BCMA Who and When: Immunotherapies in Patients with RRMM

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Welcome and Introductions

Saad Z. Usmani, MD, MBA, FACP

Chief of the Myeloma Service
Member, Memorial Sloan Kettering Cancer Center
New York, NY

Amrita Krishnan, MD

Director of Judy and Bernard Briskin
Multiple Myeloma Center
Professor of Hematology/Hematopoietic
Cell Transplantation
City of Hope, Duarte, CA

Sikander Ailawadhi, MD

Professor of Medicine
Division of Hematology-Oncology
Mayo Clinic, Jacksonville, FL

Ready. Set. Poll.

Join the session using the **QR code on your table**

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Audience Question

How confident are your right now in your ability to interpret results from clinical trials evaluating the safety and efficacy of T-cell redirecting therapies as treatment for patients with multiple myeloma?

1. Not at all confident
2. Slightly confident
3. Somewhat confident
4. Fairly confident
5. Highly confident

Audience Preview Question

What is the approximate median overall survival for patients with multiple myeloma who are penta-refractory?

1. Less than 6 months
2. 1 year
3. 2 years
4. More than 3 years

Audience Preview Question

BCMA-directed CAR T-cell therapies are currently FDA-approved for patients who have received at least how many prior lines of therapy?

1. 1
2. 2
3. 3
4. 4

Unmet Need for Patients Resistant or Refractory to MM Therapies

Refractory Status	Median OS, mo
Not Triple	11.2
Triple/Quad	9.2
Penta	5.6

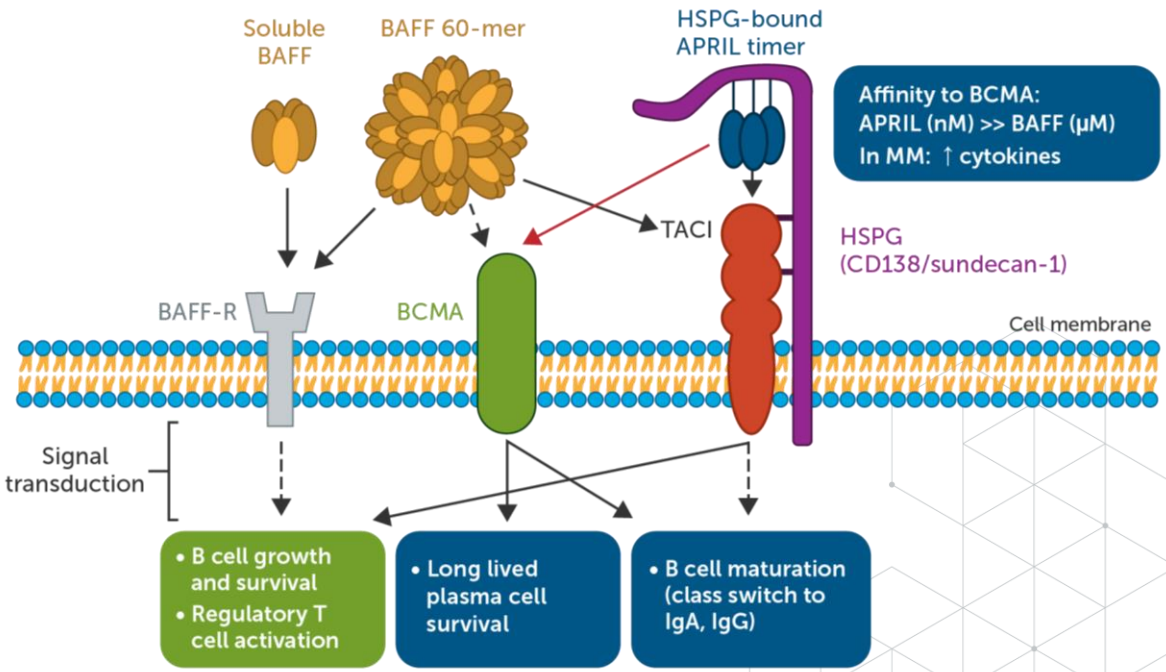
Refractory status definitions

- Not triple-refractory
  - Refractory to 1 anti-CD38 mAb (and not both PIs or immunomodulatory agents)
- Triple/Quad refractory
  - Refractory to 1 anti-CD38 mAb + 1 PI + 1 or 2 immunomodulatory agents or 1 anti-CD38 mAbs + 1 or 2 PIs + 1 immunomodulatory agent
- Penta-refractory
  - Refractory to 1 anti-CD38 mAb + 2 PIs + 2 immunomodulatory agents

Gandhi UH, et al. *Leukemia*. 2019;33(9):2266-2275.

BCMA

- B Cell Maturation Antigen (CD269, TNFRSF17) is a transmembrane glycoprotein and member of the TNFRR superfamily
- Preferentially expressed on mature B lymphocytes with limited expression on stem or nonhematopoietic cells
- Essential for survival of long-lived bone marrow plasma cells
- Overexpression and activation is associated with progression of MM



Shah N, et al. *Leukemia*. 2020;34(4):985-1005; Tai YT, et al. *Immunotherapy*. 2015;7(11):1187-1189.

FDA-Approved BCMA-Directed Therapies

Antibody-Drug Conjugate

Belantamab Mafodotin

- BCMA-directed antibody linked to the microtubule inhibitor monomethyl auristatin F
- For patients with RRMM who have received ≥ 4 prior therapies including an anti-CD38 mAb, PI, and immunomodulatory agent
- FDA-approved August 5, 2020

CAR T Cell Therapy

2 currently approved for patients with RRMM after ≥ 4 prior lines of therapies including an anti-CD38 mAb, PI, and immunomodulatory

Idecabtagene vicleucel

- FDA-approved March 26, 2021

Ciltacabtagene autoleucel

- FDA-approved February 28, 2022

Belantamab mafodotin prescribing information; Idecabtagene vicleucel prescribing information; ciltacabtagene autoleucel prescribing information.

Leveraging Community Partnerships to Optimize BCMA-Directed Therapies

Moderated Panel Discussion

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Belantamab Mafodotin

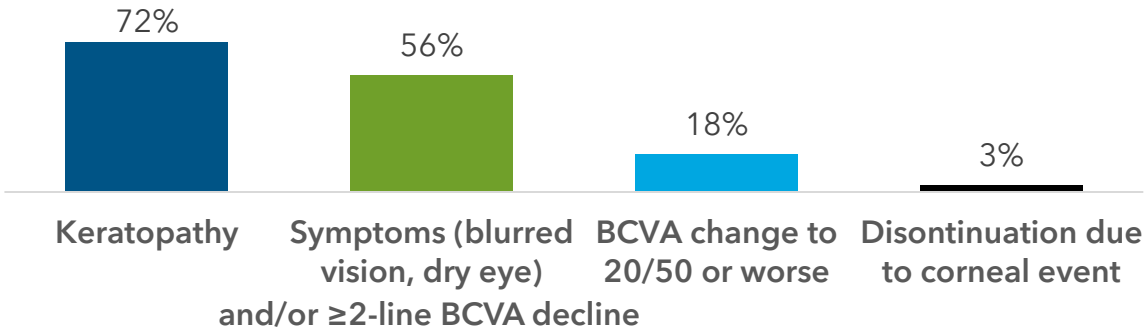
- DREAMM-2 study[1]
  - ITT population, N = 196

Heavily pretreated patient population	Belantamab Mafodotin	
	2.5 mg/kg	3.4 mg/kg
Median age, y	65	67
Median prior lines of therapy (range)	7 (3-21)	6 (3-21)
>4 prior lines of therapy, %	84	83

- Efficacy[2]
  - Efficacy between the dose cohorts was similar
  - recommended dose: 2.5 mg/kg IV q 3 wks

Efficacy in the 2.5 mg/kg cohort, n = 97 with 13-mo follow-up	Belantamab Mafodotin 2.5 mg/kg
ORR, %	32
≥ VGPR, %	19
Duration of clinical benefit, mo	11.7

- Ocular toxicities were the most common ≥gr 3 AE



1. Lonial S, et al. Lancet Oncol. 2020;21(2):207-221. 2. Lonial S, et al. Cancer. 2021;127(22):4198-4212.

Discussion Points: Belantamab Mafodotin

- Logistical advice for implementing REMS program
- When to conduct ophthalmic exams? What tests are needed?
- When to withhold or discontinue treatment?
- Other AEs of concern and management strategies
- How do you educate patients and make decisions based on individual needs?
- Which patients are the most ideal for belantamab treatment?

CAR T-Cell Therapies

Idecabtagene vicleucel[1]

Efficacy	Ide-cel, N=128
ORR, %	73
≥CR, %	33
Median DOR, mo	4.5
Median PFS, mo	8.8

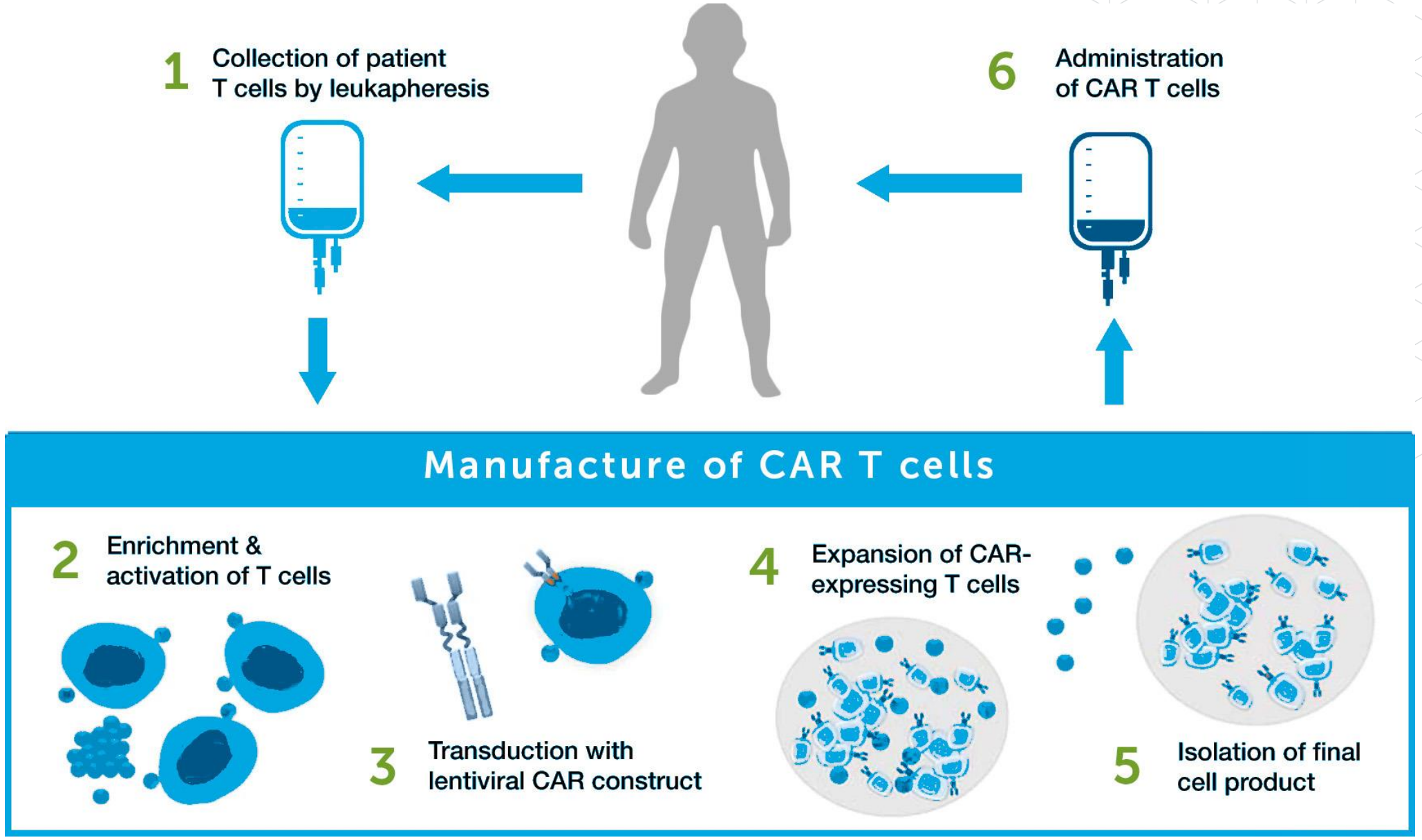
AEs of Interest	Any gr	≥ gr 3
CRS, %	84	5
Total NT, %	18	3

