Thank you for joining us.
The program will commence momentarily.

Recent Advances in Medical Oncology: Multiple Myeloma

Monday, July 13, 2020
5:00 PM – 6:00 PM ET

Faculty

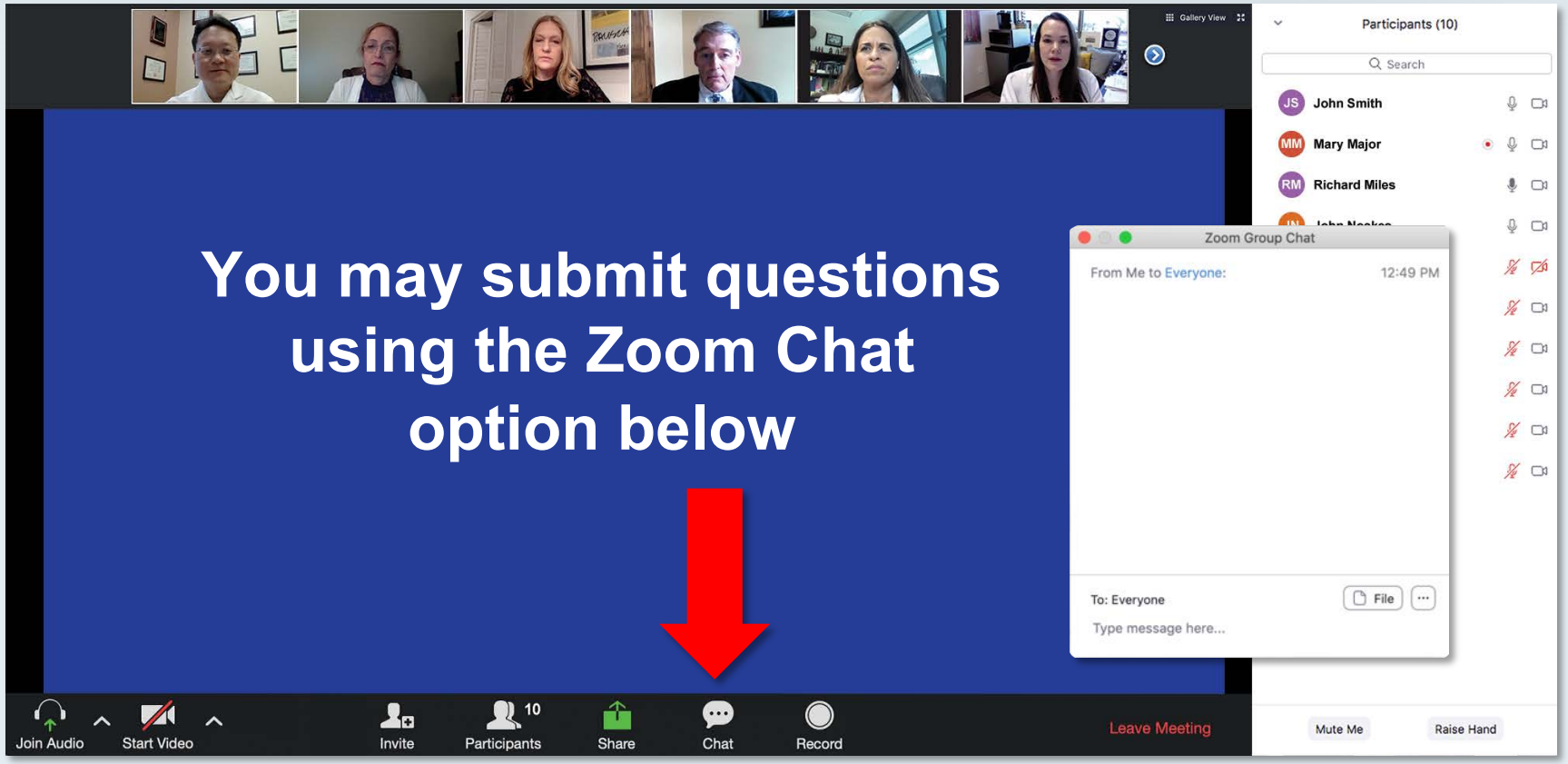
Shaji K Kumar, MD
Noopur Raje, MD

Moderator

Neil Love, MD

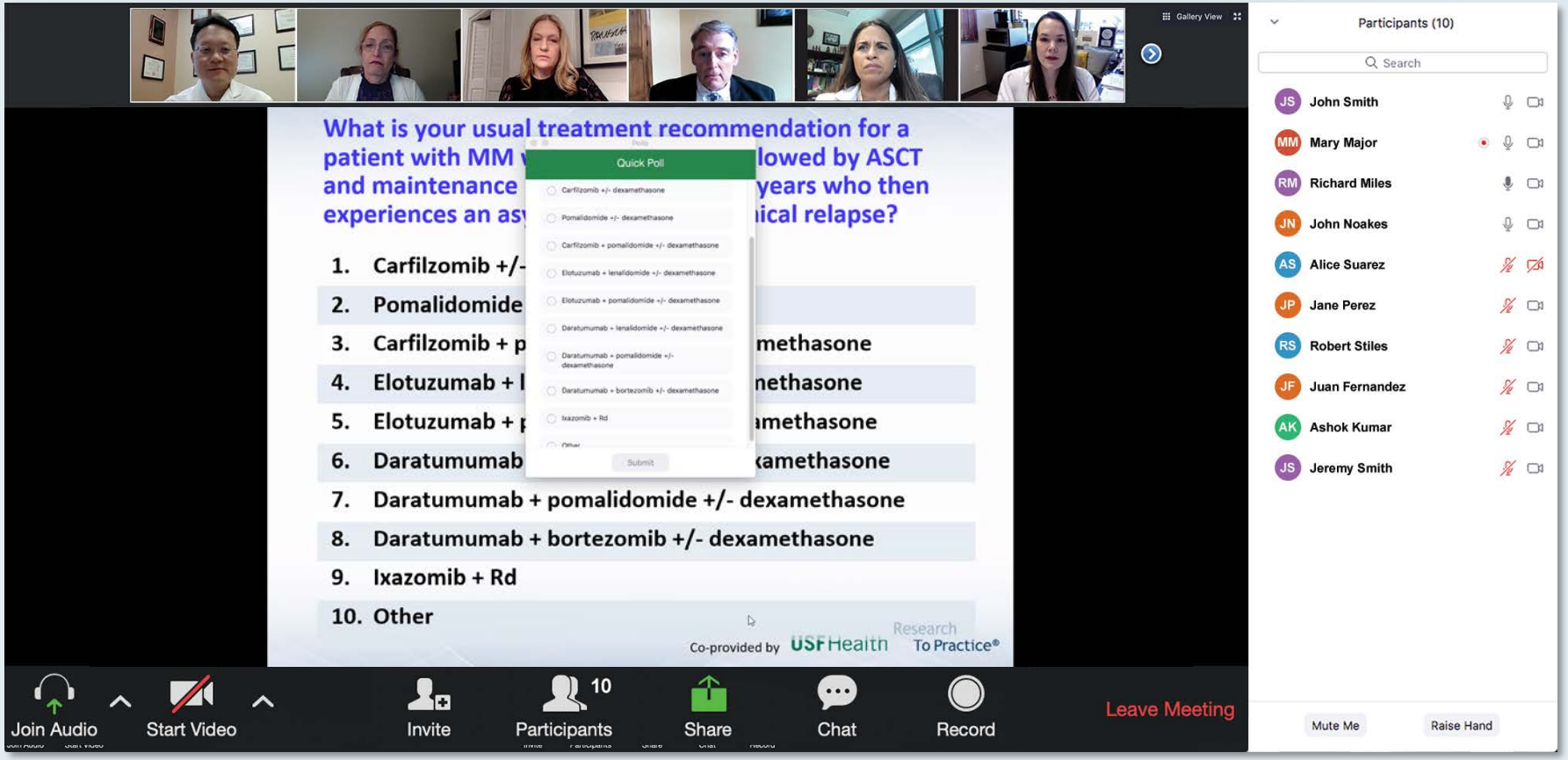
RTP RESEARCH TO PRACTICE

Dr Love and Faculty Encourage You to Ask Questions



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

Familiarizing yourself with the Zoom interface
How to answer poll questions



When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.

Dr Love — Disclosures

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Dr Kumar — Disclosures

Consulting Agreements	AbbVie Inc, Adaptive Biotechnologies, Amgen Inc, AstraZeneca Pharmaceuticals LP, Celgene Corporation, GeneCentrix Inc, Genentech, a member of the Roche Group, Janssen Biotech Inc, Kite, A Gilead Company, Merck, Molecular Partners, Oncopeptides, Takeda Oncology
Contracted Research	AbbVie Inc, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Carson, Celgene Corporation, Genentech, a member of the Roche Group, Janssen Biotech Inc, Kite, A Gilead Company, Merck, Novartis, Roche Laboratories Inc, Sanofi Genzyme, Takeda Oncology, TeneoBio
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Dr Raje — Disclosures

Consulting Agreements	Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Novartis, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology
Contracted Research	AstraZeneca Pharmaceuticals LP, Lilly

Meet The Professors

Clinical Investigators Discuss Existing and Emerging Treatment Strategies for Patients with Ovarian, Cervical and Endometrial Cancer

Tuesday, July 14, 2020

12:00 PM – 1:00 PM ET

Faculty

Michael J Birrer, MD, PhD
Kathleen Moore, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Recent Advances in Medical Oncology: Targeted Therapy for Lung Cancer

Wednesday, July 15, 2020
5:00 PM – 6:30 PM ET

Faculty

Alexander E Drilon, MD
Professor Solange Peters, MD, PhD
Suresh S Ramalingam, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Perspectives on the Current and Future Management of Multiple Myeloma

Thursday, July 16, 2020

8:00 AM – 9:00 AM ET

Faculty

Sagar Lonial, MD

Moderator

Neil Love, MD

RTP
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WITH DR NEIL LOVE

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

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

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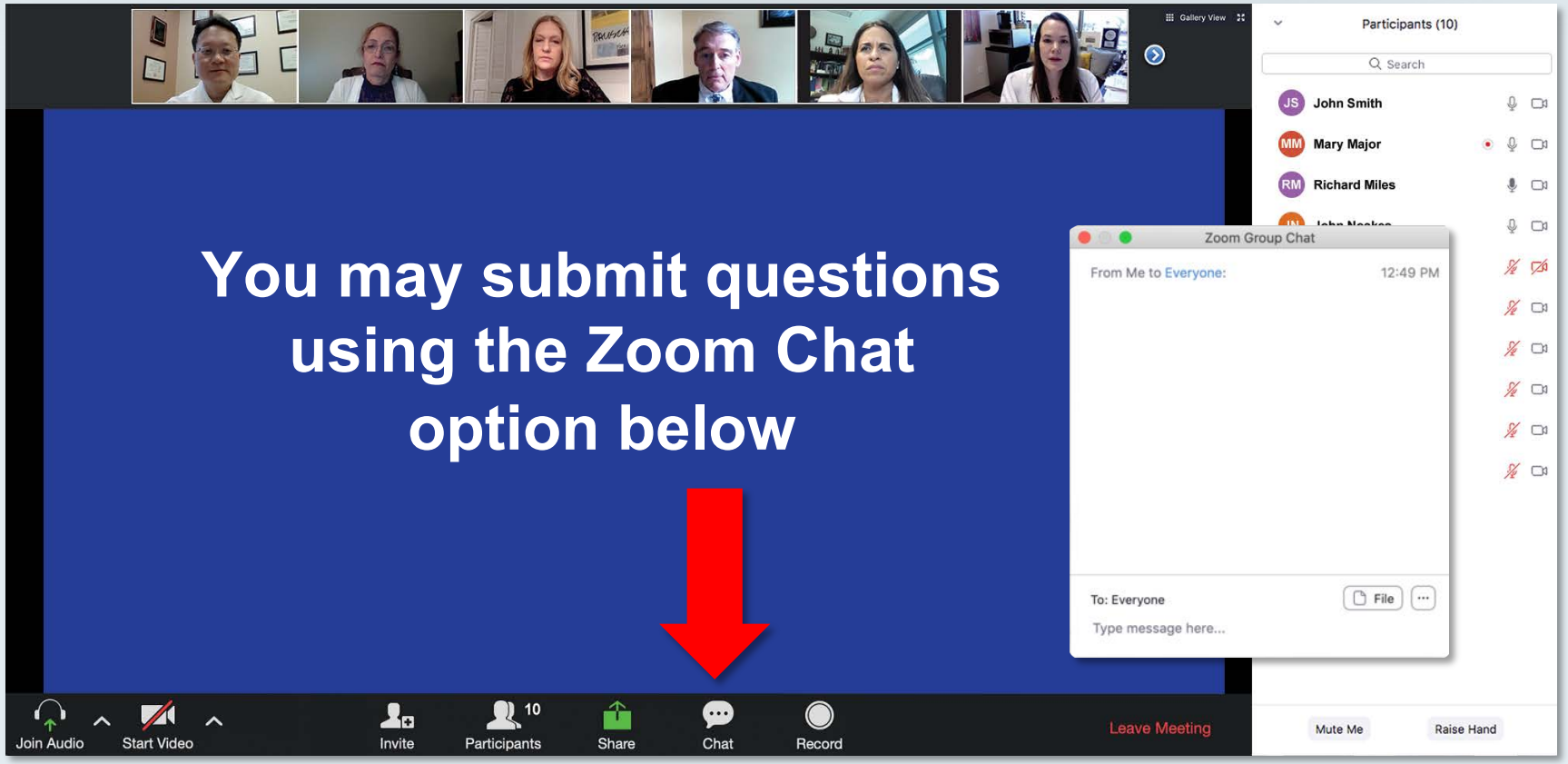

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About the Enduring Program

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RTP RESEARCH TO PRACTICE

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- **Newly diagnosed disease**
  - ENDURANCE (E1A11) trial of KRd versus RVd
  - Daratumumab-containing front-line regimens
  - Role of MRD assessment
  - Case: 67-year-old man
- **Relapsed disease**
  - Selection and sequencing of approved agents
  - Case: 72-year-old woman

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- Cereblon E3 ligase modulator (iberdomide)
- Venetoclax
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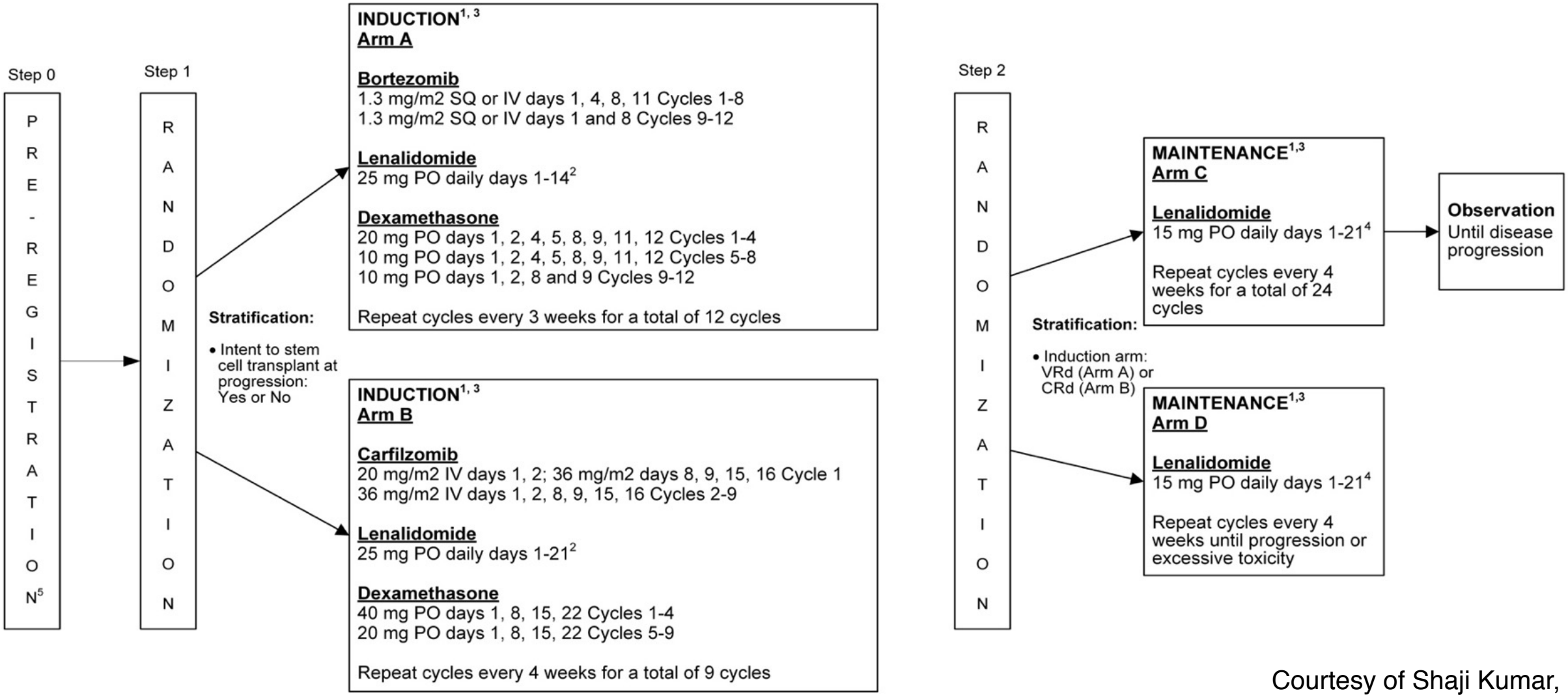
On a scale of 1 to 5, how would you rate the severity of the COVID-19 pandemic in your area? (1 = not affected at all, similar to 2019; 5 = severely affected [eg, New York at its peak])?

