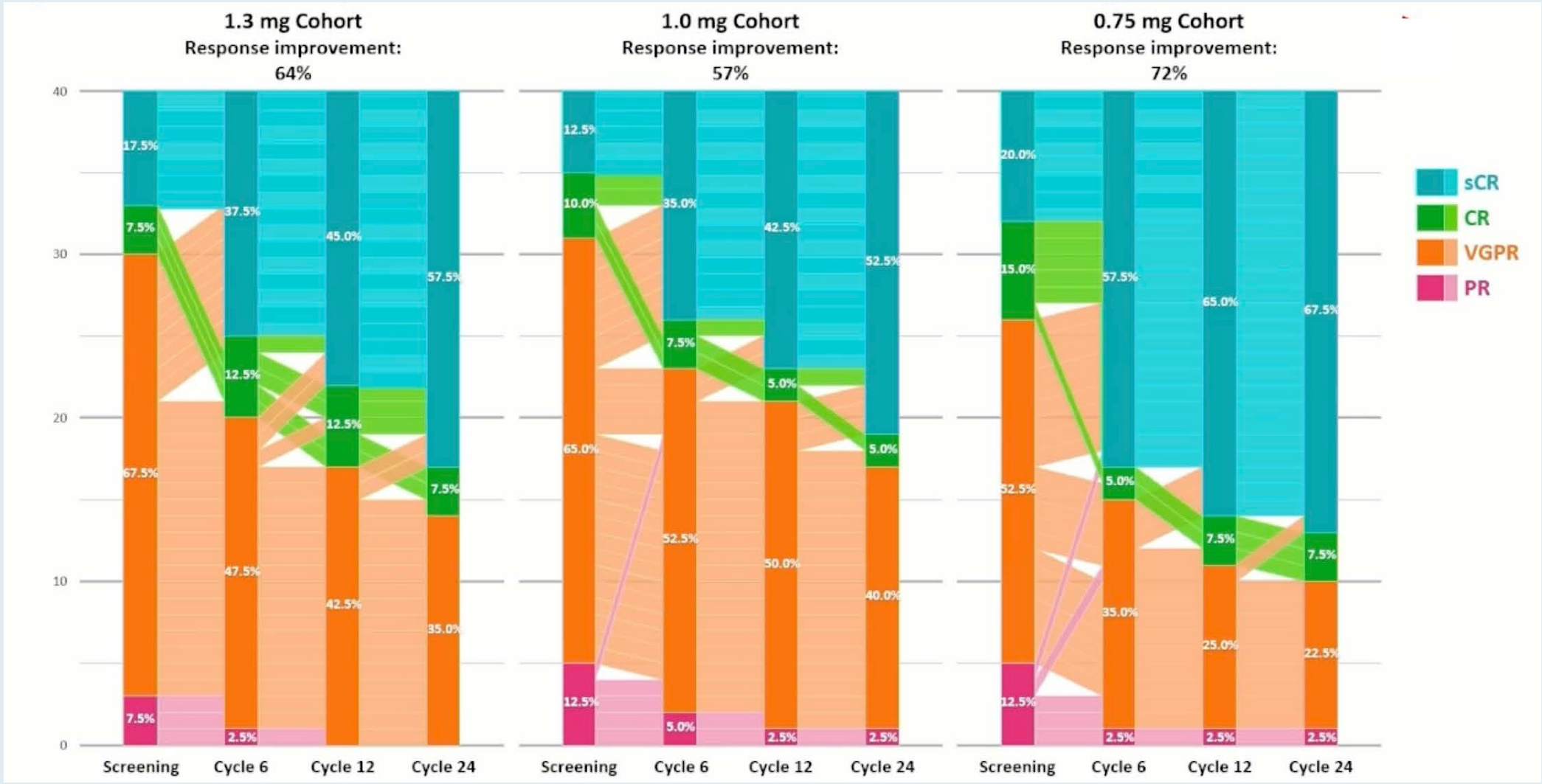


*Cohort 3 was added at a later stage.

Null hypothesis: response improvement rate within 6 month is ≤20%.

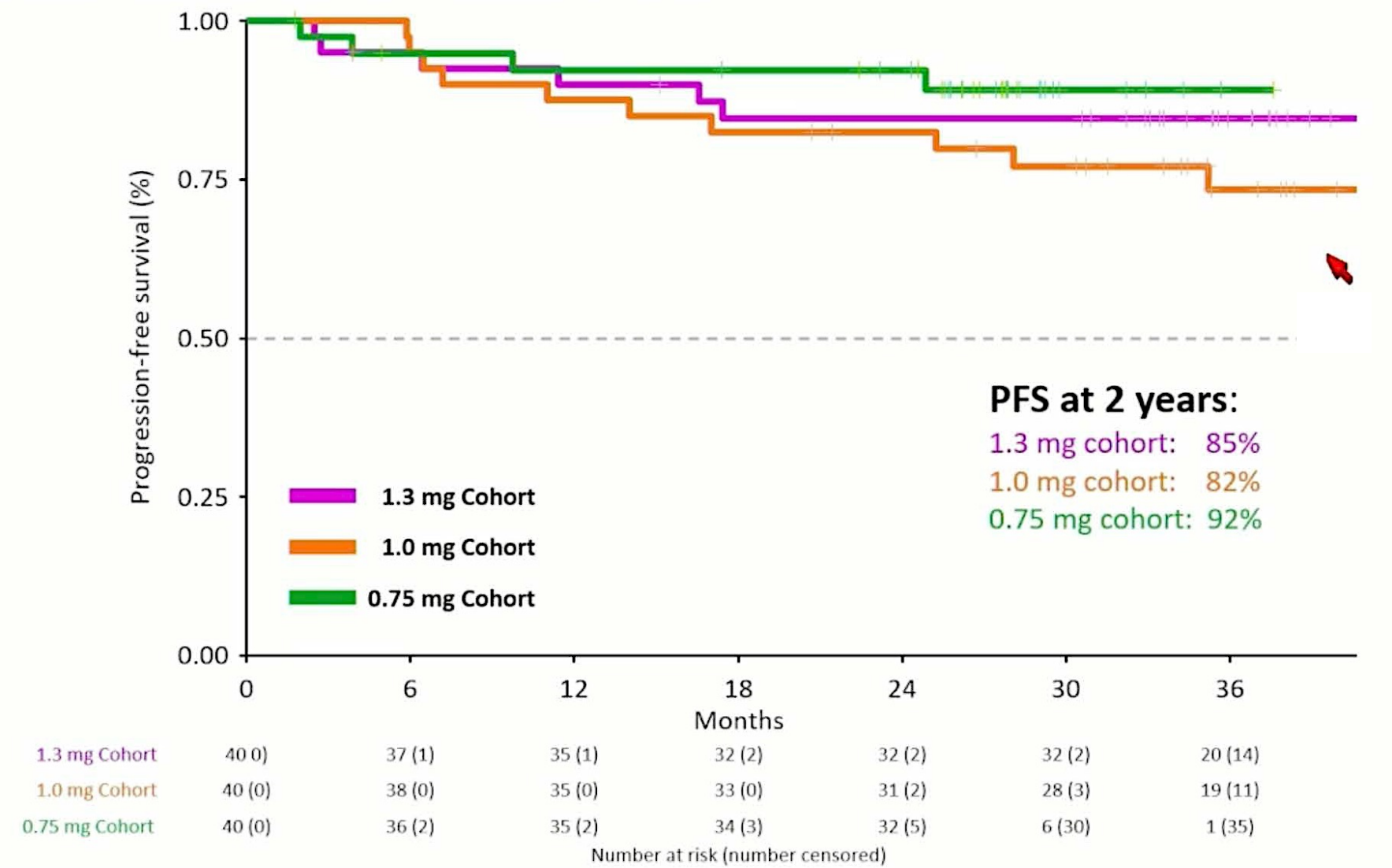
van de Donk NWCJ et al. ASH 2025;Abstract 101.

