



8th Annual

# LEAD 2026

LEADERSHIP  
EMPOWERMENT  
DEVELOPMENT

Enriching Experiences for Leaders in Hematology and Oncology

SEPT  
18-19,  
2026

## Clinical Updates in Multiple Myeloma

Yuxin Liu, MD

Dana-Farber Cancer Institute



# Disclosures

- OPNA Bio: Advisory Board
- Sanofi: Research Funding
- BMS: Research Funding

# Agenda

Continuous vs. Time-Limited  
Maintenance

ENDURANCE (ECOG-ACRIN  
E1A11)

Bispecific T-cell Engagers  
(BiTEs) in early Relapsed  
Myeloma

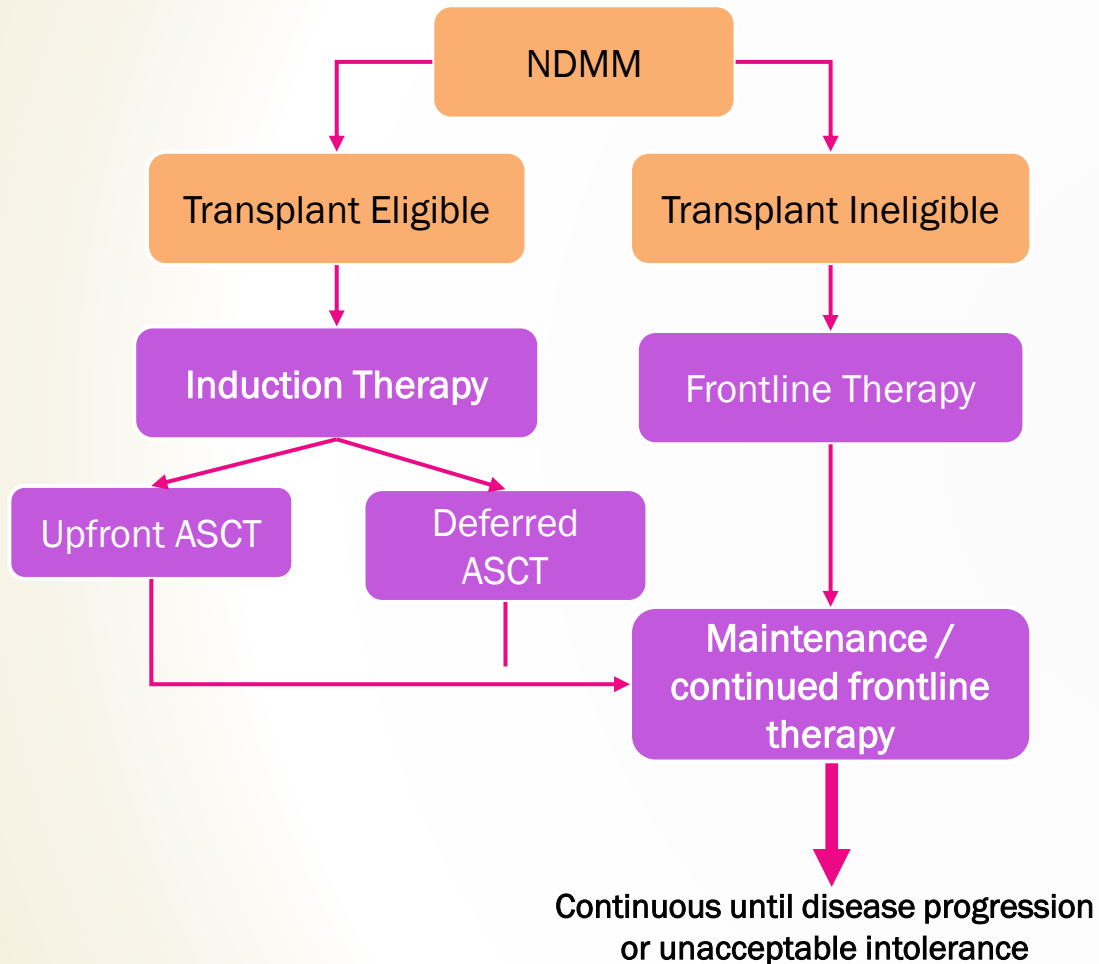
MajesTEC-3, MajesTEC-9,  
MonumentAL-3

CeLMODs: A new class of oral  
inhibitors

Iberdomide: EXCALIBER-RRMM  
Mezigdomide: SUCCESSOR-2

# Reevaluating Duration of Maintenance Therapy in Myeloma

# Continuous therapy and maintenance treatment in myeloma



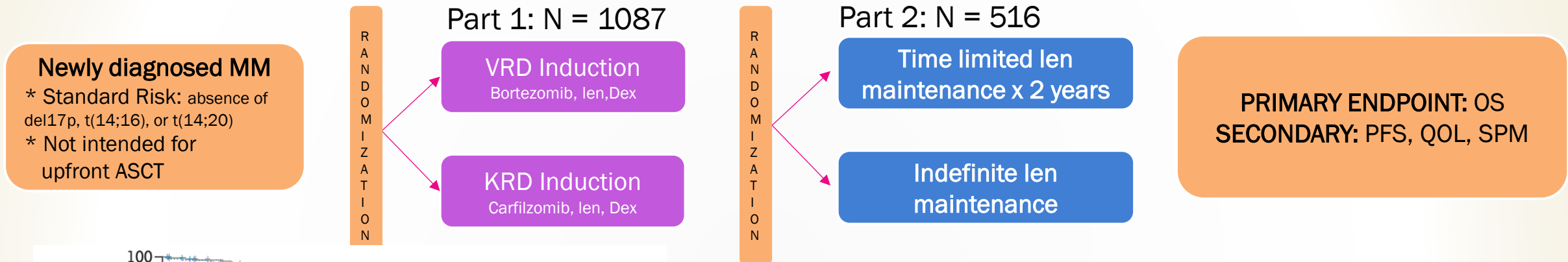
- Continuous long-term therapy in the form of maintenance or continued frontline combination therapy has been a standard of NDMM treatment
- Provides clone suppression and can help deepen response aiming to provide deep and long-term disease control (1,2)
- Lenalidomide maintenance vs. observation/placebo after ASCT improves PFS in multiple studies, and improves OS via meta-analysis (3)
- Optimal duration of maintenance remains in question
- How do we factor in transplant, depth of response, and minimal residual disease status
- Costs of continuous maintenance therapy
- Ongoing toxicity (diarrhea, rash, cytopenia), QOL impact, Secondary cancer risk, financial toxicity

1. Palumbo, A, Gay, F, Cavallo, F, et al. Continuous Therapy Versus Fixed Duration of Therapy in Patients With Newly Diagnosed Multiple Myeloma. *J Clin Oncol*. 2015;**33**(30):3459-3466.

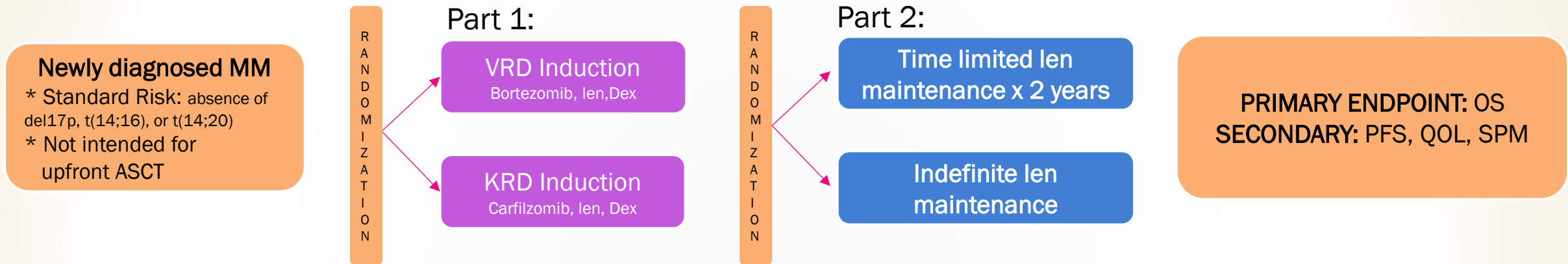
2. Ludwig, H. & Zojer, N. Fixed duration vs continuous therapy in multiple myeloma. *Hematology Am. Soc. Hematol. Educ. Program* 2017, 212–222 (2017).