a. 1
b. 2
c. 3
d. 4
e. 5

In general, has the approach to autologous stem cell transplant (ASCT) for patients with multiple myeloma (MM) changed at your institution as a result of COVID-19?

a. No
b. Yes, ASCT is currently not being performed
c. Other

E1A11: ENDURANCE Trial

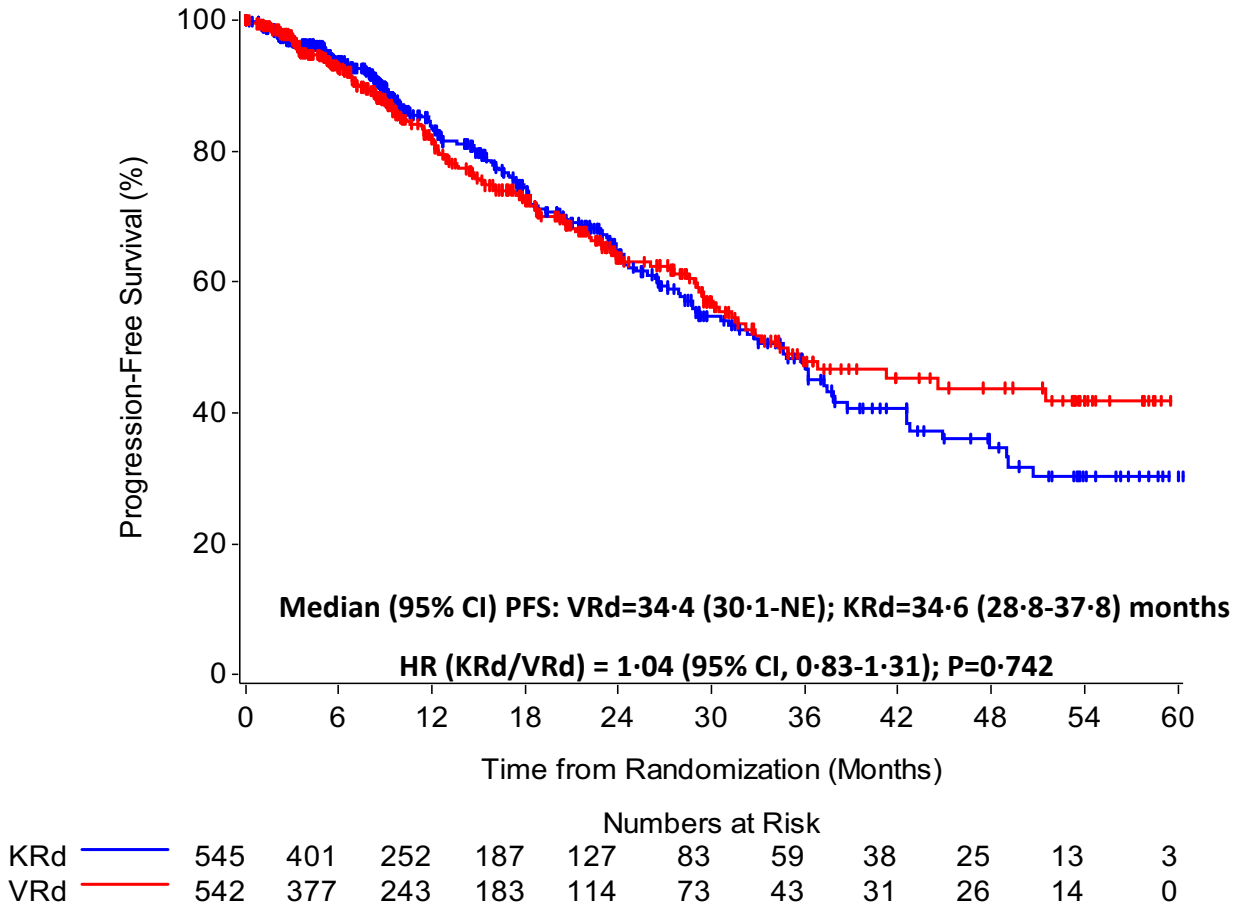


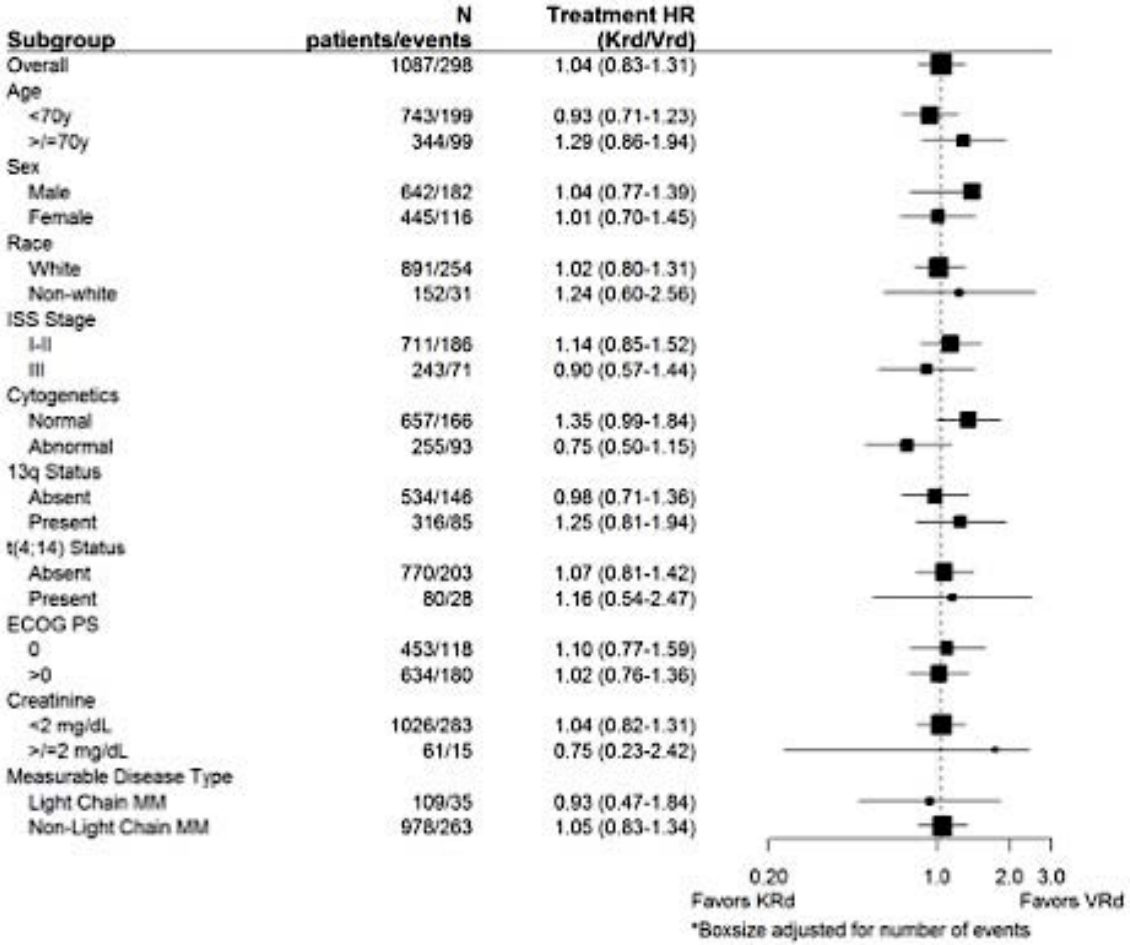
Courtesy of Shaji Kumar, MD

Kumar S et al. ASCO 2020;Abstract LBA3.

MAYO CLINIC

Progression-Free Survival from Induction Randomization





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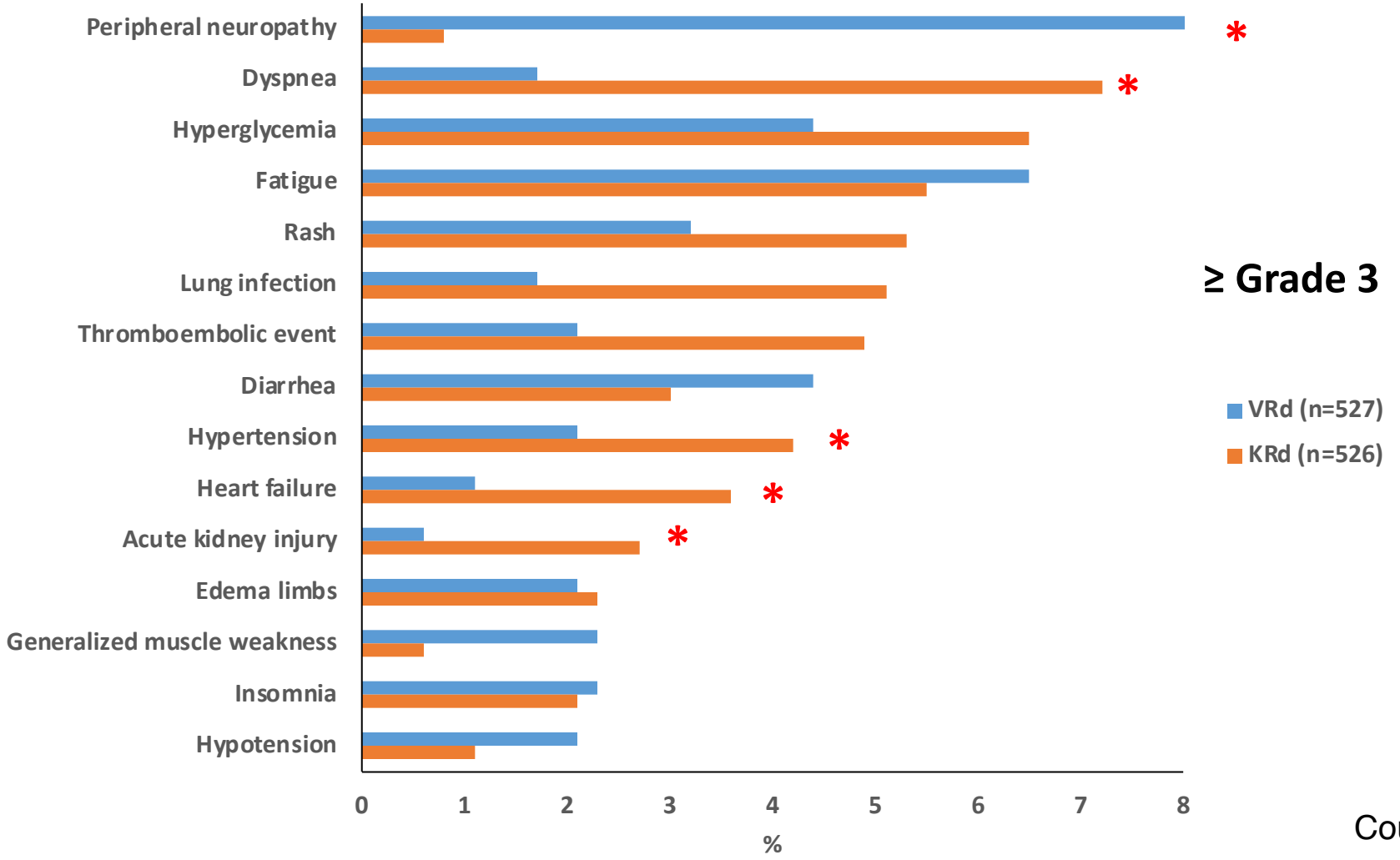
E1A11: Non-hematologic Treatment-Related AEs (≥2%)



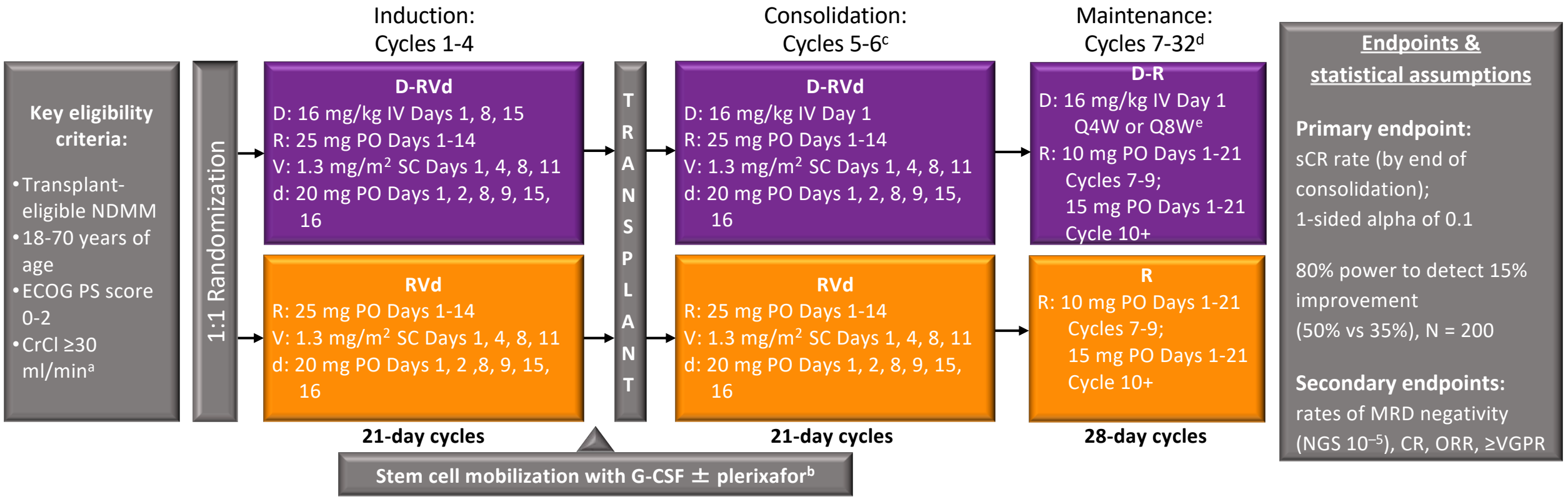
Courtesy of Shaji Kumar, MD

Kumar S et al. ASCO 2020;Abstract LBA3.