Phase II EMN26: Response Improvement over 24 Cycles



van de Donk NWCJ et al. ASH 2025;Abstract 101.

Phase II EMN26: Progression-Free Survival



van de Donk NWCJ et al. ASH 2025;Abstract 101.

RTP RESEARCH TO PRACTICE

Phase II EMN26: Authors' Conclusions

- Iberdomide maintenance resulted in an improvement in response over time in patients who received IMiD/PI-based induction +/- anti-CD38 antibody and autologous stem-cell transplantation, which compared favorably with lenalidomide maintenance.
  - Iberdomide demonstrated 46–72% improvement of response at cycle 12.
  - Lenalidomide demonstrated 31% improvement of response at cycle 12 in the EMN02 trial.
- Conversion to MRD negativity during maintenance is an important outcome post ASCT, and promising data with iberdomide were observed.
- Iberdomide showed a manageable safety profile with few grade 3–4 non-hematologic adverse events.
- The dose of 0.75 mg iberdomide was chosen as the recommended maintenance dose for further evaluation, based on comparable efficacy with superior tolerability, compared with higher doses of iberdomide.
- These data support the investigation of iberdomide vs. lenalidomide maintenance in the ongoing phase 3 registrational EXCALIBER-Maintenance trial (NCT05827016).

PI = proteasome inhibitor

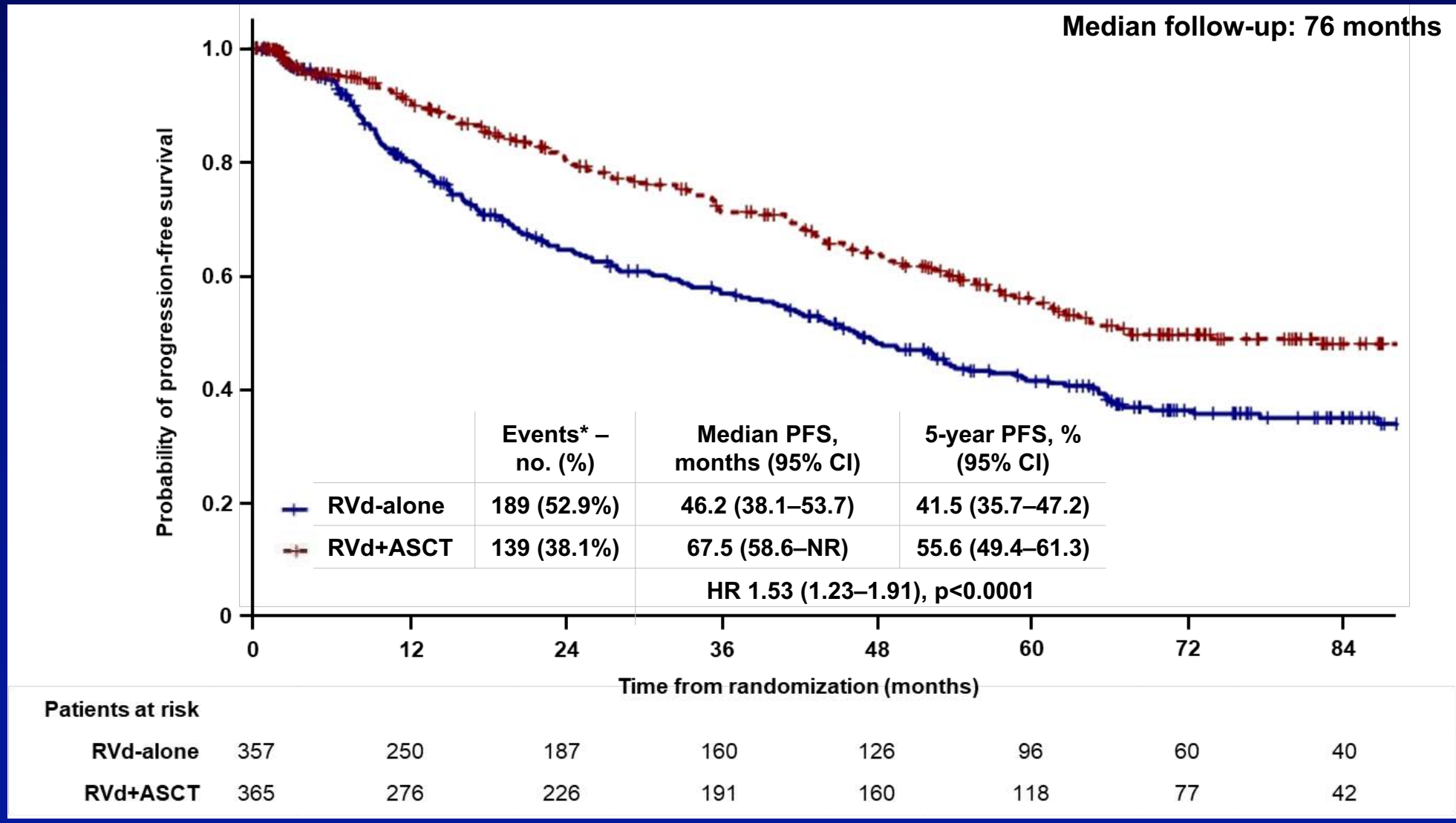
van de Donk NWCJ et al. ASH 2025;Abstract 101.

