# Selection and Sequencing of Available and Recently Approved Therapies for Patients with Relapsed/Refractory MM?


Nikhil C. Munshi, MD

Professor of Medicine
Harvard Medical School

Director Basic and Correlative Sciences
Jerome Lipper Myeloma Center
Dana-Farber Cancer Institute



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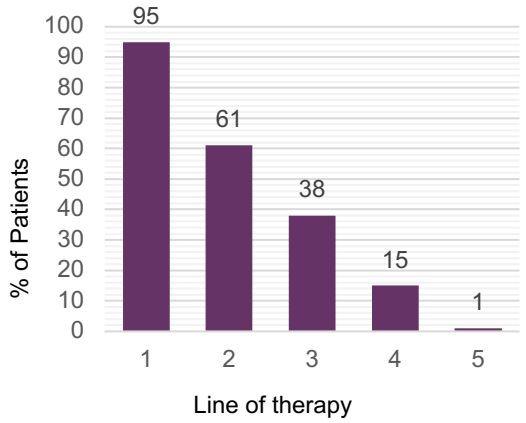
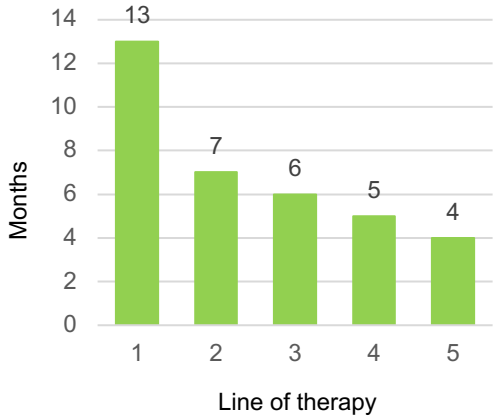
# Initial Treatment is Best Chance For Deep and Durable Remissions

**Attrition**
% of Patients Able to Get Nth Line of Therapy




**Diminishing Returns**
Median Duration of Nth Line of Therapy




- Attrition: high risk & frail elderly patients in particular will not live to Nth relapse
- Response rates and duration diminish with each successive line of therapy
- Early use of efficacious regimens to achieve *and sustain remissions* critical

Courtesy of Nikhil C Munshi, MD

Yong K et al. *Br J Haematol.* 2016;175(2):252-264.

# Indications for Retreatment

- Patients with asymptomatic rise in M-protein (biochemical relapse) can be observed to determine the rate of rise and nature of the relapse
- Clinical relapse: direct indicators of increasing disease with end organ dysfunction (MDE)
- Significant paraprotein relapse: Accelerated Doubling of the M-component in two consecutive measurements separated by < 2 months; OR
- High levels of free light chain with renal presentation
- High risk cytogenetics with biochemical progression

Courtesy of Nikhil C Munshi, MD

**Rajkumar** SV et al Blood. 2011 May 5;117(18):4691-5.

# What is the Goal of Therapy in Relapsed/Refractory Myeloma?

## Superior PFS and OS with MRD Negativity in Relapsed Refractory Multiple Myeloma

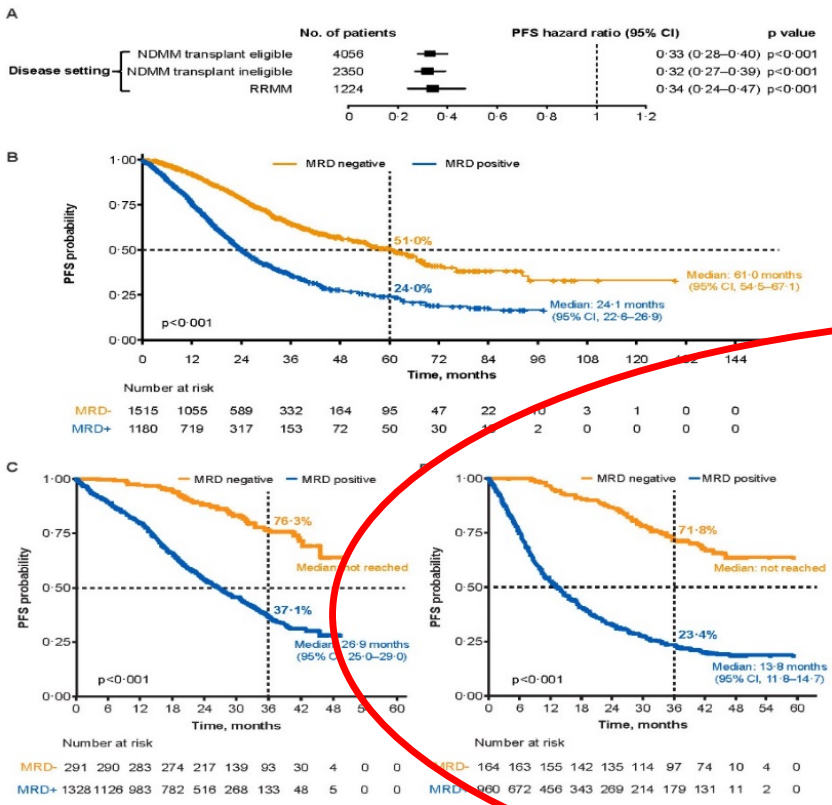
**PFS**

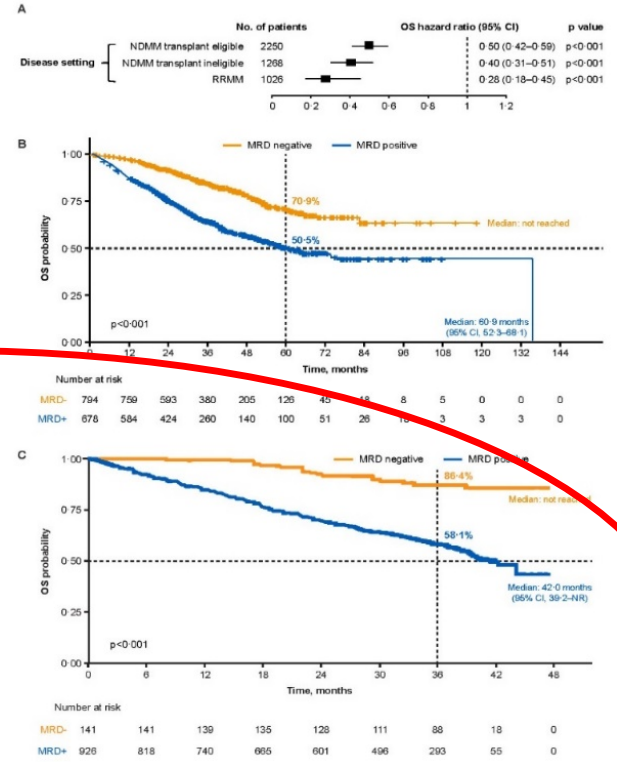
**OS**

**Newly-diagnosed Transplant Eligible**

**Newly-diagnosed Transplant Ineligible**

**Relapsed Refractory N = 1124**

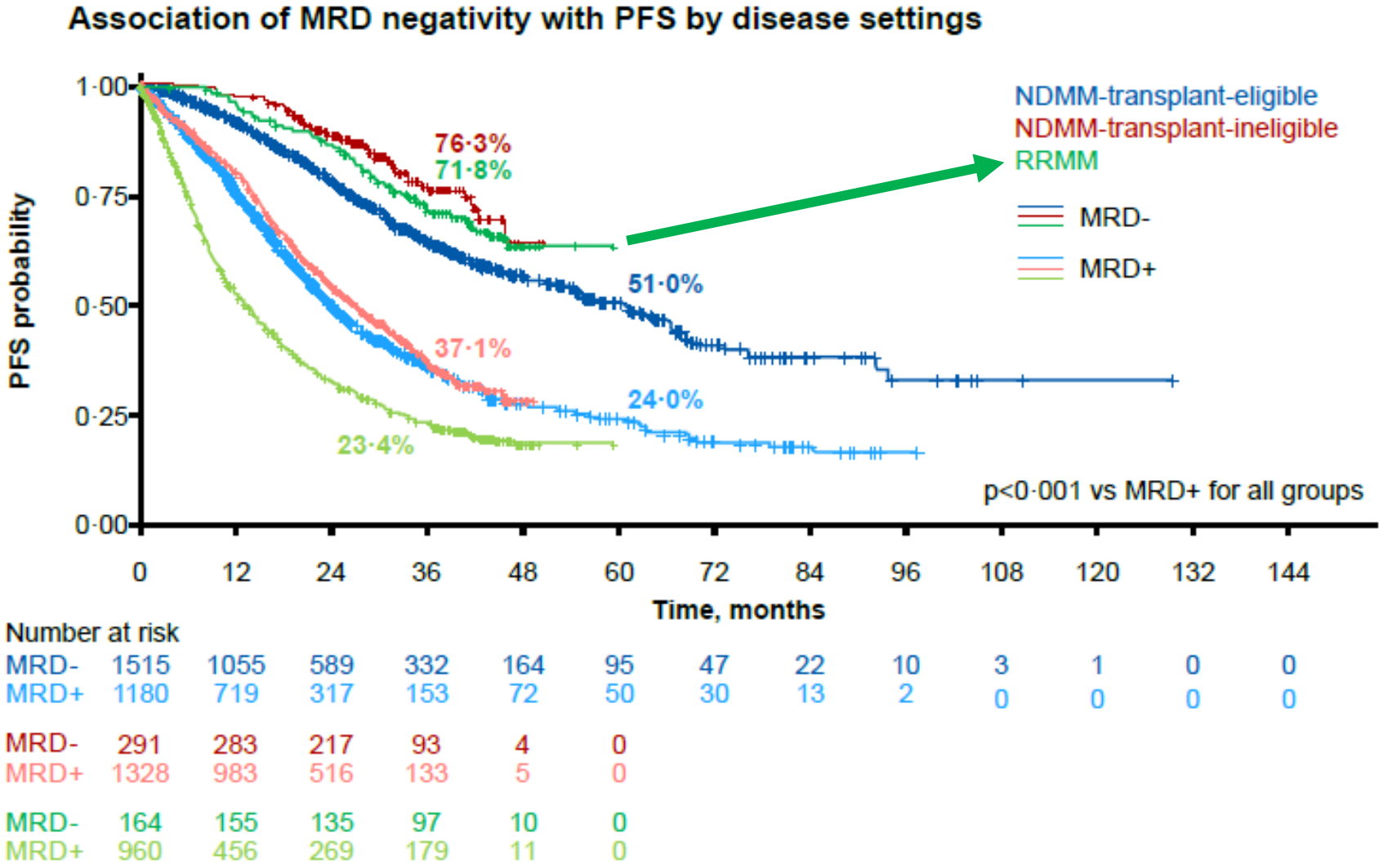



Munshi N et al., Blood Adv 2020

Courtesy of Nikhil C Munshi, MD

# MRD Negativity Provides Similar Benefit in Relapsed/Refractory Disease as in Newly-diagnosed Patient




Courtesy of Nikhil C Munshi, MD

Munshi N et al., Blood Adv 2020

# Factors to Consider for Treatment Selection

## Disease related Factors

- Nature of relapse
- Risk stratification
- Disease burden
- R-ISS staging


1. Nooka AK, et al. Blood. 2015;125:3085-3099.
2. Palumbo A, et al. N Engl J Med. 2011;364:1046-1060.
3. Palumbo A, et al. Blood. 2011;118:4519-4529.
4. Orlowski RZ, Lonial S. *Clin Cancer Res.* 2016;22:5443.