MAYO CLINIC

GRIFFIN: Randomized Phase 2

- Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 to 4/2018



Courtesy of Shaji Kumar, MD

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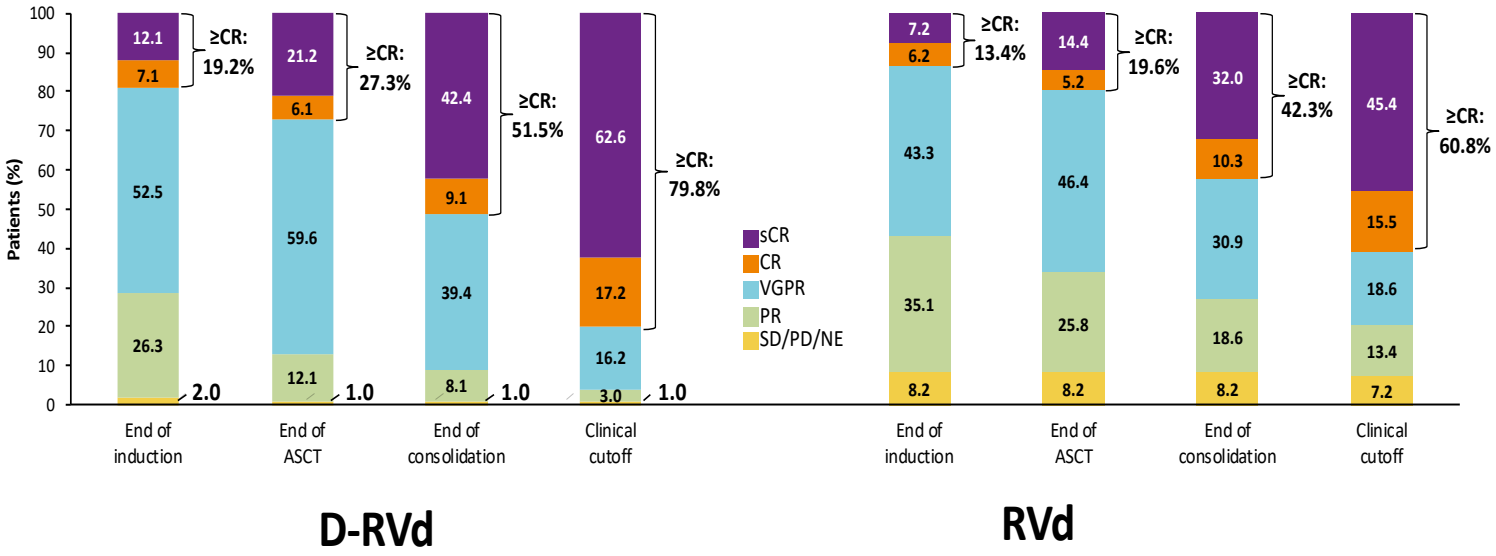
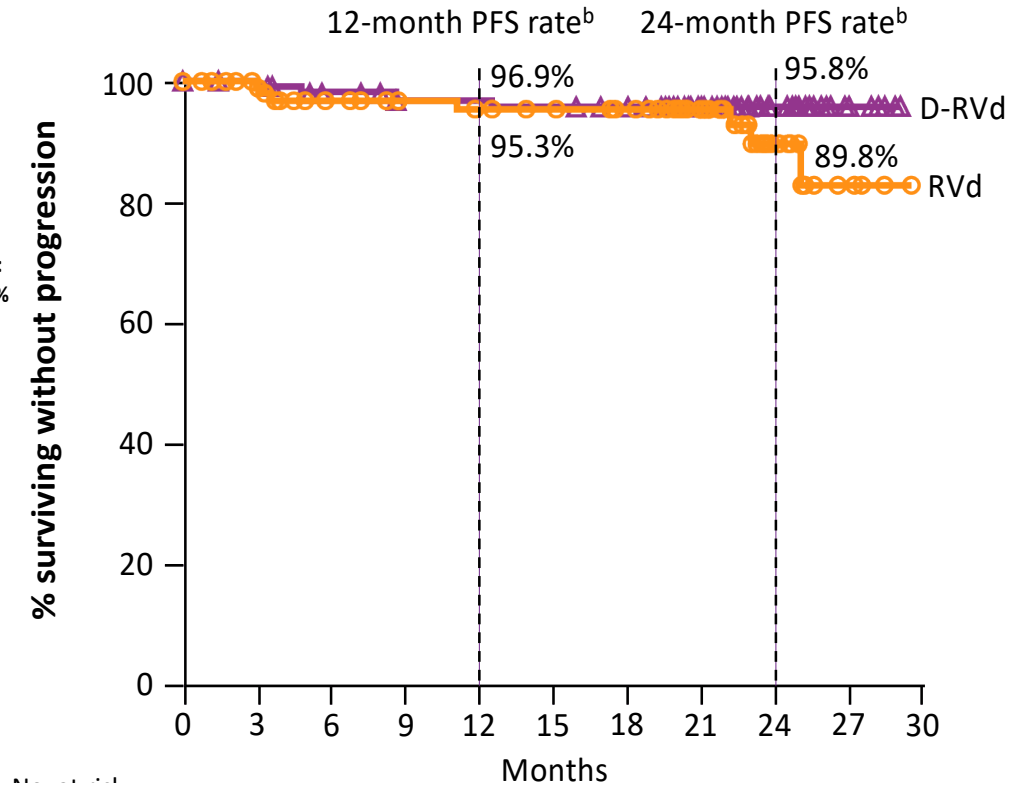
Voorhees et al, ASH 2019

Efficacy: Dara-VRd





Courtesy of Shaji Kumar, MD

Voorhees PM et al. ASH 2019;Abstract 691.

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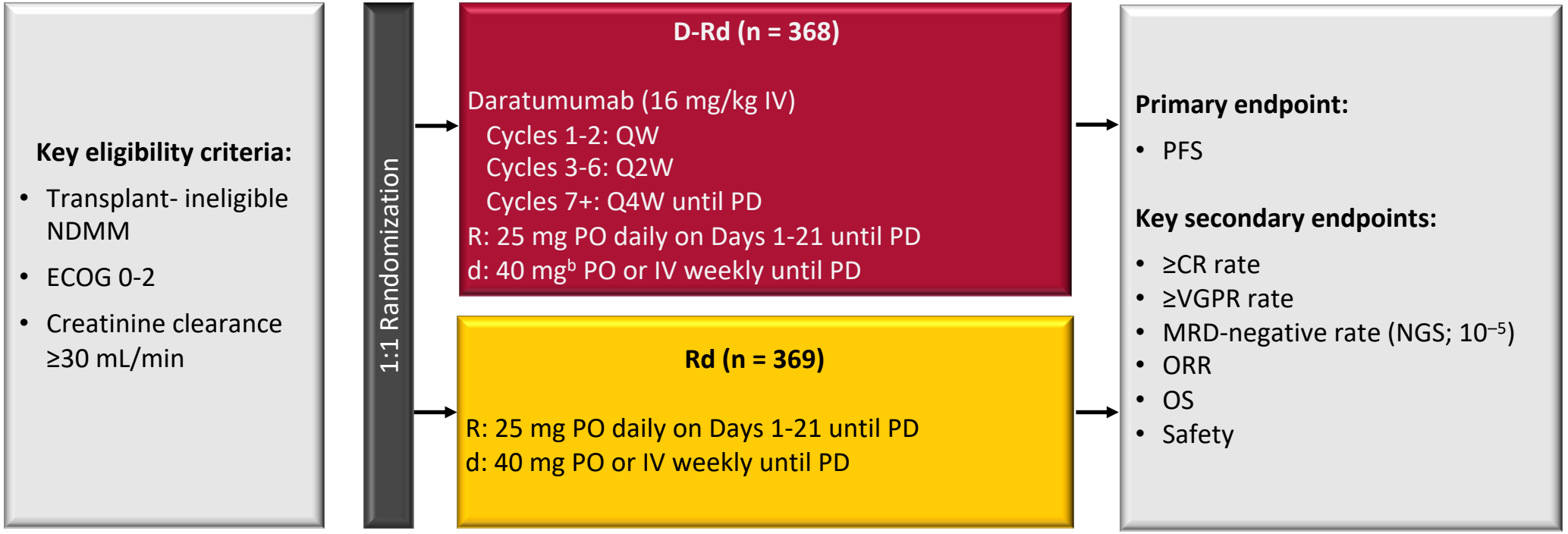
MAIA: Daratumumab Len-Dex vs. Len Dex



- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)

Courtesy of Shaji Kumar, MD

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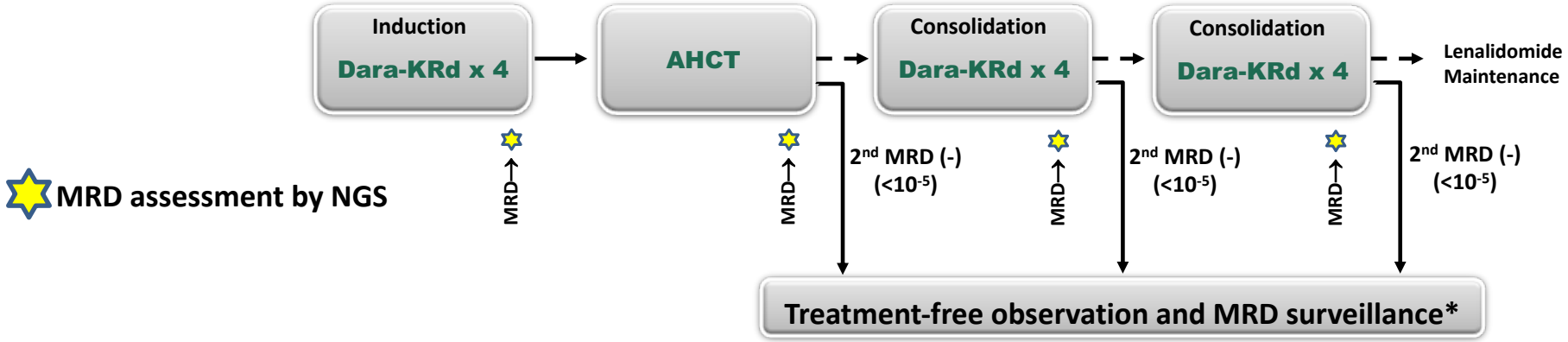
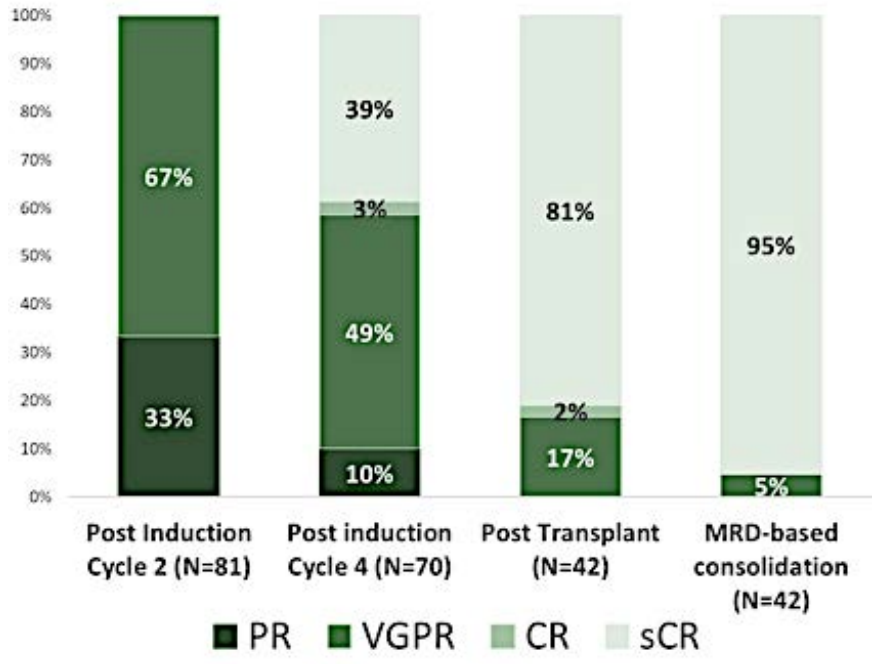
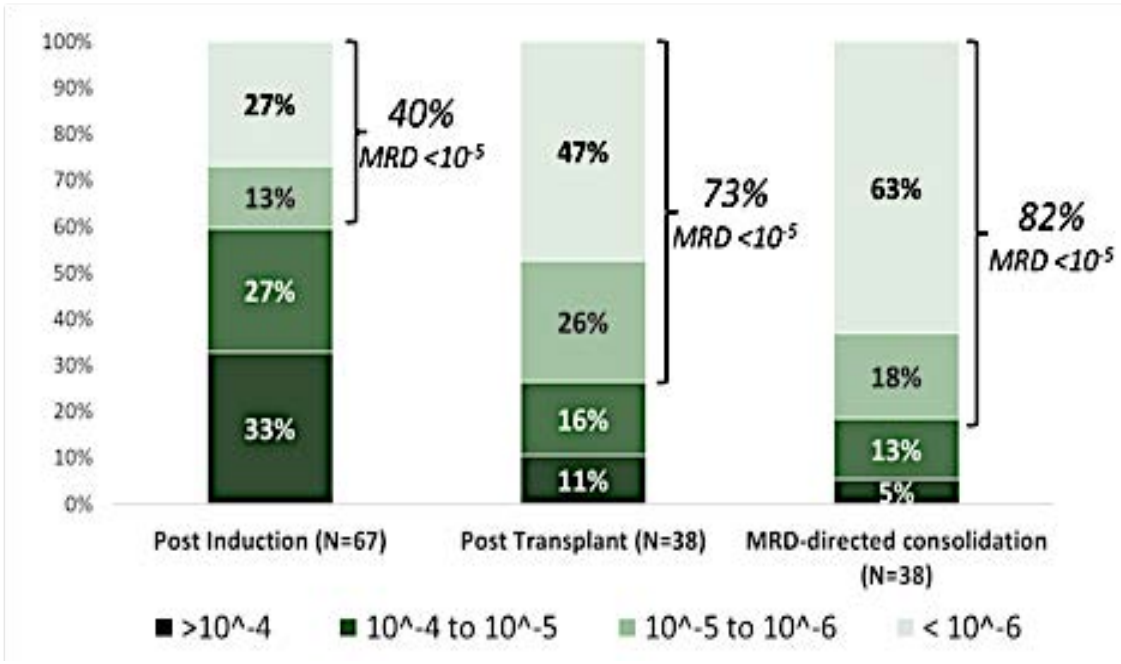
Facon et al, ASH 2018

MASTER Trial: Initial results







Costa et al, ASH 2019

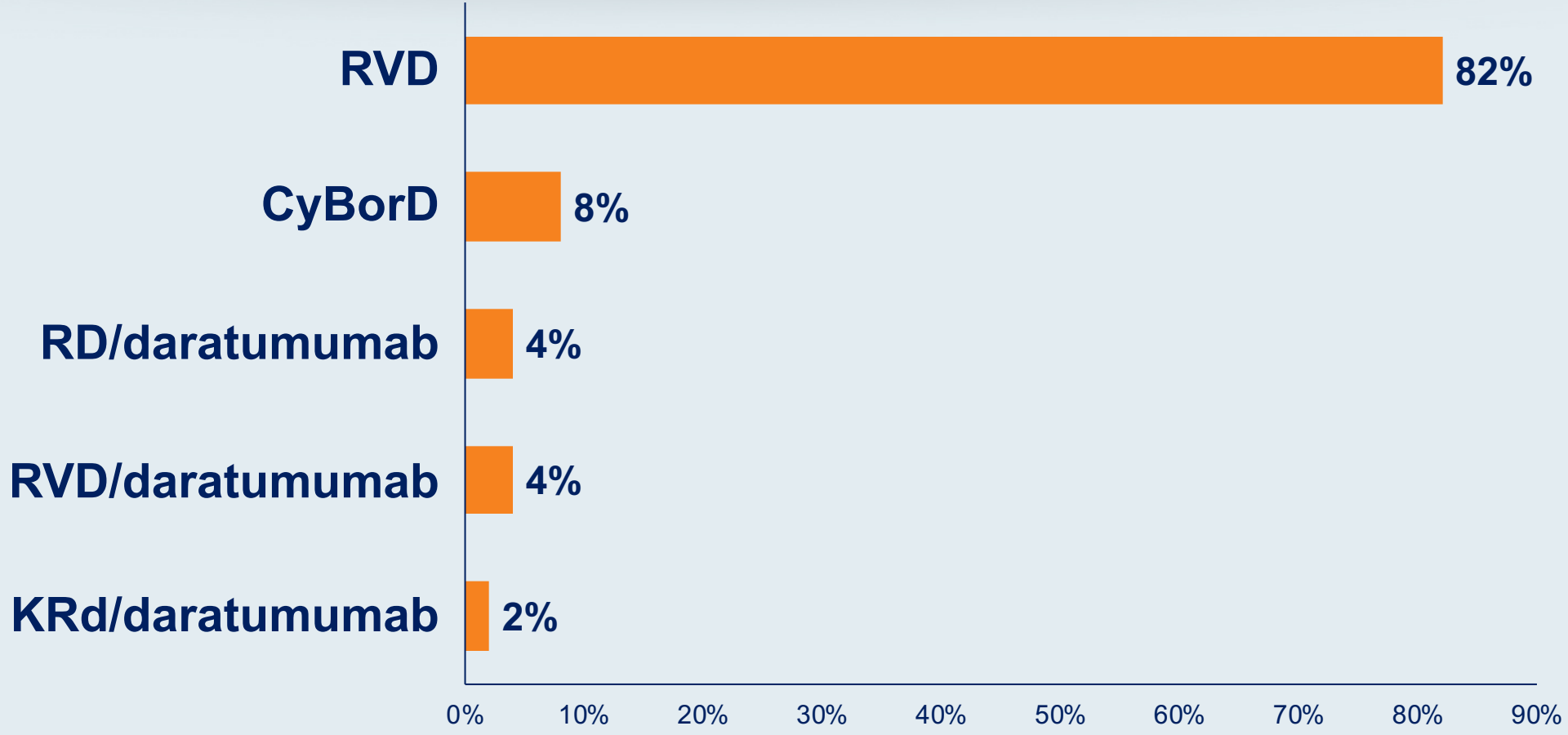
Courtesy of Shaji Kumar, MD

MAYO CLINIC

Currently, what is your usual pretransplant induction regimen for a patient with MM and no high-risk features?

a. RVD
b. Carfilzomib/Rd (KRd)
c. CyBorD
d. MPV/daratumumab
e. RD/daratumumab
f. RVD/daratumumab
g. KRd/daratumumab
h. Other

Currently, what is your usual pretransplant induction regimen for a patient with multiple myeloma (MM) and no high-risk features?