Ciltacabtagene autoleucel[2]

Efficacy	Cilta-cel, N=97
ORR, %	98
sCR, %	83
Median DOR, mo	NE
Median PFS, mo	NR

AEs of Interest	Any gr	≥ gr 3
CRS, %	95	5
ICANS, %	17	2
Other NT, %	12	9

1. Munshi NC, et al. N Engl J Med. 2021;384(8):705-716; 2. Martin T, et al. ASH 2021;138: Abstract 549.



Levine BL, et al. Methods & Clinical Development. 2016;4:92–101

Discussion Points: CAR T Cell Therapy

- Logistics for getting patients to CAR T cell therapy
  - When/how to begin referrals, suitable candidates, how to educate patients on the needs of CAR T cell therapy, facilitating access
- Managing adverse events in the first 30 days
- Managing more long-term adverse events
- Addressing unique and delayed-onset neurocognitive toxicities
- Facilitating partnerships between community practices and CAR T-administering institutions

Future Directions

- Will these therapies be used in
  - Earlier-line treatment
  - In combination
  - With other targets
- New drug classes

CAR T Cell Therapy Abstracts to Be Presented in ASCO Oral Session

- Phase 1 study of autologous anti-BCMA CAR T cell therapy
  - Frigault MJ, et al. Abstract 8003
- Phase 1 GPRC5D CAR T cell therapy
  - Huang H, et al. Abstract 8004
- BCMA/CD19 dual-targeting CAR T cell therapy
  - Du J, et al. Abstract 8005

Plasma Cell Dyscrasia Oral Abstract Presentations: Sunday, June 5 at 8:00 AM in S406

ASCO 2022. Abstracts available at: https://meetings.asco.org/2022-asco-annual-meeting/14386?presentation=207305#207305.

Audience Question

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Audience Question

BCMA-directed CAR T-cell therapies are currently available for patients who have received at least how many prior lines of therapy?

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The Nuts and Bolts of Bispecific Antibodies

Amrita Krishnan, MD
City of Hope
Duarte, California

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Audience Preview Question

Which of the following agents are considered T-cell redirecting therapies?

1. CAR T-cell therapy only
2. CAR T-cell therapy and antibody drug conjugates
3. CAR T-cell therapy and bispecific antibodies
4. Bispecific antibodies and antibody drug conjugates
5. Antibody drug conjugates, bispecific antibodies, and CAR T-cell therapies

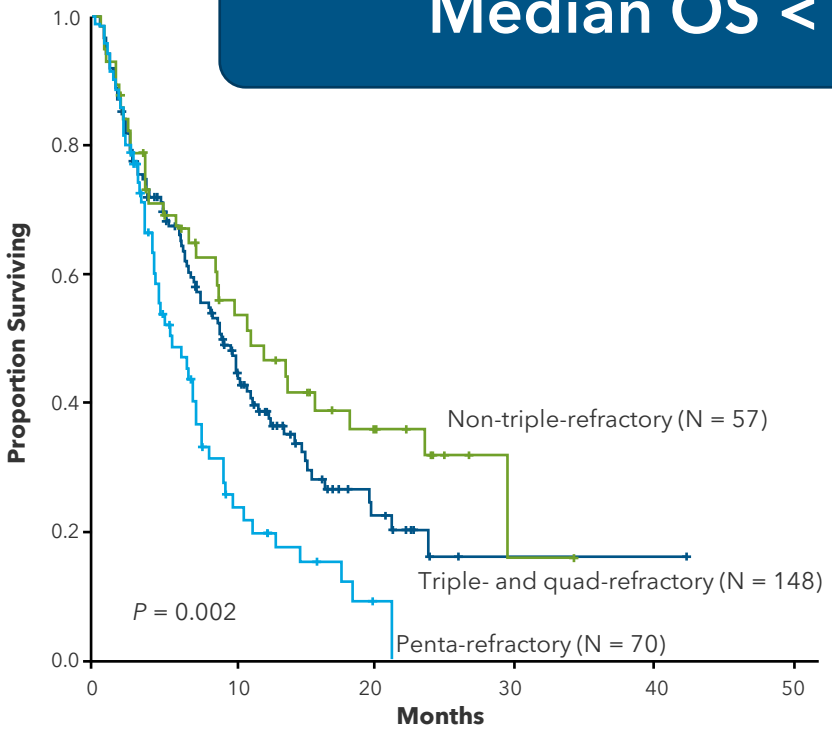
Audience Preview Question

What were the rates of grade 3/4 CRS in the teclistamab (MajesTEC-1) and elranatamab (MagnetisMM-1) monotherapy studies?

1. Less than 1%
2. 2%
3. 4%
4. 8%

Poor Outcomes in Triple-Class Refractory MM

Median OS < 12 months for refractory MM



Refractory Status	Median OS, mo
Not Triple	11.2
Triple/Quad	9.2
Penta	5.6

This is why we need new agents!

Gandhi UH, et al. *Leukemia*. 2019;33(9):2266-2275.

Treatment Options for Triple-Class Refractory Disease

Participation in Clinical Trial

- Cereblon E3 Ligase Modulators (CELMoDs)
- Novel CAR T cell therapies
- ADCs
- Bispecific antibodies

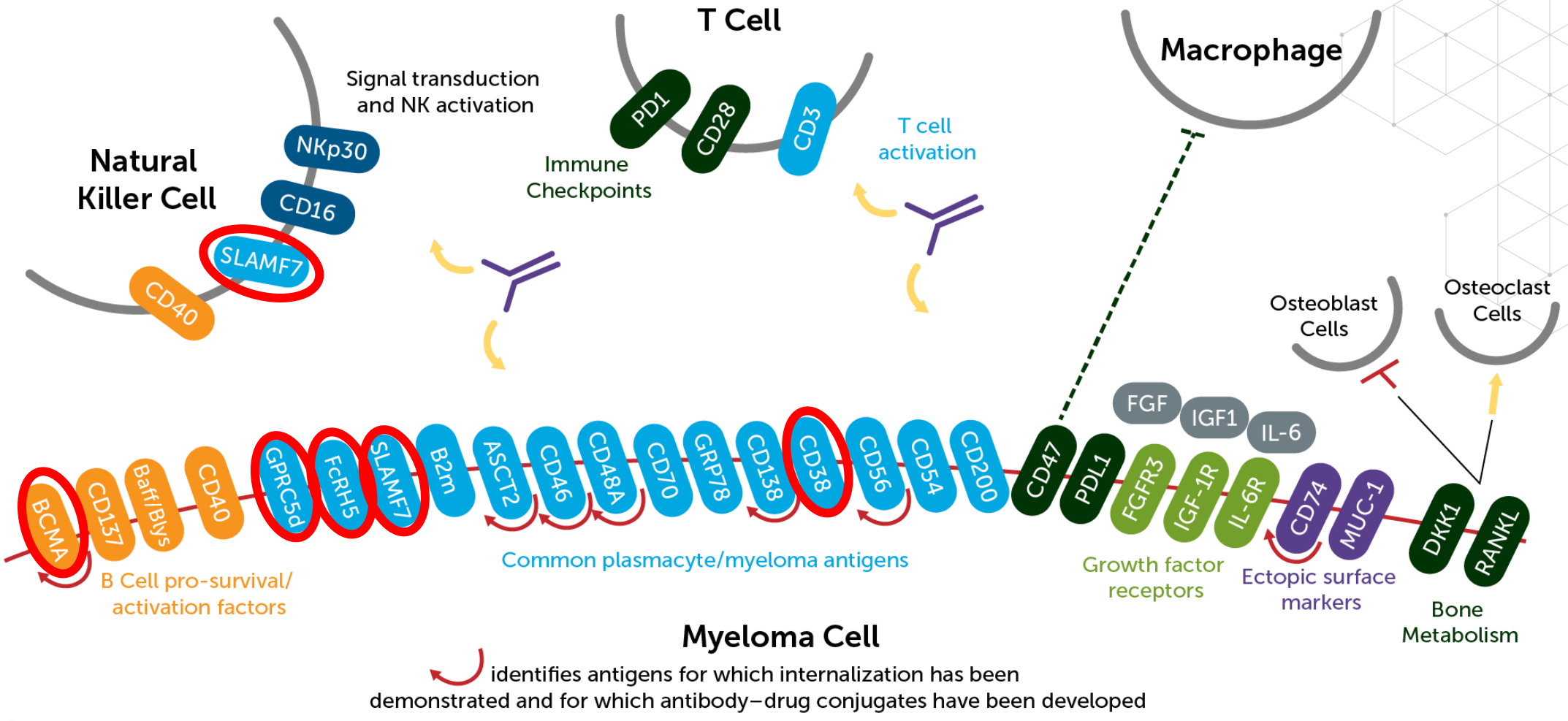
Trial Participation may not be possible

- Aggressive relapse with need to start immediate therapy
- Not fulfilling inclusion criteria/meeting exclusion criteria (ie, renal impairment, thrombocytopenia, non-secretory disease, etc.)

Use an approved and/or NCCN-recommended treatment such as belantamab mafodotin, CAR T cell therapy, selinexor or venetoclax for t(11;14) MM only. Can consider retreatment with drugs used in prior treatment lines.

NCCN Guidelines. Multiple Myeloma. V5.2022.

Immunotherapeutic Targets in Multiple Myeloma

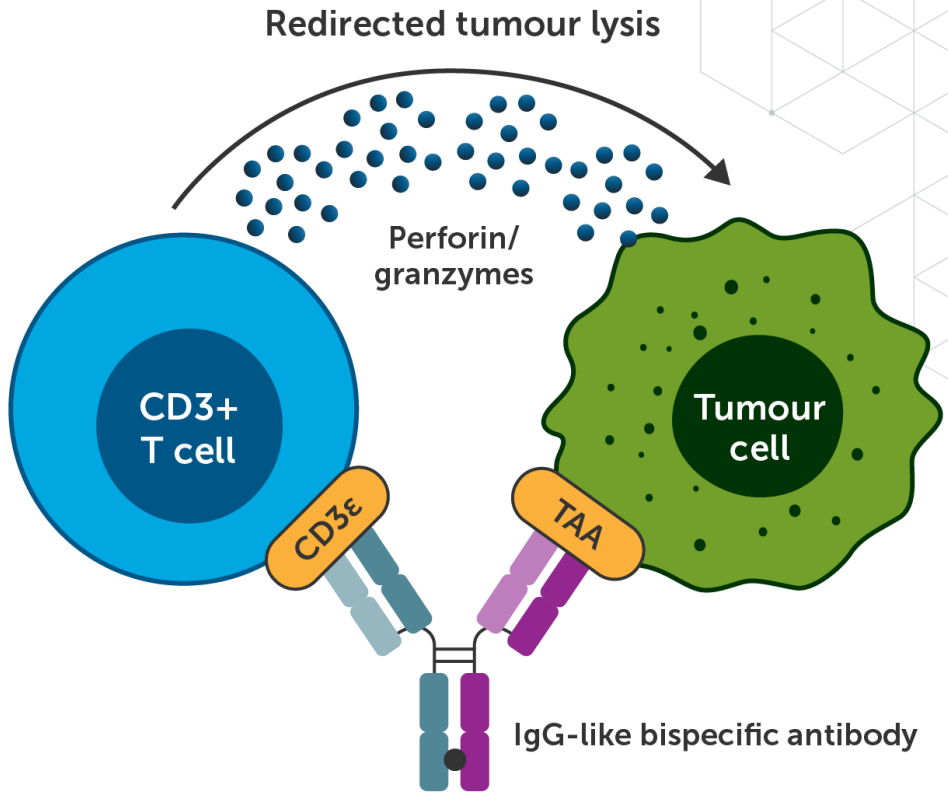


Lancman G, et al. *Hematology Am Soc Hematol Educ Program.* 2020;2020(1):264-271.