## Treatment related Factors

- Previous therapy
- Regimen-related toxicity
- Depth and duration of previous response, tumor burden at relapse
- Retreatment with previous therapies


1. Nooka AK, et al. Blood. 2015;125:3085-3099.
2. Palumbo A, et al. N Engl J Med. 2011;364:1046-1060.
3. Palumbo A, et al. Blood. 2011;118:4519-4529.

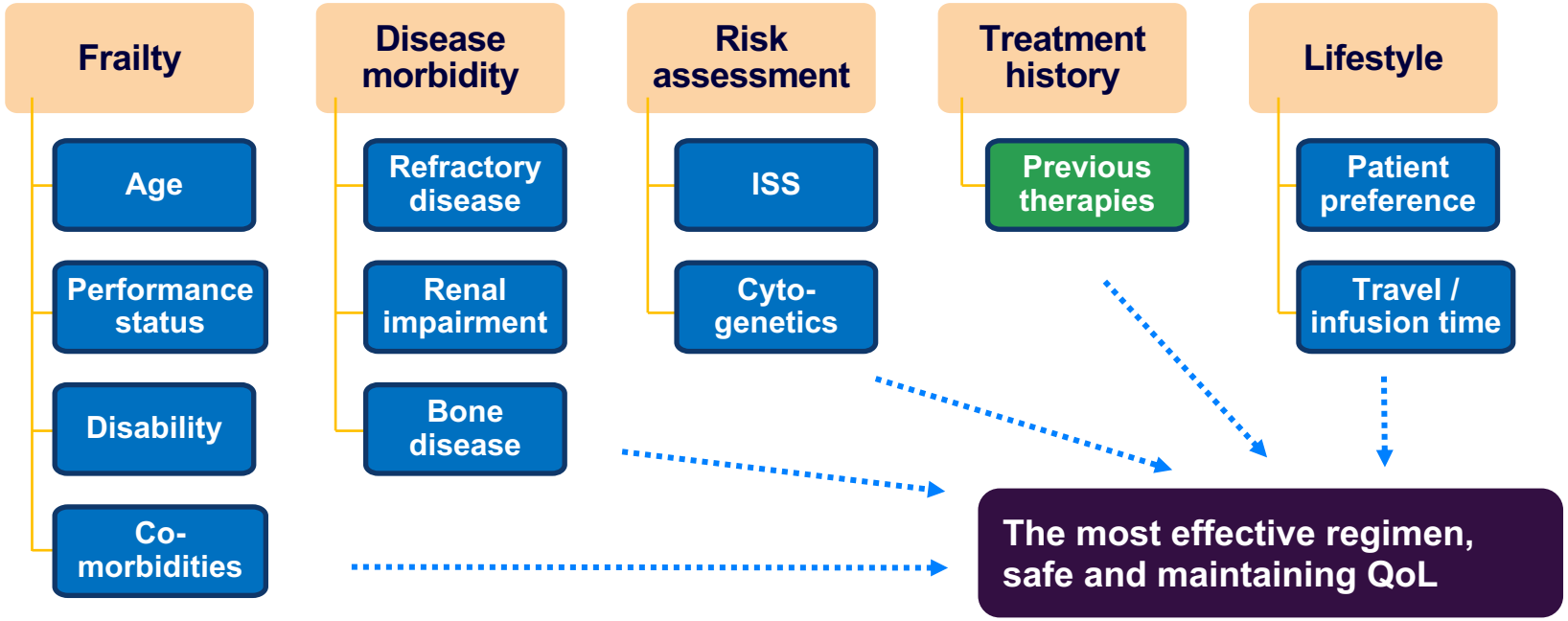

## Patient related Factors

- Renal insufficiency:
- Hepatic impairment Comorbidities and frailty
- Patient preferences


1. Nooka AK, et al. Blood. 2015;125:3085-3099.
2. Palumbo A, et al. N Engl J Med. 2011;364:1046-1060.
3. Palumbo A, et al. Blood. 2011;118:4519-4529.


Courtesy of Nikhil C Munshi, MD

# Disease and Patient-based Factors Influencing the Treatment Decision-making at the Relapsed Setting

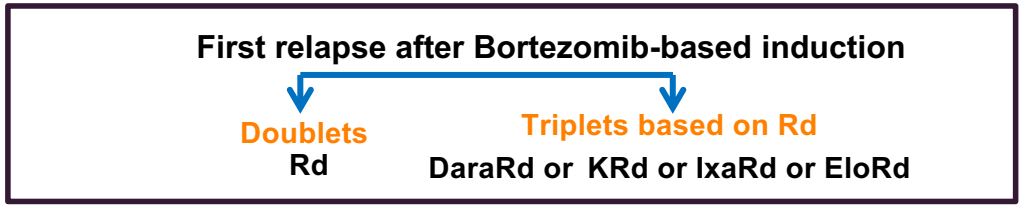



- Choice of PI- or IMiD-based partner depends on prior treatment
- Nearly all phase 3 studies show triplets perform better than doublets
- Cross trial comparisons should not be done

Clegg A et al. Lancet 2013;381:752–762; Handforth C et al. Ann Oncol 2015;26:1091–1101; Chen X et al. Clin Interv Aging 2014;9:433–441; Palumbo A et al. Blood 2015;125:2068–2074; Jhaveri D et al. Haematologica 2016;101:1–881 (Abstract E1312); Sonneveld P et al. Leukemia 2013;27:1959–1969; Faiman BM et al. Clin J Oncol Nurs 2011;15:66–76; Miceli TS et al. Clin J Oncol Nurs 2011;15:9–23; Greipp PR et al. J Clin Oncol 2005;23:3412–3420; Binder M et al. Haematologica 2016;101:P665; Merz M et al. Haematologica 2016;101:P650; Chng WJ et al. Leukemia 2016;30:1071–1078; Chung TH et al. PLoS One 2013;20:e66361; Sonneveld P et al. Leukemia 2013;27:1959–1969; Ramsenthaler C et al. BMC Cancer 2016;16:427; Williams LA et al. J Clin Oncol 2016;34:e18127; Ramasamy K et al. Haematologica 2017;102:E1457.

Courtesy of Nikhil C Munshi, MD

# Management of Patients at First Relapse
# Lenalidomide-Dexamethasone Combination Studies

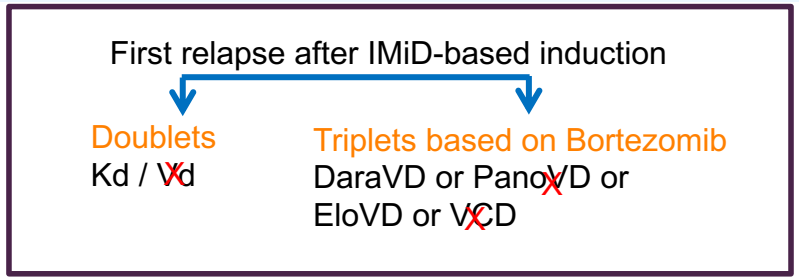



| | Ixazomib | | Elotuzumab | | Carfilzomib | | Daratumumab | |
|---|---|---|---|---|---|---|---|---|
| **N** | **IRd vs Rd 722** | | **EloRd vs Rd 646** | | **KRd vs Rd 792** | | **DRd vs Rd 569** | |
| **Efficacy** | **IRD** | **RD** | **EloRD** | **RD** | **KRD** | **RD** | **DRD** | **RD** |
| **Median f/u, mos** | 23 | | Min 48 mos | | 67 | | 32.9 | |
| **ORR** | **78.3%** | 71.5% | **79%** | 66% | **87%** | 66.7% | **93%** | 76% |
| **CR** | **12%** | 7% | **5%** | 9% | **32%** | 9.3% | **55%** | 23% |
| **Median PFS, mos** | **21** | 14.7 | **19** | 14.9 | **26** | 16.6 | **NR** | 17.5 |
| **Median OS, mos** | NR | NR | 48.3 | 39.6 | 48.3 | 40.4 | NR | NR |

Courtesy of Nikhil C Munshi, MD

Moreau P et al. *N Engl J Med*. 2016;374:1621; Dimopoulos MA et al. *Br J Haematol*. 2017;178:896.
Stewart AK et al. *N Engl J Med*. 2015;372:142; Stewart AK et al. *Blood*. 2017;130: Abstract 743.
Dimopoulos M et al. *J Hematol Oncol.* 2018;11:49; Dimopoulos MA et al. *N Engl J Med*. 2016;375:1319.

# Management of Patients at First Relapse
# Bortezomib-Dexamethasone Combination Studies




| | Pomalidomide | | Daratumumab | | Carfilzomib | | Selinexor | | Venetoclax | |
|---|---|---|---|---|---|---|---|---|---|---|
| **N** | **PVd vs Vd 559** | | **DVd vs Vd 498** | | **Kd vs Vd 929** | | **SVD vs Vd 195 vs 207** | | **VenVD vs VD 194 vs 97** | |
| **Efficacy** | **Tx** | **Control** | **Tx** | **Control** | **Tx** | **Control** | **Tx** | **Control** | **Tx** | **Control** |
| Median f/p, mos | 16 | | 26.9 | | 37.5 | | 16.5 | | 18.7 | |
| ORR | **82%** | 50% | **85%** | 63% | **76%** | 63% | **76%** | 62% | **82%** | 68% |
| CR | **16%** | 4% | **30%** | 10% | **13%** | 6% | **17%** | 11% | **13%** | 1% |
| Median PFS, mos | **11** | 7 | **16.7** | 7.1 | **18.7** | 9.4 | **13.9** | 9.46 | **22.4** | 11.5 |
| Median OS, mos | NR | NR | NR | NR | 47.6 | 40.0 | NR | 25 | NR | 25 |

Richardson et al. Lancet Oncol 2019; 20: 781–94; Palumbo A et al. *N Engl J Med*. 2016;375:754; Spencer A et al. *Haematologica.* 2018; Sep 20 [epub ahead of print]; Dimopoulos MA et al. *Lancet Oncol*. 2016;17:27; Dimopoulos et al ASCO 2020; Kumar S. EHA 2019.

Courtesy of Nikhil C Munshi, MD

# New Guidelines are Necessary for the Current RRMM Population

**First relapse after PI and/or IMiD-based induction and len-refractory**

**Anti-CD38-based regimen**

**Dara Kd**
**Dara Pom-dex**
**Dara VD or Dara RD**

**anti CD38-free regimen**

**Pom + Vd**
**Pom + Cy + Dex**
**K + Pom-dex**

**Vd + Selinexor**
Vd + Venetoclax
Kd + cyclo

Other potential combinations for this population?