3. McCarthy, et al. Lenalidomide maintenance after autologous stem-cell transplantation in newly diagnosed multiple myeloma: a meta-analysis. 2017. *J Clin Oncol*.

# ECOG-ACRIN ENDURANCE Trial: Indefinite vs. Time Limited Lenalidomide Maintenance in NDMM not undergoing transplant



# ECOG-ACRIN ENDURANCE Trial: Indefinite vs. Time Limited Lenalidomide Maintenance in NDMM not undergoing transplant



| Secondary Outcomes                                          | Indefinite     | Fixed Duration |
|-------------------------------------------------------------|----------------|----------------|
| Median PFS                                                  | 42.5 mo        | 38.9 mo        |
| Aggregate Adverse Events (Grade ≥3 Heme & Non-heme) / TEAEs | 62.4%<br>44.7% | 46.9%<br>33.5% |
| Second primary malignancy (5-year cumulative incidence)     | 11.2%          | 8.3%           |

# How do we apply the results of the ENDURANCE Trial?

- The ENDURANCE study showed that stopping lenalidomide maintenance after 2 years did not lead to a significant detriment in overall survival compared to continuous maintenance in standard risk patients not undergoing transplant
- Is this practice changing? ...Yes, but we should apply the results carefully in a very heterogeneously treated population
- How can the results be extrapolated to....
  - Patients who undergo upfront transplant?
  - Patients who receive quadruplet induction with anti-CD38 monoclonal antibody?
  - Patients with high-risk cytogenetics? Using the new IMWG-IMS genomic risk stratification?
  - How do we incorporate depth of response, MRD status, and sustained MRD negativity?
- Establishes an important precedent for future trial design to incorporate of time limited treatment

# Bispecific antibodies in early relapsed refractory myeloma

# T-cell Re-directing therapies after 4 or more prior treatments

|                               | Ide-cel | Cilta-cel | Teclistamab | Elranatamab                   | Talquetamab* | Linvoseltamab         |
|-------------------------------|---------|-----------|-------------|-------------------------------|--------------|-----------------------|
| Efficacy                      |         |           |             |                               |              |                       |
| Median Prior Lines of Therapy | 6       | 6         | 5           | 5                             | 6            | 5                     |
| ORR (%)                       | 73      | 98        | 63          | 61                            | 73           | 70.9                  |
| ≥ CR (%)                      | 33      | 83        | 39          | 35                            | NA           | 49.6                  |
| Median PFS (months)           | 8.8     | 34.9      | 11.3        | NR (15-month estimate: 50.9%) | 11.9         | NR (12-month PFS 70%) |
| Safety                        |         |           |             |                               |              |                       |
| CRS (%)                       | 84      | 95        | 72          | 58                            | 75           | 46                    |
| ICANS (%)                     | 18      | 21        | 15          | 3                             | 11           | 7.7                   |
| Infections (%)                | 69      | 58        | 76          | 70                            | 65           | 74.4                  |

\* Data presented for Talquetamab 800 µg/kg dosing

Adapted from Chari, A et al. N Eng J Med. 387:2232-2244. 2022.  
Bumma et al. 2024. J Clin Oncol 42:2702-2712



# MajesTEC-3: Teclistamab + Daratumumab in early RRMM

## Key inclusion criteria

- RRMM
- 1-3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0-2

## Key exclusion criteria

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs<sup>a</sup>

**1:1  
randomization  
N=587**

22 Oct 2021 to  
29 Sept 2023<sup>b</sup>

**Tec-Dara**  
**N=291**  
**SC dosing following Dara schedule**

**DPd/DVd<sup>\*</sup>**  
**N=296 (91% DPd)**  
**by investigator's choice<sup>c</sup>**

## Primary endpoint

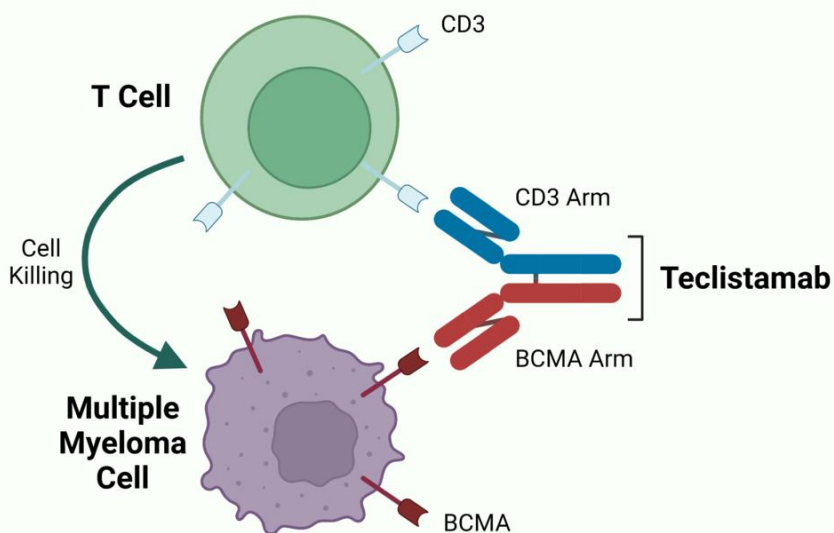
- PFS per IRC

## Key secondary endpoints

- $\geq$ CR<sup>d</sup> and ORR<sup>d</sup>
- MRD negativity ( $10^{-5}$ )
- OS
- MySIm-Q Total Symptom score

## Other secondary endpoints

- Safety
- PK and immunogenicity

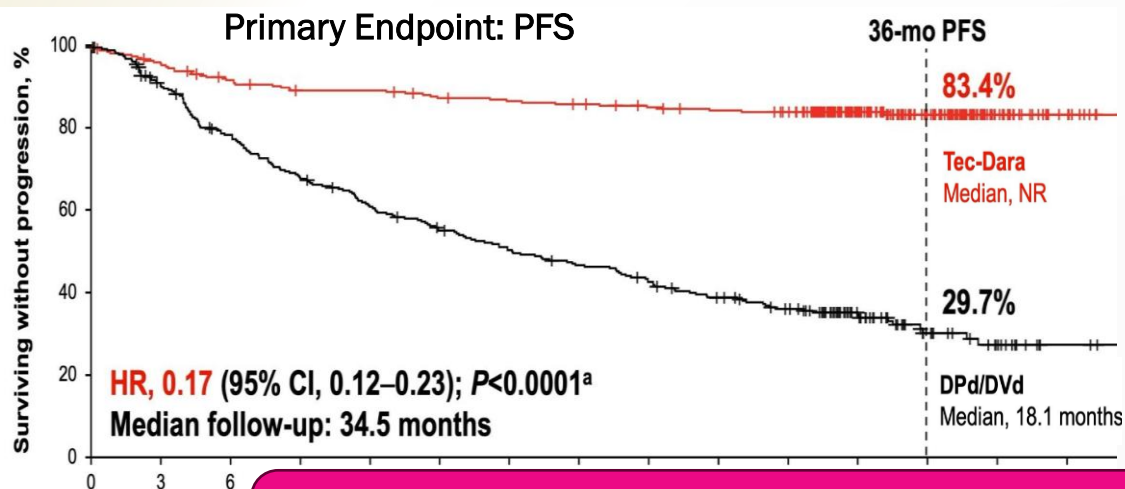


| Characteristic                | Tec-Dara<br>(n=291) | DPd/DVd<br>(n=296) |
|-------------------------------|---------------------|--------------------|
| Prior therapy exposure, n (%) |                     |                    |
| PI                            | 290 (99.7)          | 296 (100)          |
| IMiD                          | 291 (100)           | 296 (100)          |
| Anti-CD38, n (%)              | 15 (5.2)            | 16 (5.4)           |
| Refractory status, n (%)      |                     |                    |
| To last prior LOT             | 250 (85.9)          | 251 (84.8)         |
| Any PI                        | 117 (40.2)          | 104 (35.1)         |
| Any IMiD                      | 247 (84.9)          | 253 (85.5)         |
| Lenalidomide                  | 240 (82.5)          | 251 (84.8)         |
| Double (PI and IMiD)          | 99 (34.0)           | 88 (29.7)          |