MOA of T-Cell Redirection Using Bispecific Antibodies

Bispecific antibodies are an off-the-shelf treatment

Bispecific antibodies bind both a tumor cell antigen and to T lymphocyte antigen to redirect them to the malignant cell

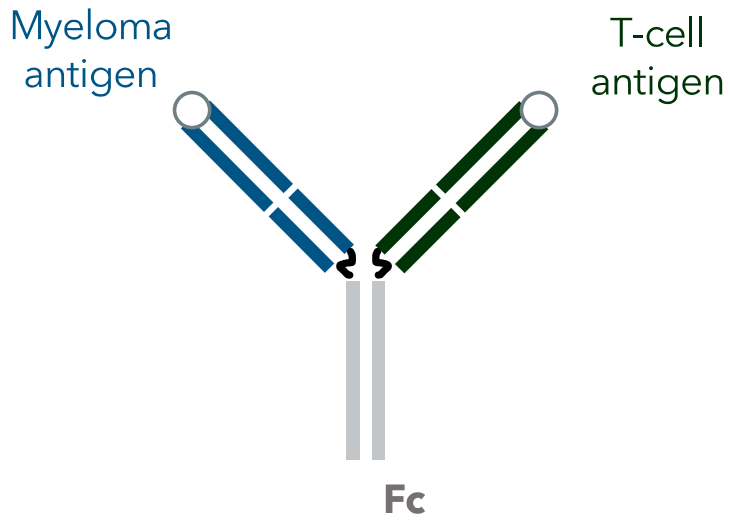


CD3 bispecific T-cell redirection mechanism of action in cancer immunotherapy

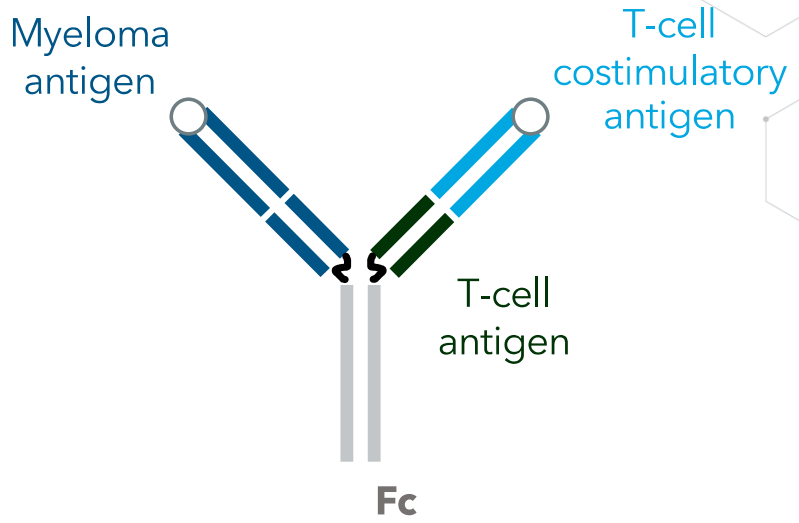
Singh A, et al. 2021;124(6):1037-1048.

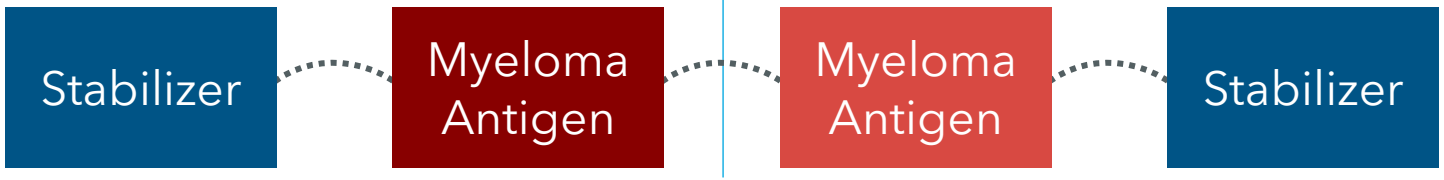
Bispecific and Trispecific Antibodies

Bispecific Antibody



Trispecific Antibody





Lancman G, et al. *Hematology Am Soc Hematol Educ Program.* 2020;2020(1):264-271.

BCMA-Directed Bispecific Antibodies in Development

	Current Phase
Teclistamab	3
Elranatamab	3
AMG 701	1/2
REGN5458	1/2
CC-93269	1
ABBV-383	1

ClinicalTrials.gov; Moreau P, Touzeau C. *Blood*. Published online April 11, 2022. doi:10.1182/blood.2021014611

Trispecific Antibodies

	Tumor Cell Target	T-cell Activation Target	3rd Target
HPN271	BCMA	CD3	Albumin
SAR442257	CD38	CD3	CD28

Jadoon Y, Siddiqui MA. Cancer Treat Res Commun. 2021;29:100468.

Non-BCMA Targeted Bispecific Antibodies

	Tumor Cell Antigen	T-cell Antigen
Cevostamab	FcRH5	CD3
Talquetamab	GPRC5D	CD3

Common Treatment-Related Toxicities Associated with Bispecific Antibodies

- CRS
- Neurologic toxicity
- Hematologic toxicity
- Infections
- IRRs

Moreau P, Touzeau C. *Blood*. Published online April 11, 2022. doi:10.1182/blood.2021014611

Comparing BCMA-Directed Immunotherapies

	Antibody Drug Conjugates	CAR T-Cell Therapy	Bispecific antibodies
Pros	• Off the shelf • Encouraging response rates • 1 hr infusion q3w • No CRS • Available in the community settings	• Unprecedented ORR including MRD$^-$ in heavily pre-treated pts • One time intervention; long chemotherapy holiday resulting in median PFS ~1 year	• Off the shelf • Deep responses • Limited severe CRS - ? Safety in frail elderly • Can be given in community settings after 1st cycle
Cons	• Ocular toxicity – requires close collaboration with ophthalmology; potential impact on pt quality of life • Thrombocytopenia • Continuous treatment until progression • Modest ORR and PFS in triple class/penta refractory	• Manufacturing time • Requires complex infrastructure • CRS ? role in frail elderly • Impact of bridging chemo on remission duration • long-term cytopenias • Cost given relapses (even in MRD-) • Management challenging	• ? need for admissions with initial doses until CRS risk low • Dosing/schedule to be determined • Need for continuous treatment until progression • Toxicities require further study – infections, neurotoxicity

Lancman G, et al. Hematology Am Soc Hematol Educ Program (2020) 2020 (1): 264–271.

Preparing for Future T Cell-Redirecting Therapy with Bispecific Antibodies

Saad Z. Usmani, MD
Memorial Sloan Kettering Cancer Center
New York, New York

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BCMA-Directed Bispecific Antibodies

	N	Triple-class refractory, %	ORR, %	All / gr 3/4 CRS, %
Teclistamab	165	78	62	72 / <1
Elranatamab	55	91	69*	87 / 0
REGN5458	68	100	73*	38 / 0
AMG701	75	68	83*	61 / 7
CC-93269	30	Not reported	89*	77 / 4
ABBV-383 (TNB-383B)	103	62	64*	52/3

*At recommended dose

ClinicalTrials.gov; Moreau P, Touzeau C. *Blood*. Published online April 11, 2022. doi:10.1182/blood.2021014611; Jadoon Y, Siddiqui MA. *Cancer Treat Res Commun*. 2021;29:100468.

AMG-420 and AMG-701

Bispecific Antibody	AMG-420	AMG-701
Treatment	Continuous IV 4/6 weeks	Weekly IV
Patients, n	42	75
Median prior lines, n	3.5	6
Triple-class refractory, %	IMiD + PI - 36; Dara - 21	68
ORR at therapeutic dose, %	70 5 MRD- (400 µg/d)	36 (3-12mg)
Duration of Response, mo	9	3.8 14/17 (ongoing)
AEs, % All (≥ grade 3) CRS Infections Neutropenia Anemia Thrombocytopenia Deaths Other	 38 (2) 33(24) NR NR NR 4 (10%) Polyneuropathy (5)	 61 (7) (17) 23 40 20 4 (5) Neurotoxicity 8 (0)

Topp, et al. *J Clin Oncol*. 2020; Harrison, et al. ASH 2020

MajesTEC-1: Teclistamab Monotherapy in Heavily Pretreated MM, Phase 1 Design

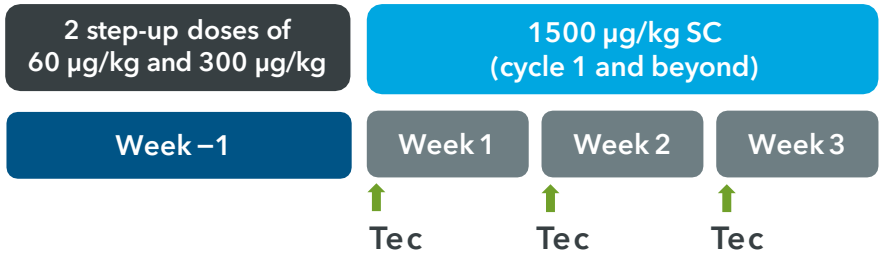
Key Objectives

- Part 1: Identify RP2D
- Part 2: Safety and tolerability at RP2D
- Antitumor activity, pharmacokinetics, pharmacodynamics

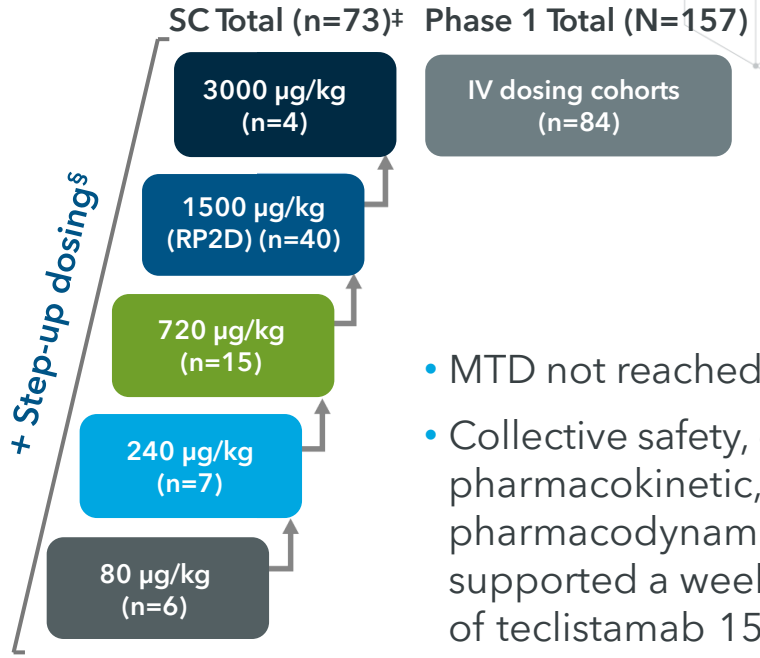
Key Eligibility Criteria

- Adults with measurable MM
- R/R or intolerant to established MM therapies
- Hemoglobin ≥8 g/dL, platelets ≥75 × 10^9/L, ANC ≥1.0 × 10^9/L
- No prior BCMA-targeted therapy

Dosing Schedule at RP2D



Premedications† were limited to step-up doses and first full dose
- No steroid requirement after first full dose

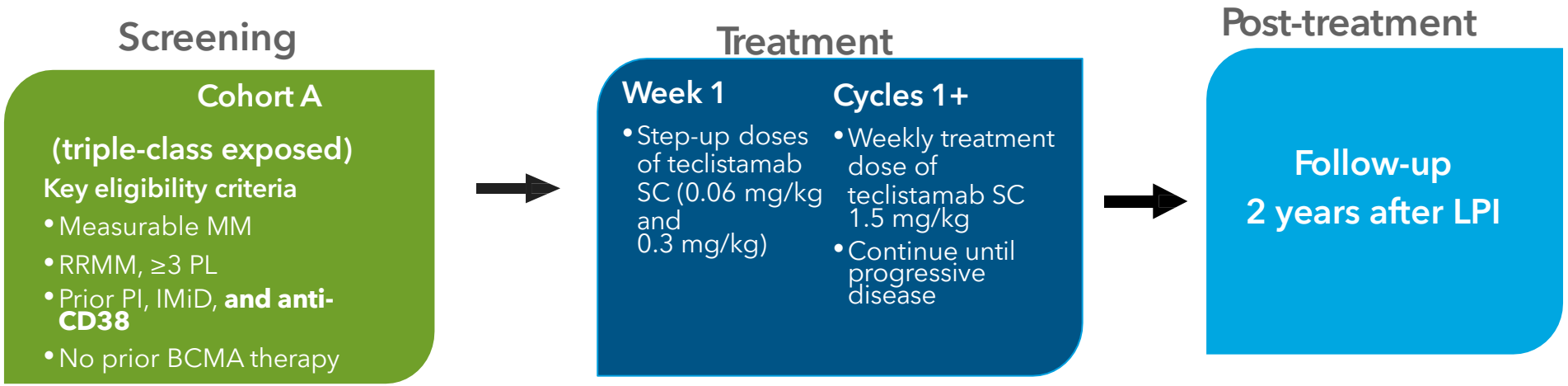


- MTD not reached
- Collective safety, efficacy, pharmacokinetic, and pharmacodynamic data supported a weekly SC dose of teclistamab 1500 µg/kg as the RP2D

Moreau P, et al. Blood. 2021;138(Supplement 1):896.