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*

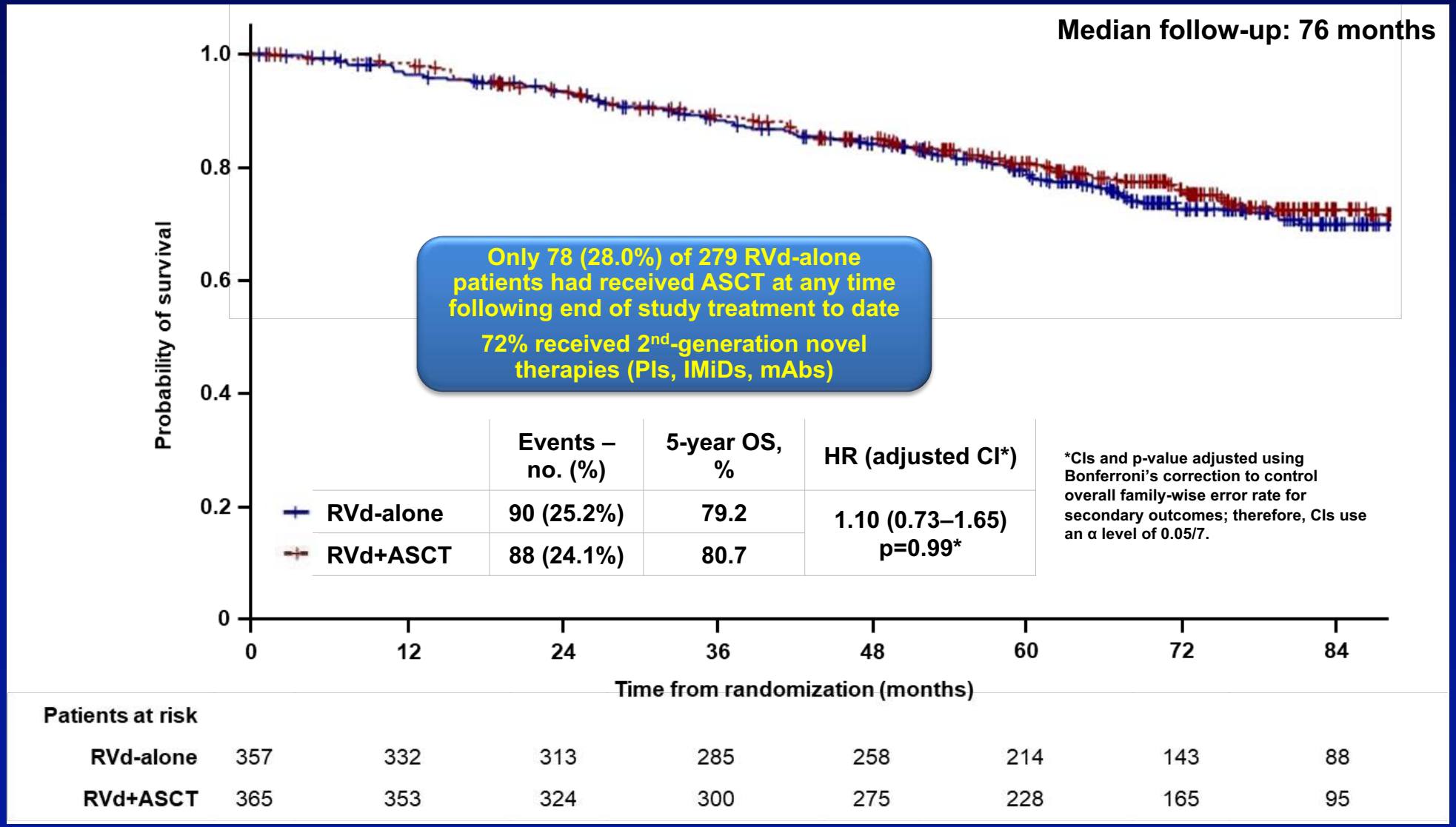
DETERMINATION 1: Improved PFS with RVd + ASCT vs RVd Alone (Primary Endpoint – Δ 21.3 months between medians)



Richardson PG, et al. N Engl J Med 2022;387(2):132–47.

Data cutoff: 12/10/21. *PFS events: disease progression or death.

DETERMINATION: No OS improvement with RVd + ASCT vs RVd Alone (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	

*CIs and p-value adjusted using Bonferroni's correction to control overall family-wise error rate for secondary outcomes; therefore, CIs use an α level of 0.05/7.

Patients at risk								
RVd-alone	357	332	313	285	258	214	143	88
RVd+ASCT	365	353	324	300	275	228	165	95

Richardson PG, et al. N Engl J Med 2022;387(2):132–47.

Data cutoff: 12/10/21.

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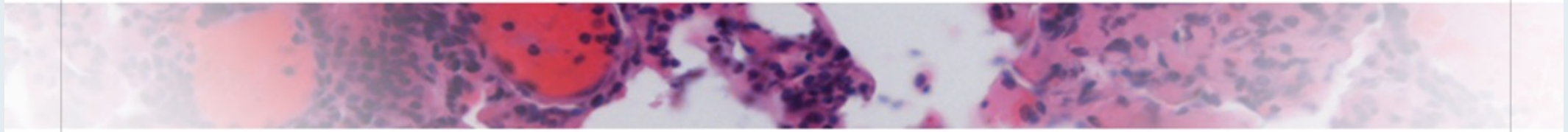


The Impact of Duffy Genotype on Progression-Free Survival With Lenalidomide, Bortezomib, and Dexamethasone (RVd) Alone Or RVd Plus ASCT in Patients with Newly Diagnosed Multiple Myeloma (NDMM): Updated Subgroup Analysis of the Phase 3 DETERMINATION Trial

Lauren E. Merz, Rebecca L. Zon, Susanna J. Jacobus, Mehmet K. Samur, Jeffrey A. Zonder, Abdullah M. Khan, Hani Hassoun, Larry D. Anderson Jr, Yvonne Efebera, Tondre Buck, Racquel D. Innis Shelton, Monique A. Hartley-Brown, Sagar Lonial, Erica L. Campagnaro, Peter M. Voorhees, Robert Z. Orlowski, Caitlin Costello, Noopur S. Raje, Eva Medvedova, Philip L. McCarthy, Carter P. Milner, Cristina Gasparetto, Mounzer E. Agha, Krisstina Gowin, Rammurti T. Kamble, Sundar Jagannath, Nitya Nathwani, Melissa Alsina, Sergio Giralt, Jacob Laubach, Omar Nadeem, Irene Ghobrial, Clifton C. Mo, Kenneth C. Anderson, Nikhil C. Munshi, Paul G. Richardson

RTP RESEARCH TO PRACTICE

DETERMINATION: Differential PFS Effect by Race in NDMM

Overall (N=357 vs N=365): no OS benefit with RVd+ASCT

- RVd-alone vs RVd+ASCT, 5-yr OS 79.2% vs 80.7%, HR 1.10 (95% CI 0.73–1.65)