Courtesy of Nikhil C Munshi, MD

# Therapeutic Advances in Multiple Myeloma

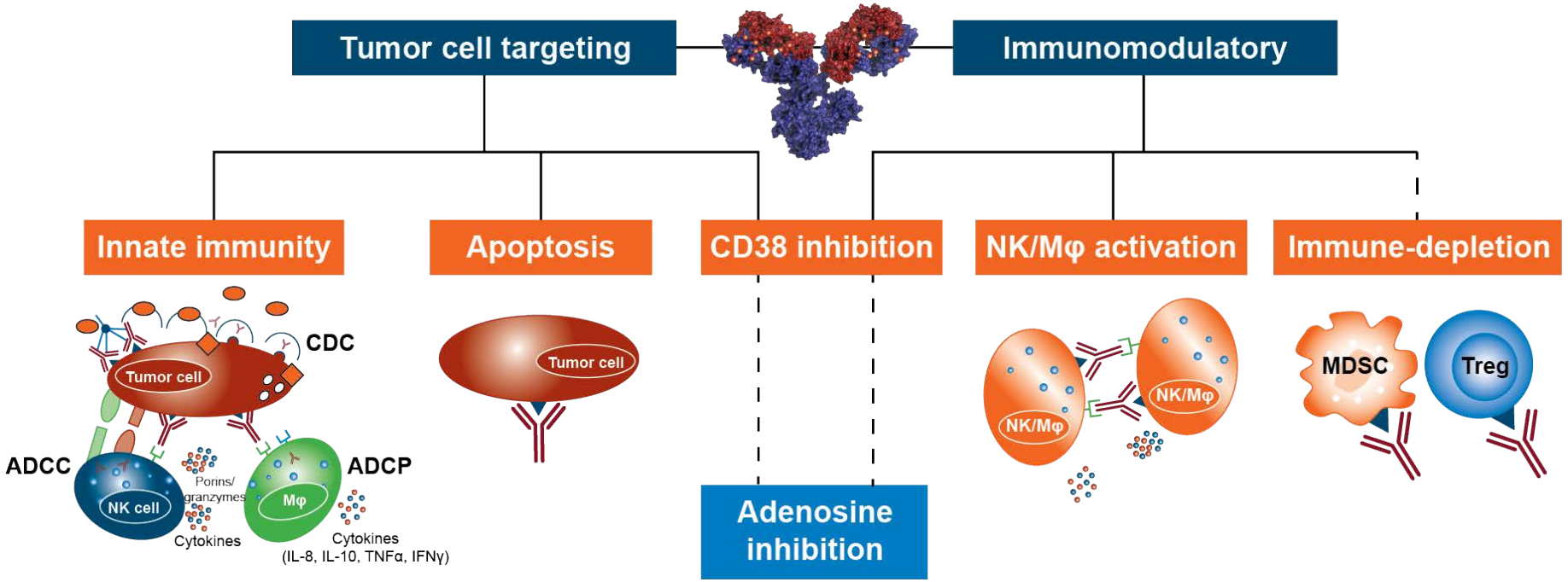
- ~~11~~ 12 new Agents in last 15 years:
- Proteasome inhibitors: bortezomib, Carfilzomib, Ixazomib
- Immunomodulator: thalidomide, lenalidomide, pomalidomide
- HDAC inhibitor: Panobinostat
- Monoclonal antibodies: elotuzumab, daratumumab Isatuximab, Belantamab mafodotin
- Exportin inhibitor: Selinexor
- Alkylating Agent: bendamustine
- Existing older agents: melphalan, dexamethasone. cyclophosphamide, anthracycline, etoposide
- Near approval: Ide-cel, Cilta-cel, melflufen, venetoclax, BCMA-bispecifics

- 2-, 3-, 4-drug combinations - effective in relapsed/refractory myeloma

Courtesy of Nikhil C Munshi, MD

# Isatuximab: Mechanism of Action

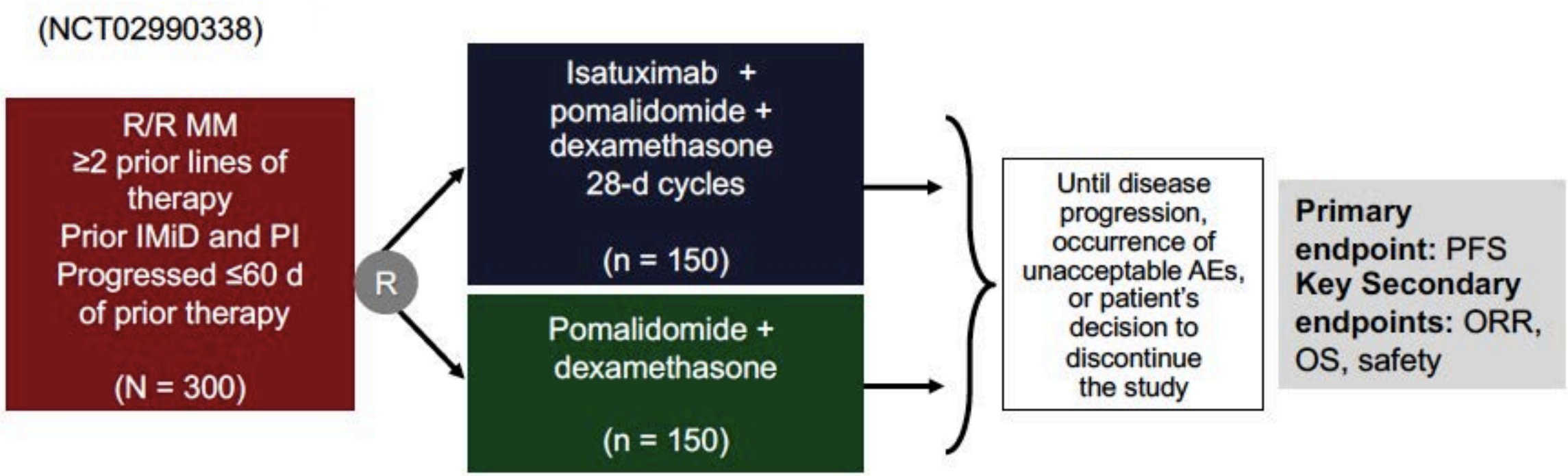
- Active in combination studies in R/R MM




- **Effective combinations**
  - **ICARIA-MM – Isa Pd**
  - **IKEMA – Isa Kd**

Courtesy of Nikhil C Munshi, MD

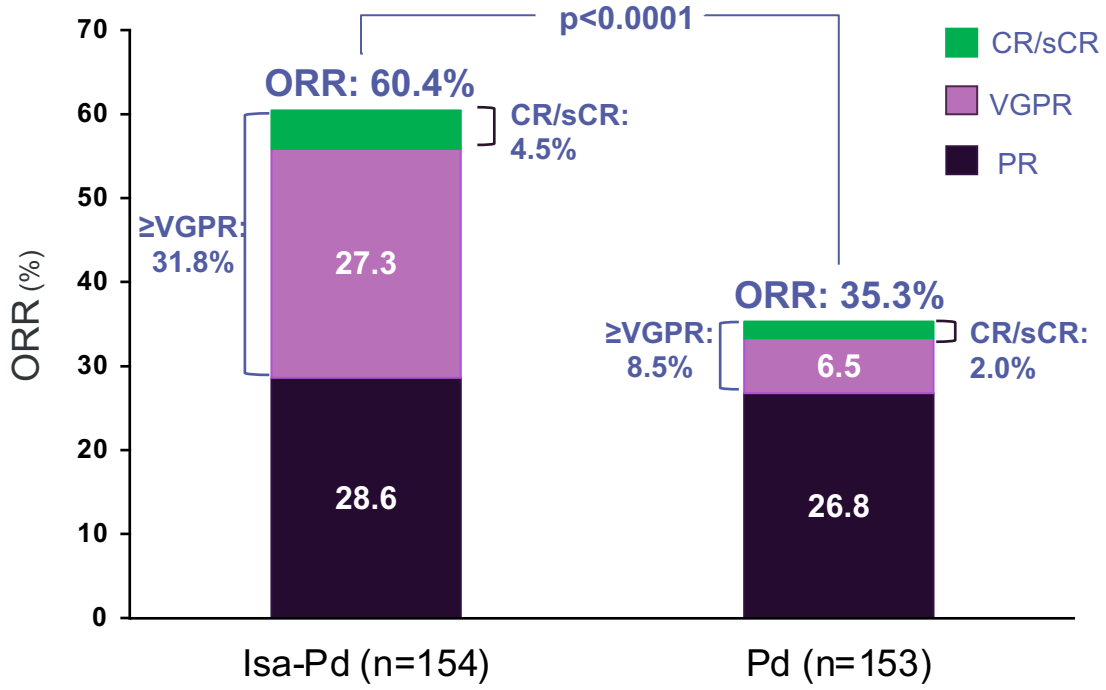
# ICARIA-MM: Isa-Pd Versus Pd in RRMM




Attal, M et al. Lancet 394: 859, 2019.

Courtesy of Nikhil C Munshi, MD

# ICARIA-MM: Significant Improvement in Response with Isa-Pd Compared to Pd




**Median time to 1st response: Isa-Pd 35 days vs Pd 58 days**

**True CR rate in Isa-Pd underestimated because of isatuximab interference with M-protein measurement**

| | Isa-Pd (n=154) | Pd (n=153) |
|---|---|---|
| nCR, % | 15.6 | 3.3 |

**MRD negativity at $10^{-5}$ (ITT): 5.2% for Isa-Pd vs 0% for Pd**

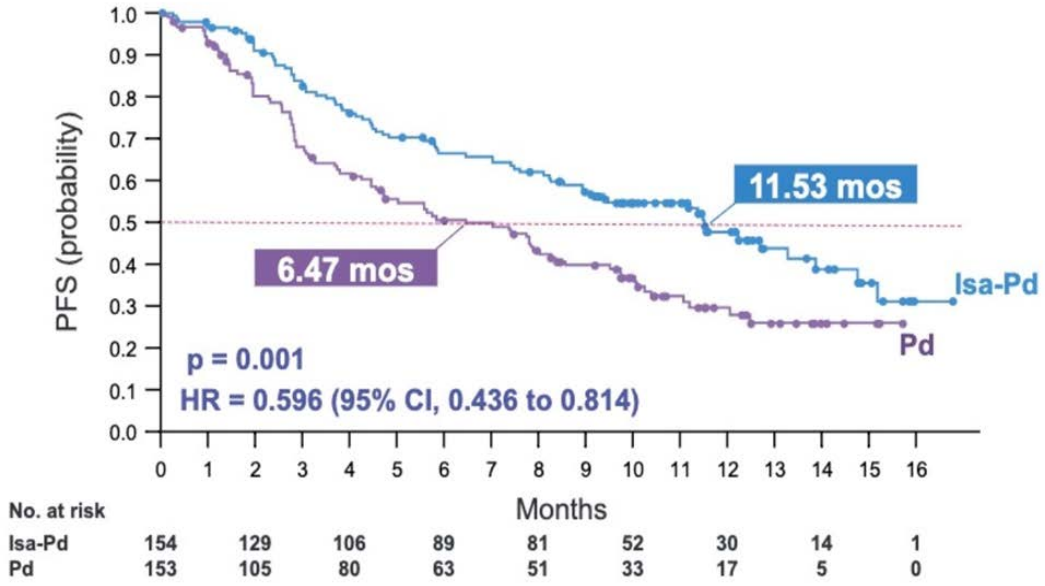
**Addition of Isa to Pd resulted in significant improvement in overall and depth of response**