MajesTEC-1: Phase 2 Study Design

- Phase 1/2, open-label, multicohort, multicenter dose escalation study of teclistamab monotherapy in patients with RRMM who previously received ≥3 prior lines and were triple-class exposed

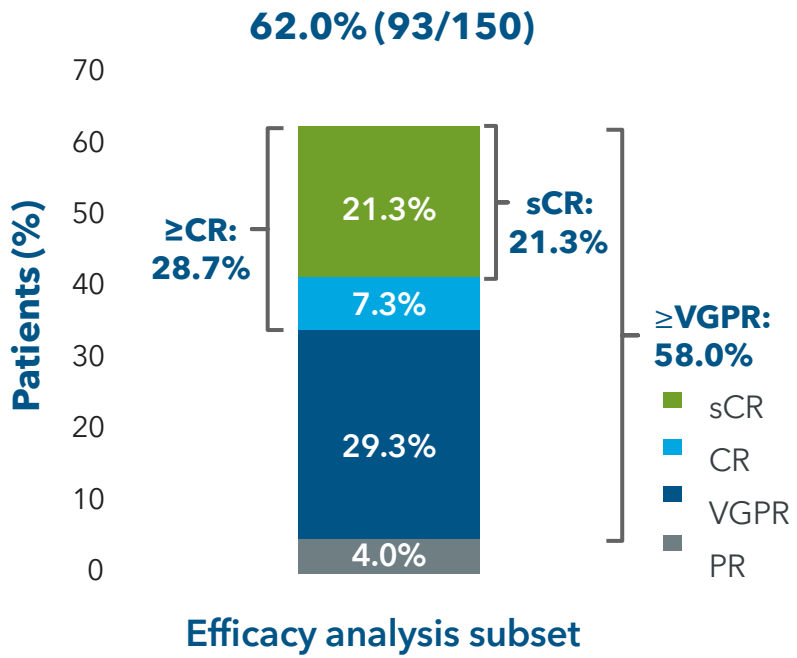


- **Primary endpoint: ORR**
- **Key secondary endpoints:** DOR, ≥VGPR, ≥CR, sCR, TTR, MRD status, PFS, OS, safety, pharmacokinetics, immunogenicity, PRO

Moreau P, et al. *Blood*. 2021;138(Supplement 1):896.

MajesTEC-1: Overall Response Rate for Teclistamab Monotherapy

ORR



Efficacy

- Median follow-up of 7.8 months
- Median TTFR: 1.2 months
- MRD-neg rate: 24.7% (10^{-5}); 16.7% (10^{-6})
- Median DOR: not reached
- 9 month EFS in responders: 85.9
- 9 mo PFS: 58.5%
- Median OS: not reached

Moreau P, et al. Blood. 2021;138(Supplement 1):896.

MajesTEC-1: Overall Safety Profile

AEs ≥20%, n (%)	Teclistamab Monotherapy, N = 165	
	Any Grade	Grade 3/4
Neutropenia	108 (65.5)	94 (57.0)
Anemia	82 (49.7)	57 (34.5)
Thrombocytopenia	63 (38.2)	35 (21.2)
Lymphopenia	56 (33.9)	53 (32.1)
CRS	118 (71.5)	1 (0.6)
Injection site erythema	42 (25.5)	0 (0)
Fatigue	41 (24.8)	3 (1.8)
Nausea	40 (24.2)	1 (0.6)
Headache	36 (21.8)	1 (0.6)
Diarrhea	34 (20.6)	4 (2.4)

- 1 pt discontinued due to AE
- 53% had serious AEs
- Infections occurred in 63%
- 72% had evidence of hypogammaglobulinemia

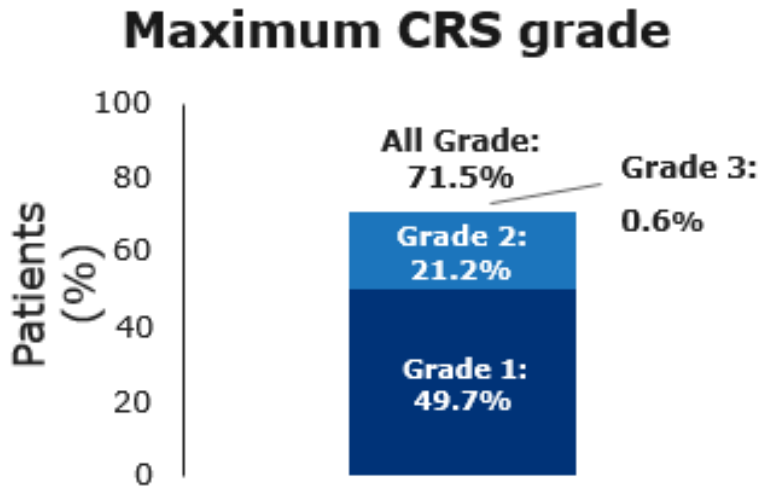
There were 9 deaths due to AEs; none were related to teclistamab

- COVID-19 (n=7)
- Pneumonia (n=1)
- Hemoperitoneum (n=1)

Moreau P, et al. Blood. 2021;138(Supplement 1):896.

MajesTEC-1: CRS and NT

CRS



- Median time to onset: 2 days
- 2.4% received ≥1 dose of tocilizumab

Neurotoxicity

Neurotoxicity, n (%)	Safety Analysis Set N=165
Any	21 (12.7)
Headache	14 (8.5)
ICANS	5 (3.0)
Encephalopathy	2 (1.2)
Tremor	2 (1.2)

- All events grade 1 or 2
- 7.3% required support
- Median onset: 2.5 d

Moreau P, et al. *Blood*. 2021;138(Supplement 1):896.

Teclistamab After Exposure to Other BCMA-Targeted Agents in MajesTEC-1

SCREENING

Cohort C

Key eligibility criteria

- Documented, measurable RRMM
- RRMM, ≥3 prior lines
- Prior PI, IMiD, and anti-CD38 mAb
- **Prior BCMA-targeted treatment (CAR-T and/or ADC)**

TREATMENT

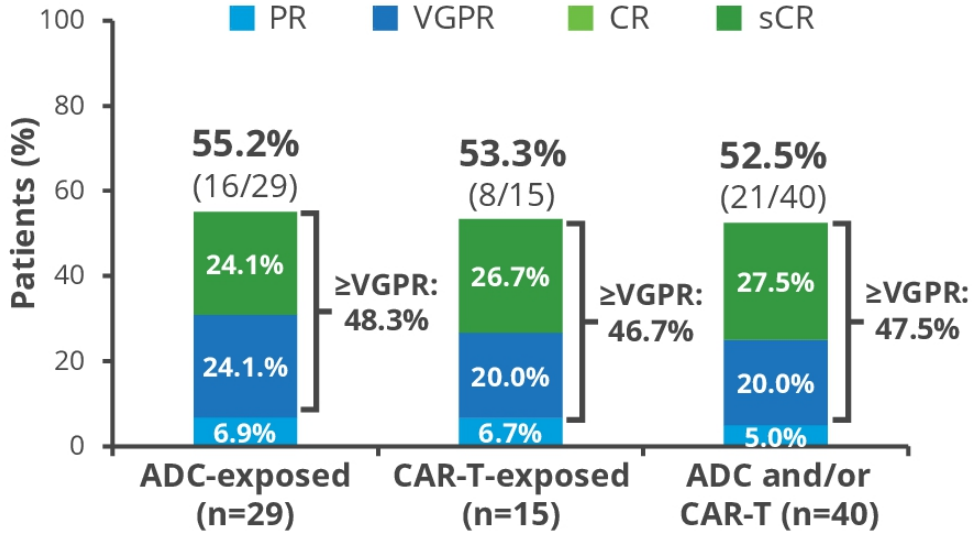
Week 1

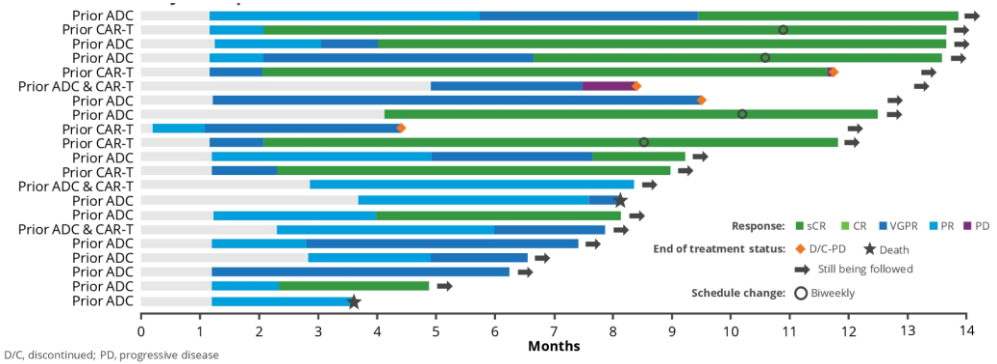
- Step-up doses of teclistamab (0.06 and 0.3 mg/kg)

Cycles 1+

- Weekly[a] teclistamab SC 1.5 mg/kg
- Continue until progressive disease

Simon's 2-stage design[b]



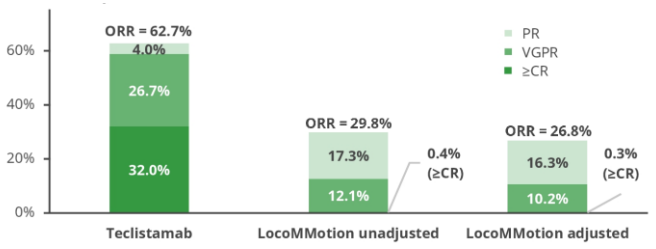


D/C, discontinued; PD, progressive disease

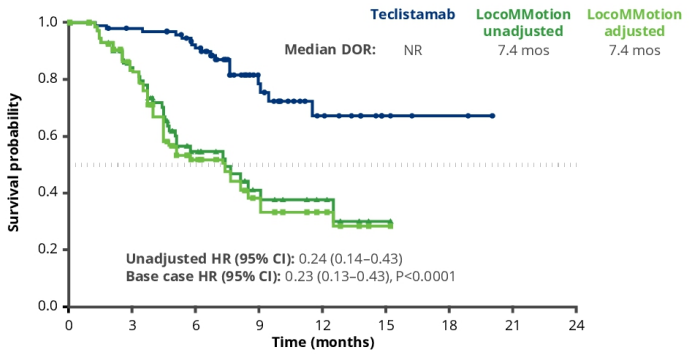
Touzeau C, et al. ASCO Annual Meeting. 2022. Abstract 8013.