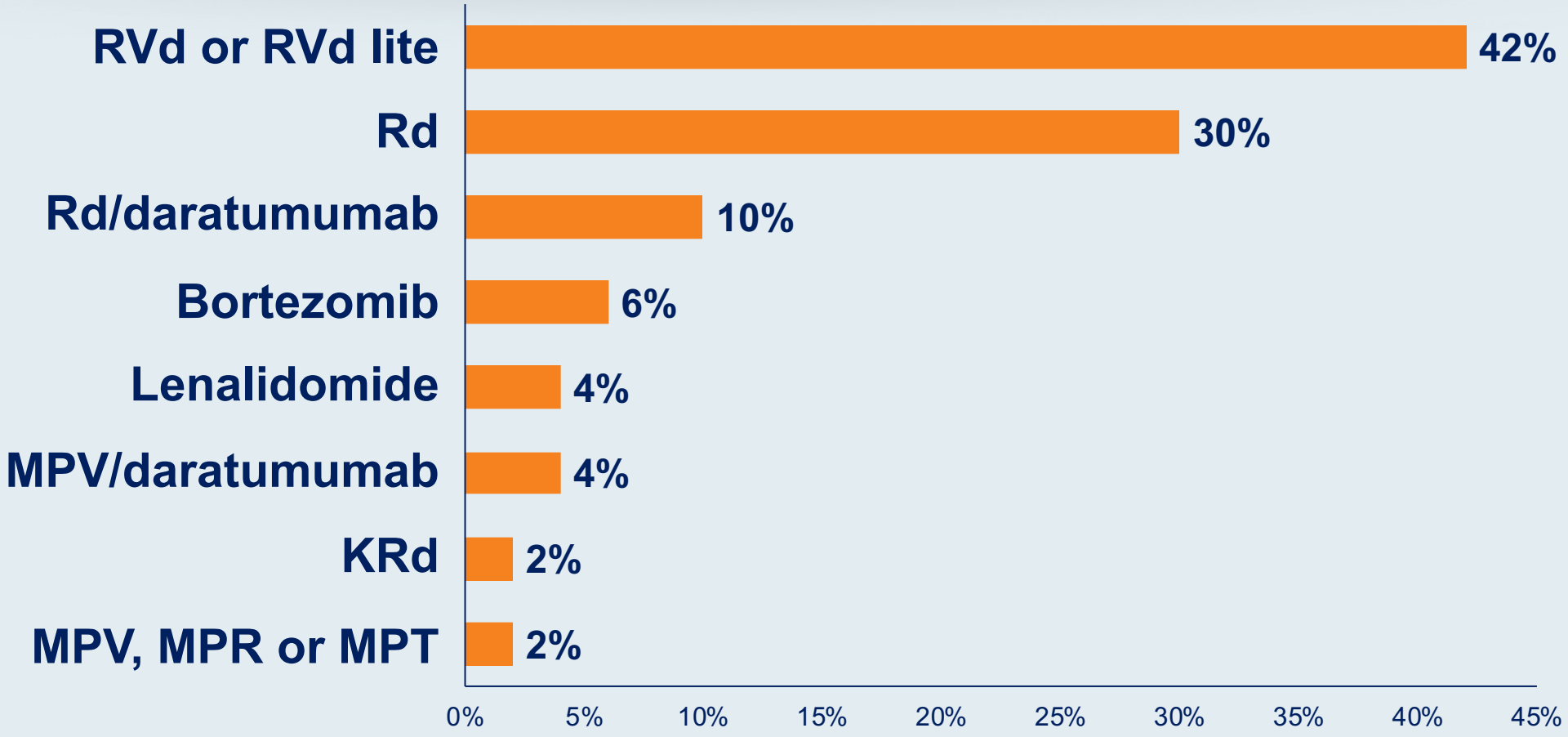
R = lenalidomide; V = bortezomib; d = dexamethasone; K = carfilzomib

Survey of 50 US-based medical oncologists.

What is your usual induction regimen for an 80-year-old patient with MM with normal renal function and no high-risk features?

a. Lenalidomide
b. Rd
c. Bortezomib
d. RVd or RVd lite
e. KRd
f. MPV/daratumumab
g. Rd/daratumumab
h. Other

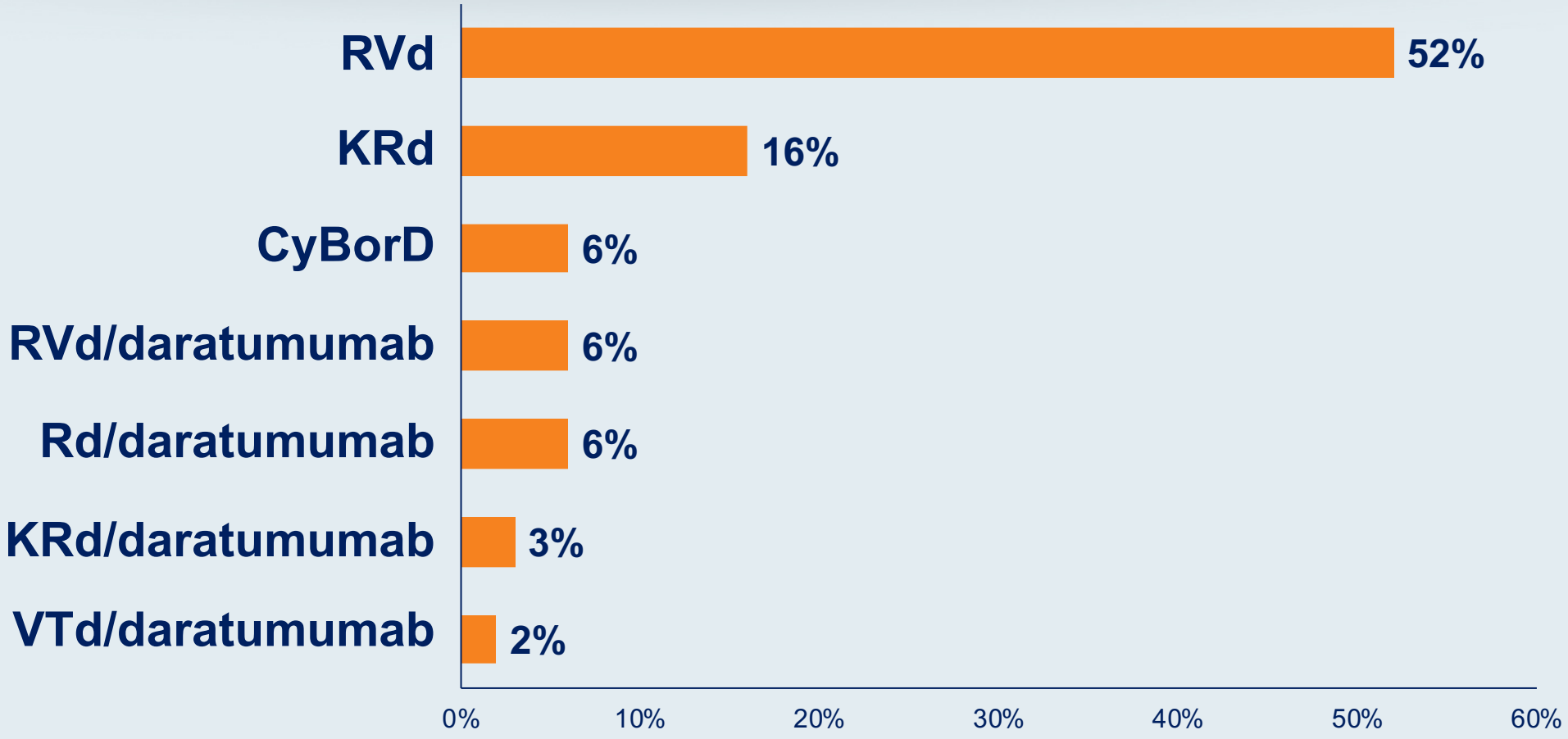
What is your usual induction regimen for an 80-year-old patient with MM, normal renal function and no high-risk features?



M = melphalan; V = bortezomib; d = dexamethasone; P = prednisone; R = lenalidomide; T = thalidomide

Survey of 50 US-based medical oncologists.

Regulatory and reimbursement issues aside, what is your preferred pretransplant induction regimen for a 65-year-old patient with MM and del(17p)?



Survey of 50 US-based medical oncologists.

Case Presentation – Dr Kumar: 67-Year-Old Man with Newly Diagnosed MM

- 67-year-old male presents with low back pain, X-rays shows lytic lesions
- Additional work up:
- Hb: 11.2 g/dL, normal EBC, Platelets
- Serum creatinine: 1.1 mg/dL, normal calcium.
- Serum protein electrophoresis: 2.1 g/dL IgG kappa monoclonal protein
- Bone marrow: 40% plasma cells, FISH: t(4;14), otherwise normal
- PET: multiple FDG avid lesions, no soft tissue involvement
- What is the next step?

Therapy of newly diagnosed MM: key considerations

Patient characteristics

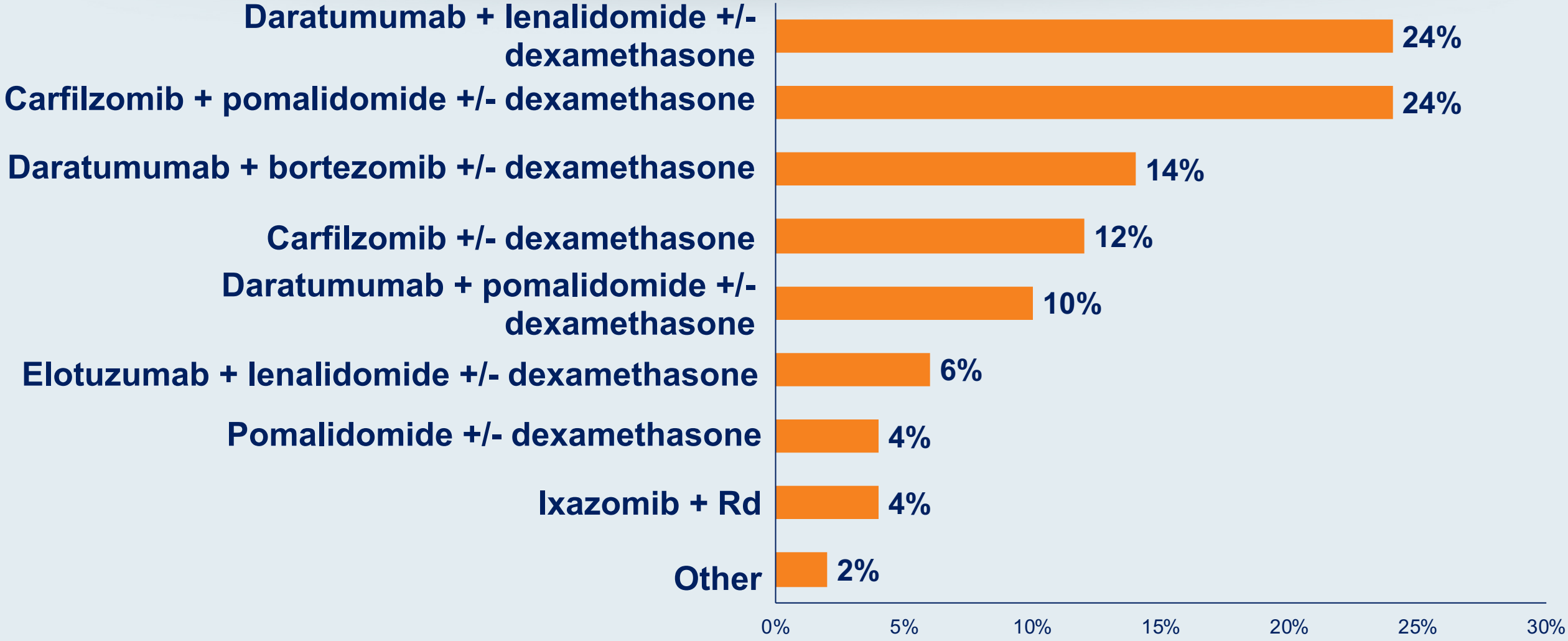
- Age
- Frailty/performance status
- Co-morbidities
  - Diabetes
  - Neuropathy
  - CAD
- Social support
- Cost / insurance issues

Disease characteristics

- Disease complications
  - Renal failure
  - Neurological complications
- Extramedullary disease
  - PCL, EMD
- Risk stratification
  - RISS
  - Others

Courtesy of Shaji Kumar, MD

What is your usual treatment recommendation for a patient with MM treated with RVd → autologous stem cell transplant and maintenance lenalidomide for 1.5 years who then experiences an asymptomatic biochemical relapse?



Survey of 50 US-based medical oncologists.

Case Presentation – Dr Kumar: A 72-Year-Old Woman with Standard Risk, R/R MM

- 72-year-old female, diagnosed with standard risk MM 6 years ago
- Induction with VRd for 4 cycles followed by single autologous SCT
- Achieved a CR, and started lenalidomide maintenance
- Relapsed after 3 years, started on daratumumab + bortezomib and dexamethasone: on maintenance daratumumab
- Achieved a VGPR, now with new back pain and PET shows new FDG avid lesions
- What would be the next step?

When should we start treatment for relapse?

- Patients with clinical progression/ CRAB clearly needs treatment
- Those with biochemical progression only may not need immediate treatment
  - Standard risk disease with slow trend up
- Treatment indicated in:
  - High risk disease with any progression
  - Presentation with renal or neurological complications
  - Rapid doubling of M spike

Courtesy of Shaji Kumar, MD

MAYO CLINIC

General principles

- Duration of initial response defines biology
- Triplet (two active classes + dex) preferred over doublet
  - At least one drug from a non-refractory class
- Consider PS, age and comorbidities when selecting drug/ doses
- Take into account prior toxicities/ residual toxicities
- Treat to maximum response and maintain on one drug till progression or tolerability

Courtesy of Shaji Kumar, MD

How do we select treatment?

- Prior drug exposure/ refractory status
- High risk vs. standard risk
- Age, frailty and comorbidity
- Toxicity with prior drugs
- Transplant eligibility/ prior transplant
- Patient preference/ goals of care
- Logistics of drug administration

Courtesy of Shaji Kumar, MD

MAYO CLINIC

Selecting the optimal regimen

Lenalidomide refractory, bortezomib sensitive

Bortezomib based
Dara-bortezomib-Dex Selinexor-Bortezomib-Dex Elotuzumab-Bortezomib-dex Panobinostat-Bortezomib-Dex

Pomalidomide based
Pomalidomide-bortezomib-Dex
Elo-Pom Dex

Bortezomib refractory, Lenalidomide sensitive

Carfilzomib based
Carfilzomib-lenalidomide-Dex

IMiD based
Elotuzumab-lenalidomide-dex

Lenalidomide AND Bortezomib refractory

Carfilzomib based
Carfilzomib-Dara-Dex
Carfilzomib-Isatuximab-Dex
Carfilzomib-Pom Dex

MoAb based
Dara-Pom-Dex
Isa-Pom Dex

Other
Selinexor

Courtesy of Shaji Kumar, MD

MAYO CLINIC

Risk stratification

- Duration of initial response/ primary refractory disease
- Acquisition of new abnormalities (1qamp, del17p)
- ISS/RISS
- Performance status
- Presence of EMD
- Circulating plasma cells

Courtesy of Shaji Kumar, MD

MAYO CLINIC

What should we do for high risk?