<sup>\*</sup> DPd: Daratumumab, Pomalidomide, dexamethasone; DVd: Daratumumab, bortezomib, dexamethasone

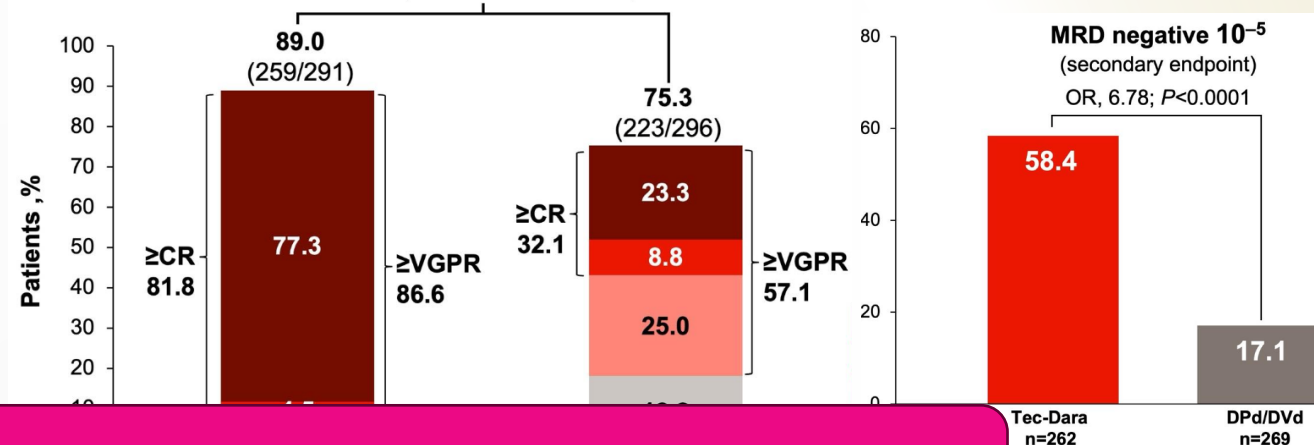
# MajesTEC-3: Teclistamab + Daratumumab in early RRMM

## Primary Endpoint: PFS

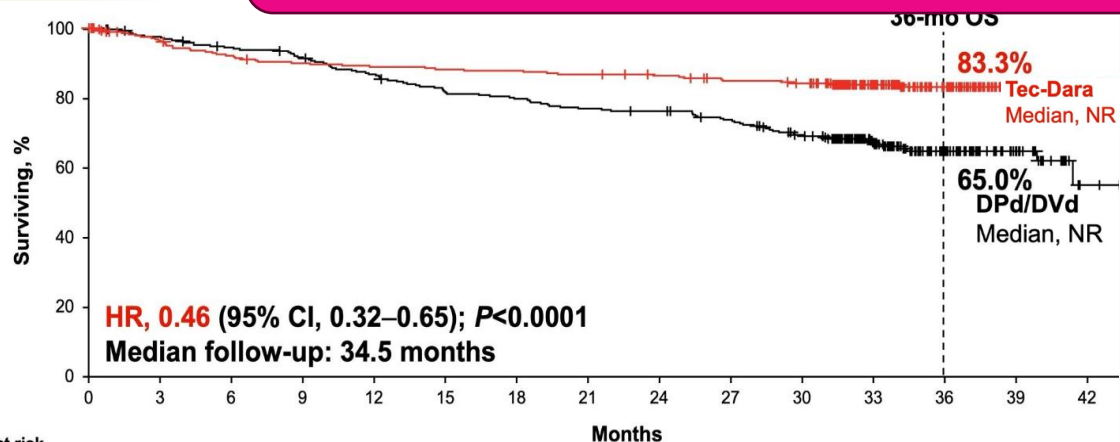


ORR: OR, 2.65 (95% CI, 1.68–4.18);  $P<0.0001$

$\geq$ CR: OR, 9.56 (95% CI, 6.47–14.14);  $P<0.0001$



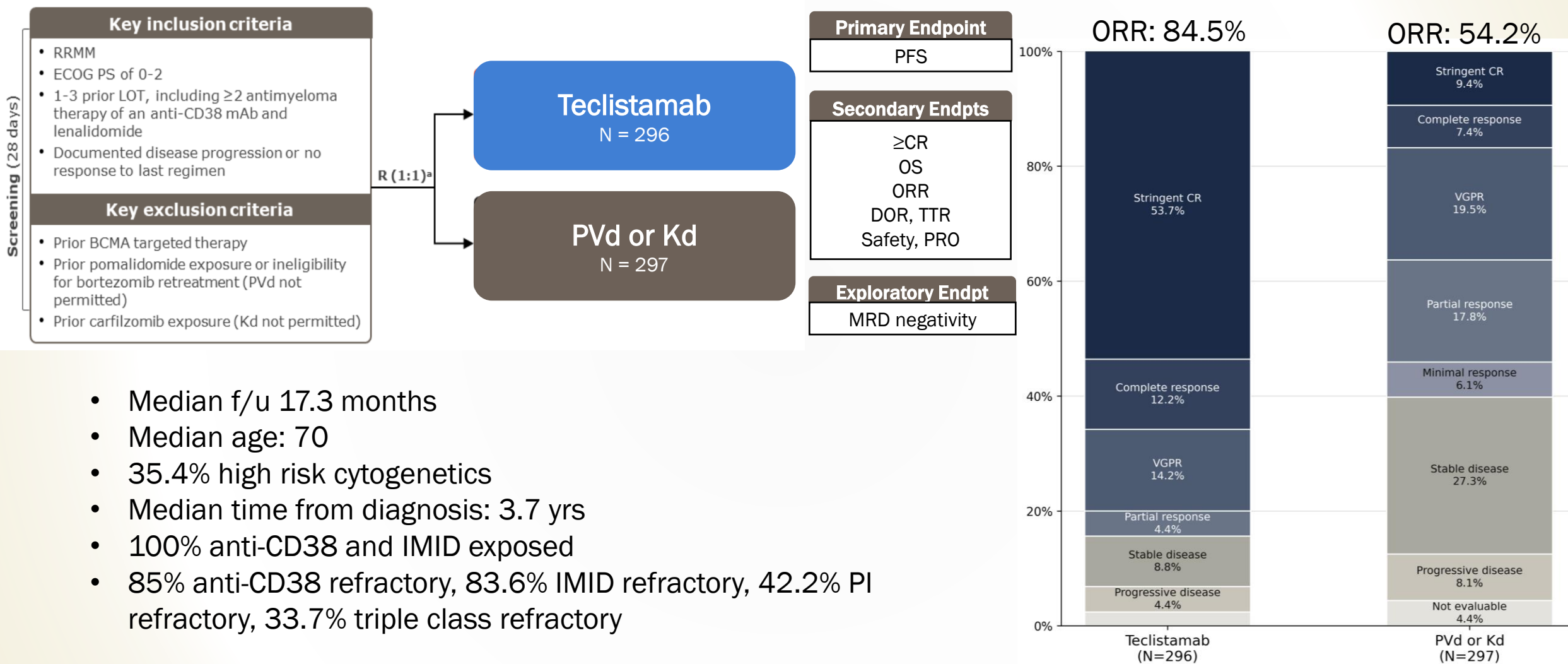
Tec-Dara is FDA approved after one prior treatment lines in March 2026