Teclistamab in the Context of Current Therapy: LocoMMotion Study in Triple-Class Exposed RRMM

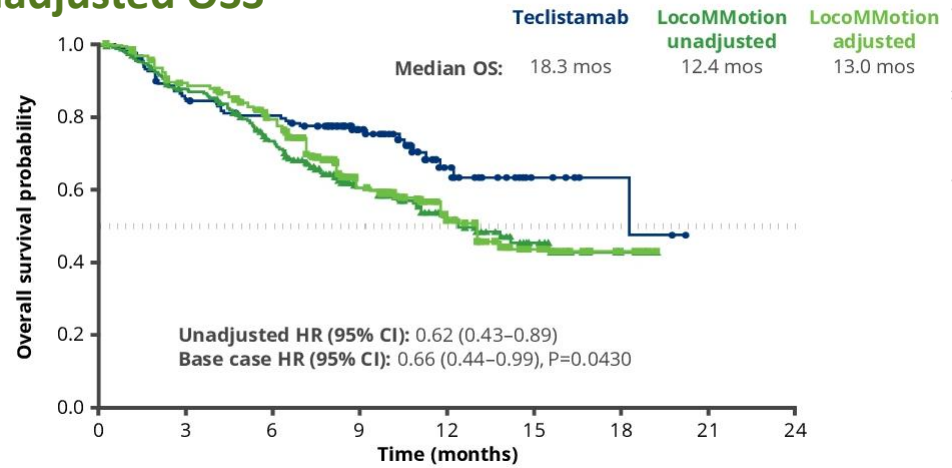
Patient Eligibility Criteria	MajesTEC-1 (N=150)	LocoMMotion (RWPC cohort) (N=248)
	• Triple-class exposure • ≥3 prior LOT • Measurable disease • ECOG performance status <2 • Progression on last LOT	• Triple-class exposure • ≥3 prior LOT • Measurable disease • ECOG performance status <2 • Progression on last LOT



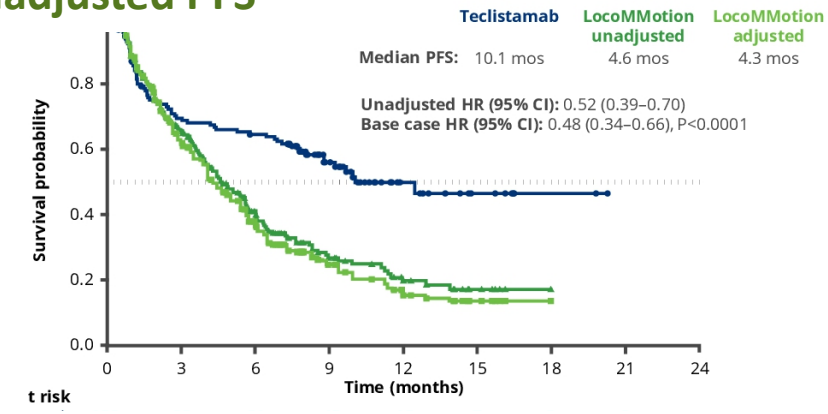
DOR



Unadjusted OSS



Unadjusted PFS



van de Donk NWCJ, et al. ASCO Annual Meeting. 2022. Abstract 8016.

Teclistamab + Daratumumab, Phase 1b

Key eligibility criteria

- Adults with measurable MM
- ≥3 prior LOT, including a PI and IMiD
- Prior anti-CD38 therapy allowed (90-day washout period)
- Prior BCMA-directed therapies were allowed

Tec + dara dosing schedules

Dara	Tec SC		Patients enrolled
1800 mg SC (per approved schedule[5]) Cycles 1–2: QW Cycles 3–6: Q2W Cycles 7+: Monthly	1.5 mg/kg QW[a]	→	n=21
	3 mg/kg Q2W[a]	→	n=39
	3 mg/kg QW	→	n=5

Baseline Characteristics	Teclistamab + Daratumumab, N = 65
Median prior lines, n	5
Prior BCMA, %	12
CD38 refractory,%	63
Triple-Class / Penta Refractory, %	59 / 31
Toxicity*	
CRS, All (Gr 3/4), %	68 (0)
Infections, All (Gr 3/4), %	68 (28)

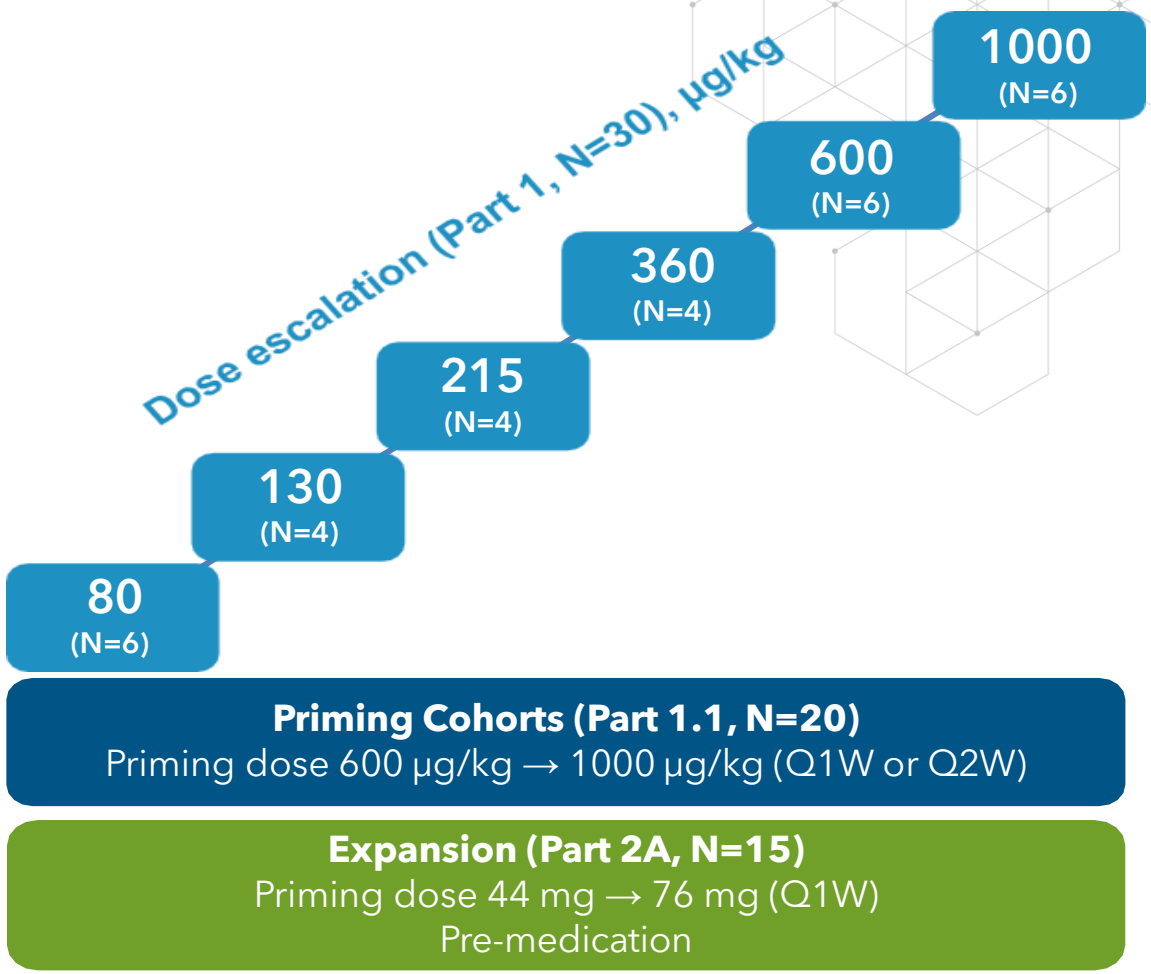
*1 patient had grade 1 ICANs

Response	Daratumumab SC 1800 mg +		
Teclistamab	1.5 mg/kg qW, n = 20	3 mg/Kg q2W, n = 27	3 mg/kg qW, n = 4
ORR, %	75	74	100
CR/sCR, %	30	11	50

Rodriguez-Otero, et al. ASCO 2022. Abstract 8032 .

MagnetisMM-1: Elranatamab Monotherapy

- Dose escalation (Part 1, n = 30): elranatamab 80-1000 µg/kg weekly
- Priming cohorts (Part 1.1, n = 20): single priming dose (600 µg/kg) followed 1 week later by full dose (1000 µg/kg) q1w or q2w
- Expansion (Part 2A, n = 15): single priming dose (44 mg) followed by full dose (76 mg) weekly
  - Pre-medication was given with priming dose and first full dose.
- Data cutoff was July 26, 2021.



Sebag M, et al. Blood. 2021;138(Supplement 1):895.

MagnetisMM-1: Baseline Characteristics

- Median age: 64 y
- High-risk cytogenetics, 27%
- Median prior antimyeloma therapies: 6 (range, 2-15)

Prior Treatment Exposure	Elranatamab Monotherapy SC, N = 55
Triple-class refractory, n (%)	**50 (90.9)**
Prior PIs, n (%)	**55 (100)**
Bortezomib	52 (94.5)
Carfilzomib	47 (85.5)
Ixazomib	17 (32.7)
Prior immunomodulatory agents, n (%)	**55 (100)**
Lenalidomide	54 (98.2)
Pomalidomide	52 (94.5)
Thalidomide	9 (16.4)
Prior anti-CD38 therapy, n (%)	**54 (98.2)**
Daratumumab	52 (94.5)
Isatuximab	4 (7.3)
Other	1 (1.8)
Prior BCMA-targeted therapy, n (%)	**13 (23.6)**
Anti-BCMA ADC	8 (14.5)
CAR-T	9 (16.4)

Sebag M, et al. Blood. 2021;138(Supplement 1):895; Jakubowiak AJ, et al. ASCO Annual Meeting. 2022. Abstract 8014.

MagnetisMM-1: TEAEs

Adverse Event	Monotherapy SC (N=55)				
	Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematologic, n(%)					
Neutropenia	0	2 (3.6)	14 (25.5)	25 (45.5)	41 (74.5)
Anemia	2 (3.6)	8 (14.5)	26 (47.3)	0	36 (65.5)
Lymphopenia	0	0	3 (5.5)	26 (47.3)	29 (52.7)
Thrombocytopenia	6 (10.9)	6 (10.9)	5 (9.1)	10 (18.2)	27 (49.1)
Leukopenia	7 (12.7)	6 (10.9)	5 (9.1)	10 (18.2)	18 (50.9)
Non-hematologic, n (%)					
CRS	28 (50.9)	20 (36.4)	0	0	48 (87.3)
Injection site reaction	27 (49.1)	4 (7.3)	0	0	31 (56.4)
Fatigue	6 (10.9)	13 (23.6)	3 (5.5)	0	22 (40.0)
Diarrhea	12 (21.8)	8 (14.5)	3 (5.5)	0	22 (40.0)

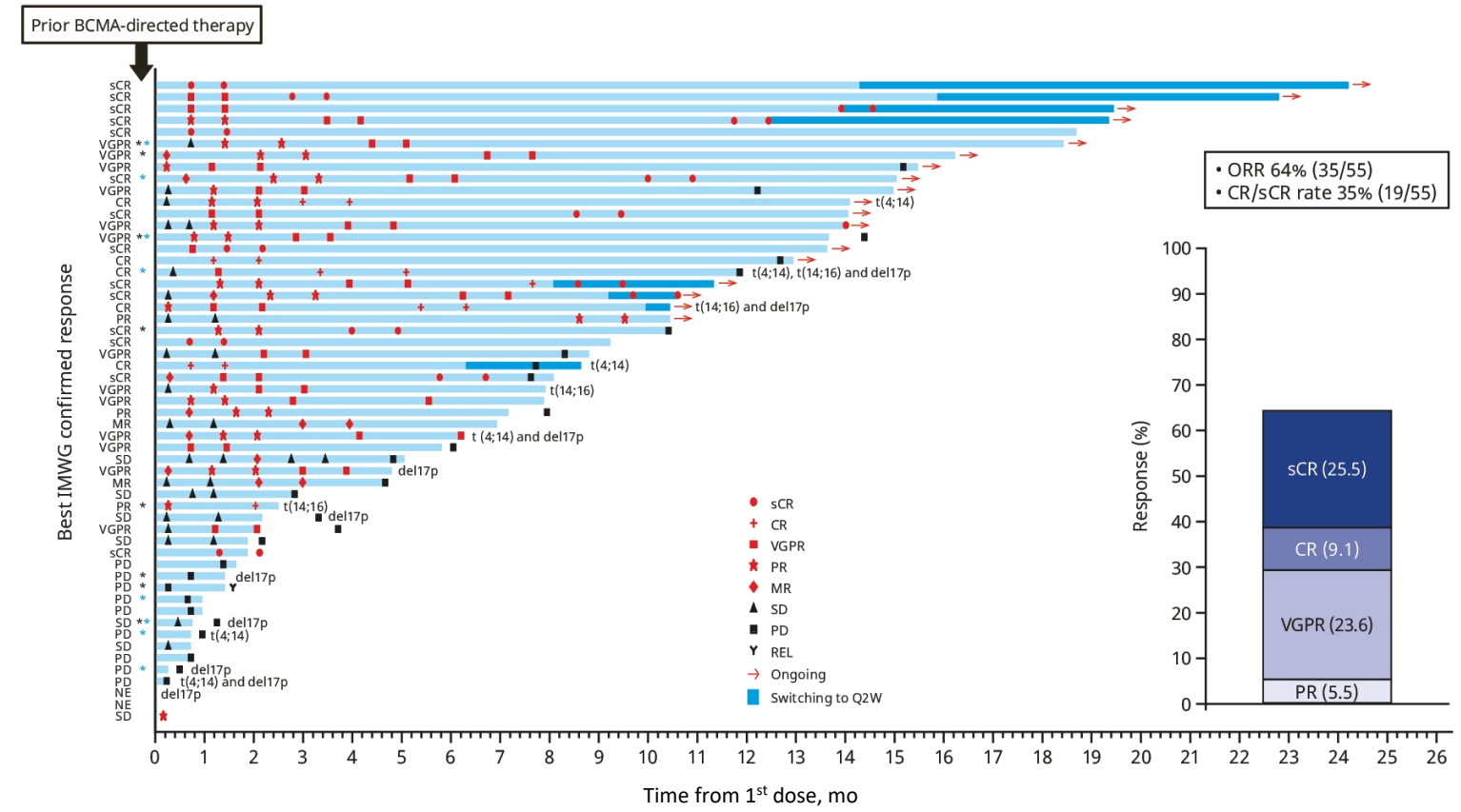
Effect of Priming on CRS	Elranatamab SC at Recommended Monotherapy Dose		
	Escalation n = 6	Priming n = 20	Expansion n = 15
Priming / Pre-medicationa	**No / No**	**Yes / No**	**Yes / Yes**
Overall, n (%)	6 (100)	20 (100)	10 (66.7)
Grade 1	4 (66.7)	10 (50.0)	5 (33.3)
Grade 2	2 (33.3)	10 (50.0)	5 (33.3)
Duration, days, median (range)	4.0 (1–10)	3.0 (2–7)	3.0 (1–4)