- Multi-drug combination (triplets)
- Use drug classes that patient has not been exposed to
- Treat to maximum response, maintain with one/both drugs (no dex)
- MRD negativity leads to better outcomes
- Certain drug classes may be more relevant

Courtesy of Shaji Kumar, MD

Impact of toxicity with prior treatments/ comorbidities

- Peripheral neuropathy
  - avoid bortezomib
  - Consider carfilzomib, ixazomib if PI desired
- Cardiac failure
  - Avoid carfilzomib, anthracyclines
- Renal insufficiency
  - Dose adjust/ avoid lenalidomide
- Skin reaction with IMiDs
  - If severe skin reaction, avoid this class

Courtesy of Shaji Kumar, MD

MAYO CLINIC

Patient preference/ logistics

- All oral regimens allow less frequent clinic visits
  - However, compliance needs to be monitored
- IV infusions require clinic visit
  - Frequency of administration important factor
  - IV versus SQ has significant impact on patient choice
- Combinations with less hematological toxicity will allow for less frequent testing and clinic visits

Courtesy of Shaji Kumar, MD

MAYO CLINIC

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- BCMA-targeted therapy
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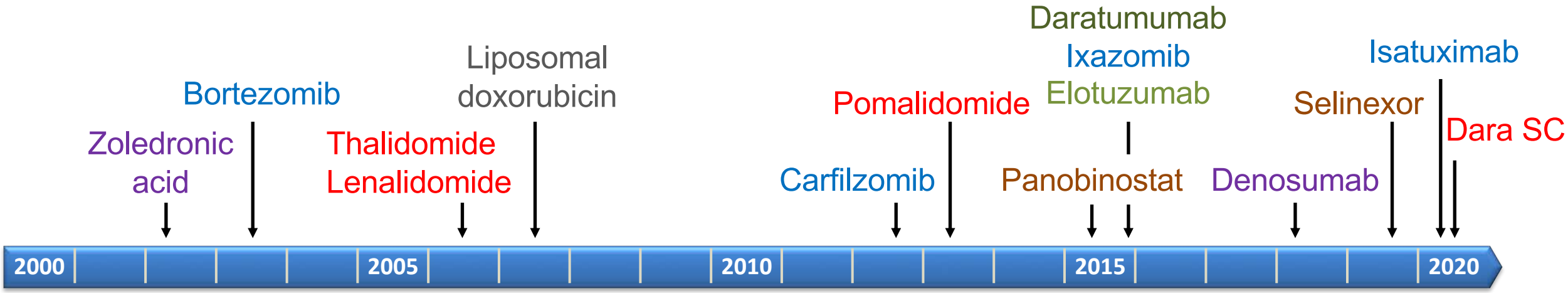
Myeloma Drugs Approved Since 2000



Initial FDA approval date in multiple myeloma

Courtesy of Noopur Raje, MD

Standard Practice in 2020

- Triplets in newly-diagnosed patients: RVD/KRD/VCD
  - Phase II trial (2010)[1]
  - Phase III data from SWOG S0777 (2016)[2]: RVd > Rd
  - Phase II data (2013/2016)[3]
- Transplant and maintenance SOC[4]
- Daratumumab initially approved in 2015 in patients with ≥3 prior lines of treatment
  - Now approved in first line with VMP[5]
    Dara-Rd vs Rd (MAIA)[6]
  - Ongoing trials comparing and Dara-RVd vs RVd (GRIFFIN)
- Triplets such as KRd or PVD > doublets[7,8]
- **Continuous therapy is the accepted treatment paradigm for myeloma**

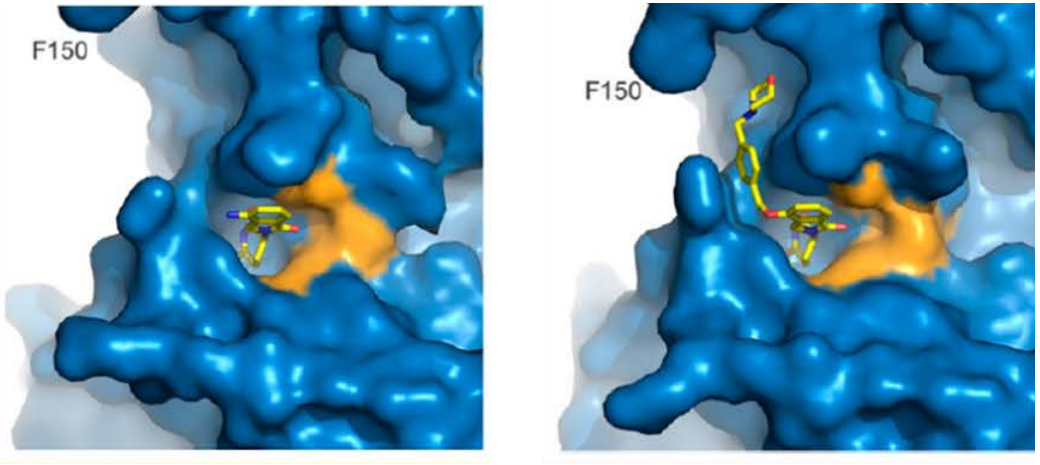
1. Richardson PG, et al. *Blood*. 2010; 2. Durie BGM, et al. *Lancet*. 2017; 3. Jakoboviak A, et al. *Blood*. 2013; 4. McCarthy A. *N Engl J Med*. 2015;
5. Mateos MV, et al. *N Engl J Med*. 2018; Facon T, et al. *N Engl J Med*. 2019; 7. Stewart AK, et al. *N Engl J Med*. 2015; 8. Richardson PG, et al. ASCO. 2018.

Courtesy of Noopur Raje, MD

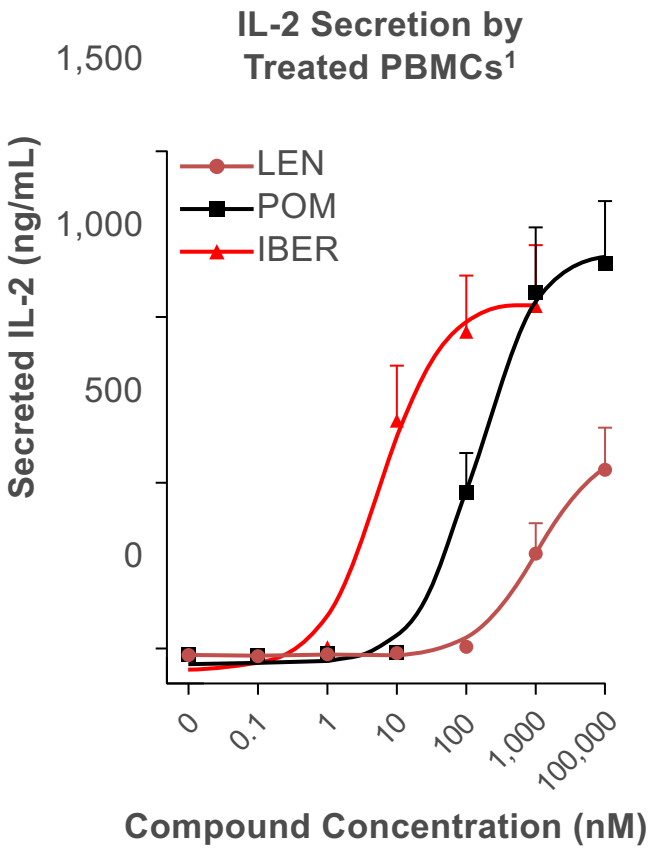
Iberdomide: Mechanism of Action

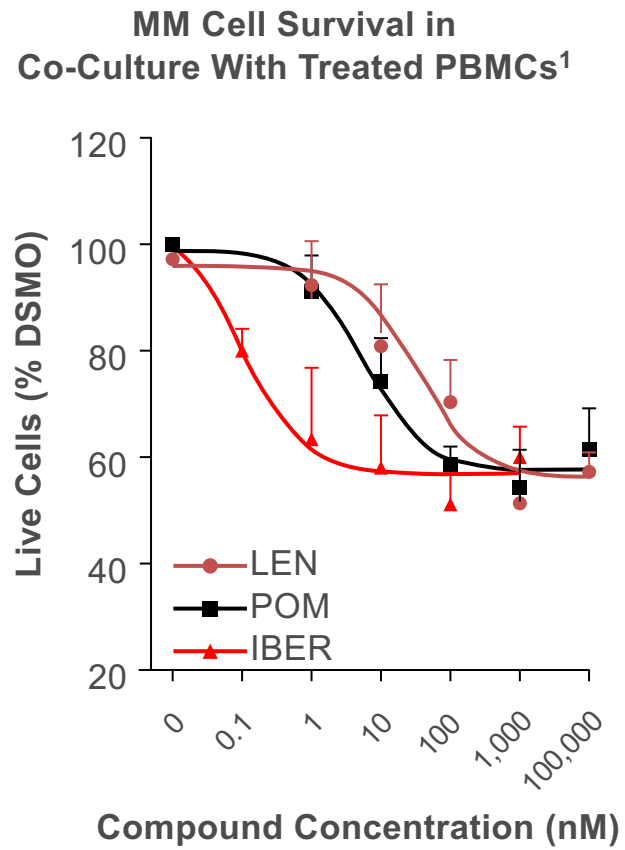
Iberdomide enhances in vitro immune stimulatory activity versus lenalidomide and pomalidomide[1]

LEN[2] **IBER[2]**



EC_{50}, nM[2]	Ikaros	Aiolos
LEN	67	87
POM	24	22
IBER	1	0.5





1. Bjorklund CC, et al. Unpublished data. 2. Matyskiela ME, et al. J Med Chem. 2018;61:535-542

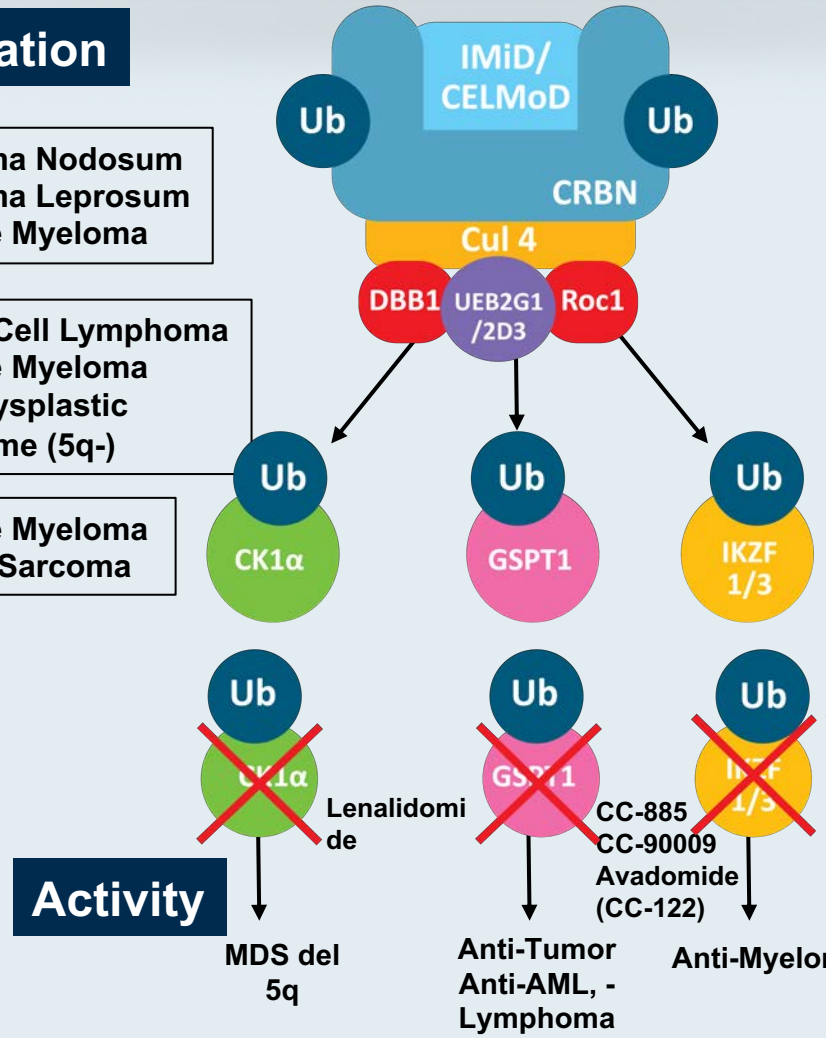
Courtesy of Noopur Raje, MD

First-in-Human Phase I Study of the Novel CELMoD Agent CC-92480 Combined with Dexamethasone (DEX) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM)

Richardson PG et al.
ASCO 2020;Abstract 8500.

CC-92480/Dexamethasone Combined with Bortezomib or Daratumumab or Carfilzomib

IMiD®	Indication
Thalidomide	Erythema Nodosum Erythema Leprosum Multiple Myeloma
Lenalidomide	Mantle Cell Lymphoma Multiple Myeloma Myelodysplastic Syndrome (5q-)
Pomalidomide	Multiple Myeloma Kaposi Sarcoma



Clinical trials	CELMoDs®
Multiple Myeloma Diffuse Large B-Cell Lymphoma CNS Lymphoma Glioblastoma Hepatocellular Carcinoma Chronic Lymphocytic Leukemia	CC-122
Multiple Myeloma Systemic Lupus Erythematosus	CC-220
Acute Myeloid Leukemia	CC-90009
Multiple Myeloma	CC-92480 Indisulam
Acute Myeloid Leukemia? (in vitro)	CC-885

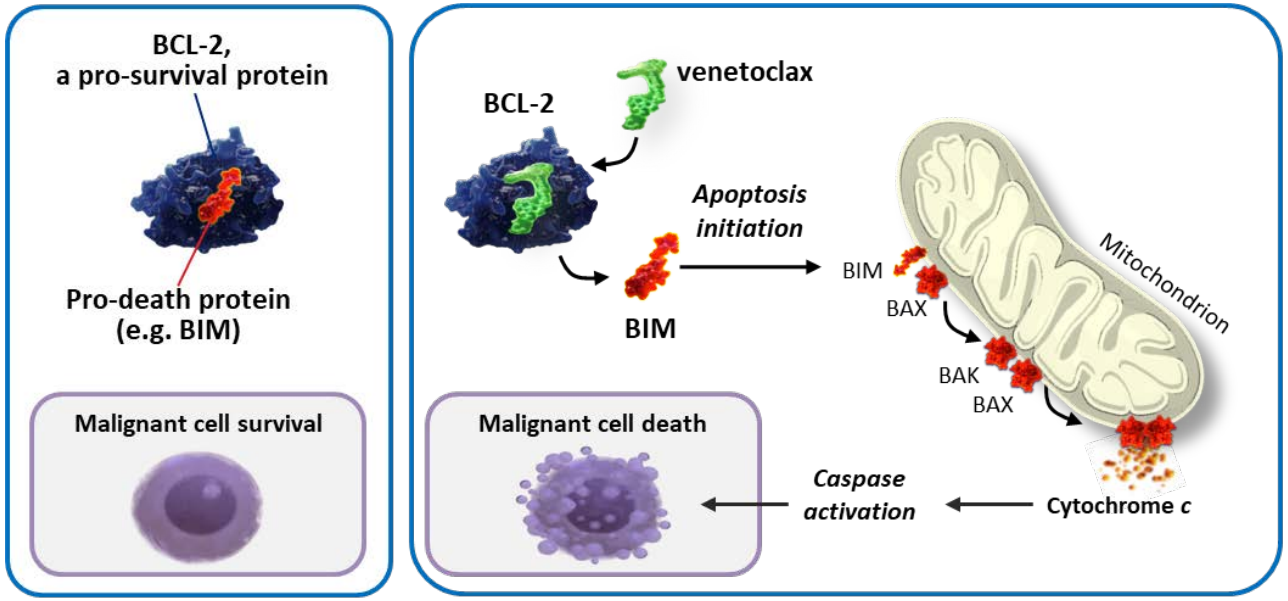
Abbreviation: CK1a: casein kinase 1a;
CELMods: Cereblon E3 Ligase Modulation Drugs;
CRL4: cullin-4 RING E3 ligase;
CRBN: Cereblon; CNS: Central Nervous System;
CUL4: Cullin-4; DDB1: DNA damage-binding protein 1;
GSPT1: G1 To S Phase Transition 1;
IKZF1: Ikaros zinc-finger protein 1;
IKZF3: Aiolos zinc-finger protein 3;
IMiDs: Immunomodulatory Drugs;
MDS: Myelodysplastic Syndrome;
Roc1: Ring finger protein;
UB: Ubiquitination
UBE2G1/2D3: Ubiquitin-conjugating enzymes