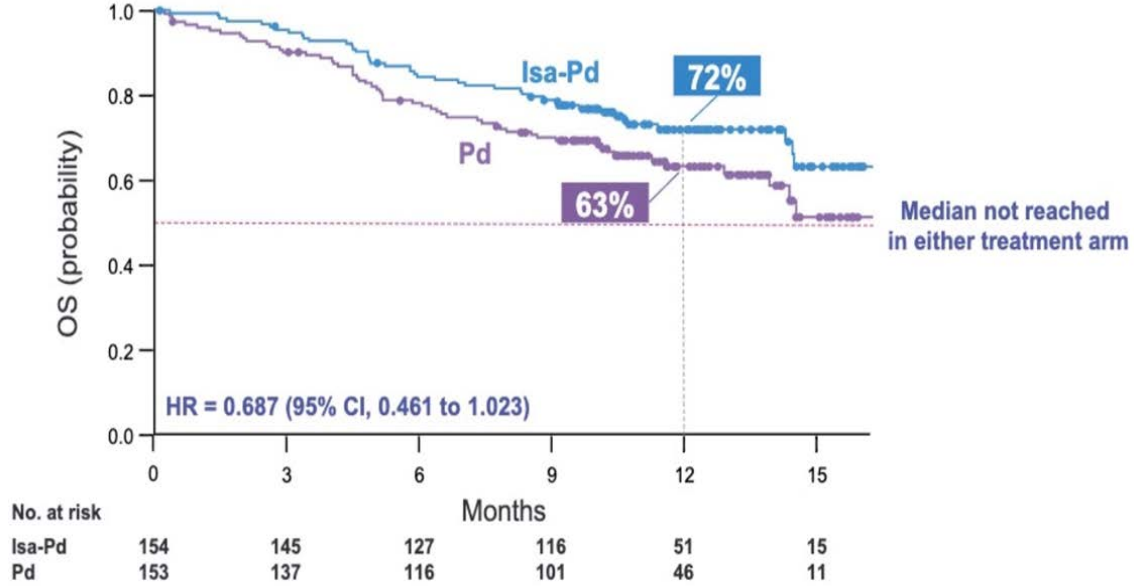
Data cut-off 11 Oct, 2018
CR complete response; d, dexamethasone; IRC, Independent Review Committee; Isa, isatuximab; ITT, intent-to-treat; MRD, minimal residual disease; nCR, near complete response; ORR, overall response rate; P, pomalidomide; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
*All criteria for a complete response were met except that immunofixation remained positive [Richardson PG, et al. *N Engl J Med.* 2003;348(26):2609-2617]

Courtesy of Nikhil C Munshi, MD

# ICARIA-MM: Significant Improvement in Survival with Isa-Pd Compared to Pd

- 307 patients, after a median number of 3 lines, 95% len-refractory
- Significant and clinically meaningful improvement in PFS; consistent across subgroups



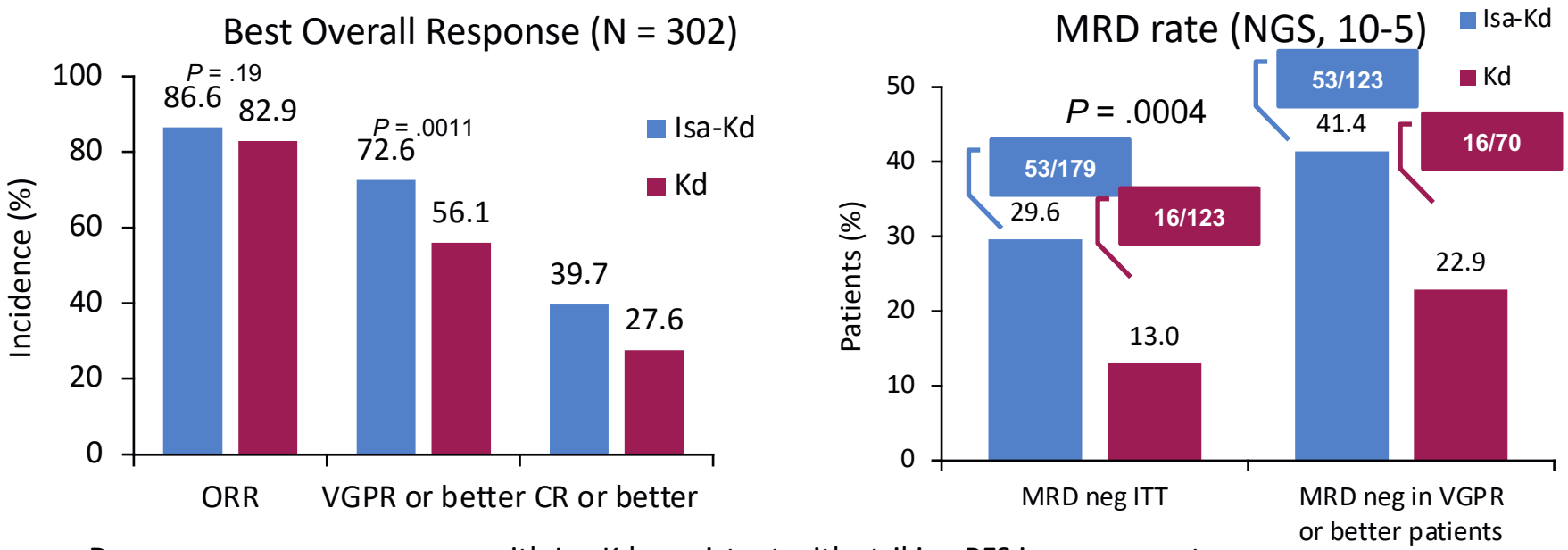




CI, confidence interval; HR, hazard ratio; IRC, independent review committee; OS, overall survival; PFS, progression-free survival; Isa-Pd, isatuximab-pomalidomide-dexamethasone; Pd, pomalidomide-dexamethasone.

Richardson P et al. Lancet. 2019;394(10214):2096-2107.

Courtesy of Nikhil C Munshi, MD

# IKEMA: Carfilzomib/Dexamethasone ± Isatuximab: Response

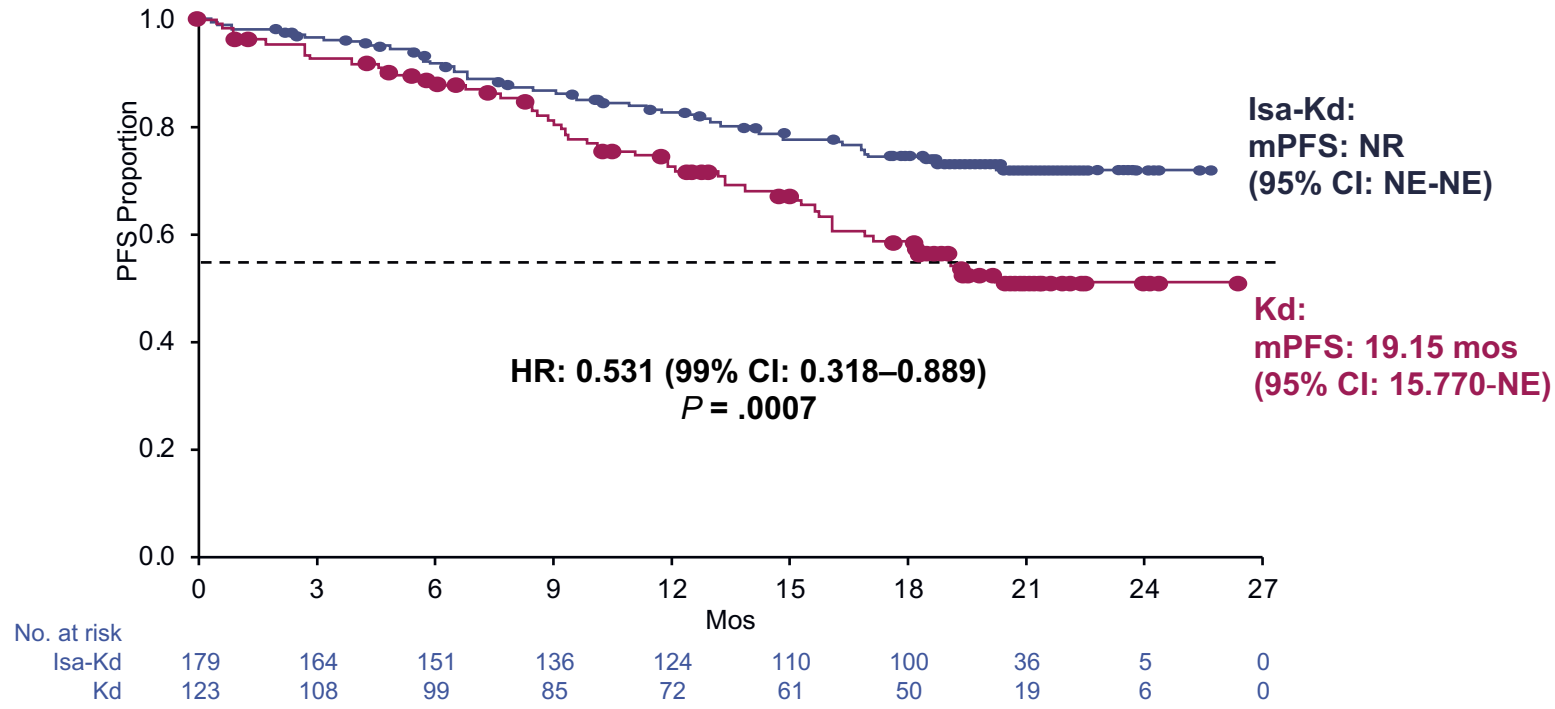



- Deeper responses were seen with Isa-Kd consistent with striking PFS improvement
- MRD negativity rate with Isa-Kd was approximately 30% in ITT population

Courtesy of Nikhil C Munshi, MD

Moreau. EHA 2020. Abstr LB2603.

# IKEMA: Isa-Kd Showed Improvement in PFS vs Kd : 47% Reduction of Risk

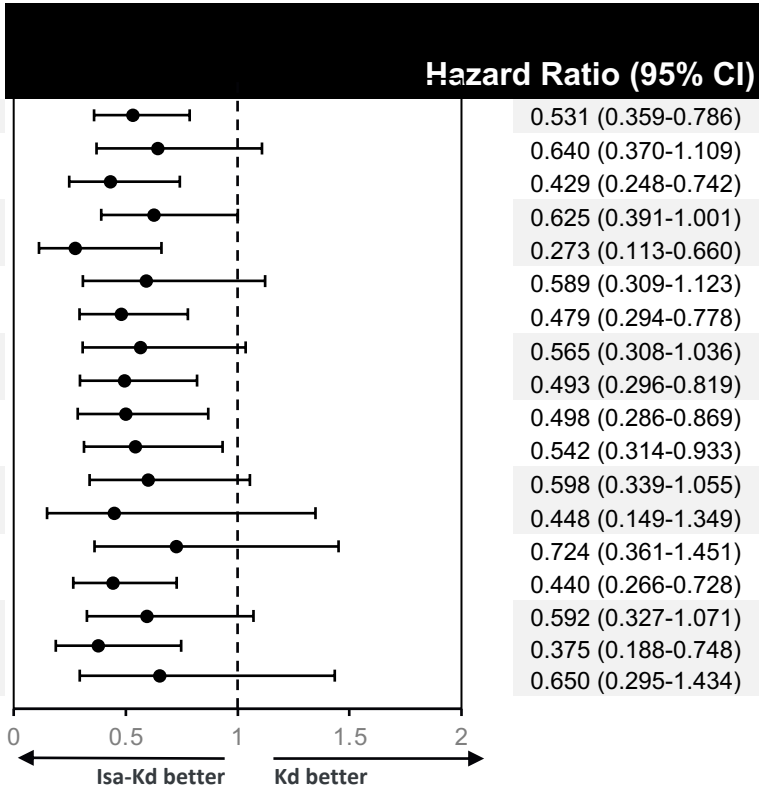



Moreau. EHA 2020. Abstr LB2603.