- Among the 55 patients, there was one DLT of Grade 4 thrombocytopenia in the q2W priming cohort.

Sebag M, et al. Blood. 2021;138(Supplement 1):895; Jakubowiak AJ, et al. ASCO Annual Meeting. 2022. Abstract 8014.

MagnetisMM-1: Response

- N = 55, Median follow-up: 10.6 mo
- ORR: 64%
  - ≥ CR: 35% (all evaluable patients MRD-negative [13/13])
  - 54% ORR in patients with prior BCMA-directed therapy



Jakubowiak AJ, et al. ASCO Annual Meeting. 2022. Abstract 8014.

Bispecific Antibody Abstracts to Be Presented in ASCO Oral Session

- MagnetisMM-3: phase 2 elranatamab in RRMM
  - Lesokhin AM, et al. Abstract 8006
- MajesTEC-1: Updated efficacy and safety for teclistamab in RRMM
  - Nooka AK, et al. Abstract 8007

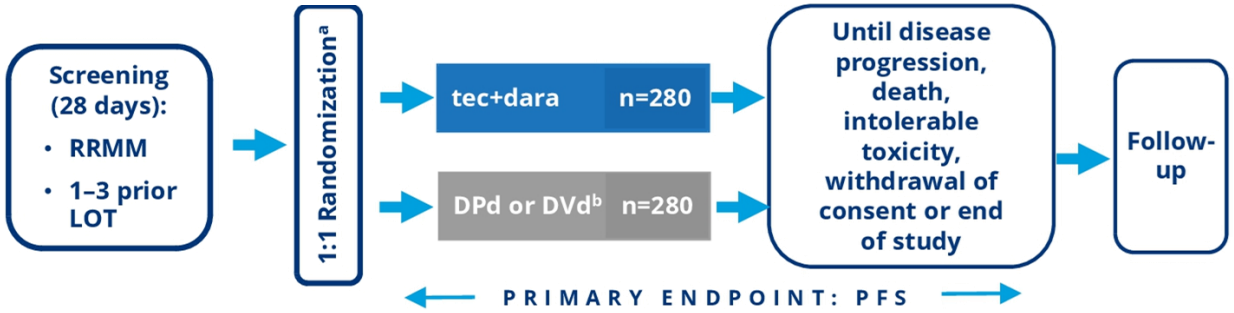
Plasma Cell Dyscrasia Oral Abstract Presentations: Sunday, June 5 at 8:00 AM in S406

ASCO 2022. Abstracts available at: https://meetings.asco.org/2022-asco-annual-meeting/14386?presentation=207305#207305.

ASCO 2022: Phase 3 TIP

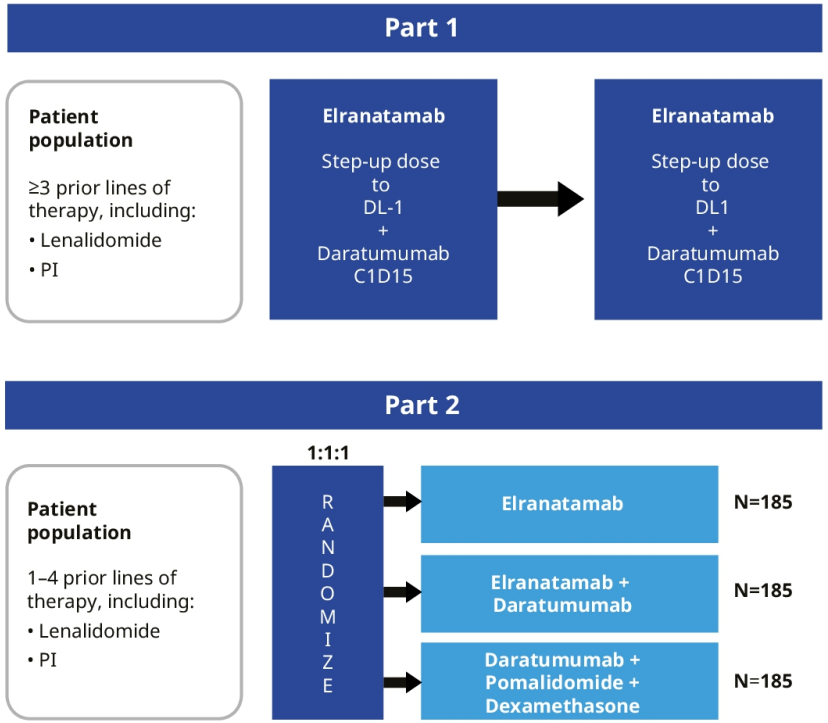
MajesTEC-3

- Teclistamab + dara vs dara/pom/dex or dara/bor/dex (investigator's choice) in RRMM



MagnestisMM-5

- Elranatamab monotherapy or elranatamab + dara vs dara/pom/dex (dara and elranatamab SC)



Mateos M-V, et al. ASCO 2022. Abstract TPS 8072; Gosicki S, et al. ASCO 2022. Abstract TPS80-74.

Summary

- There are several bispecific antibody platforms in clinical trials
- Compared to CAR T cell therapy, they have:
  - Potential advantages: off the shelf, better safety profile, SC administration
  - Potential disadvantages: continuous therapy
- BCMA-directed bispecific antibodies are showing impressive safety and efficacy in RRMM
  - Moving to earlier lines of therapies
  - Combination with mAbs and immunomodulatory agents
  - Need to incorporate in frontline strategies in high-risk MM (several concepts are in development)
- Novel targets for bispecific antibodies are in early clinical development, making all IO-based MM therapy strategies realistic in the near future.

Incorporating Emerging Immunotherapies into the MM Treatment Paradigm

Moderated Panel Discussion

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Discussion Points

- Does the sequence of the therapy for bispecific antibodies matter?
- What is needed to make bispecific antibodies safer in the outpatient setting?
- Can bispecific antibody strategies be fixed duration?
- Will there be an impact in patients with high-risk disease?
- What would it take for T cell redirection to beat ASCT?
- What non-BCMA targets are you most excited about, and how do you anticipate those being used in treatment of MM?

Audience Question

Which of the following agents are considered T-cell redirecting therapies?

1. CAR T-cell therapy only
2. CAR T-cell therapy and antibody drug conjugates
3. CAR T-cell therapy and bispecific antibodies
4. Bispecific antibodies and antibody drug conjugates
5. Antibody drug conjugates, bispecific antibodies, and CAR T-cell therapies

Audience Question

What were the rates of grade 3/4 CRS in the teclistamab (MajesTEC-1) and elranatamab (MagnetisMM-1) monotherapy studies?

1. Less than 1%
2. 2%
3. 4%
4. 8%

Addressing Access to Care in MM

Sikander Ailawadhi, MD
Mayo Clinic
Jacksonville, Florida

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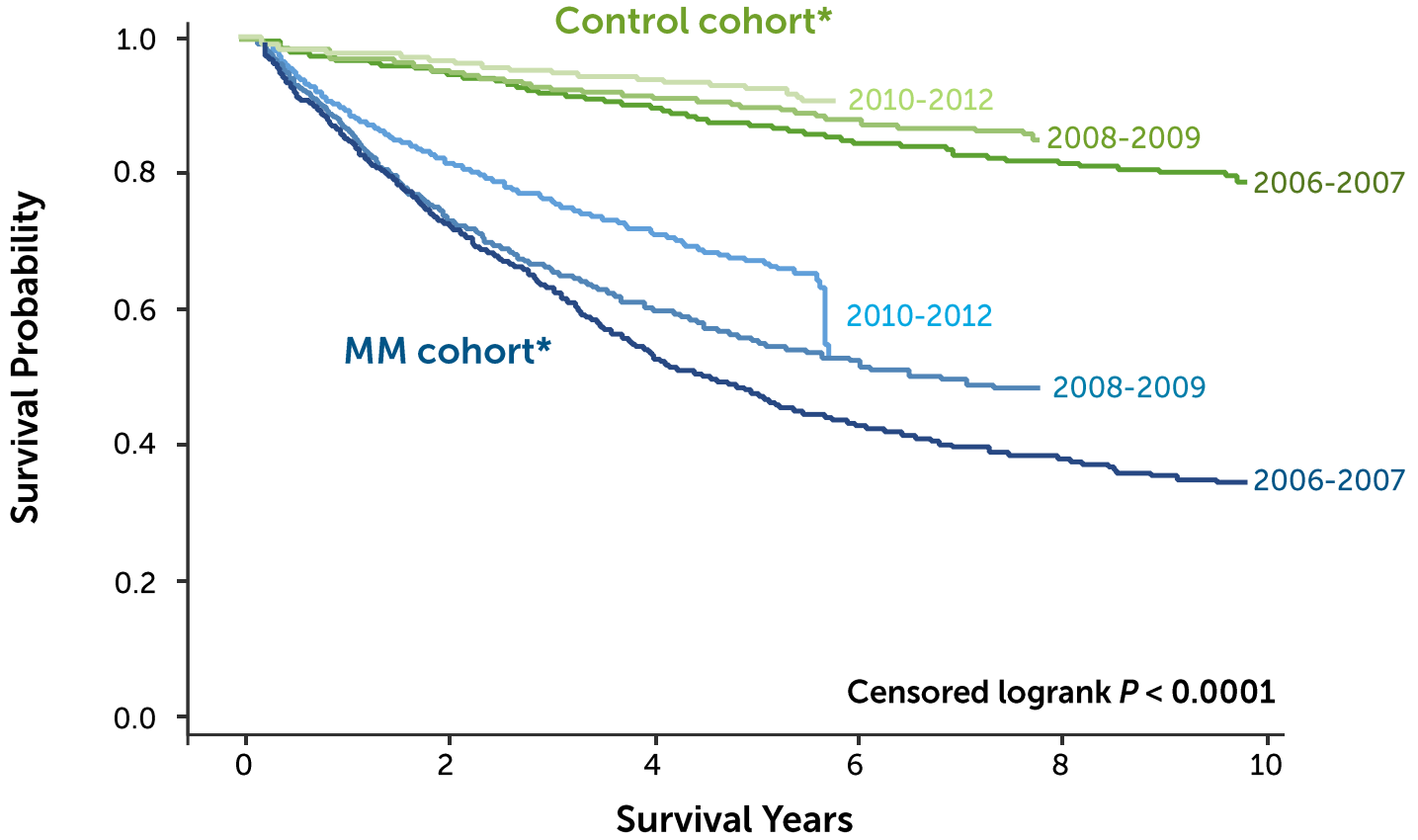
Audience Preview Question

In which of the following racial/ethnic populations is stem cell transplant utilized the least for patients with multiple myeloma?