## Adverse Events

- Grade 3/4 infections: 54.1% Tec-Dara; 43.4% DPd/DVd
- Grade 3 infections higher w/ Tec-Dara in the first 6 months
- 13 (4.6%) deaths due to infections with Tec-Dara
  - 12 in the the first 6 months of treatment (3 COVID-19)
  - 9 of 12 patients did not receive IVIG
- 84.5% Hypogammaglobulinemia in Tec-Dara arm (Protocol amended 2/2023 to reinforce IVIG)

# MajesTEC-9: Teclistamab monotherapy in early RRMM



- Median f/u 17.3 months
- Median age: 70
- 35.4% high risk cytogenetics
- Median time from diagnosis: 3.7 yrs
- 100% anti-CD38 and IMiD exposed
- 85% anti-CD38 refractory, 83.6% IMiD refractory, 42.2% PI refractory, 33.7% triple class refractory

\* PvD: Pomalidomide, bortezomib, dexamethasone; Kd: Carfilzomib, dexamethasone

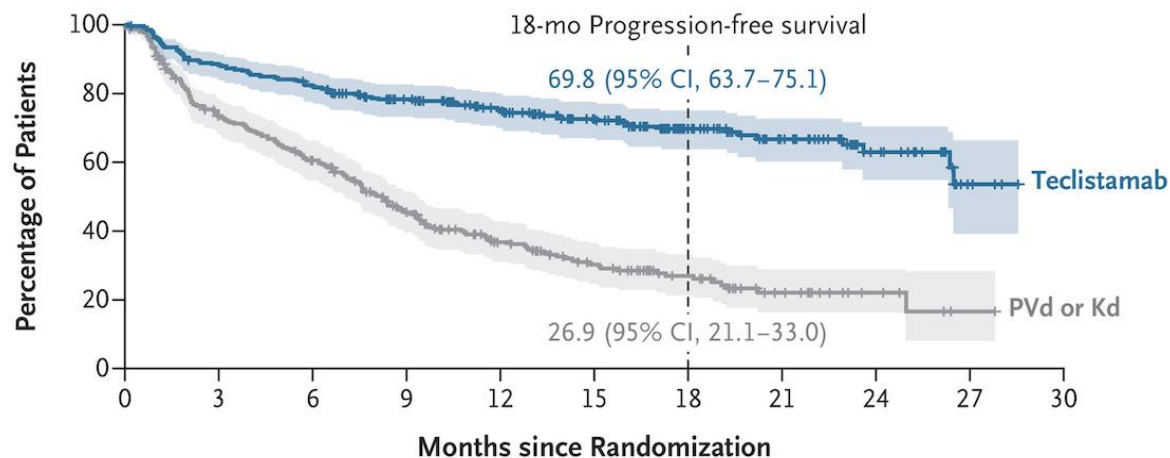
**LEAD 2026:** Leadership, Empowerment, and Development

Touzeau C et al. N Engl J Med. 2026 Jul 30;395(5):440-45



# MajesTEC-9: Teclistamab monotherapy in early RRMM

Progression-free Survival

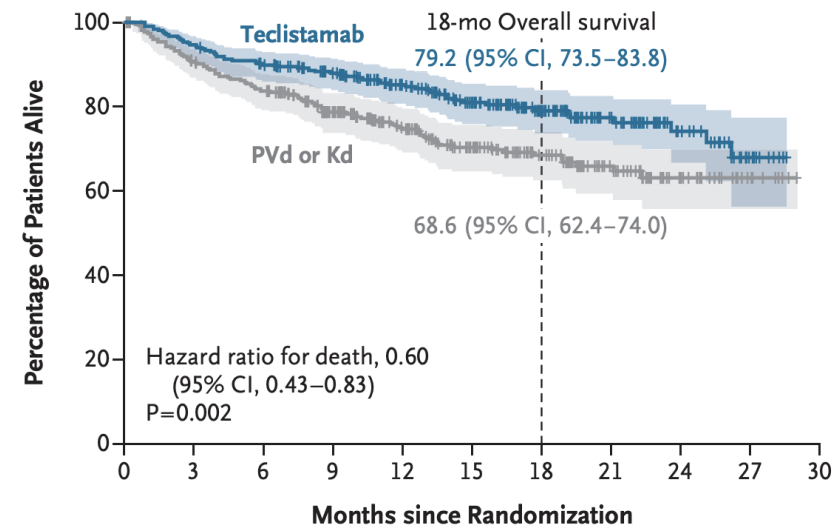


No. at Risk

|             |     |     |     |     |     |     |    |    |    |   |   |
|-------------|-----|-----|-----|-----|-----|-----|----|----|----|---|---|
| Teclistamab | 296 | 258 | 239 | 206 | 172 | 141 | 92 | 57 | 27 | 6 | 0 |
| PVd or Kd   | 297 | 199 | 162 | 112 | 74  | 51  | 33 | 16 | 6  | 1 | 0 |

Teclistamab significantly improved PFS vs PVD or Kd (HR = 0.29; 95% CI 0.23-0.38  $p < 0.001$ ). Median PFS NR for tec; 8.2 mo for PVD/Kd

Overall Survival



No. at Risk

|             |     |     |     |     |     |     |     |    |    |    |   |
|-------------|-----|-----|-----|-----|-----|-----|-----|----|----|----|---|
| Teclistamab | 296 | 280 | 263 | 237 | 195 | 159 | 107 | 66 | 33 | 11 | 0 |
| PVd or Kd   | 297 | 264 | 243 | 210 | 172 | 137 | 91  | 54 | 25 | 8  | 0 |

## Safety

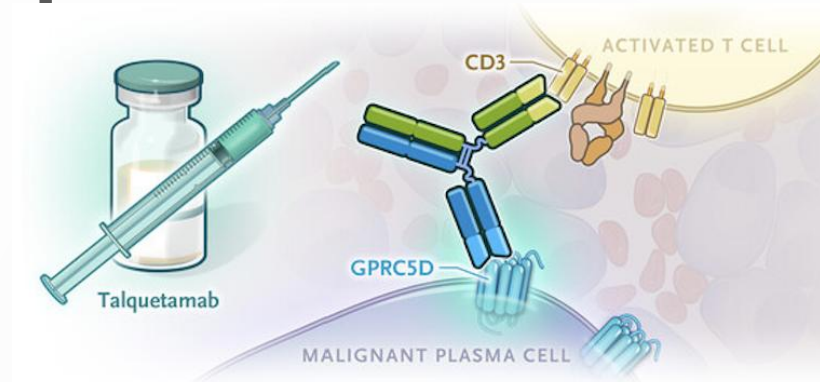
Grade 3/4 AEs: 84.9% of Teclistamab vs. 76.3% PVD/Kd (Grade 5: 6.35% vs. 3.5%, respectively)

CRS: 66% Teclistamab; mostly grade 1/2. ICANS = 4.1%

Grade 3/4 Infections were common: 41.6% with teclistamab vs. 29% with PVD/Kd



# MonumenTAL-3: Talquetamab-Daratumumab in early RRMM



## Study Design

### MonumenTAL-3

1:1:1<sup>b</sup> N=864

Tal-DP  
(n=287)

Tal-D  
(n=287)

DPd  
(n=290)

## Eligibility Criteria

- Age ≥18 years
- Measurable RRMM<sup>a</sup>
- ECOG PS 0-2
- ≥1 prior LOTs including lenalidomide and a PI.