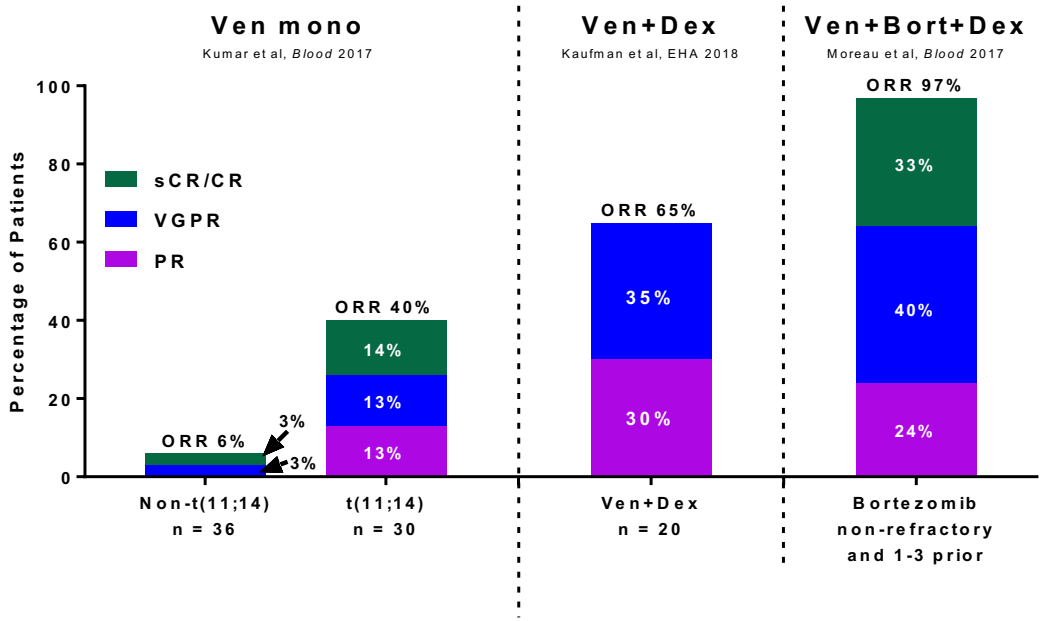
Holstein et al, Next-Generation Drugs. Targeting the Cereblon Ubiquitin Ligase. JCO 2018.
Lu G et al eLife 2018
Gandhi AK et al Br Haem 2014
Krönke J et al Science 2014
Hansen JD et al J Med Chem 2020
Uehara, T et al Nat Chem Biol 2017

McCarthy P. ASCO 2020 Discussant

Venetoclax Targets BCL-2 in Multiple Myeloma

- Pro-survival proteins BCL-2, MCL-1, and BCL-X_L promote multiple myeloma (MM) cell survival
- Venetoclax (Ven) is a selective, potent, oral BCL-2 inhibitor
- Ven had encouraging clinical efficacy in t(11;14) MM as monotherapy and in a broader patient population in combination with Bd, with a tolerable safety profile in Phase 1 studies

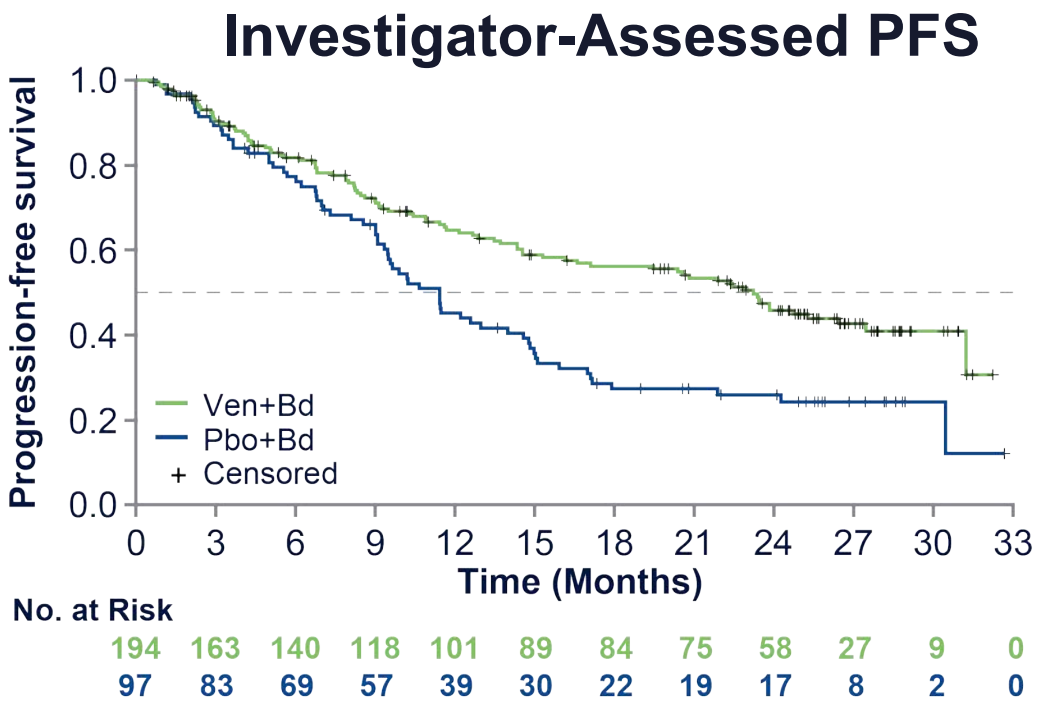


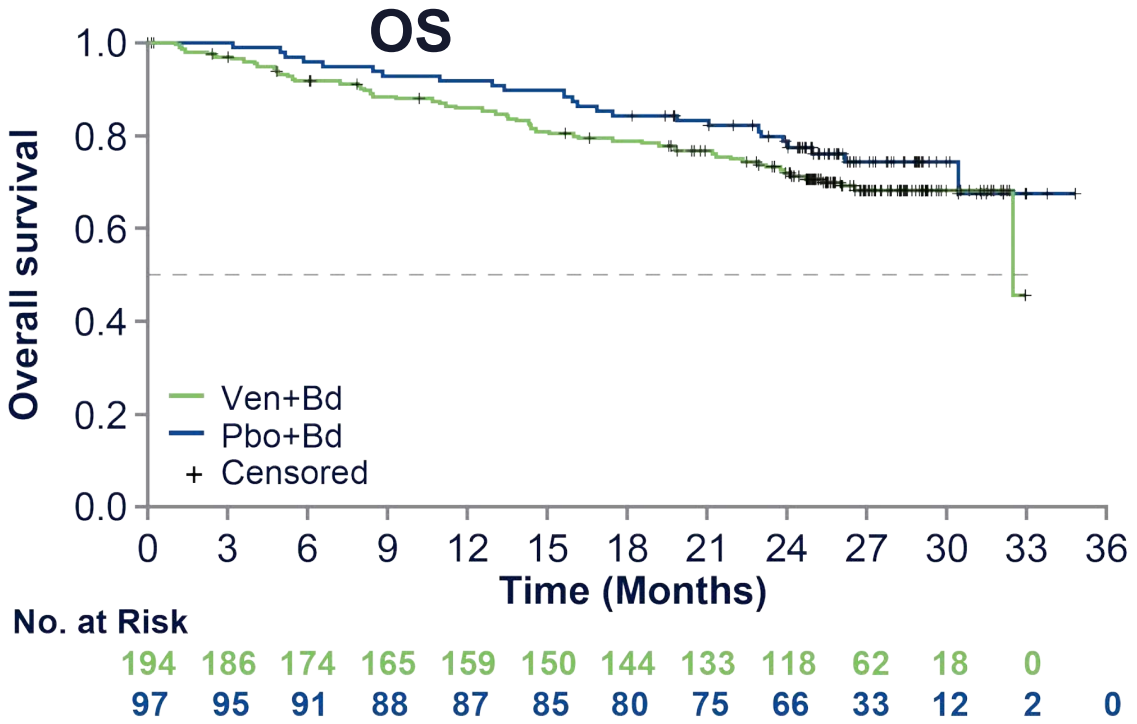


Courtesy of Noopur Raje, MD

BELLINI TRIAL Update:

PFS and OS in All Patients (ITT)





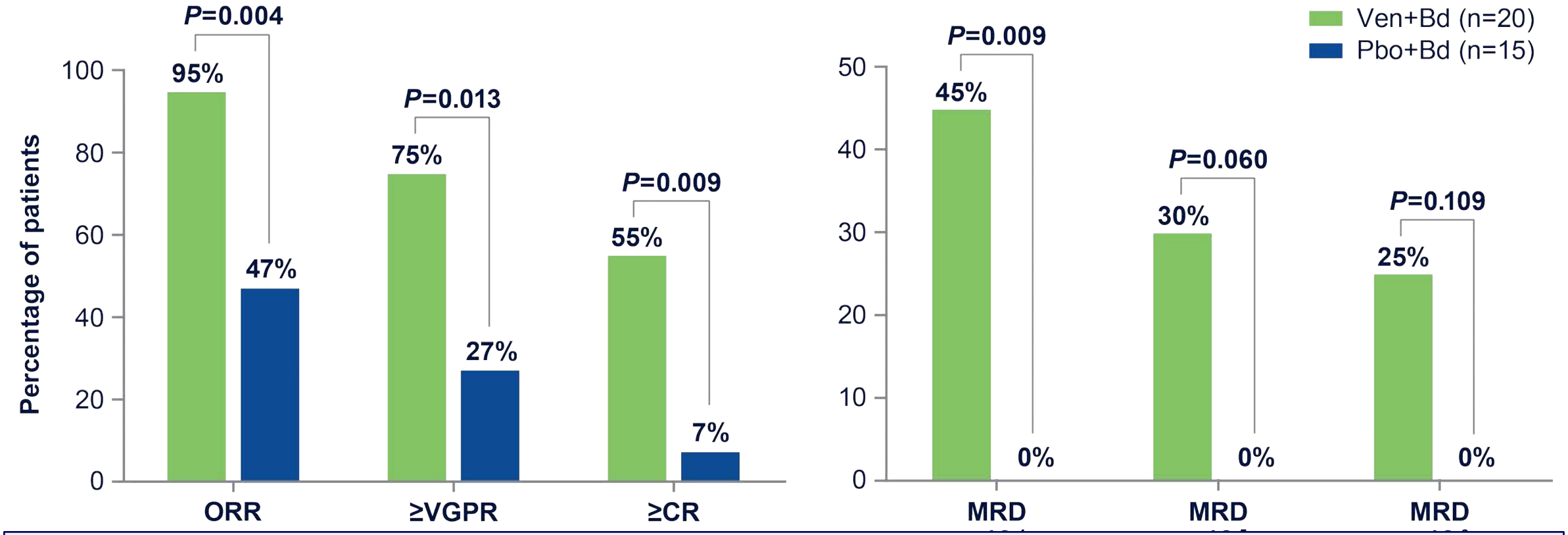
PFS	Ven+Bd	Pbo+Bd
Median, months	23.2	11.4
HR (95% CI)	0.60 (0.44, 0.83)	
P value	0.001	

OS	Ven+Bd	Pbo+Bd
Median, months	32.5[a]	Not reached
HR (95% CI)	1.32 (0.82, 2.12)	
P value	0.256	

Clinical Data Cutoff: 15 Jul 2019

Courtesy of Noopur Raje, MD

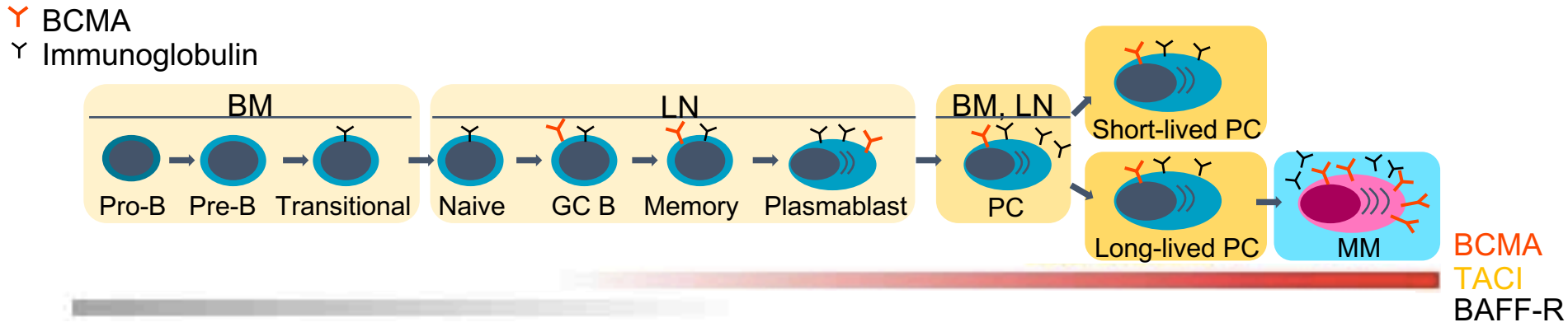
Clinical Response Rates and MRD Negativity Rates in Patients with t(11;14)

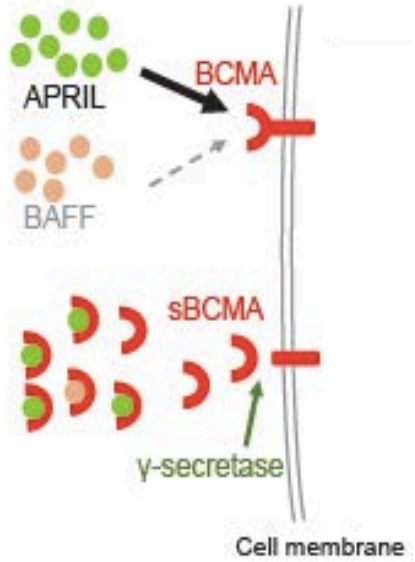


Patients with t(11;14) achieved higher rates of response, including MRD negativity with venetoclax compared with placebo