Wh… (75… PF…

- R… H…

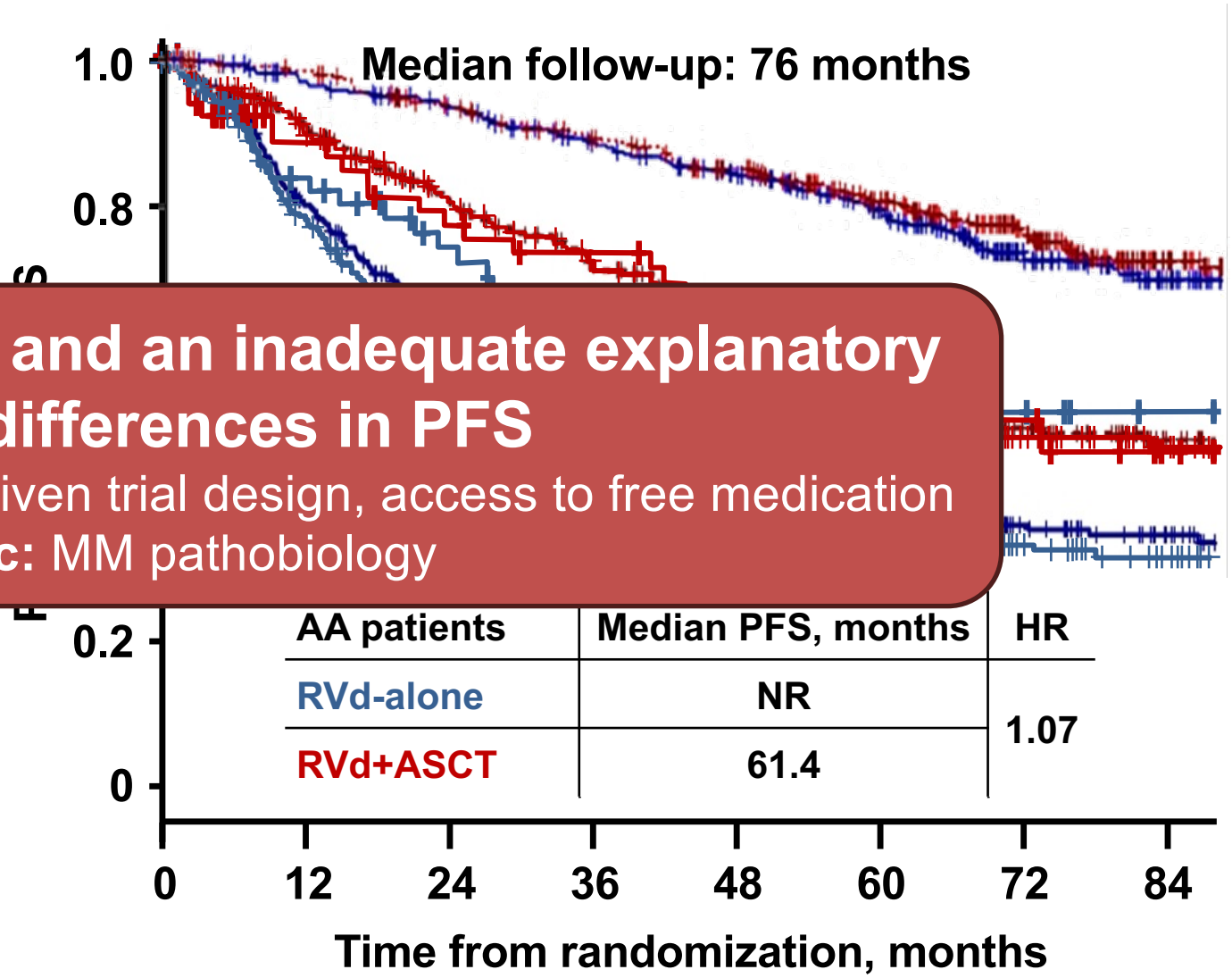
African American patients (18.5% vs 18.1% of ITT patients): PFS appeared similar between arms

- RVd-alone vs RVd+ASCT HR 1.07 (95% CI 0.61–1.89)

Race is social construct and an inadequate explanatory model for differences in PFS

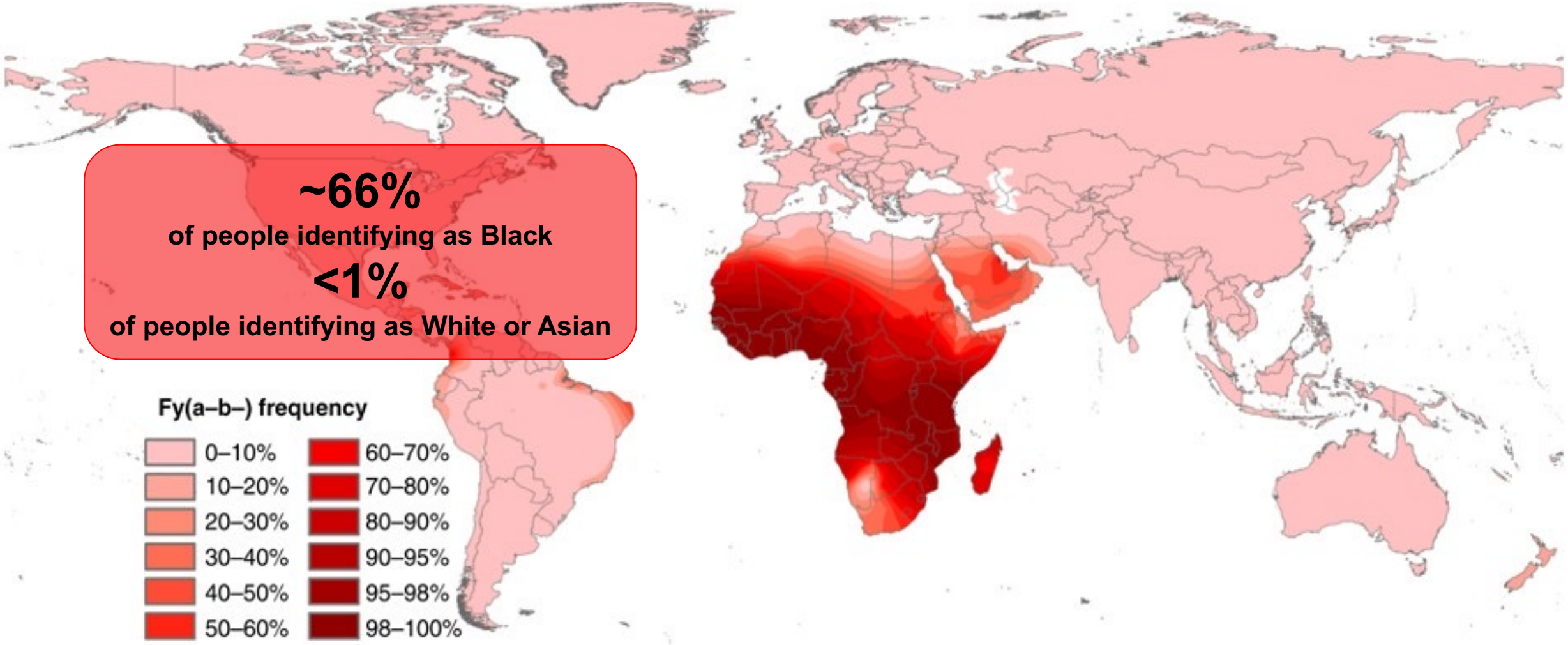
→ **Socioeconomic:** minimized given trial design, access to free medication

→ **Genetic:** MM pathobiology



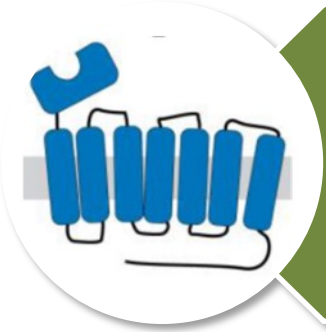
Richardson PG, et al. DETERMINATION Investigators. Triplet Therapy, Transplantation, and Maintenance until Progression in Myeloma. N Engl J Med 2022;387(2):132–47.
Zonder JA, et al. Blood 2023;142(suppl 1):4762.