Courtesy of Nikhil C Munshi, MD

# IKEMA: PFS Subgroup Analyses

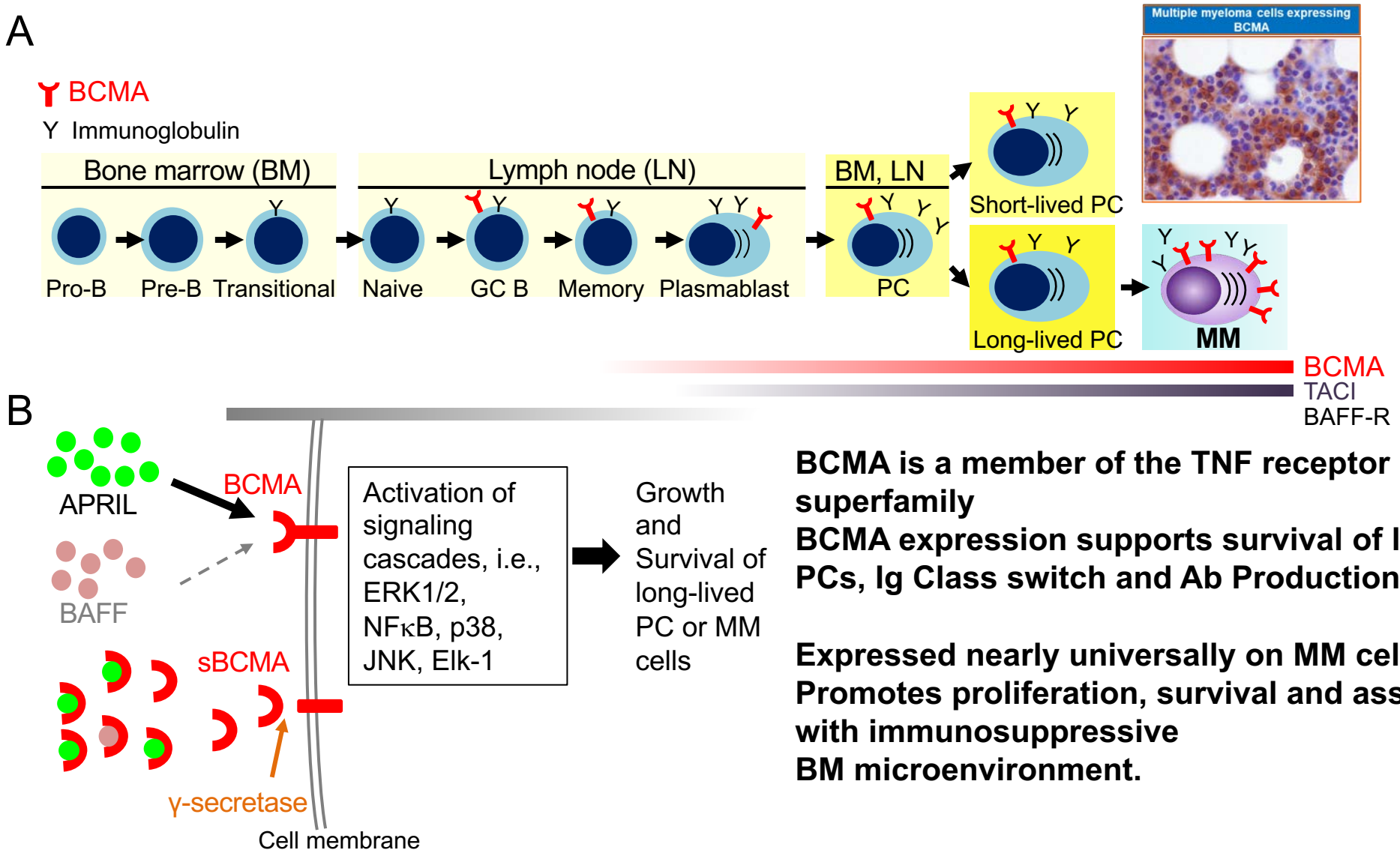
| Subgroup | | Isa-Kd | Kd | Hazard Ratio (95% CI) |
|---|---|---|---|---|
| | | No. of events/total no. | | |
| **All patients** | | 48/179 | 55/123 | 0.531 (0.359-0.786) |
| **Age** | < 65 yrs | 25/88 | 26/66 | 0.640 (0.370-1.109) |
| | ≥ 65 yrs | 23/91 | 29/57 | 0.429 (0.248-0.742) |
| **Baseline eGFR (MDRD)** | ≥ 60 mL/min/1.73 m² | 32/122 | 38/93 | 0.625 (0.391-1.001) |
| | < 60 mL/min/1.73 m² | 10/43 | 10/18 | 0.273 (0.113-0.660) |
| **Number of prior lines of therapy** | 1 | 18/80 | 19/55 | 0.589 (0.309-1.123) |
| | > 1 | 30/99 | 36/68 | 0.479 (0.294-0.778) |
| **Prior PI treatment*** | Yes | 22/81 | 20/47 | 0.565 (0.308-1.036) |
| | No | 26/98 | 35/76 | 0.493 (0.296-0.819) |
| **Prior IMiD treatment*** | Yes | 22/81 | 29/62 | 0.498 (0.286-0.869) |
| | No | 26/98 | 26/61 | 0.542 (0.314-0.933) |
| **Refractory to Len** | Yes | 23/57 | 25/42 | 0.598 (0.339-1.055) |
| | No | 5/15 | 9/17 | 0.448 (0.149-1.349) |
| **High-risk cytogenetic status** | Yes | 17/42 | 15/31 | 0.724 (0.361-1.451) |
| | No | 27/114 | 35/77 | 0.440 (0.266-0.728) |
| **ISS staging at study entry** | I | 20/89 | 24/71 | 0.592 (0.327-1.071) |
| | II | 17/63 | 16/31 | 0.375 (0.188-0.748) |
| | III | 11/26 | 14/20 | 0.650 (0.295-1.434) |




Moreau. EHA 2020. Abstr LB2603.

Courtesy of Nikhil C Munshi, MD

# B-Cell Maturation Antigen (BCMA)
# A Promising Target in Multiple Myeloma



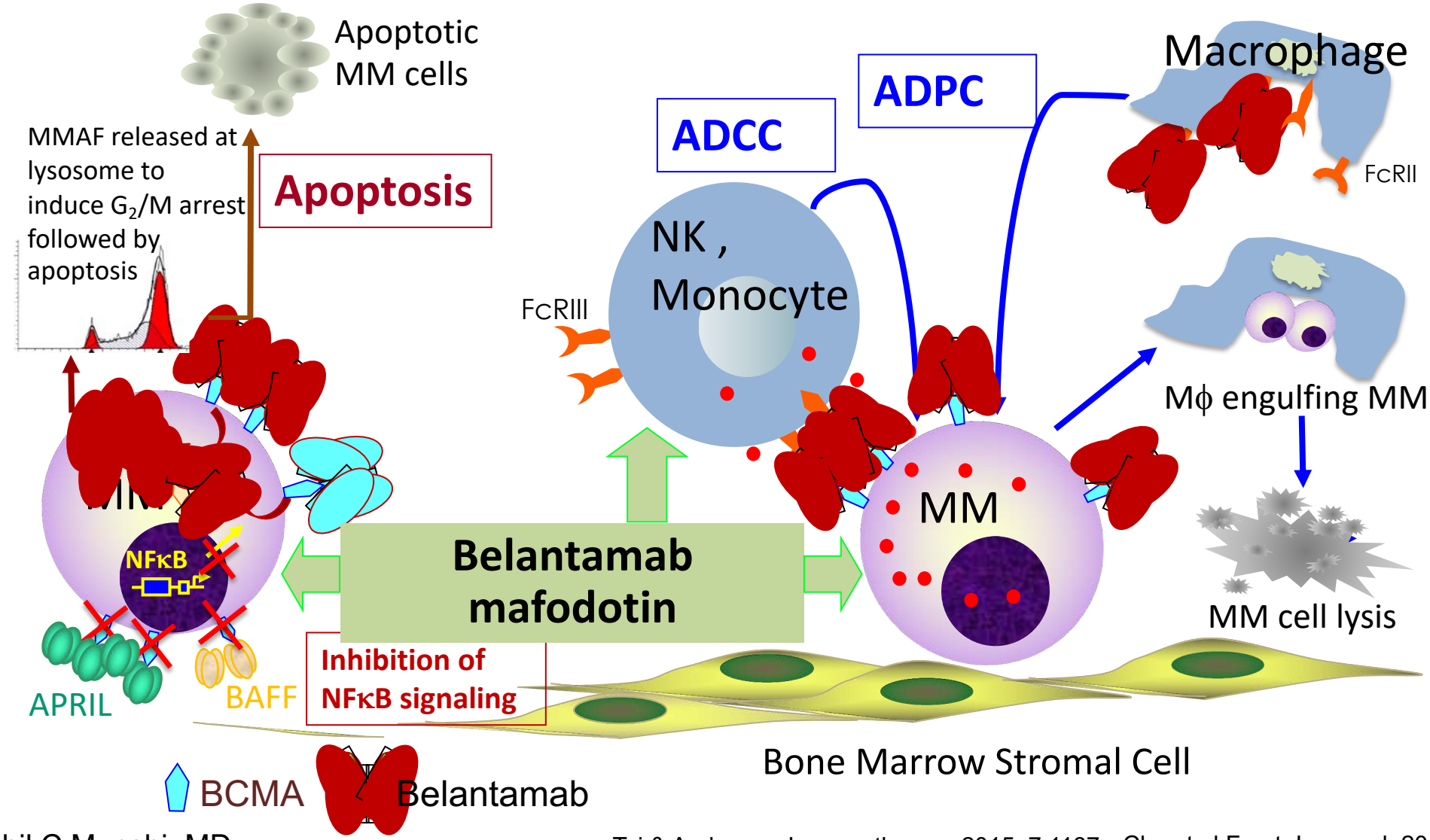

**BCMA is a member of the TNF receptor superfamily**
**BCMA expression supports survival of long-lived PCs, Ig Class switch and Ab Production**

**Expressed nearly universally on MM cells**
**Promotes proliferation, survival and associated with immunosuppressive BM microenvironment.**