## Endpoints

- PFS per IRC
- ORR (≥PR)<sup>c</sup>, ≥CR, MRD-negative CR (10<sup>-5</sup>), OS
- Safety, PK, immunogenicity

## Patient Characteristics

- Median Age: 64
- High risk cytogenetics; 30.9%
- ISS stage 3: 10.5%
- Median prior lines of therapy 2
- Prior stem cell transplant 68.9%
- 100% IMiD and PI exposed;
- 11.9% anti-CD38 mAB exposed
- 1.2% anti-BCMA exposed

Tal-DP: Talquetamab, Daratumumab, Pomalidomide; Tal-D: Talquetamab, Daratumumab; DPd: Daratumumab Pomalidomide, dexamethasone

**LEAD 2026:** Leadership, Empowerment, and Development

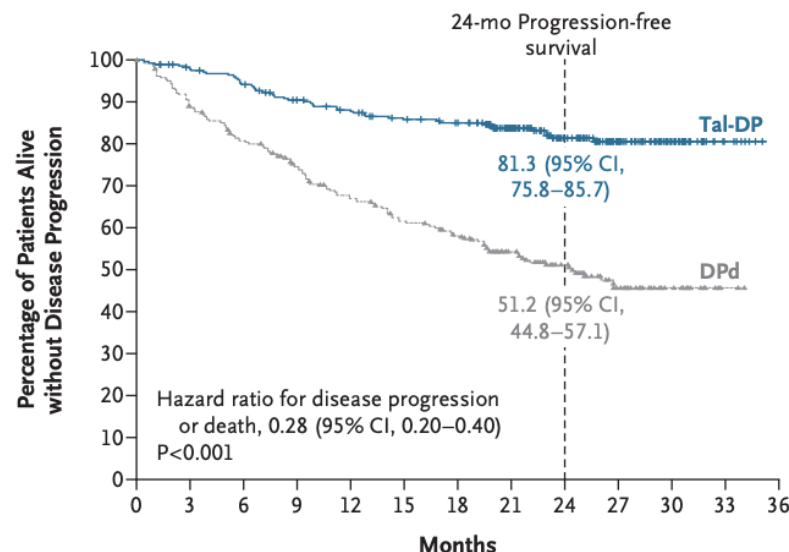
Mina R, et al. N Engl J Med. 2026 Aug 13;395(7):671-683

 **Bio Ascend**<sup>™</sup>  
A Vianium Group Company

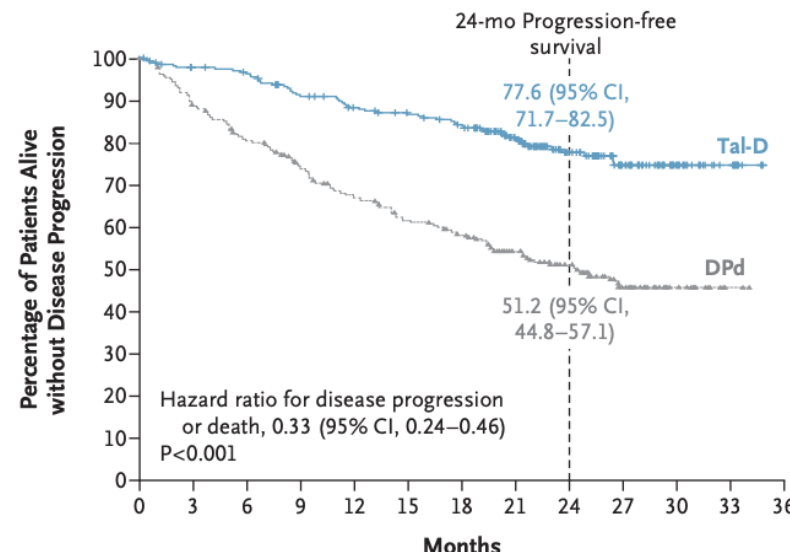
 **University of Nebraska**  
Medical Center

# MonumenTAL-3: Talquetamab-Daratumumab in early RRMM

**A Progression-free Survival, Tal-DP vs. DPd**



**B Progression-free Survival, Tal-D vs. DPd**



| Parameter, n (%)                    | Tal-DP (n=287) | Tal-D (n=287) | DPd (n=290) |
|-------------------------------------|----------------|---------------|-------------|
| ORR <sup>c</sup>                    | 253 (88.2)     | 254 (88.5)    | 225 (77.6)  |
| ≥CR                                 | 204 (71.1)     | 198 (69.0)    | 100 (34.5)  |
| MRD-negative CR (10 <sup>-5</sup> ) | 150 (52.3)     | 133 (46.3)    | 46 (15.9)   |

Estimated 24-mo OS: 89.2% Tal-DP, 87.9% Tal-D vs. 79.1% DPd (Tal-DP vs. DPd HR 0.47, Tal-D vs. DPd HR 0.51)

## Safety

- **Serious AEs:** 63% of Tal-DP; 52.6% Tal-D, 53.7% DPd
- **Grade 3/4 Neutropenia:** *more common in Pom-containing regimens* -76.4% Tal-DP, 29.2% Tal-D, 86.2% DPd
- **CRS:** 67.8% Tal-DP, 58.4% Tal-D (predominantly grade 1 or 2)
- **ICANS:** : 2.9% Tal-DP, 1.1% Tal-D
- **Grade 3/4 Infections:** 37.7% Tal-DP, 29.2% Tal-D, 42.4% DPd
- **Hypogammaglobulinemia:** 81.5% Tal-DP, 70.1% Tal-D, 62.5% DPd
- **GPRC5D associated skin, nail, dysgeusia** was common with Tal-DP and Tal-D
- **Ataxia/balance disorders:** 14.5% of Tal-DP, 12.4% Tal-D
- **Fatal AEs:** 1.8% of Tal-DP, 4.9% Tal-D, 4.6% in DPd

Tal-DP: Talquetamab, Daratumumab, Pomalidomide; Tal-D: Talquetamab, Daratumumab; DPd: Daratumumab Pomalidomide, dexamethasone

**LEAD 2026:** Leadership, Empowerment, and Development

Mina R, et al. N Engl J Med. 2026 Aug 13;395(7):671-683



# Landscape of T-cell Direction Therapies in early relapse

|                                    | Teclistamab                    |                                  | Talquetamab                                    | Cilta-Cel                        | Belantamab mafodotin                  |
|------------------------------------|--------------------------------|----------------------------------|------------------------------------------------|----------------------------------|---------------------------------------|
| MOA                                | BCMA Bispecific antibody       |                                  | GPRC5D Bispecific Antibody                     | BCMA CAR-T                       | BCMA Antibody Drug Conjugate          |
| Study                              | MajesTEC-3 / 9                 |                                  | MonumenTAL-3                                   | CARTITUDE-4                      | DREAMM-7                              |
| Phase                              | III                            |                                  | III                                            | III                              | III                                   |
| Combinational Agents               | Daratumumab                    | Monotherapy                      | Daratumumab, Pomalidomide                      | N/A                              | Bortezomib/Dex                        |
| Lines of Therapy                   | 1-3                            |                                  | 1-3                                            | 1-3                              | >1 (FDA approved after 2 prior lines) |
| Prior anti-CD38 exposed/refractory | 5.2% exposed/<br>0% refractory | 100% exposed /<br>85% refractory | 11.6% exposed/<br>0% refractory                | 25.5% exposed/<br>24% refractory | 1% exposed/<br>0% refractory          |
| PFS                                | 83.4% at 36 mo                 | 69.8% at 18 mo                   | Tal-DP: 81.3% at 24 mo<br>Tal-D 77.6% at 24 mo | 59.4% at 30 mo                   | mPFS 36.6 mo                          |
| OS                                 | 83.3% at 36 mo                 | 79.2% at 18 mo                   | Tal-DP: 89.2% at 24 mo<br>Tal-D 87.9% at 24 mo | 76.4% at 30 mo                   | 74% at 36 mo                          |

Costa LJ et al. N Engl J Med. 2026 Feb 19;394(8):739-752; Touzeau C et al. N Engl J Med. 2026 Jul 30;395(5):440-453; Mina R, et al. N Engl J Med. 2026 Aug 13;395(7):671-683

San-Miguel J et al. N Engl J Med. 2023 Jun 5; 389:335-347. Hungria V et al. N Engl J Med. 2024 Jun 13;391:393-407.