Frequency of the Duffy null Genotype



Howes RE, et al. The global distribution of the Duffy blood group. Nat Commun 2011;2:266.

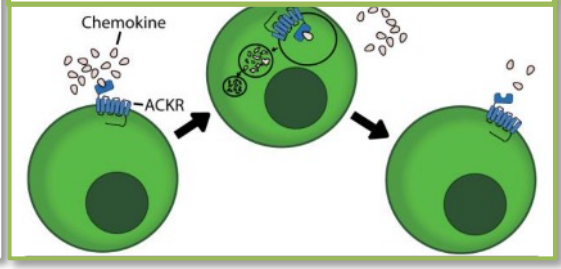
Roles of the Duffy Antigen



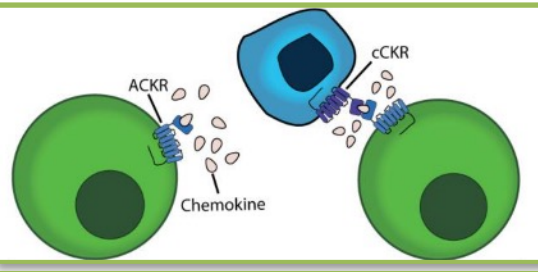
DARC/ACKR1 – atypical chemokine receptor

- Ligands:
  - CCL1, CCL2, CCL5, CCL6, CCL8, CCL11, CCL12, CCL14, CCL16, CCL17
  - CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL8, CXCL9, CXCL10, CXCL11, CXCL13

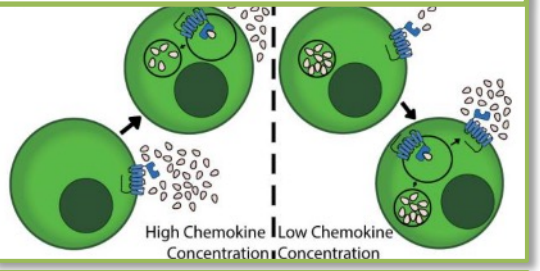
Chemokine scavenging



Chemokine presentation



Chemokine reservoir



Cytokine/chemokine homeostasis

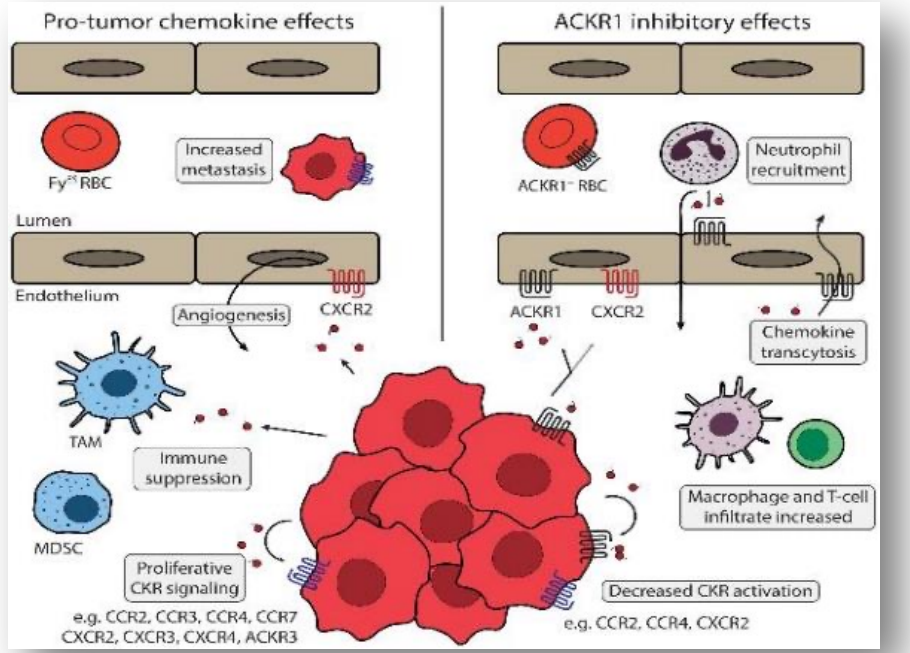
Null form is protective against *Plasmodium vivax*

Establishes normal absolute neutrophil reference intervals

- **Duffy non-null: 2,000 – 7,500/μL**
- **Duffy null: 1,200 – 5,500/μL**

Crucial decoy receptor ~ including cytokine/chemokine homeostasis

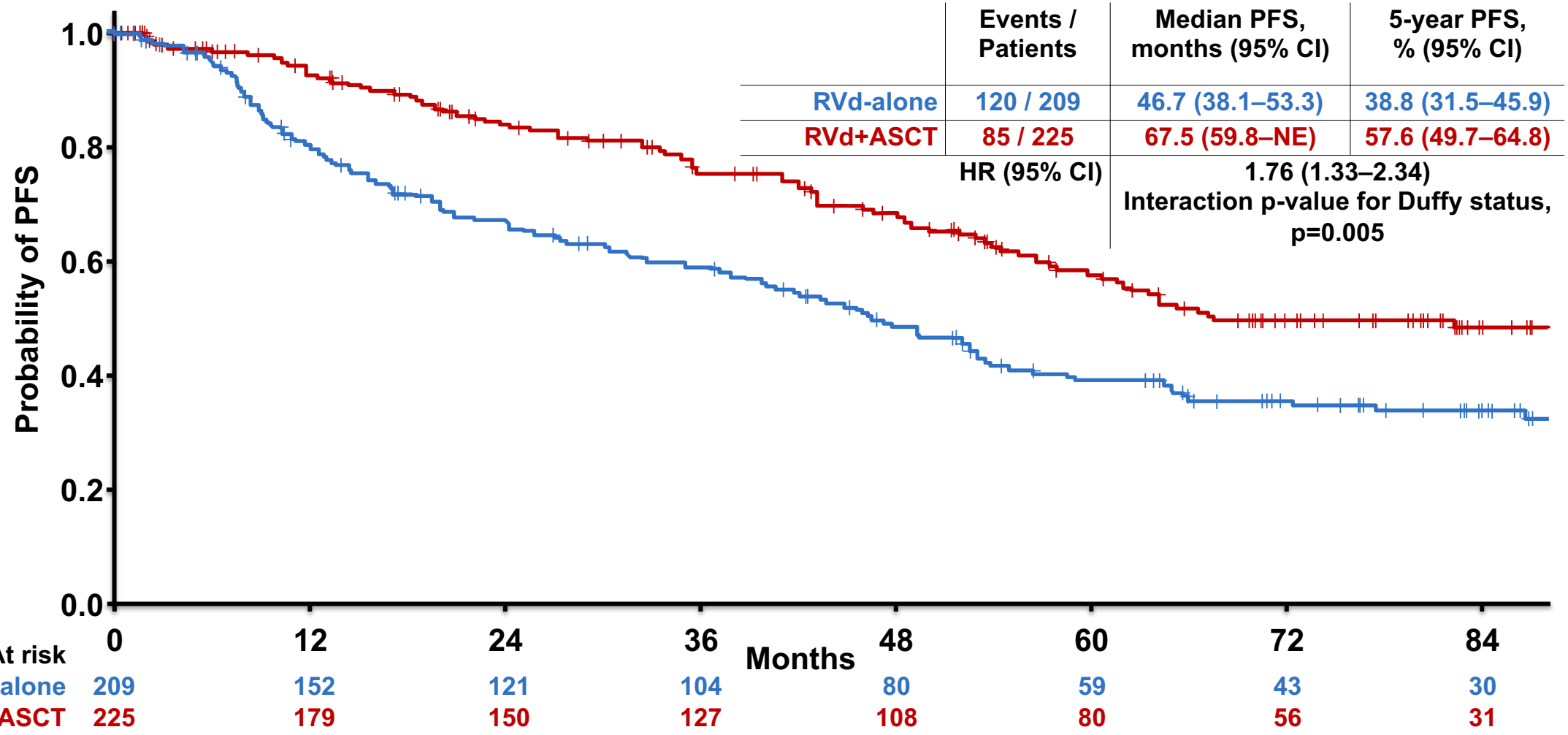
Chemokine signaling in TME may be regulated by DARC expression