1. African American
2. Asian
3. Caucasian
4. Hispanic/Latino

Outcomes in MM: Improving Survival Over Time

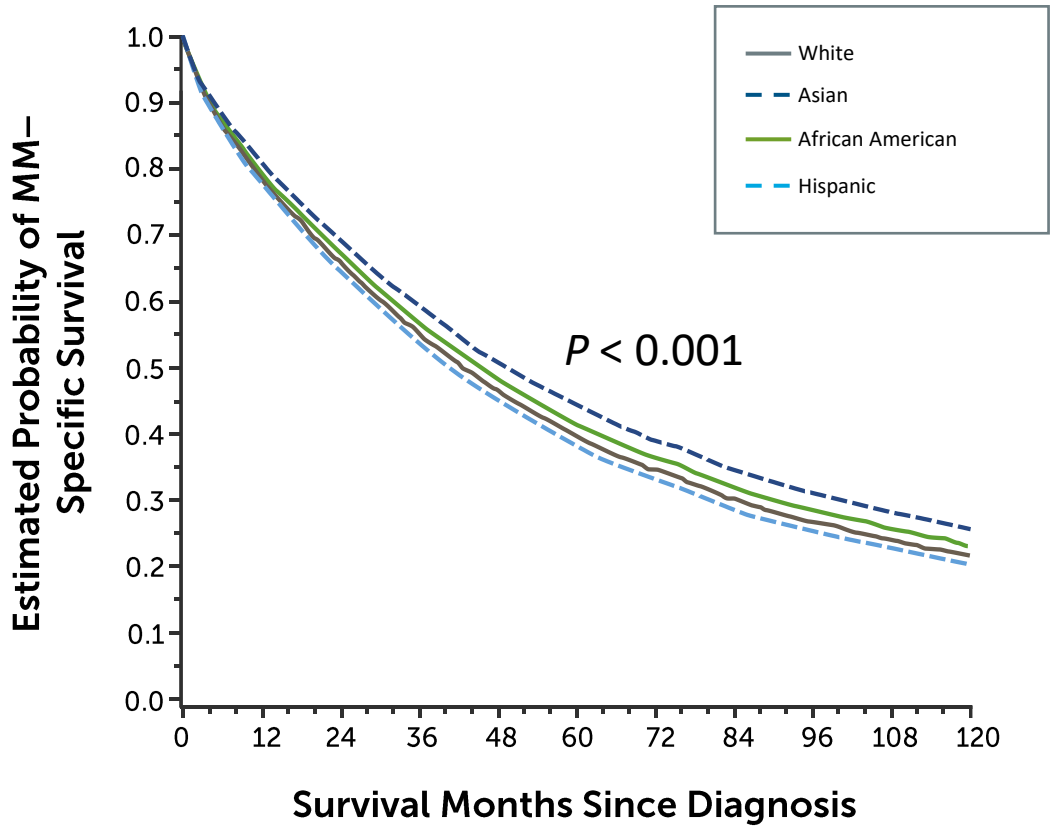


*Year ranges represent the year of diagnosis.

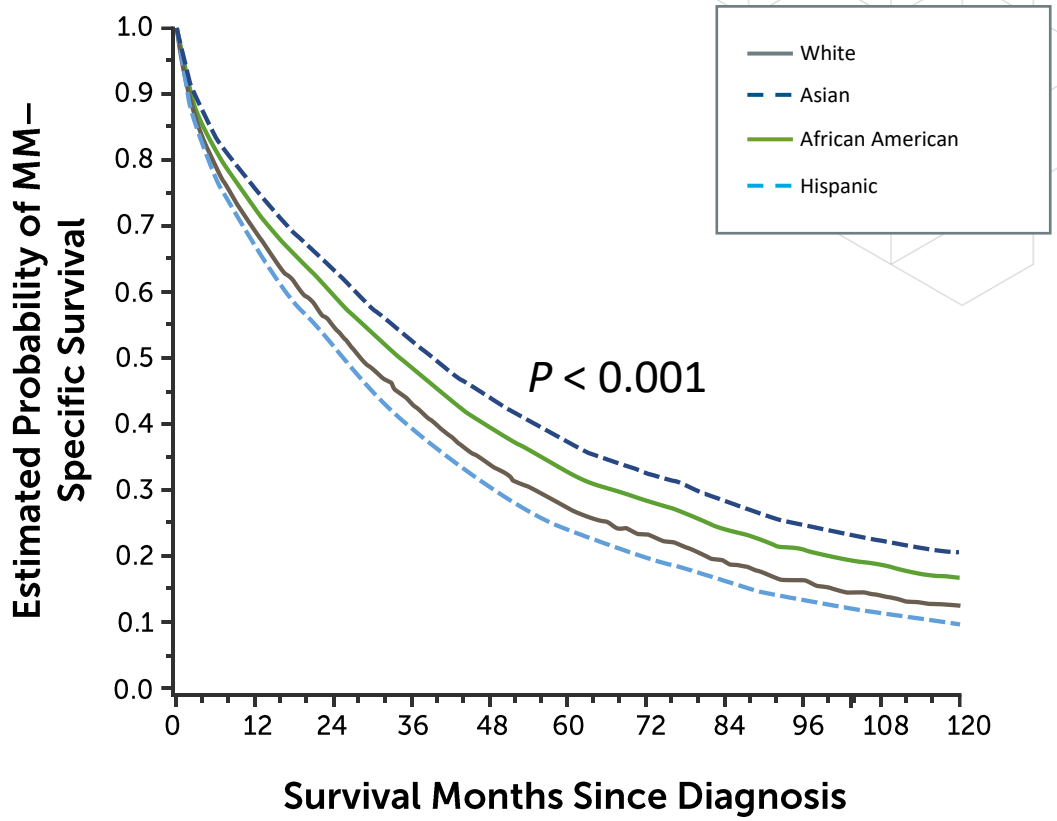
Fonseca R, et al. *Leukemia*. 2017;31(9):1915-1921.

Outcomes in Multiple Myeloma: Differences by Race/Ethnicity

All Patients

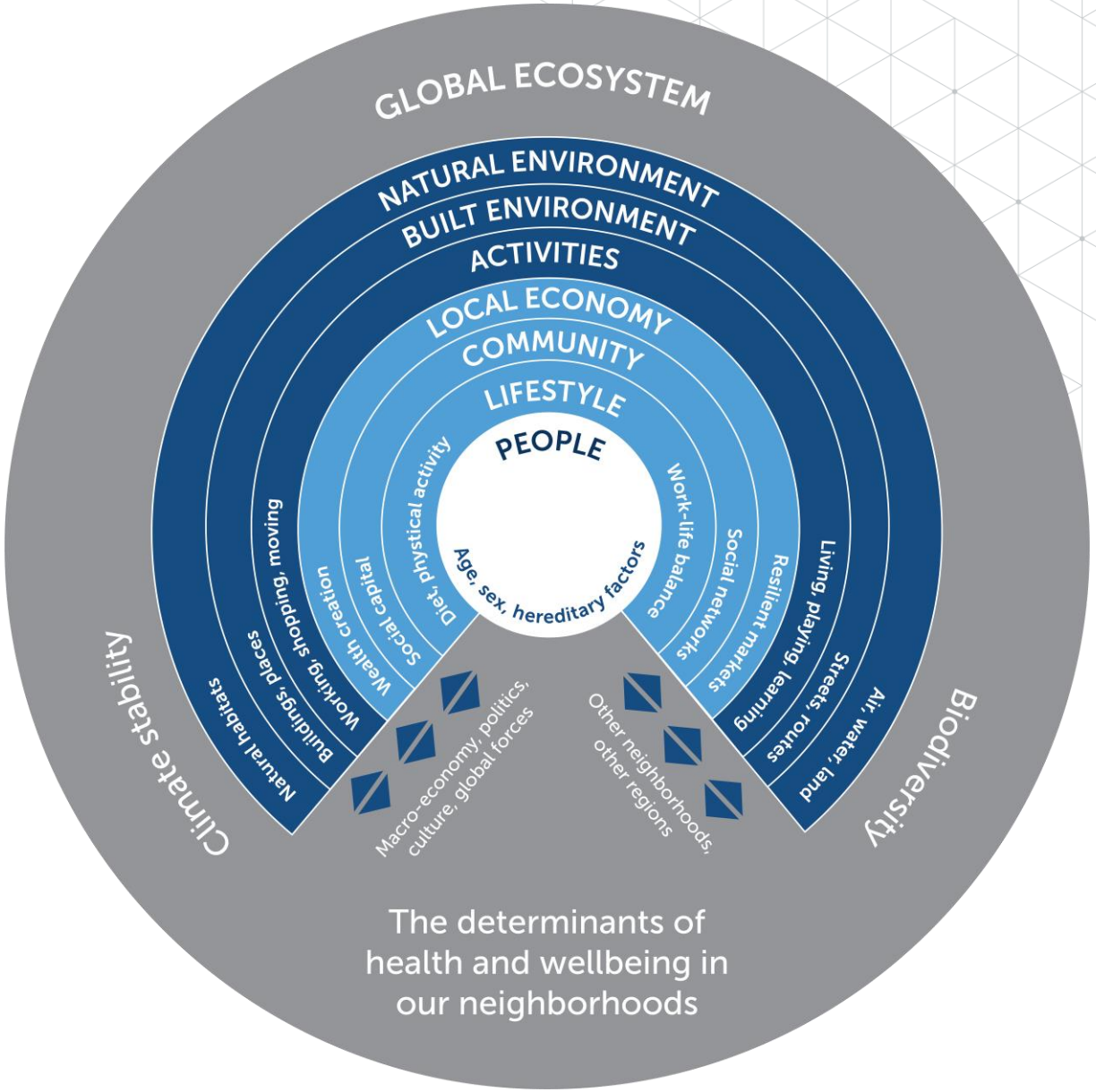


Patients ≥75 Years



Ailawadhi S, et al. *Br J Haematol*. 2012;158(1):91-98.

Determinants of Health: Sociocultural and Economic



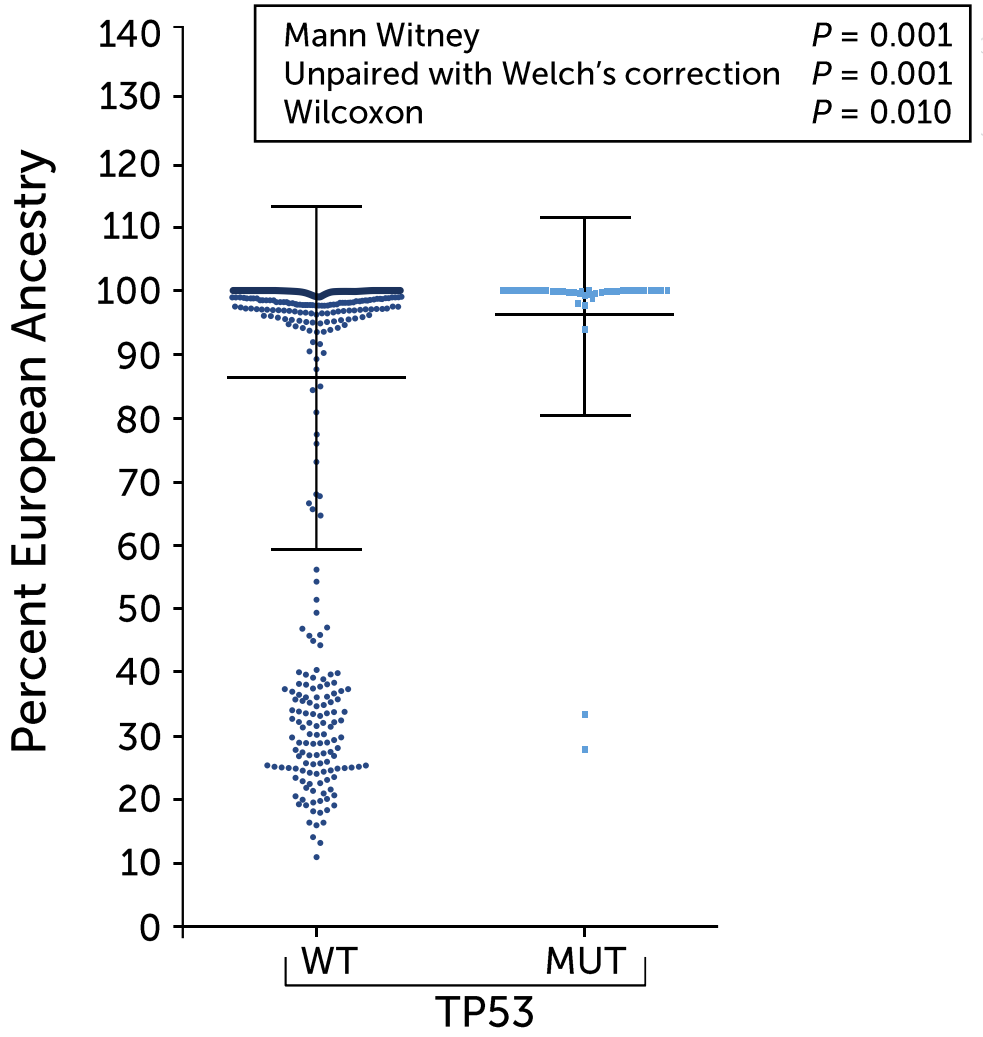
Barton H, Grant M. *J R Soc Promot Health.* 2006;126(6):252-253.