Bio Ascend™  
A Celis Gene Company

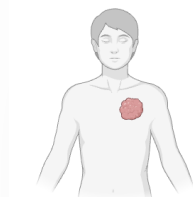
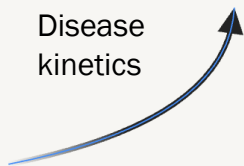
# Considerations in Immunotherapy & T-cell engager therapy Sequencing

## Disease Characteristics

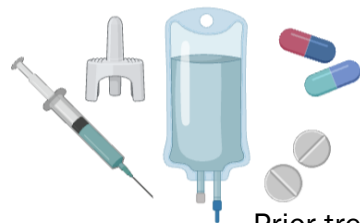
Cytogenetics



Disease kinetics



Extramedullary disease



Prior treatment history

## Patient Comorbidities



## Logistics & Access



Access to CAR-T center  
Manufacturing time  
Inpatient hospitalization needs  
Caregiver Requirements

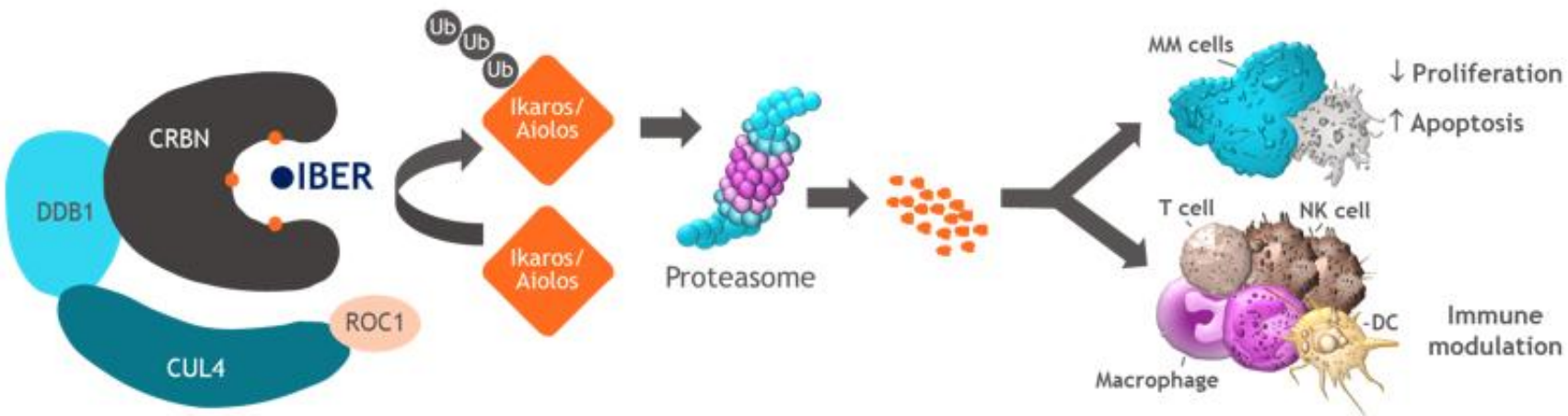


## Patient Preference



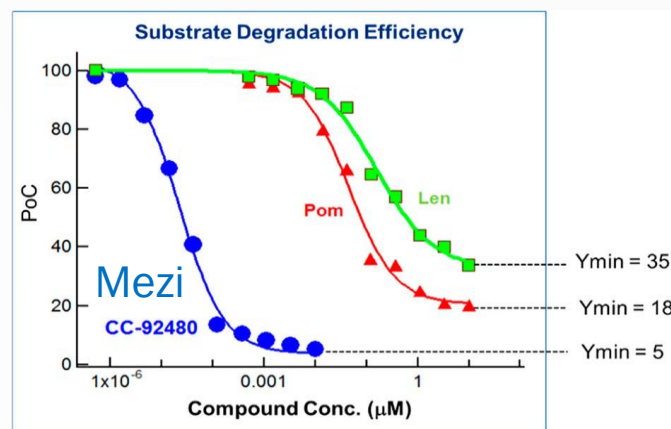
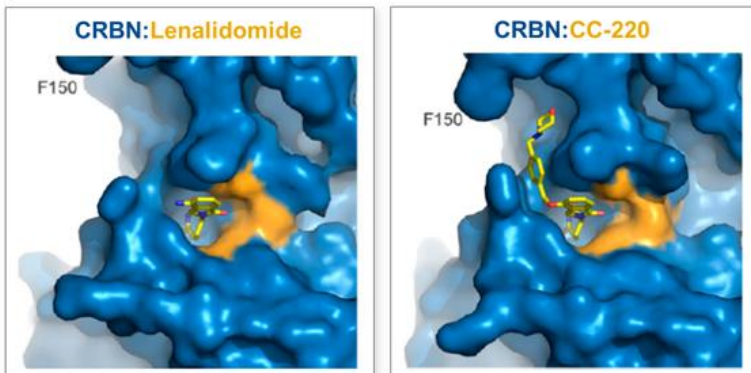
# CELMoDs: a new class of novel oral inhibitors

# CELMoDs: Iberdomide (CC-220) and Mezigdomide (CC-92480) are novel oral cereblon (CRBN) E3 ligase modulators



- Exist as a single S isomer, conferring more efficient binding leading to more potent anti-tumor and immune modulation compared to IMiDs
- Better tolerability than IMiDs. Less rash, fatigue, and GI toxicity
- Potential to enhance activity of immune-based therapies including CAR-T