Courtesy of Nikhil C Munshi, MD

Cho et al Front. Immunol. 2018. 01821

# Belantamab mafodotin - a BCMA Auristatin Immunotoxin Induces Strong Anti-MM Effects via multiple MOAs

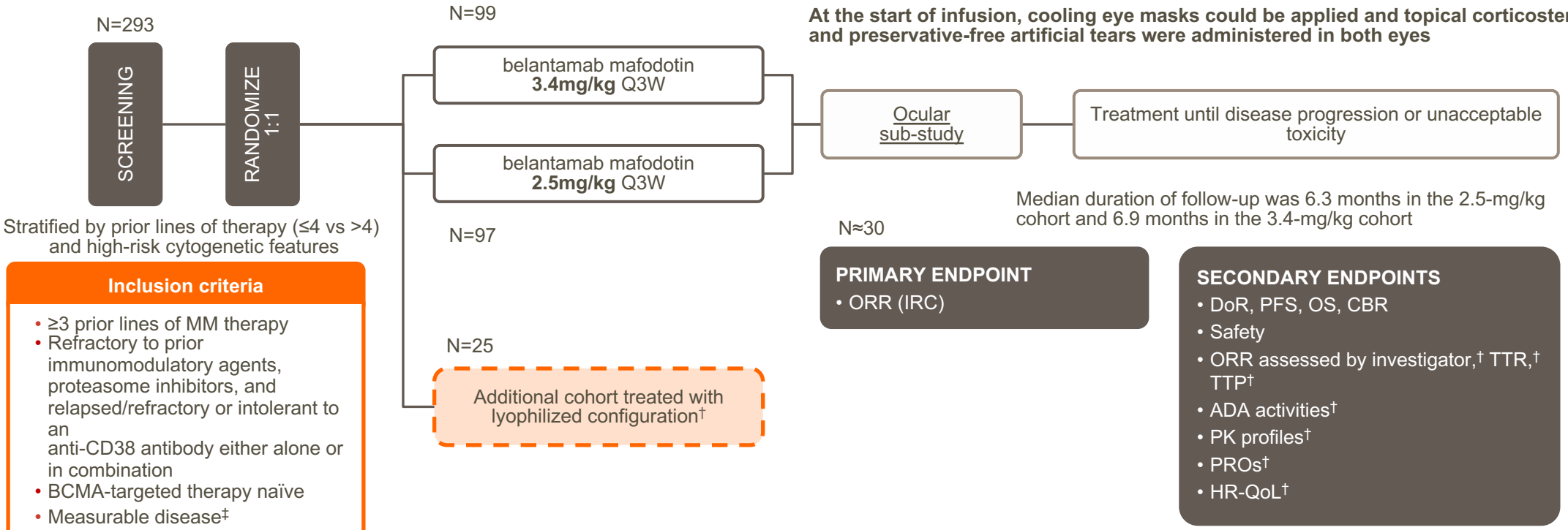



Courtesy of Nikhil C Munshi, MD Tai et al Blood 2014 123:3128 Tai & Anderson Immunotherapy 2015 ;7:1187 Cho et al Front. Immunol. 2018. 01821

# A Phase II, Open-label, Randomized, 2-dose study in Relapsed Refractory Multiple Myeloma

## Study design DREAMM-2

**Refractory to an immunomodulatory drug, proteasome inhibitor, and refractory/intolerant to an anti-CD38 monoclonal antibody**

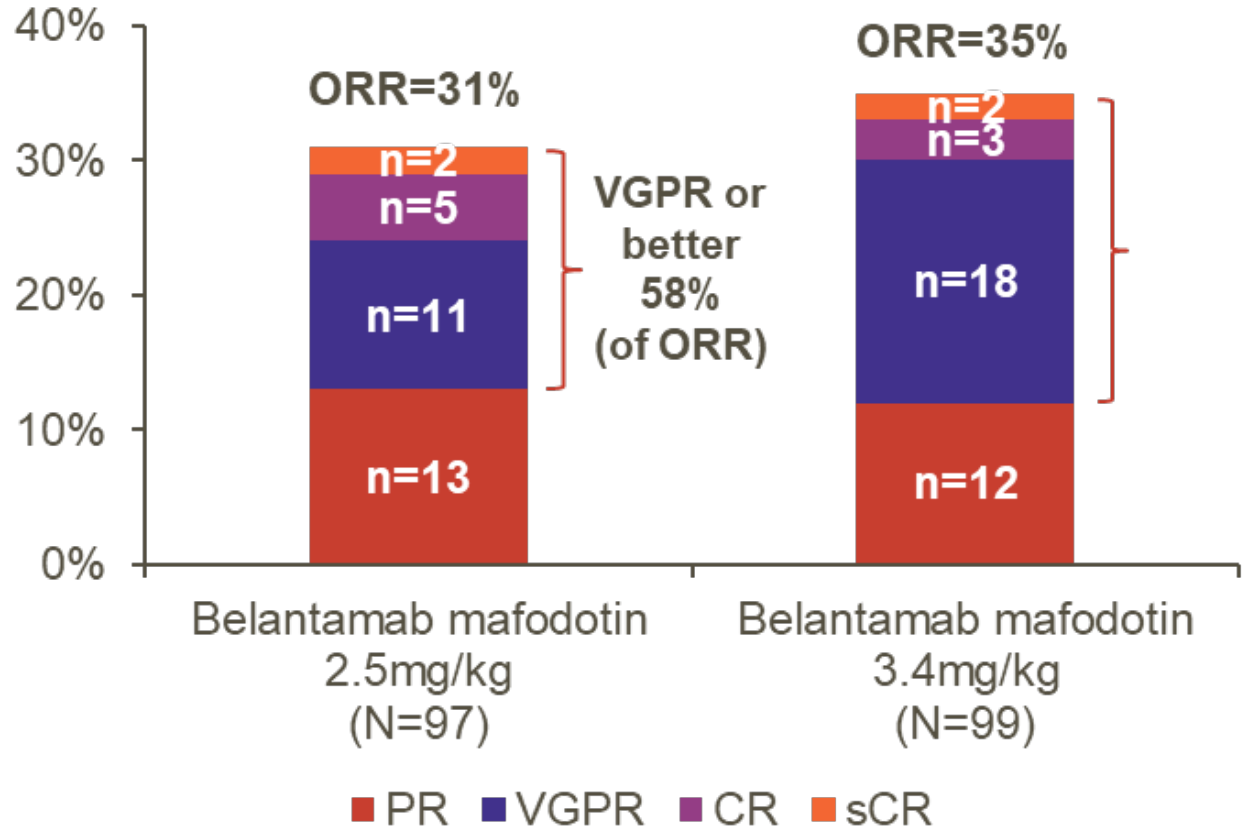



**1.** Lonial S et al. *Lancet Oncol.* 2020;21(2):207-221. **2.** Lonial S et al. Poster presented at: American Society of Clinical Oncology Annual Meeting;. Poster 436.

Courtesy of Nikhil C Munshi, MD

# Belantamab mafodotin: Overall response

**DREAMM-2 13-month follow-up**

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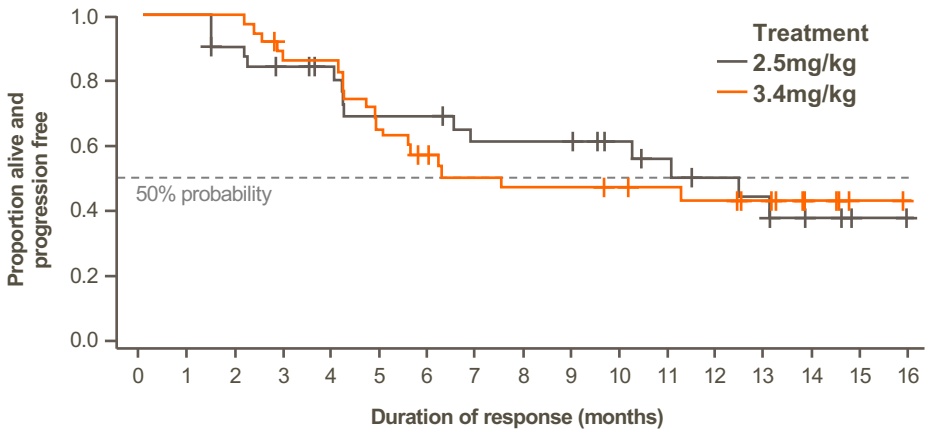
Courtesy of Nikhil C Munshi, MD

# Belantamab mafodotin: Survival Outcome in heavily pretreated MM Patients

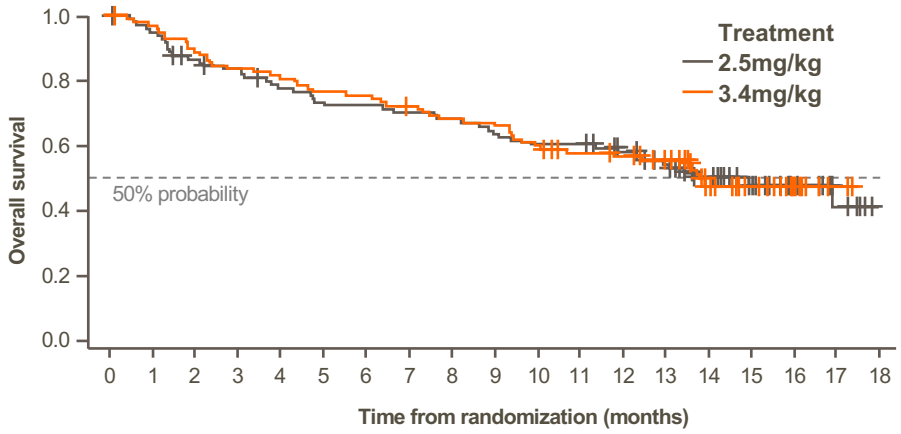
**DREAMM-2 13-month follow-up**

| | belantamab mafodotin 2.5mg/kg (n=97) | belantamab mafodotin 3.4mg/kg (n=99) |
|---|---|---|
| **mOS** | 14.9 months (95% CI: 9.9-NR) | 14.0 months (95% CI: 10-NR) |
| **mDOR** | 11.0 months (95% CI: 4.2-NR) | 6.2 months (95% CI: 4.8-NR) |
| **mPFS** | 2.8 months (95% CI: 1.6-3.6) | 3.9 months (95% CI: 2.0-5.8) |

## Duration of response




## Overall survival

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Courtesy of Nikhil C Munshi, MD

# Belantamab mafodotin: Common adverse events Keratopathy and Thrombocytopenia

DREAMM-2

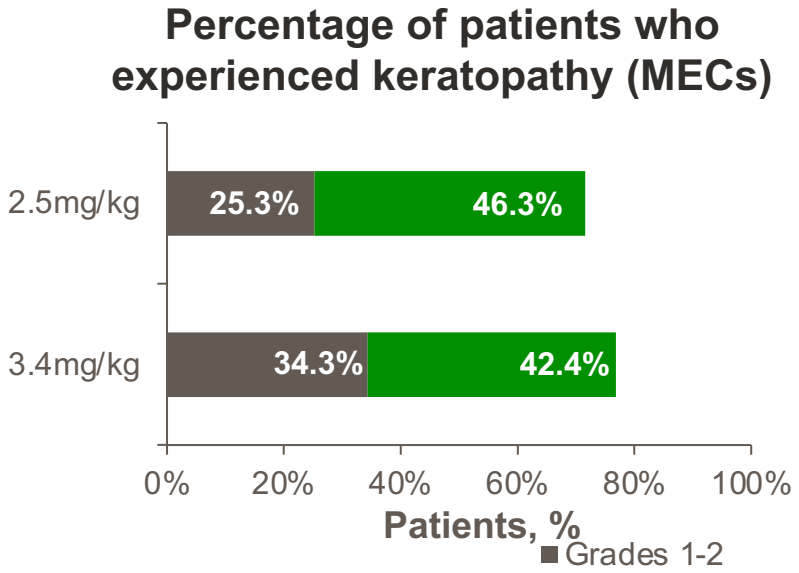
| Adverse events* | Any grade, n (%) | | Grades ≥ 3, n (%) | |
|---|---|---|---|---|
| | 2.5mg/kg n=95 | 3.4mg/kg n=99 | 2.5mg/kg n=95 | 3.4mg/kg n=99 |
| Any event | 93 (98) | 99 (100) | 80 (84) | 83 (84) |
| Keratopathy (MECs) - changes to the superficial corneal epithelium | 68 (72) | 76 (77) | 44 (46) | 42 (42) |
| Thrombocytopenia | 36 (38) | 56 (57) | 21 (22) | 32 (32) |
| Anemia | NR | NR | 20 (21) | 27 (27) |
| Neutropenia | NR | NR | 10 (11) | 17 (17) |
| Pneumonia | NR | NR | 6 (6) | 11 (11) |