Lack of expression on erythrocytes in Duffy null	Reduced binding to inflammatory cytokines	Exaggerated inflammatory reaction, with increased inflammasome and sequelae
→ Preserved expression of DARC on endothelium and Purkinje cells, with potential for asymmetric dysfunction	→ Potential role in MM pathobiology → Excess inflammatory response	→ Complex downstream effects (e.g. upregulation of APOBEC; additional tissue injury)

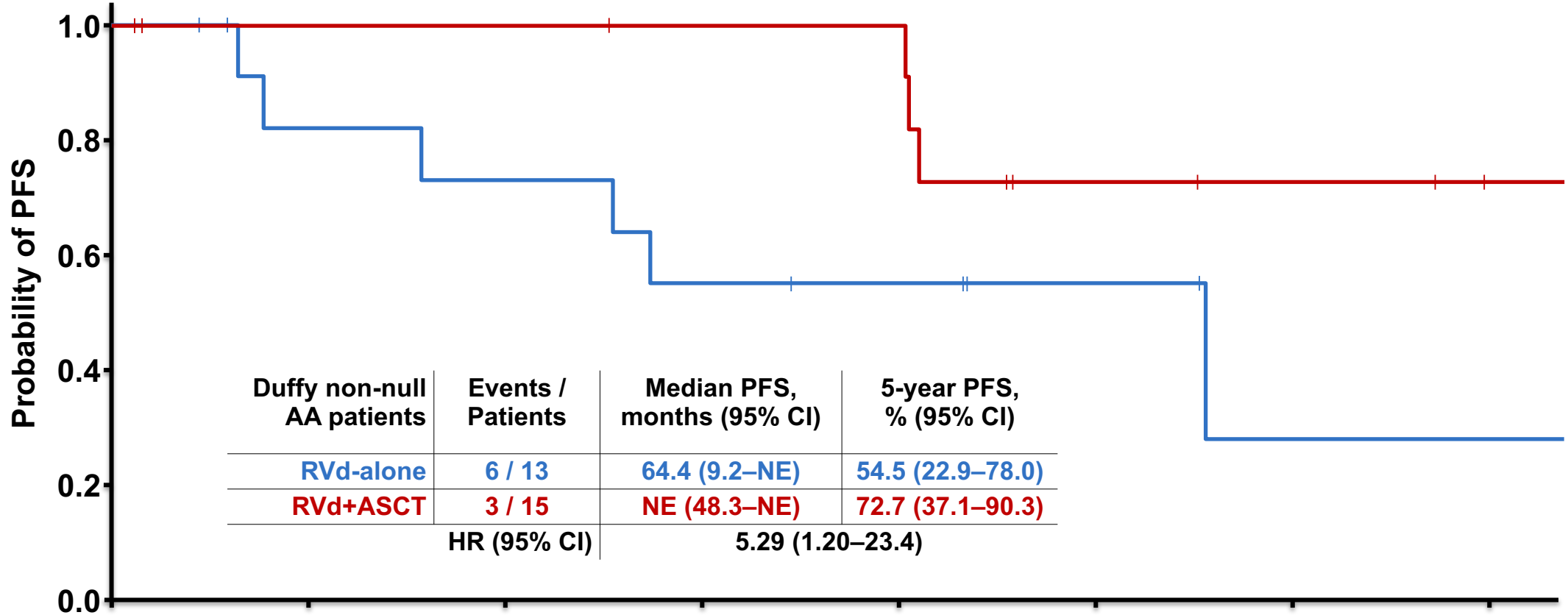
Jinna N, et al. Cells 2022;11(23):3818. Lindsay HG, et al. Int J Mol Sci 2023;24(22):16493. Crawford KS, Volkman BF. Front Immunol. 2023;14:1111960. Rappoport N, et al. Br J Haematol 2019;184:497–7. Morgan G. COMy; 2023. Richardson PG. Korean Society of Hematology, sponsored symposium; 2024. Richardson PG. LLM NYC Annual Meeting; 2025.

PFS in Duffy non-null Patients Consistent with ITT Analysis, in Favor of RVd+ASCT