Courtesy of Noopur Raje, MD

BCMA as target for myeloma therapy





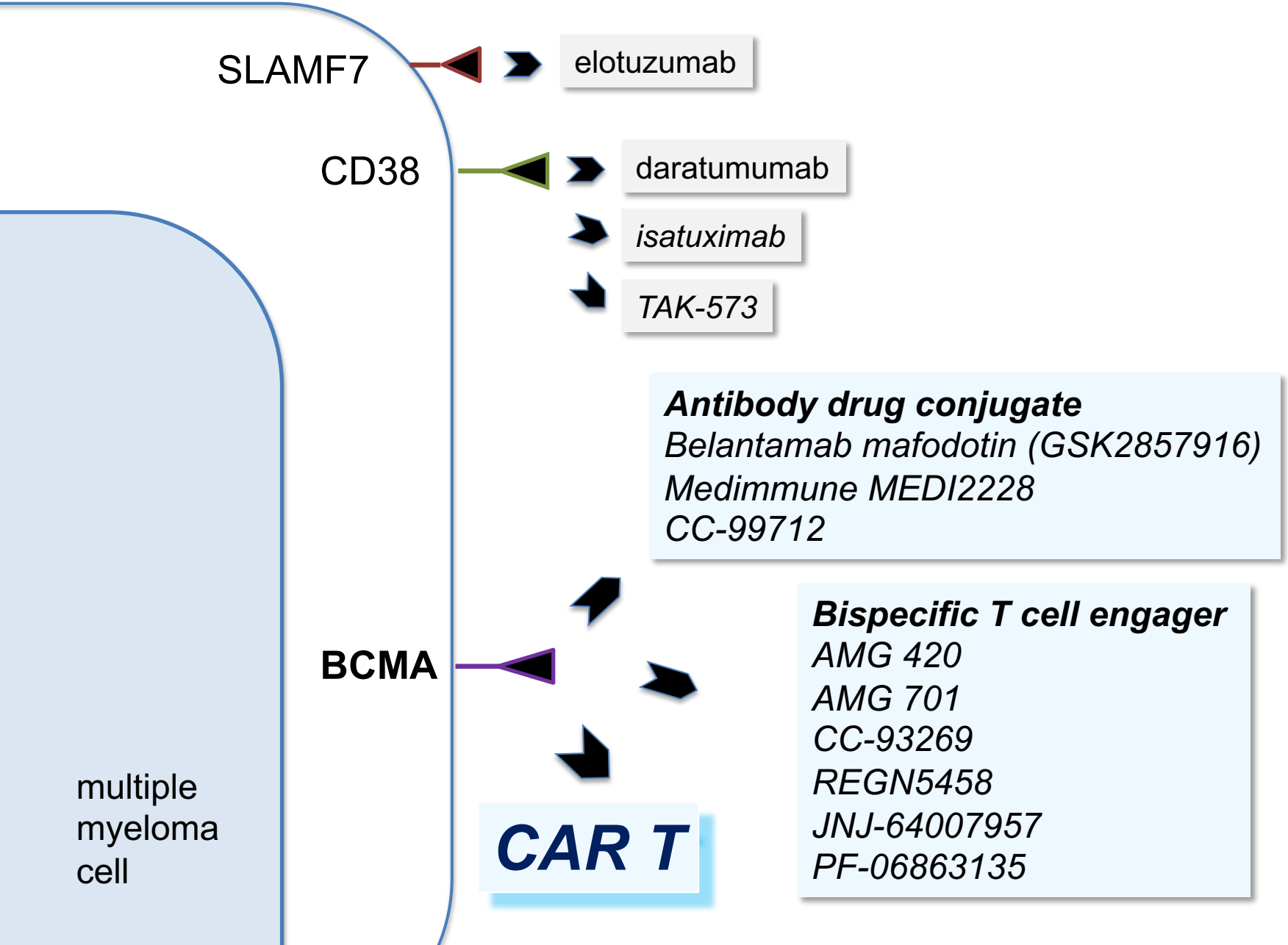
- BCMA is an antigen expressed specifically on PCs and myeloma cells
- Cell surface receptor of TNF superfamily
- Higher expression in myeloma cells than normal PCs
- Not expressed in other tissues
- Key role in B-cell maturation and differentiation
- Promotes myeloma cell growth, chemotherapy resistance, and immunosuppression in the bone marrow microenvironment
- Expression of BCMA increases as the disease progresses from MGUS to advanced myeloma
- Additional ligands for BMCA include APRIL and TACI

APRIL, a proliferation-inducing ligand; BAFF-R, B-cell activating factor receptor; GC, germinal center; sBCMA, soluble BCMA; TACI, transmembrane activator and CAML interactor.

Courtesy of Noopur Raje, MD

Cho SF et al., *Front Immunol* 2018;9:1821. Moreaux J et al. *Blood* 2004;103:3148-57. Sanchez E et al., *Br J Haematol* 2012;158:727-38.

Therapies targeting BCMA



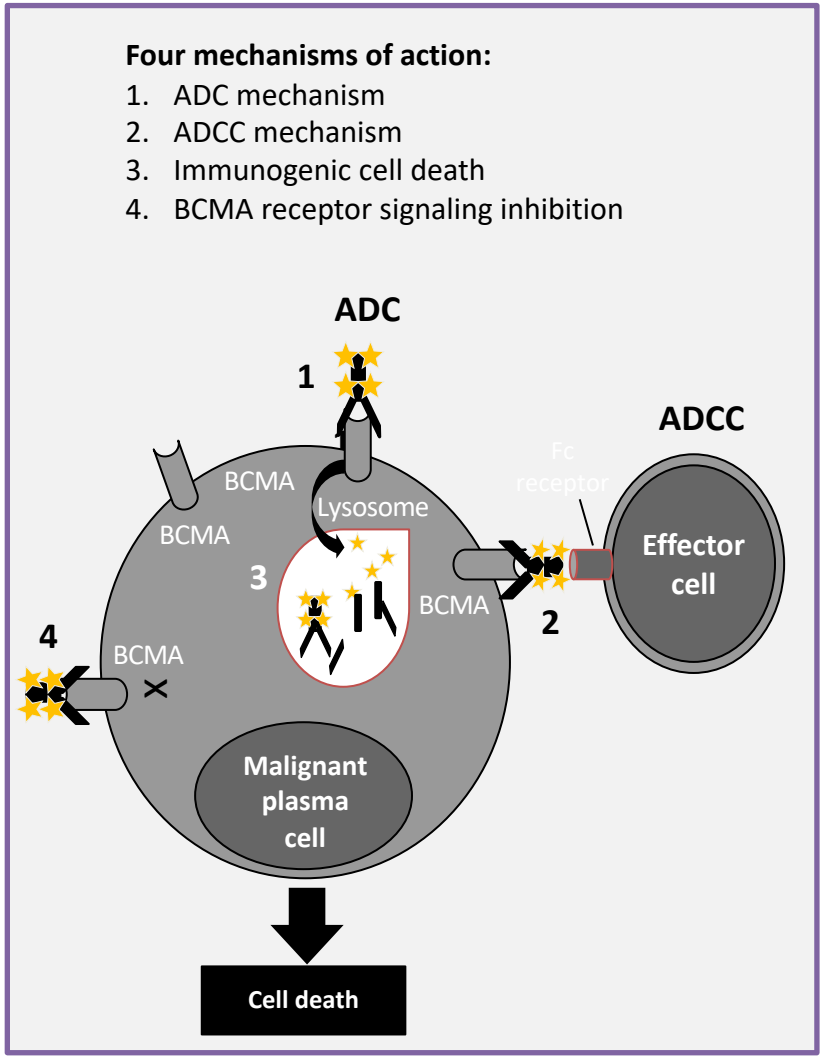
Courtesy of Noopur Raje, MD

Belantamab Mafodotin

- **GSK2857916**: humanized, afucosylated IgG1 **anti-BCMA conjugate antibody**; neutralization of soluble BCMA
  - Preclinical studies demonstrate its selective and potent activity[1]

GSK2857916[1,2]

Cytotoxic agent	–MMAF (non-cell permeable, highly potent auristatin
Afucosylation	–Enhanced ADCC
Linker	–Stable in circulation

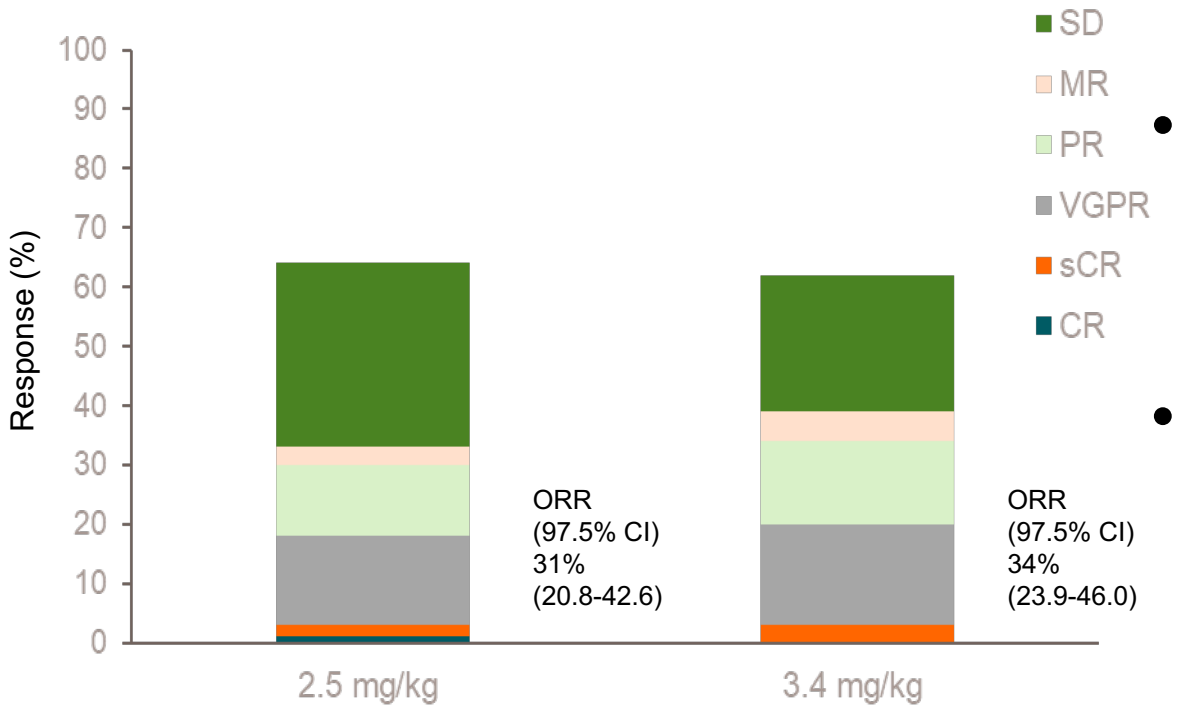


ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; BCMA, B-cell maturation antigen; IgG, immunoglobulin G; MMAF, monomethyl auristatin F.

1. Tai YT, *et al. Blood* 2014;**123**(20):3128–38;
2.Trudel S, *et al.* Abstract 741; Presented at ASH 2017; Atlanta, Georgia., Lancet Oncology 2018

Courtesy of Noopur Raje, MD

Belantamab Mafodotin: Interim Phase 2 Results



- Overall IRC-assessed ORR with 2.5 mg/kg (N = 97): 31% (97.5% CI, 20.8-42.6)
- Overall IRC-assessed ORR with 3.4 mg/kg (N = 99): 34% (97.5% CI, 23.9-46.0)

Lonial S, et al. *Lancet Oncol* 2019;21(2):2017-221

Courtesy of Noopur Raje, MD

Belantamab Mafodotin: Safety Results

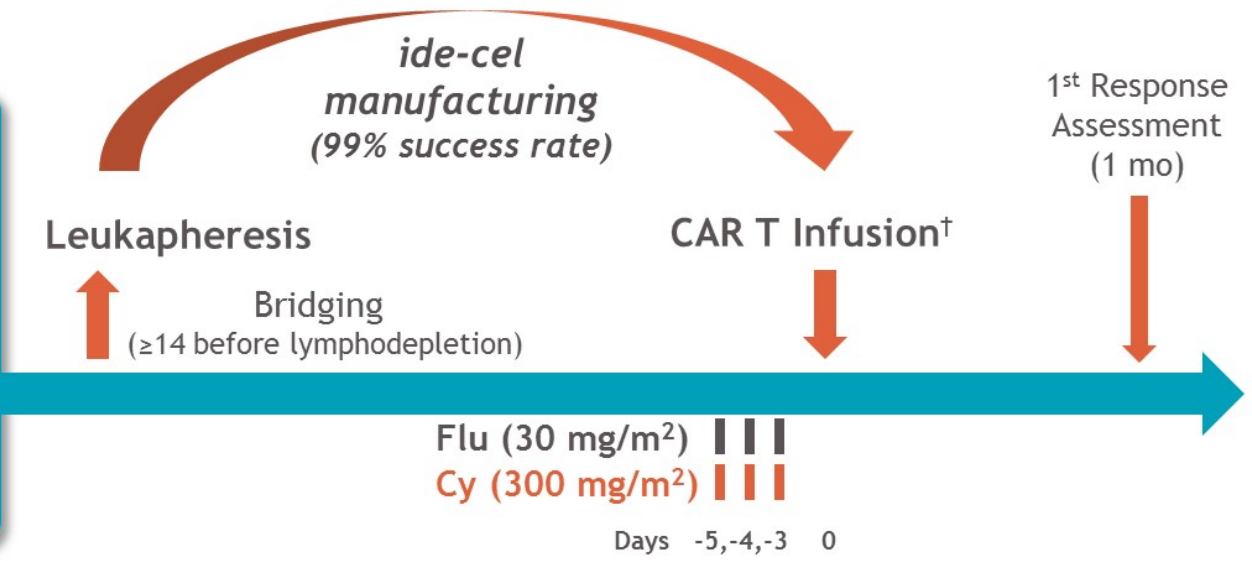
- Overall, serious AEs occurred in 40% of patients in the 2.5 mg/kg cohort and 47% in the 3.4 mg/kg cohort
- The most common grade 3/4 AEs associated with belantamab mafodotin were keratopathy, thrombocytopenia, and anemia
- AEs of special interest included:
  - Thrombocytopenia (occurred in 35% and 59% of the cohorts, respectively)
  - Infusion-related reactions (21% and 16%)
  - Keratopathy/corneal events (71% and 75%)

Lonial S, et al. *Lancet Oncol* 2019;21(2):2017-221

Courtesy of Noopur Raje, MD

Phase II Pivotal KarMMa Study of Ide-cel

- RRMM
- ≥3 prior regimens with ≥2 consecutive cycles each (or best response of PD)
- Previously exposed to:
  - IMiD agent
  - Proteasome inhibitor
  - Anti-CD38 antibody
- Refractory to last prior therapy per IMWG*



Endpoints

- **Primary**: ORR (null hypothesis ≤50%)
- **Secondary**: CRR (key secondary; null hypothesis ≤10%), Safety, DOR, PFS, OS, PK, MRD‡, QOL, HEOR
- **Exploratory**: Immunogenicity, BCMA expression/loss, cytokines, T cell immunophenotype, GEP in BM

Study Status as of Jan 14, 2020

Screened N=158

Leukapheresed N=140

Treated N=128
(Target Dose CAR+ T cells)

150 × 10⁶	n=4
300 × 10⁶	n=70
450 × 10⁶	n=54

Median Follow-up (mo)

150 × 10⁶	18.0
300 × 10⁶	15.8
450 × 10⁶	12.4
Total	13.3

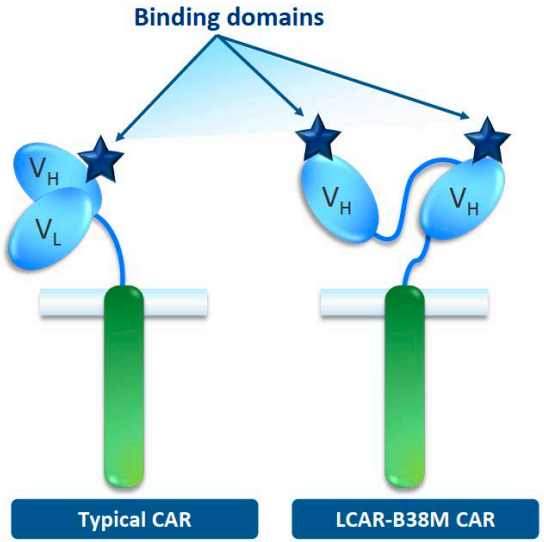
CRR, complete response rate; Cy, cyclophosphamide; DOR, duration of response; Flu, fludarabine; GEP in BM, gene expression profile in bone marrow; HEOR, health economics and outcomes research; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PK, pharmacokinetics; QOL, quality of life.
*Defined as documented disease progression during or within 60 d from last dose of prior antimyeloma regimen. †Patients were required to be hospitalized for 14 d post-infusion. Ide-cel retreatment was allowed at disease progression for best response of at least stable disease. ‡By next-generation sequencing.