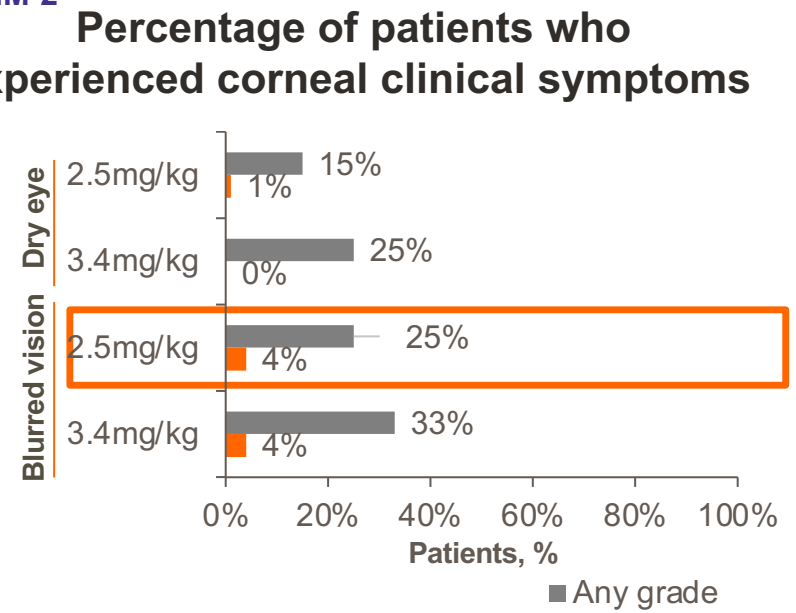
**1.** Lonial S et al. *Lancet Oncol.* 2020;21(2):207-221. **2**. Lonial S et al. Poster presented at: American Society of Clinical Oncology Annual Meeting;. Poster 436.

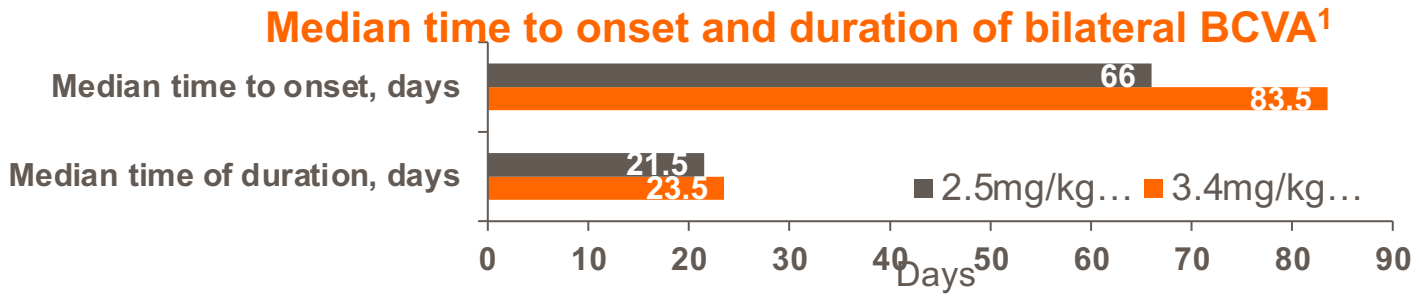
Courtesy of Nikhil C Munshi, MD

# Keratopathy with Belantamab mafodotin Dose modifications

DREAMM-2




**First events resolved in 82% in 2.5mg/kg group AND 100% in 3.4mg/kg group**

**1.** Lonial S et al. *Lancet Oncol.* 2020;21(2):207-221. **2**. Lonial S et al. Poster presented at: American Society of Clinical Oncology Annual Meeting;. Poster 436.

Courtesy of Nikhil C Munshi, MD

# Future Options: DREAMM-6 Belantamab/Bor/dex

- All patients had evaluable responses
- ORR: 78% (95% CI: 52.4-93.6)[1]
  - Higher than previously reported ORRs for Vd in patients with ≥ 1 prior therapy (50% to 63%)[2-4]
- Median duration of response not yet reached

| Best Confirmed Response, n (%) | Belantamab mafodotin + Vd (N = 18) |
|---|---|
| Clinical benefit rate* | 15 (83) |
| ORR | 14 (78) |
| ▪ VGPR | 9 (50) |
| ▪ PR | 5 (28) |
| MR | 1 (6) |
| SD | 3 (17) |

*sCR + CR + VGPR + PR + MR.

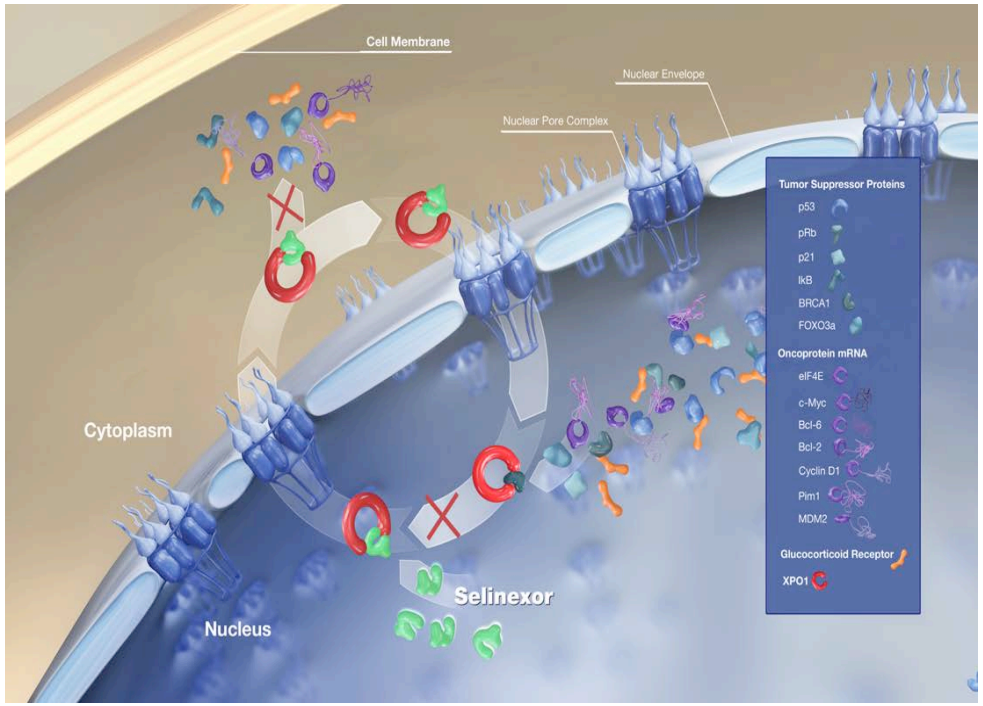
Nooka, AK et al. 2020 ASCO Abstract # 8502.

Courtesy of Nikhil C Munshi, MD

# Targeting XPO-1

**Selinexor approved for use in pts with RRMM who have received four prior therapies (including pts refractory to two proteasome inhibitors or IMiDs and an anti-CD38 antibody)**

**Selinexor is an oral XPO-1 inhibitor that induces nuclear retention and activation of TSPs and the GR in the presence of steroids, and suppresses oncoprotein expression[1]**

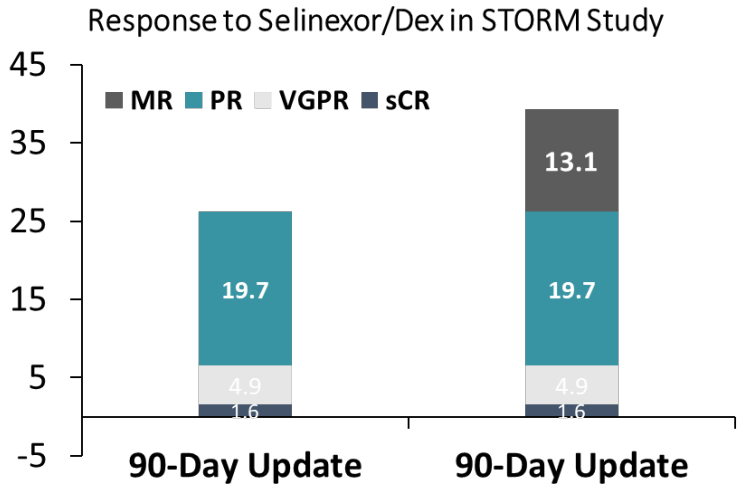



Courtesy of Nikhil C Munshi, MD

*[1]Schmidt et al., Leukemia, 2013, [2]Tai et al., Leukemia, 2013, [3]Argueta et al., Oncotarget, 2018 [4]Turner et al, 2017 unpublished*

# Targeting Nuclear Transport
# *Selinexor*

- Inhibits XPO1
  - XPO1 is the major nuclear export protein
  - XPO1 is overexpressed in MM
- Results of STORM Study
  - N = 122; median 7 prior treatments
  - 86% refractory to bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab
  - mDOR = 4.4 months
  - Associated with hematologic and GI toxicity
    - Aggressive supportive care needed

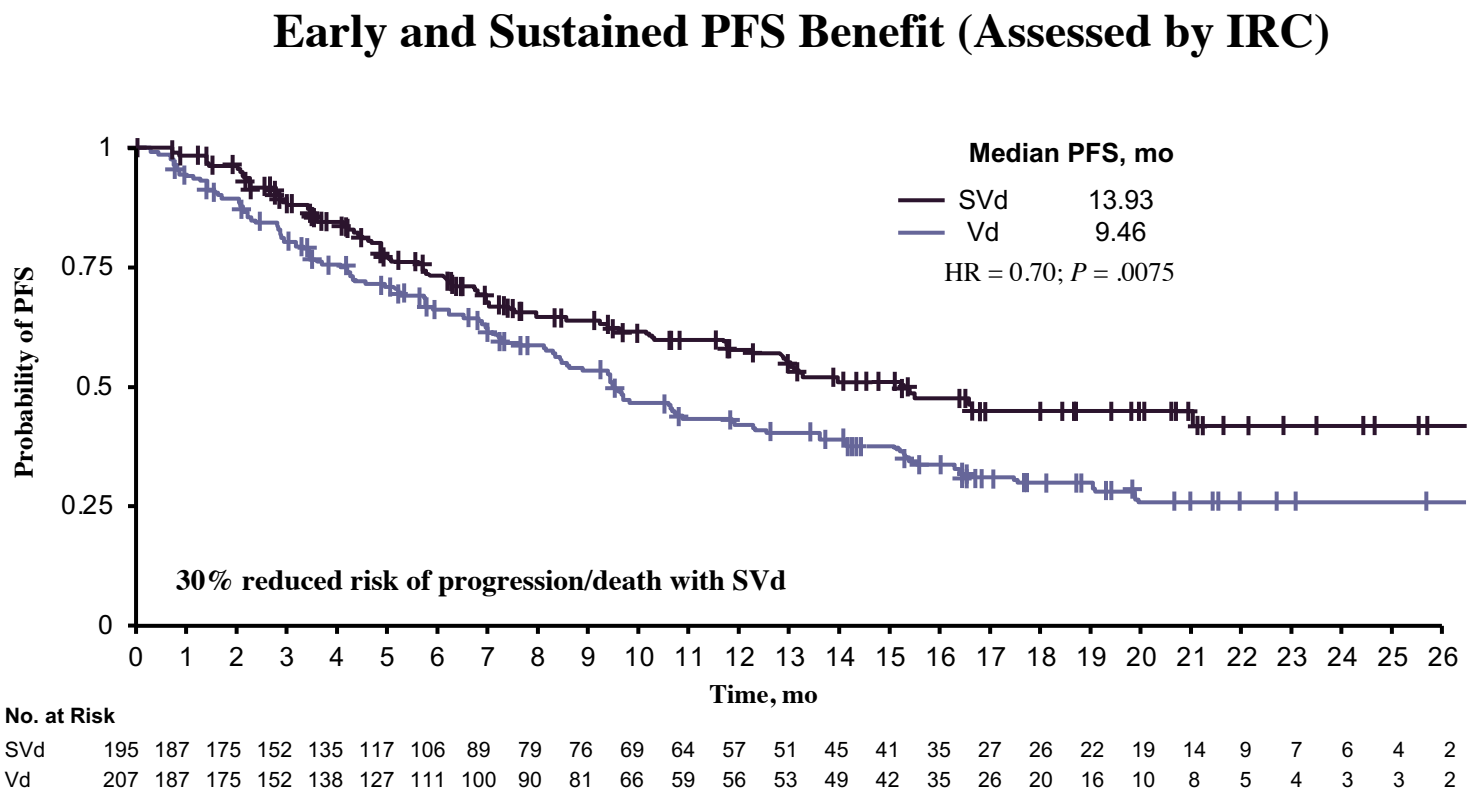



FDA-Approved July 2019
In combination with Dex in adults with RRMM after ≥ 4 prior therapies (≥ 2 PIs, ≥ 2 immunomodulatory drugs, and an anti-CD38 antibody)


- Chari A, et al. *N Engl J Med.* 2019;381:727-738.