Binding surface interactions with CRBN<sup>1</sup>

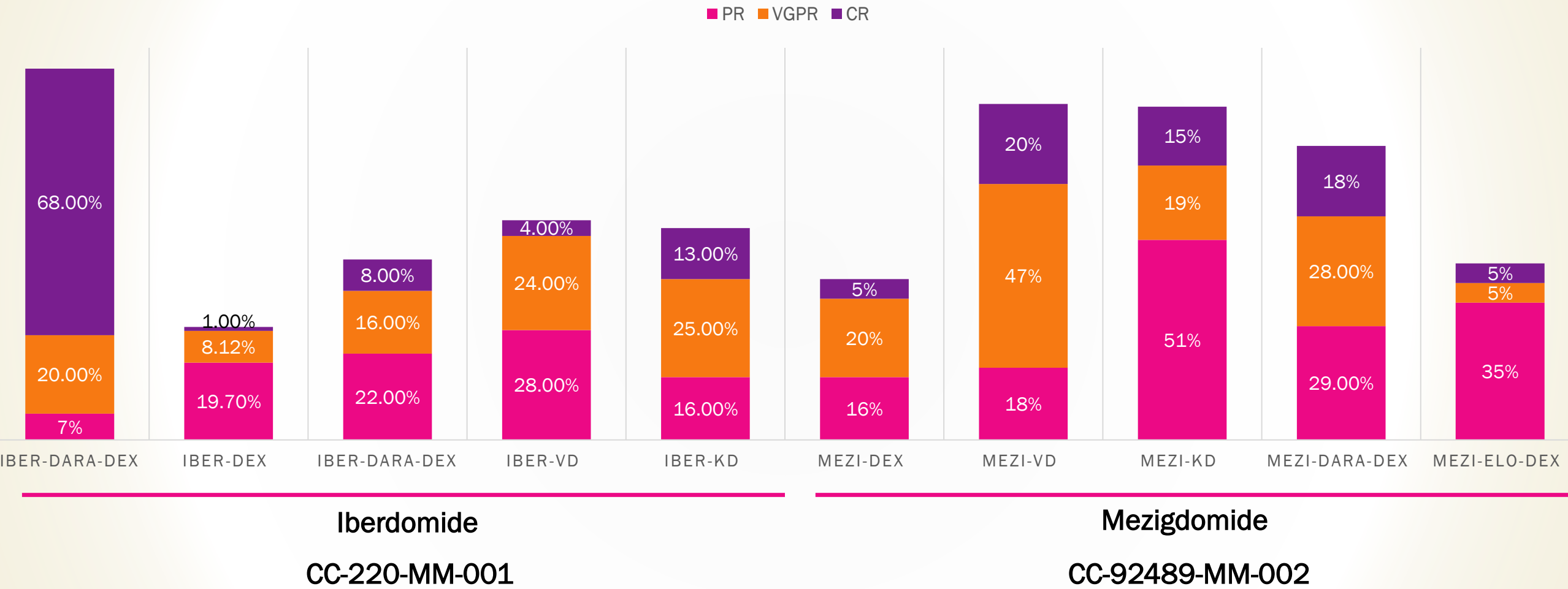


Substrate degradation<sup>1</sup>

| EC <sub>50</sub> , nM <sup>2</sup> | Ikaros | Aiolos |
|------------------------------------|--------|--------|
| LEN                                | 67     | 87     |
| POM                                | 24     | 22     |
| IBER                               | 1      | 0.5    |

1. Hansen JD, et al. *J Med Chem* 2020;63:6648–6676. 2. Lu G, et al. *Science* 2014;343:305–309. 3. John LB, Ward AC. *Mol Immunol* 2011;48:1272–1278.

# CELMoD Performance in Phase I/II RRMM Trials

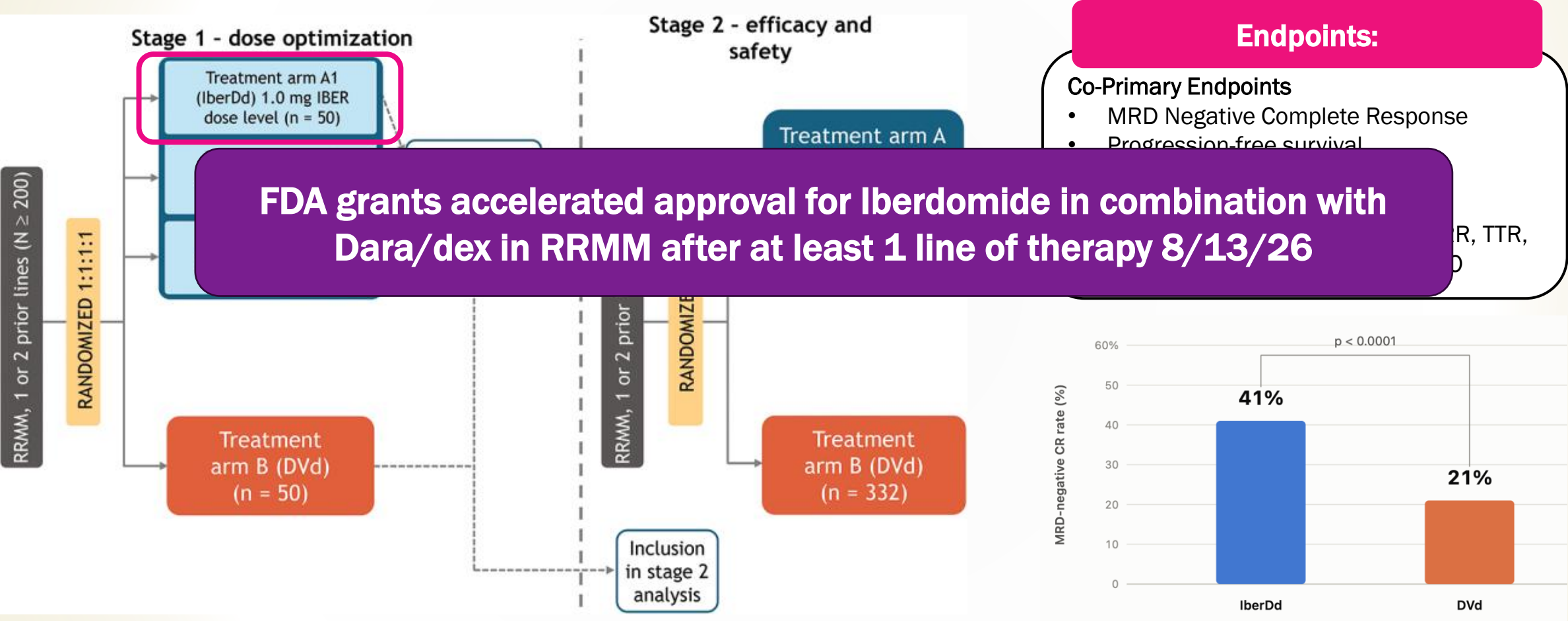


Lonial, Sagar et al. The Lancet Haematology, Volume 9, Issue 11, e822 - e832  
Oriol. Clin Lymphoma Myeloma Leuk 2023; 23(Suppl 2):S31. Sureda Balari A et al. Clin Lymphoma Myeloma Leuk 2025(suppl1):S897  
Sandhu. Blood 2024; 144(supplement1)1025. Richardson PG et al. Blood. 2023;142(suppl1):1013. Richardson PG. NEJM 2023.

**LEAD 2026:** Leadership, Empowerment, and Development



# EXCALIBER-RRMM: Phase III Iberdomide, Daratumumab, Dex in RRMM



IberDd = iberdomide + daratumumab + dexamethasone; DVd = daratumumab + bortezomib + dexamethasone.