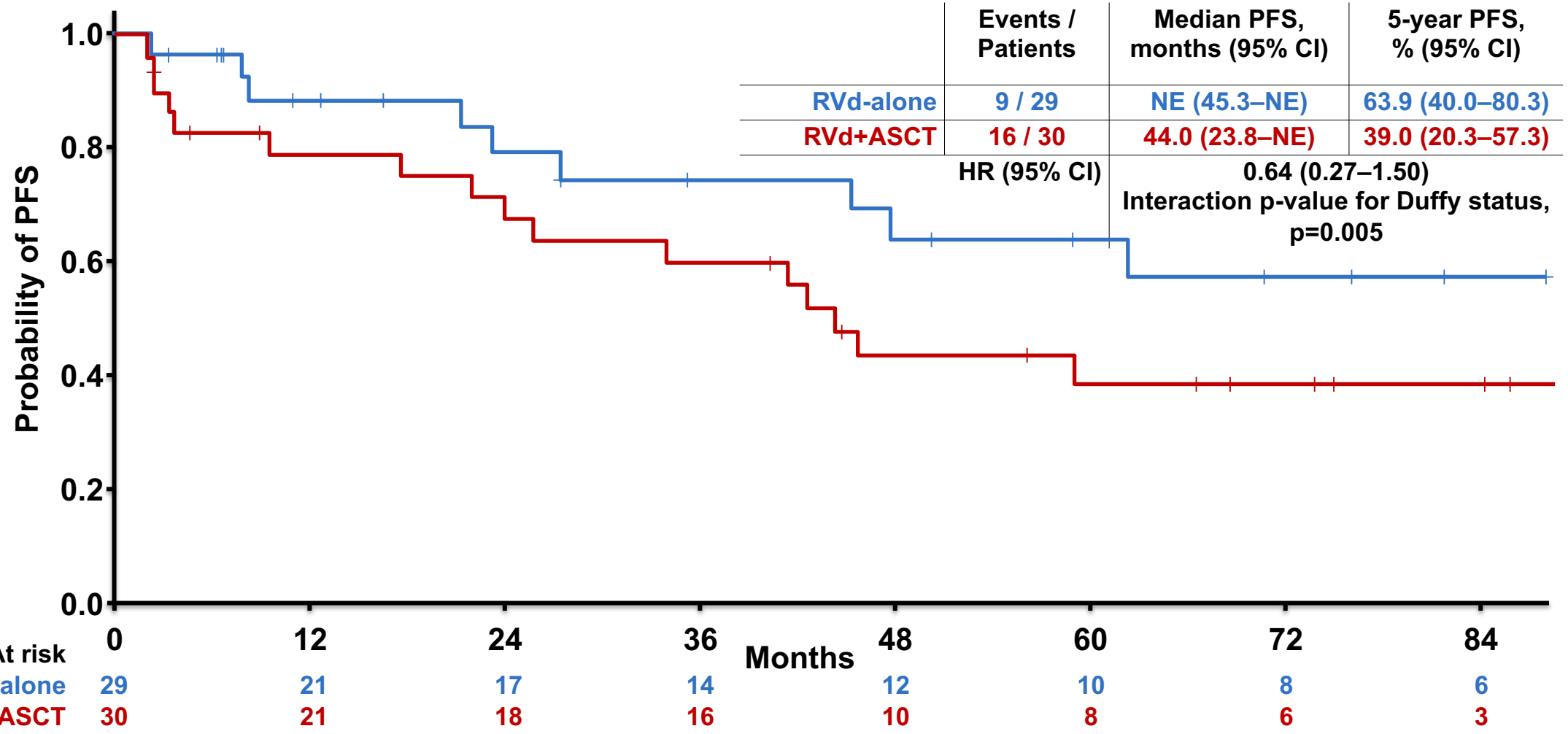
	Events / Patients	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	120 / 209	46.7 (38.1–53.3)	38.8 (31.5–45.9)
RVd+ASCT	85 / 225	67.5 (59.8–NE)	57.6 (49.7–64.8)
HR (95% CI)		1.76 (1.33–2.34)	
Interaction p-value for Duffy status, p=0.005			

PFS in African American Duffy non-null Patients Consistent with ITT Analysis, in Favor of RVd+ASCT



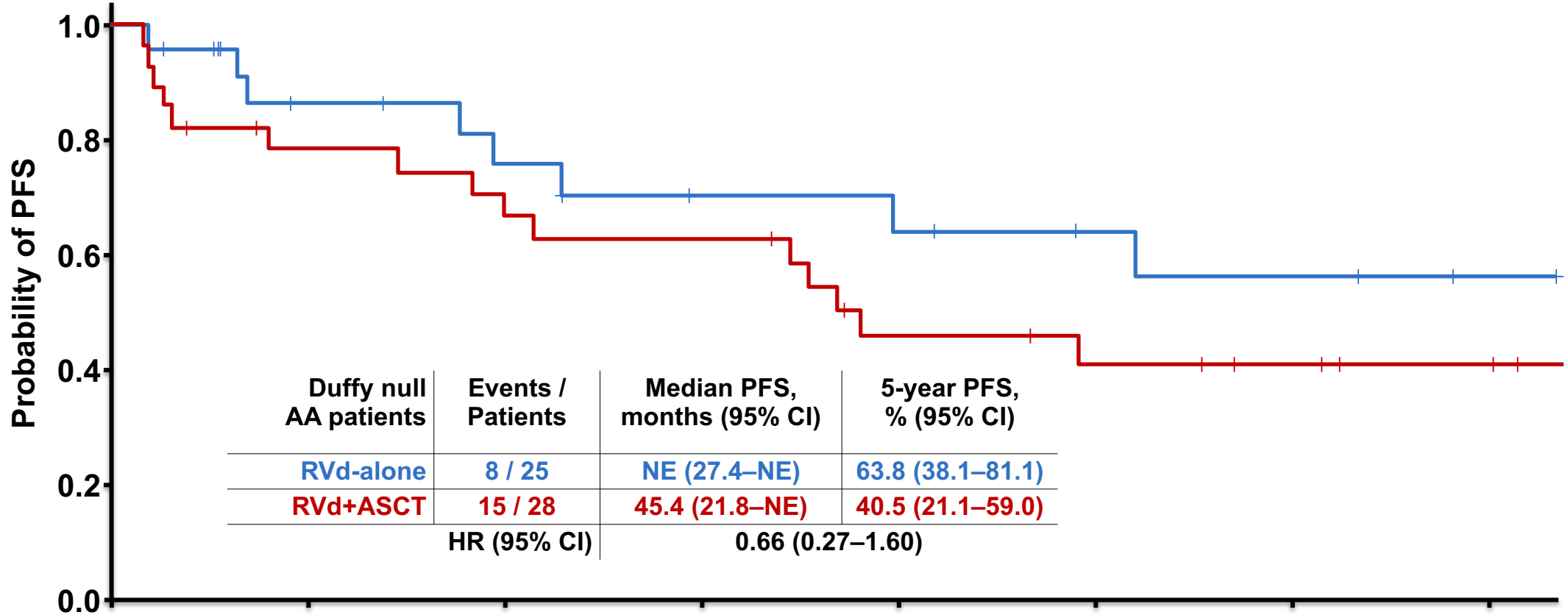
Duffy non-null AA patients	Events / Patients	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	6 / 13	64.4 (9.2–NE)	54.5 (22.9–78.0)
RVd+ASCT	3 / 15	NE (48.3–NE)	72.7 (37.1–90.3)
	HR (95% CI)	5.29 (1.20–23.4)	

PFS in Duffy null Patients Longer with RVd-alone, Opposite of ITT, in Favor of Deferred ASCT



	Events / Patients	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	9 / 29	NE (45.3–NE)	63.9 (40.0–80.3)
RVd+ASCT	16 / 30	44.0 (23.8–NE)	39.0 (20.3–57.3)
	HR (95% CI)	0.64 (0.27–1.50)	
		Interaction p-value for Duffy status, p=0.005	

PFS in African American Duffy null Patients Longer with RVd-alone, Opposite of ITT, in Favor of Deferred ASCT



Duffy null AA patients	Events / Patients	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	8 / 25	NE (27.4–NE)	63.8 (38.1–81.1)
RVd+ASCT	15 / 28	45.4 (21.8–NE)	40.5 (21.1–59.0)
	HR (95% CI)	0.66 (0.27–1.60)	

At risk	0	12	24	36	48	60	72	84
RVd-alone	25	17	14	11	10	8	7	5
RVd+ASCT	28	20	17	16	10	8	6	3