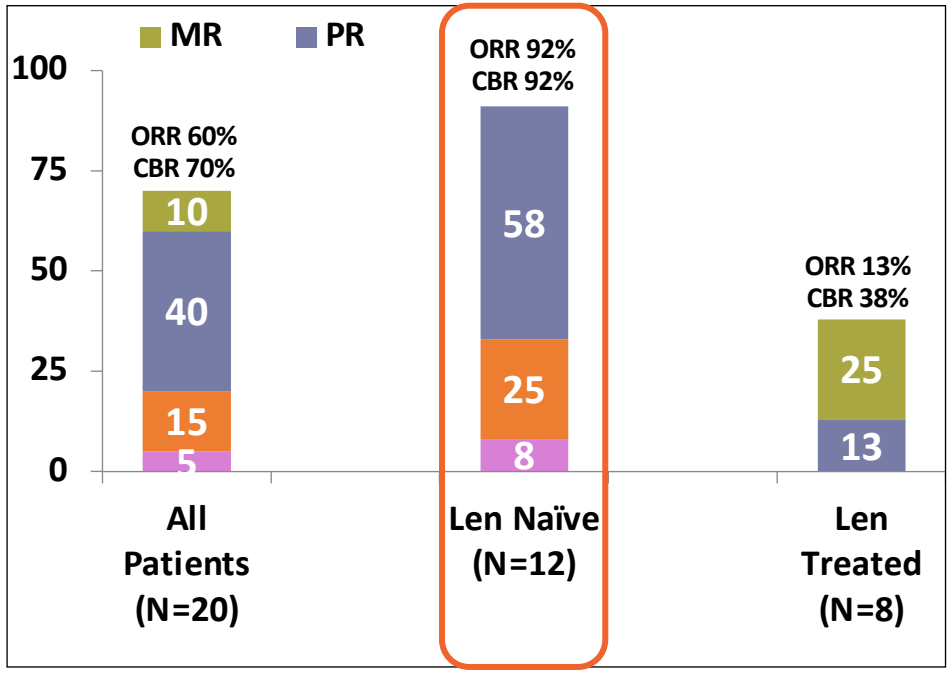

Courtesy of Nikhil C Munshi, MD

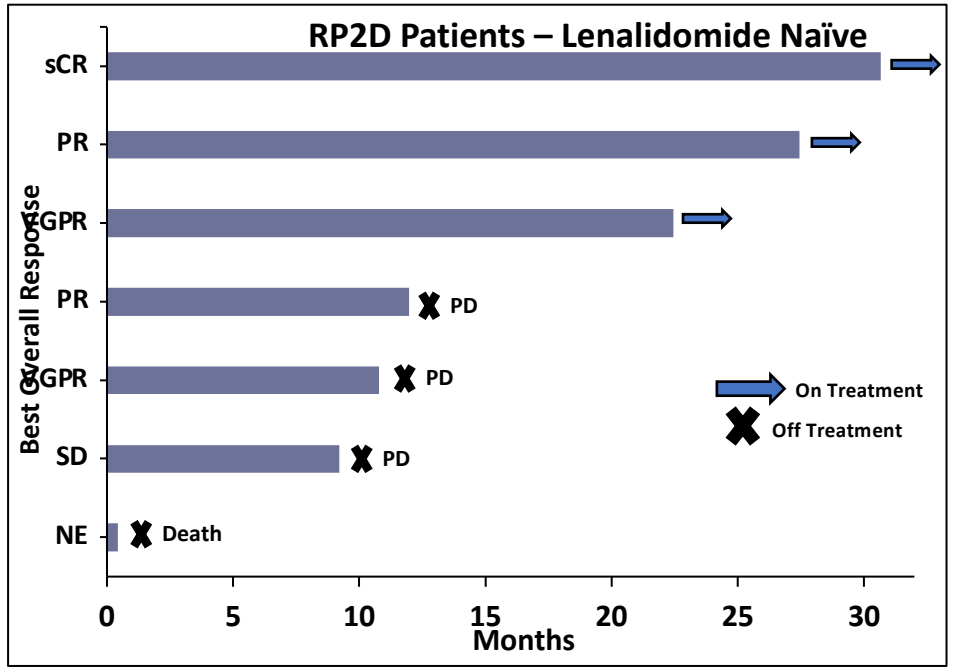
# Phase 3 BOSTON Trial: Selinexor Plus Vd in RRMM




Courtesy of Nikhil C Munshi, MD

# Selinexor-Lenalidomide-Dexamethasone: Efficacy




- The median time to response (≥PR) was 1 month
- Among lenalidomide naïve RP2D patients, the median time on treatment was 12 months

Responses were adjudicated according to the *International Myeloma Working Group* criteria,*four patients not evaluable for response withdrew consent prior to disease follow-up. Two unconfirmed PRs, ORR=Overall Response Rate (sCR+VGPR+PR), CBR=Clinical Benefit Rate (ORR+MR), sCR=Stringent Complete Response, VGPR=Very Good Partial Response, PR=Partial Response, MR=Minimal Response. Responses as of August 1, 2019 based on interim unaudited data.

Courtesy of Nikhil C Munshi, MD

# Conclusions

- Select from daratumumab-, elotuzumab-, and isatuximab-based triplets
- No solid data to support a specific sequence or preference for one agent over another
- Data from high-risk subgroups show that they benefit, but not as much as standard risk
- Possibility that proteasome inhibitor-based triplets may have a greater benefit in high-risk

Courtesy of Nikhil C Munshi, MD

# Conclusions

- Exciting novel approaches in pipeline, including both small molecules and new immunotherapies (S. Jagannath)
  - SINE, BCL2, MCL1 inhibitors
  - BiTEs, bispecific antibodies
- Immunotherapies such as CAR T-cells are showing impressive activity in the relapsed and refractory setting
  - Challenges remain, including toxicity, manufacturing time, and cost
- Due to earlier use of novel agents, relapsed and especially refractory disease is becoming more challenging to manage
- Better use of our current drugs in new combinations can have efficacy even if these agents were given previously
- Novel(er) drugs available on clinical trials offer the possibility of new mechanisms of action and may overcome prior drug resistance

Courtesy of Nikhil C Munshi, MD

# Case 1: Young patient with relapsed/refractory disease – 4th line

**61-year-old lady with active legal practice presented with new onset back pain and anemia**

- Serum M spike: 4 g/dL; Serum IgG 5460 mg/dL
- SFLC: kappa: 184 mg/L; lambda: 1.86 mg/L; kappa:lambda ratio: 98.9
- Bone marrow Bx: 70% plasma cells
- FISH: amp 1q;
- Conventional cytogenetics: no abnormality

- Hb 11.6 g/dL (dropped from 13.2 g/dL two months prior)
- Sr. Calcium 9.6 mg/dL
- Sr Creatinine: 0.9 mg/dL
- Sr. albumin: 4 g/dL; LFTs: WNL
- B2M: 3.84 ug/dL
- Bone survey: L3 and T8 compression; fracture of Left 3rd rib

- Diagnosed with IgG lambda light chain multiple myeloma, with amp 1q

Courtesy of Nikhil C Munshi, MD

# Case 1 (Continued): Young patient with relapsed/refractory disease – 4th line

**61-year-old lady with IgG λ multiple myeloma, with amp 1q**

- VRd x 5 with minimal response (45% reduction) → changed to CyBorD with PR
- Autologous cell stem cell transplant →
- Relapsed 4 months post ASCT
- – Carfilzomib/cyclophosphamide/dexamethasone.
  - – Response 3 months
- - Daratumumab/pomalidomide/dexamethasone
  - – Response 4 months
- Multiple lines of therapy with initial response with quick subsequent relapse
- **What would be the next line of therapy?**

Courtesy of Nikhil C Munshi, MD

# Case 2: Young patient with 1st relapse

- **62-year-old male in good physical condition. Presented for evaluation of recent fatigue and shortness of breath. Labs are as follows**
  - M-spike, IgG kappa: 6.1 g/dL
  - Beta-2-microglobulin: 9.8 mg/dL
  - Bone marrow aspirate: 90% plasma cells
  - FISH: t(11;14)

  - Hemoglobin: 7.8 g/dL
  - Calcium: 9.0 mg/dL
  - Creatinine 1.5 mg/dL
  - Albumin: 2.6 g/dL
  - Skeletal survey: Diffuse lytic lesions

- VRd → ASCT → lenalidomide maintenance x 24 mo. → PD
- **What are his options at first relapse?**

Courtesy of Nikhil C Munshi, MD

# Case 3: Older patient with relapsed disease – 3rd line

- 75-year-old male with CAD – 2 vessel disease, Mild diabetes and hypertension.
- Presented with rib pain, fatigue, and anemia

| | | | |
|---|---|---|---|
| Hemoglobin | **8.1** g/dL | M-protein | 4.9 (**IgA-kappa**) |
| Calcium | 9.5 mg/dL | Kappa/Lambda/FLC | 91/3.3/32.4 |
| Creatinine | 1.5 mg/dL | Urine M-protein | 27 mg/24 hours |
| PET-CT | Vertebral Compression **fractures;** rib lesions | Albumin | 3.2 g/dL |
| BM biopsy | 80% (kappa-restricted) | Beta-2-microglobulin | **8.1** mg/dL |
| Cytogenetics | Normal | LDH | 125 |
| FISH | **t(4;14), del(17p),del 13** | ECOG PS | 1 |

- Initial therapy with RVD-lite x 8 cycles → PR but neuropathy Gr2; R maintenance x 1.5 years → relapsed while on R 10 mg qd
- Dara-PomDex → PR, remission for 14 months, but now PD
- During the past 3 years close follow-up for his cardiac function; EF ~50%
- **What are the treatment options for this patient?**

Courtesy of Nikhil C Munshi, MD