EudraCT: 2017-002245-29
ClinicalTrials.gov: NCT03361748

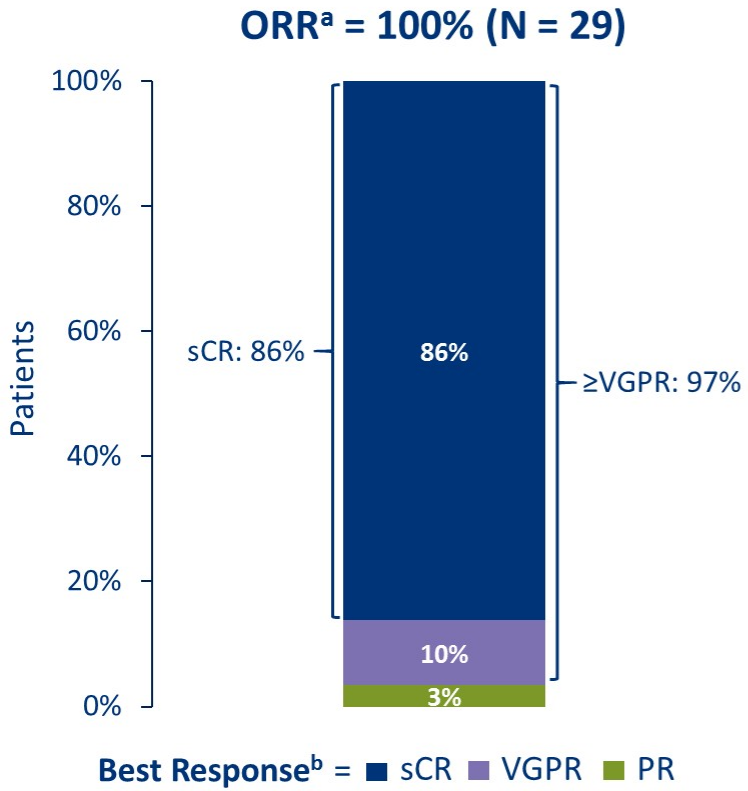
Courtesy of Noopur Raje, MD

Presented By Nikhil Munshi at TBD

JNJ-4528 (A BCMA-Directed CAR T-Cell Therapy)



CARTITUDE-1: Overall Response Rate



- 25 of 29 (86%) patients achieved sCR
- ORR and depth of response were independent of BCMA expression on myeloma cells at baseline
- Median time to first response = 1 mo (1 – 3)
- Median time to CR = 3 mo (1 – 13)

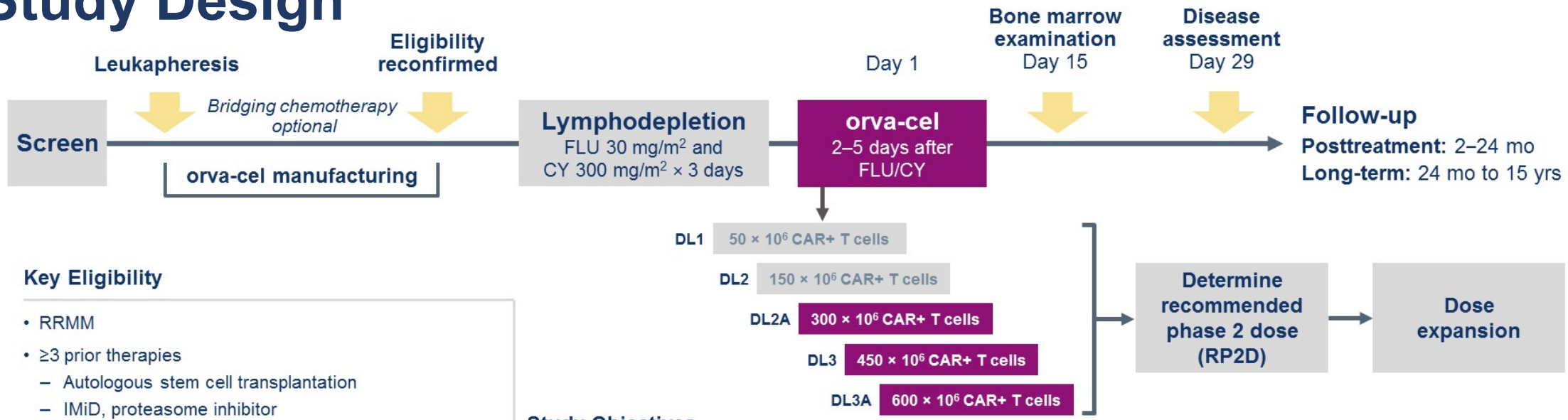
[a]PR or better; Independent Review Committee-assessed, [b]No patient had complete response, stable disease, or progressive disease as best response. CR=complete response; ORR=overall response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

56th ASCO Annual Meeting 2020, Berdeja et al. Abstract #8505

Courtesy of Noopur Raje, MD

Presented By Jesus Berdeja at ASCO 2020

EVOLVE Trial of Orvacabtagene Autoleucel (Orva-cel): Study Design



Key Eligibility

- RRMM
- ≥3 prior therapies
  - Autologous stem cell transplantation
  - IMiD, proteasome inhibitor
  - Anti-CD38 (combination or monotherapy)
- Refractory to last line of therapy
- ECOG performance status 0–1
- CrCl ≥60 ml/min, ANC ≥1000 cells/mm^3, PLT ≥50/mm^6, Hb ≥8 g/dL
- No selection based on BCMA expression
- BCMA cohort: relapse after prior anti-BCMA directed therapy at any time

Study Objectives

Phase 1

Primary

- To evaluate safety and tolerability (DLTs, adverse events)
- To determine a recommended phase 2 dose (RP2D)

Secondary

- To determine orva−cel pharmacokinetics (C_{max}, T_{max}, AUC)
- To evaluate preliminary antitumor activity

Phase 2

Primary

- To evaluate the antitumor activity of orva−cel, as determined by ORR, at the RP2D

ANC, absolute neutrophil count; AUC, area under the curve; BCMA, B-cell maturation antigen; C_{max}, maximum concentration; CrCl, creatinine clearance; CY, cyclophosphamide; DL, dose level; DLT, dose-limiting toxicity; FLU, fludarabine; Hb, hemoglobin; IMiD, immunomodulatory agent; MRD, minimal residual disease; ORR, objective response rate; PLT, platelet; T_{max}, time to maximum concentration.

Courtesy of Noopur Raje, MD

Presented By Sham Mailankody at ASCO 2020

Characteristic Summary of CAR T-Cell Therapies in MM

	KarMMa: idecabtagene vicleucel (n=128)	EVOLVE: orvacabtagene autoleucel (n=62)	CARTITUDE-1: JNJ-4528 (n = 29)
Age	61 (33-78)	61 (33-77)	60 (50-75)
High Risk Cytogenetics, %	35	41*	27
Tumor Burden in BM, %	>50% PC = 51	—	≥60% PC = 24
Extramedullary PCs, %	39	23	10
Median prior lines of therapy	6 (3-16)	6 (3-18)	5 (3-18)
Triple refractory, %	84	94	86
Bridging therapy, %	88	63	79
Unique properties	Human BCMA, 4-1BB, CD3z	Modified spacer, CD4:CD8 enriched for CM	Median cell dose **0.72x10^6** cells/kg 2 BCMA single chain antibodies

* Included +1q21

Presented By Krina Patel at ASCO 2020

CAR T-Cell Therapy in MM

Safety

	KarMMa	EVOLVE	CARTITUDE-1
↓ANC ≥G3, %	89	90	100
↓plts ≥G3, %	52	47	69
CRS: all, ≥G3,%	84, 6	89, 3	93, 7
Med. time to CRS, duration, days	1 (1-12) 5 (1-63)	2 (1-4) 4 (1-10)	7 (2-12) 4 (2-64)
ICANS: all, ≥G3,%	17, 3	13, 3	10, 3
HLH/MAS, %	--	5	? 7 (lfts)
Infections: all, ≥G3 %	69, --	40, 13	--, 19
Toci/steroid/ anakinra use, %	52/15/0	76/52/23	79/21/21

? This was not listed at MAS/HLH, I am just speculating → could this have been early MAS

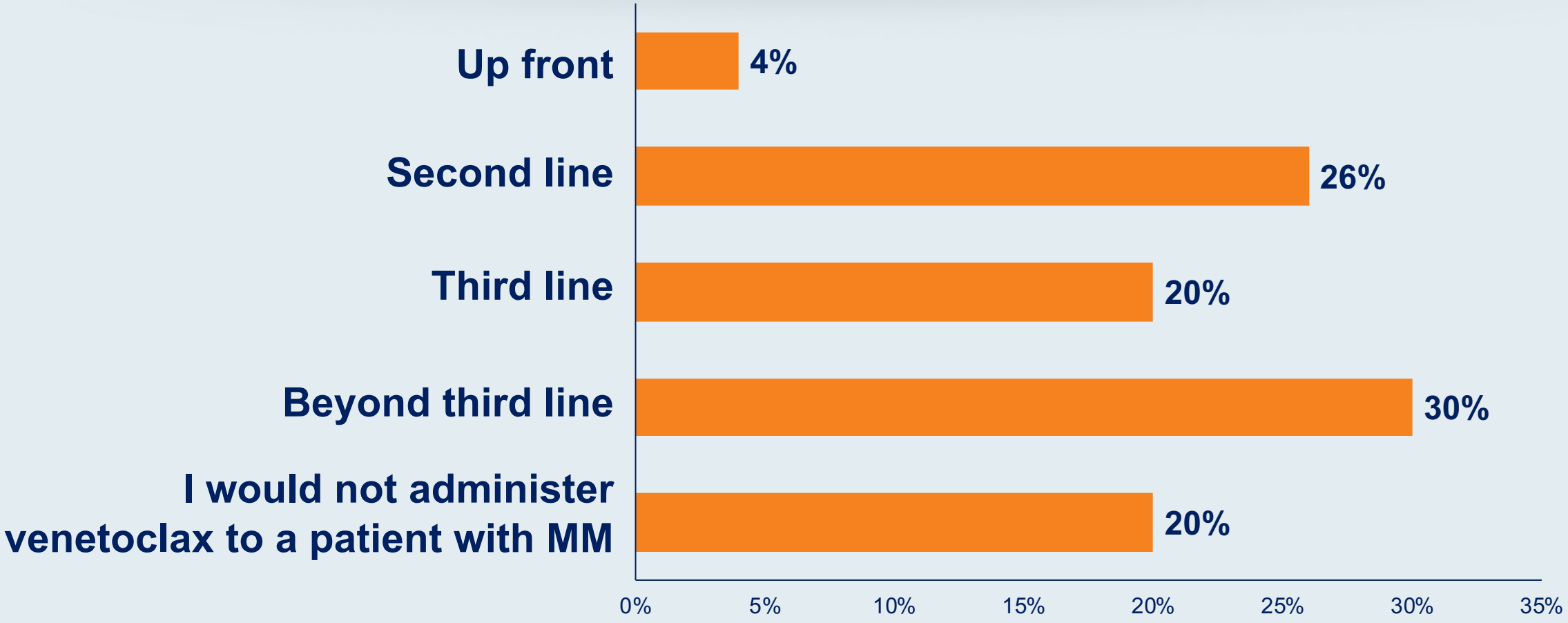
Efficacy

	KarMMa (n = 128)	EVOLVE (n = 62)	CARTITUDE-1 (n = 29)
ORR, %	73 (66-81)	92	100
sCR/CR, %	33	36	86
MRD neg ≥10^{-5}, % (of evaluable)	94	84	81
PFS/DoR, months	8.8/10.7	NR*	NR**
Screened Apheresed Treated	150 140 128	--	35 35 29

* 300 x10^6 cell dose cohort (lowest) = PFS 9.3 months, other med F/U = 8.8 and 2.3 month
** 9 mo PFS = 86%

Presented By Krina Patel at ASCO 2020

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

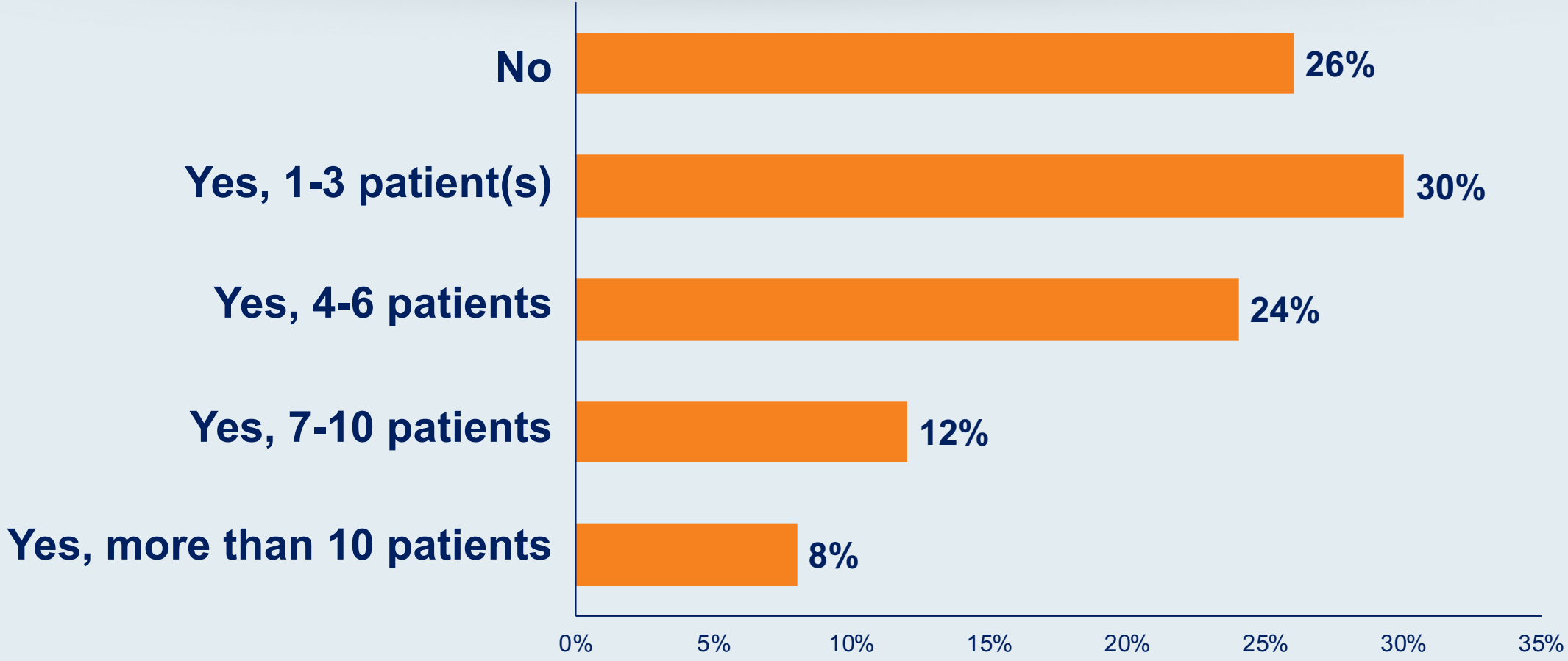


Survey of 50 US-based medical oncologists.

Is there an age beyond which you would not recommend BCMA-targeted CAR T-cell therapy for an otherwise healthy patient with relapsed MM?

a. No
b. Yes, age 70
c. Yes, age 75
d. Yes, age 80
e. Yes, age 85
f. Yes, age 90
g. Yes, age 95
h. Yes, age 100

Have you referred any patients with MM for BCMA-targeted CAR T-cell therapy?



Survey of 50 US-based medical oncologists.

Case Presentation – Dr Raje: A 70-Year-Old Man with Standard Risk, Stage II MM

- 70-yr-old male diagnosed with ISS/R-ISS stage II multiple myeloma with standard-risk CG
- Initial treatment: RVd therapy; achieved a VGPR and subsequently received HDM and autograft
  - After 26 mos of maintenance therapy, his M spike had gone up from 0.2 g/dL to 0.6 g/dL and, subsequently, to 1.0 g/dL
- Treated with carfilzomib with pomalidomide and dexamethasone; achieved a PR
- Was admitted with pneumonia and new pathological fracture with an increase in M protein to 1 g/dL
  - Started on daratumumab with bortezomib

In your current practice, which of the following therapeutic strategies would you be most likely to recommend?

a. Isatuximab
b. Selinexor
c. Anti-BCMA bispecific antibody clinical trial
d. Anti-BCMA CAR T-cell therapy clinical trial
e. Belantamab mafodotin clinical trial
f. I don’t know

Meet The Professors

Clinical Investigators Discuss Existing and Emerging Treatment Strategies for Patients with Ovarian, Cervical and Endometrial Cancer

Tuesday, July 14, 2020

12:00 PM – 1:00 PM ET

Faculty

Michael J Birrer, MD, PhD
Kathleen Moore, MD

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Thank you for joining us!

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