DETERMINATION 2

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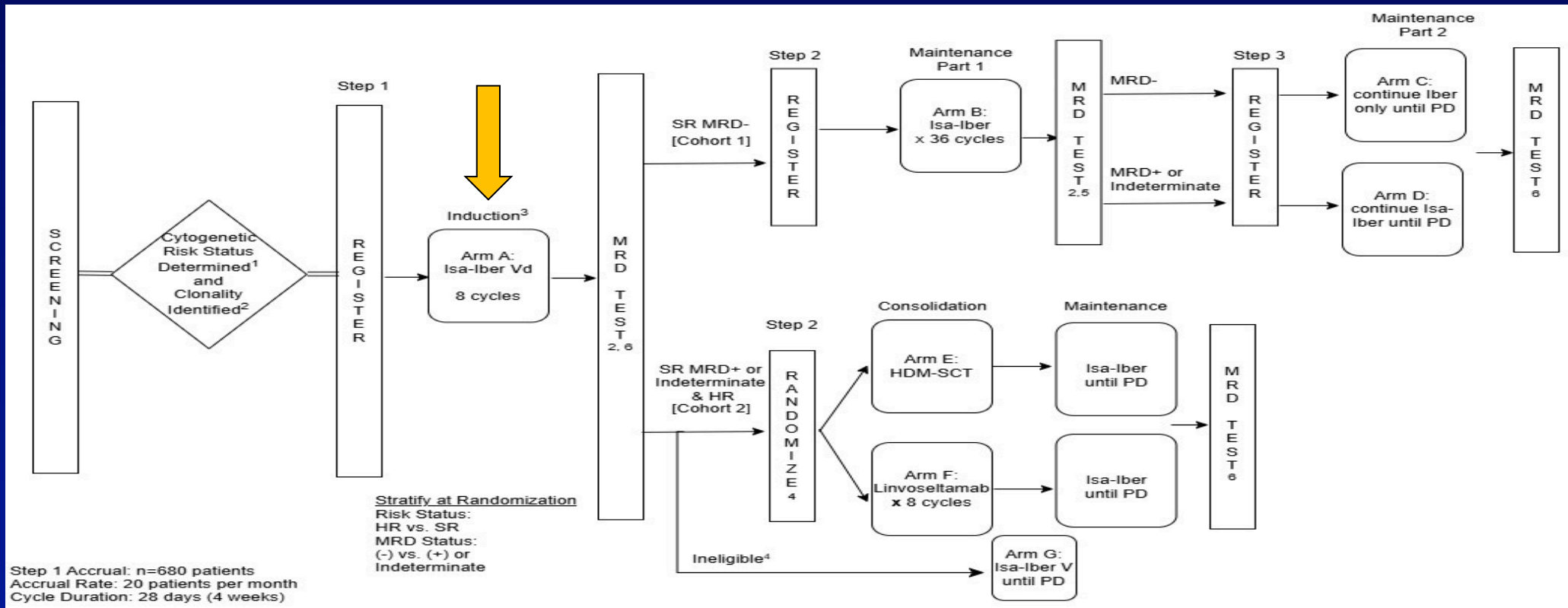
NDMM in 2025: A Tale of Two Cities ~ high risk (genetic, functional) versus standard risk

DETERMINATION 2 Schema (Revised for N = 720 Patients)



[1]Cytogenetic risk status based on FISH and next-generation sequencing (NGS) by PlasmaSEQ (TP53 mutational testing); Patients without risk established at screening are registered as Standard-Risk (SR)

[2]Clonality ID type test and all subsequent MRD tests based on NGS using Adaptive Biotechnologies clonoSEQ® assay; Patients with no dominant sequences identified at screening will be followed by next-generation flow cytometry (NGF)

[3]Stem cell mobilization to occur between 4-6 cycles of induction

[4]Only eligible patients are randomized to consolidation; Ineligible patients may continue on-study in Arm G

[5]Step 2 treatment and Step 3 [Cohort 1] assignments are dependent on post-induction and post-3 years maintenance MRD tests, respectively; Patients therefore must have completed treatment per protocol to be eligible to continue on study; Only patients who achieve IMWG very good partial response (VGPR) or better status require an evaluable sample at these timepoints for MRD testing; Patients with indeterminate MRD test results along with patients not achieving IMWG VGPR status are assumed to be MRD-positive

[6]MRD test conducted 1-year post-registration [Cohort 1] and 1-year post-randomization [Cohort 2] for the outcome of MRD-negative complete response (CR); Only patients who achieve IMWG VGPR or better status require an evaluable sample at these timepoints for MRD testing

Agenda

Introduction: Clinical Trials We LOVE to Discuss

Module 1: Mechanism of Action of Cereblon E3 Ligase Modulators (CELMoDs)

Module 2: Available Efficacy Data with CELMoDs in the Management of Relapsed/Refractory Multiple Myeloma (MM)

Module 3: Extramedullary Disease

Module 4: Spectrum and Management of CELMoD-Associated Adverse Events

Module 5: Ongoing Phase II and III Trials Evaluating CELMoDs for MM

Module 6: Other Trials in Progress

Other CELMoD Trials in Progress

- **GEM21menos65.** A Phase III Trial for NDMM Patients Who Are Candidates for ASCT Comparing Extended VRD Plus **Early Rescue Intervention vs Isatuximab-VRD vs Isatuximab-V-Iberdomide-D**
- A Randomized Phase III Trial Assessing **Iberdomide Versus Iberdomide Plus Isatuximab Maintenance Therapy Post Autologous Hematopoietic Stem-Cell Transplantation** in Patients With Newly Diagnosed Multiple Myeloma
- Multicenter, Phase II, National and Open-label Study to Evaluate **Iberdomide-dexamethasone Alone or in Combination With Standard MM Treatment Regimens in Transplant Ineligible** Newly Diagnosed Patients
- IBEX: Phase 2 Trial of **Iberdomide + SQ Daratumumab As Post-Autologous Stem Cell Transplant Maintenance** Therapy in Multiple Myeloma
- A Phase I/II Study of **Elotuzumab and Iberdomide and Dexamethasone Post Idecabtagene Vicleucel** in Relapsed and Refractory Multiple Myeloma
- A Phase 2, Single Arm Multicenter, Study Testing **Mezigdomide, Carfilzomib, and Dexamethasone** (480Kd) in Participants With Relapsed or Refractory Multiple Myeloma (RRMM)
- A Phase 1b/2a, Multicenter, Open-label Study to Determine the Recommended Dose and Schedule, and Evaluate the Safety and Preliminary Efficacy of **Mezigdomide in Combination With Elranatamab** in Participants with Relapsed and/or Refractory Multiple Myeloma (RRMM)

Exploring Current Patterns of Care in the Community: Selection of First-Line and Maintenance Therapy for Patients with Extensive-Stage Small Cell Lung Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, February 4, 2026
5:00 PM – 6:00 PM ET

Faculty

Hossein Borghaei, DO, MS
Anne Chiang, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME and ABIM MOC credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

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