# SUCCESSOR-2: Phase 3 trial of Mezigdomide, carfilzomib, dex vs. Carfilzomib/dex in RRMM

## Eligibility

RRMM who received  $\geq 1$  prior LOT with lenalidomide and anti-CD38 mAB

~525 patients  
1-3 prior lines

Stage 1: Mezi-Kd  
Dose optimization

Stage 2  
3:2 Random

Mezi-Kd

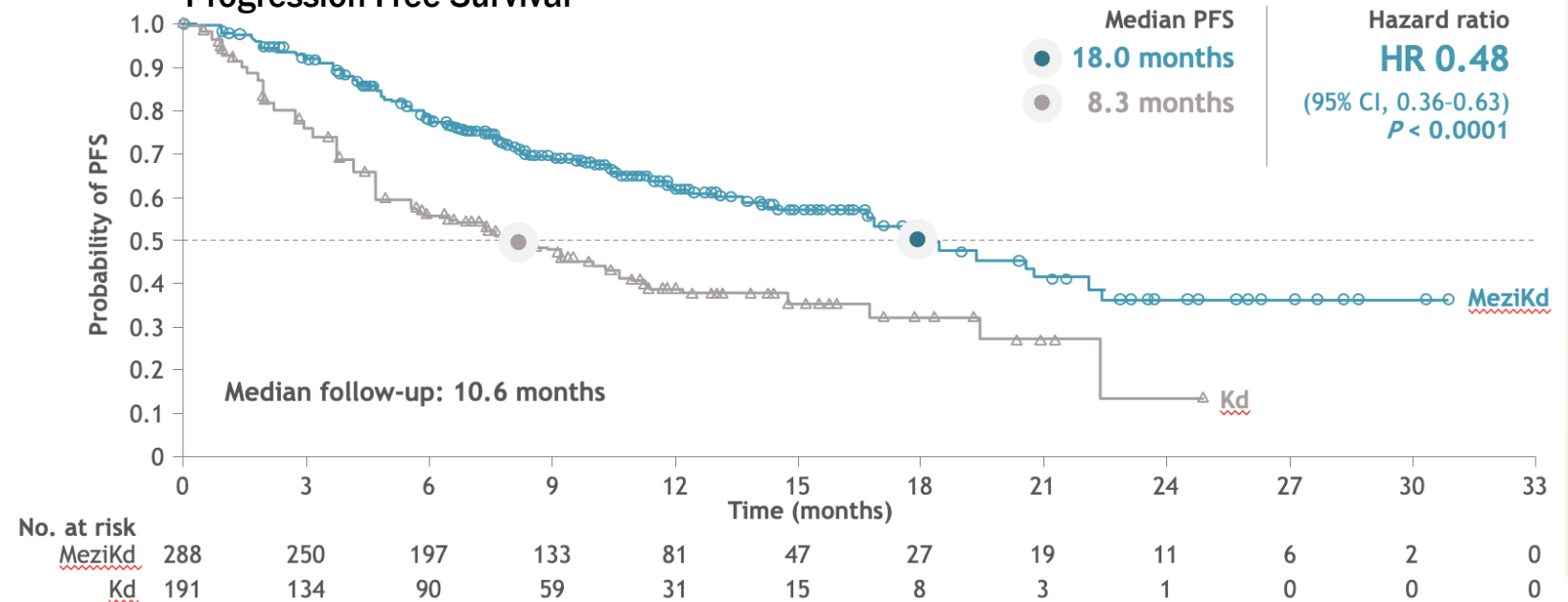
Kd

Primary Endpoint:  
PFS

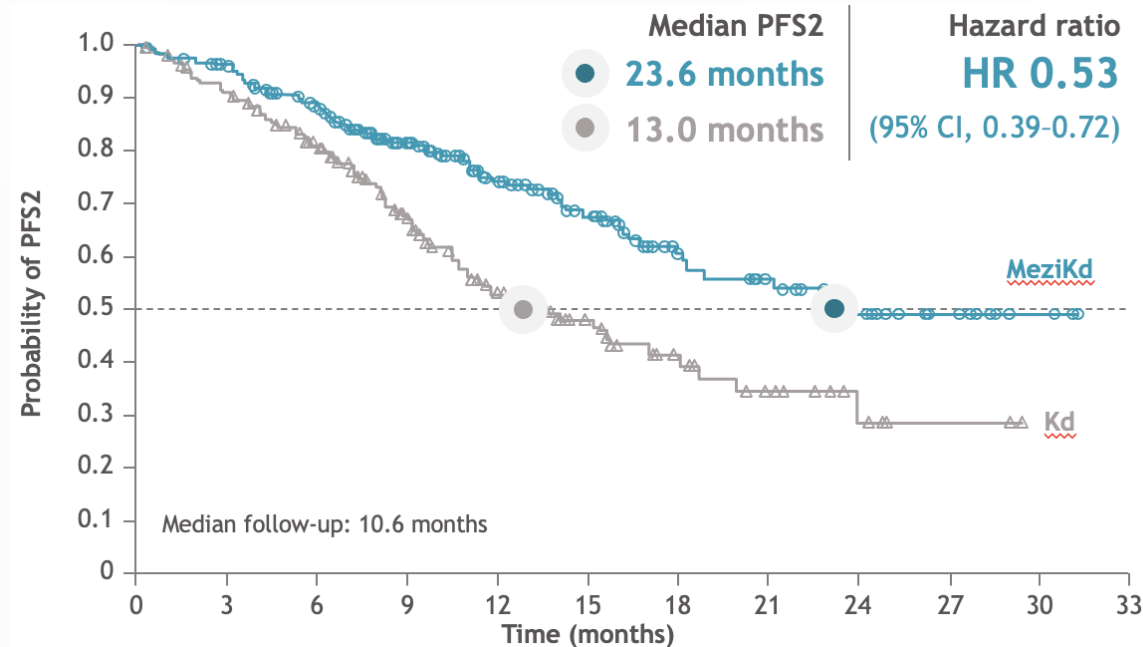
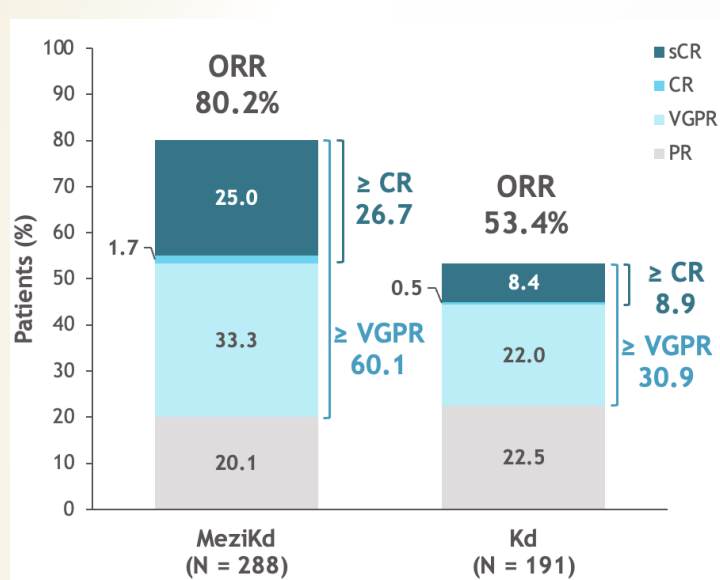
## Patient Characteristics

- 25.1%  $\geq 75$  years
- 24.6% soft-tissue plasmacytomas
- 28.3% high risk cytogenetics
- 86% refractory to anti-CD38 mAB
- 92% triple class exposed; 38.8% triple class refractory

## Progression Free Survival



# SUCCESSOR-2: Phase 3 trial of Mezigdomide, carfilzomib, dex vs. Carfilzomib/dex in RRMM



Positive OS trend favoring MeziKd with 10.6 mo median follow-up HR 0.79 (95% CI: 0.54-1.15)

## Safety

- Serious AEs (Grade 3/4): 83.7% MeziKd; 56.5% Kd
- Grade 3/4 Neutropenia: 61.1% MeziKd\*, 9.1% Kd; *on-target reversible AE with Mezigdomide w/ GCSF support*
- Grade 3/4 Infections: 34.1% MeziKd, 15.6% Kd
- Grade 3/4 Hypertension: 3.8% MeziKd, 9.1% Kd
- Grade 3/4 VTE 2.8% MeziKd, 0.5% Kd

# Conclusion:

- The ENDURANCE study demonstrated that more is not always better in the context of indefinite lenalidomide maintenance in standard risk NDMM transplant deferred myeloma
- Further evaluation of time limited treatment is needed especially as more efficacious quadruplet induction treatments are now being employed and as more novel therapies are moving up earlier
- The treatment landscape of early relapsed myeloma is changing. Bispecific antibodies are up into earlier lines of treatment with the FDA approval of Teclistamab-Daratumumab after 1 prior line of therapy along with the demonstrated efficacy of Tec monotherapy and Talquetamab combinations.
- A new drug class is here! The first CELMoD, Iberdomide, has been FDA approved in combination with Daratumumab/dexamethasone in RRMM
- Mezigdomide in combination with Carfilzomib/dexamethasone has also demonstrates significant PFS advantage compared to Kd in RRMM and is granted a PDUFA date in May 2027 by FDA

# Thank you!