Factors Affecting Outcomes: Complex and Inter-related

Race and Disease Biology in MM

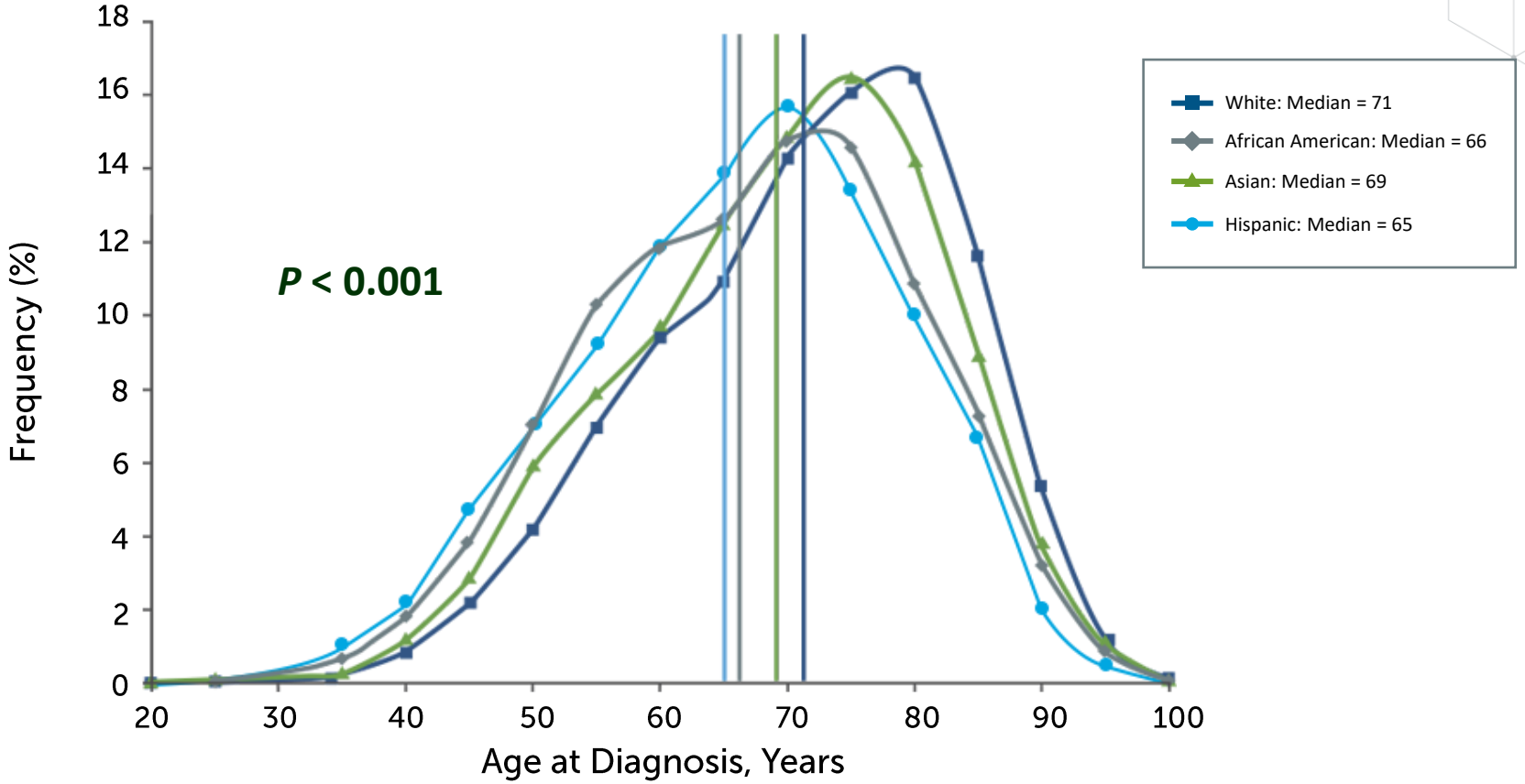
- Differences in mutation frequency in African and European descent in myeloma:

Lower incidence of high-risk mutations in African Americans



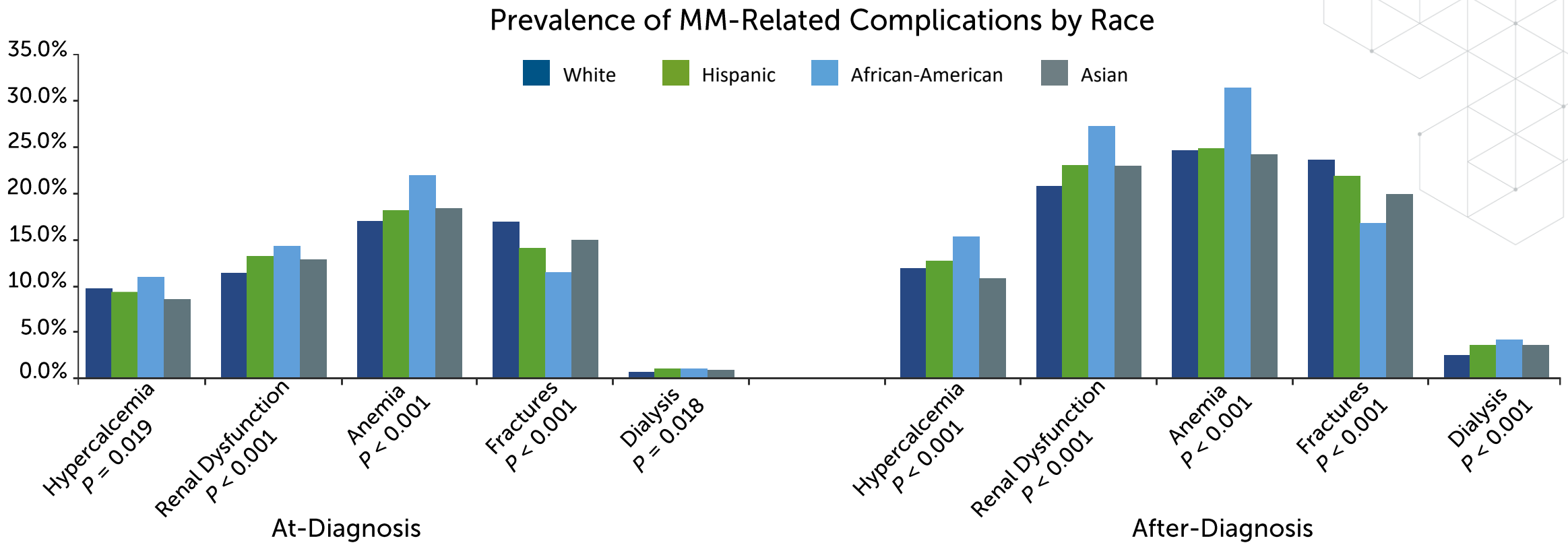
Manojlovic Z, et al. *PLoS Genet*. 2017;13(11):e1007087.

Race and Clinical Presentation in Multiple Myeloma



Ailawadhi S, et al. *Br J Haematol*. 2012;158(1):91-98.

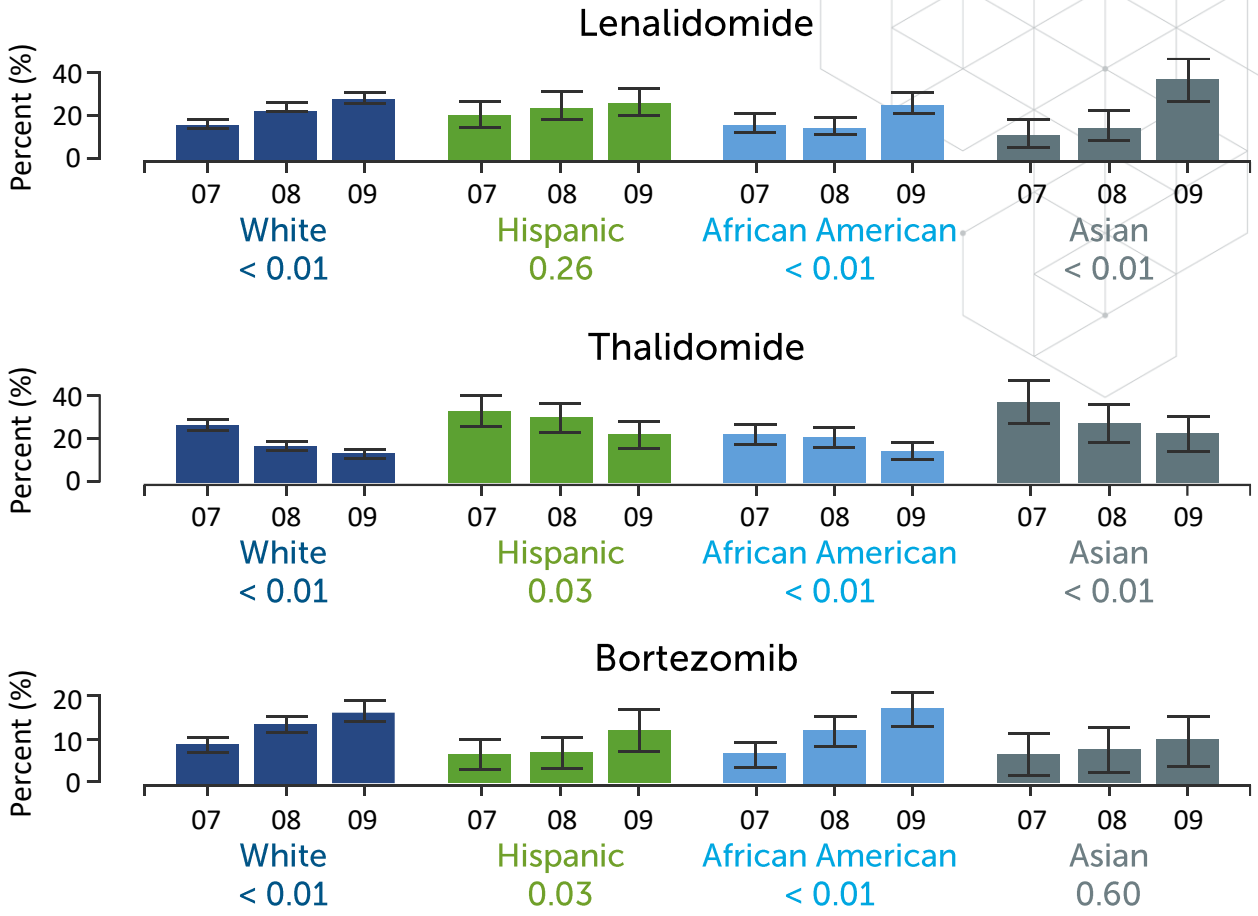
Race and Clinical Presentation in Multiple Myeloma



Ailawadhi S, et al. *Cancer*. 2018;124(8):1710-1721.

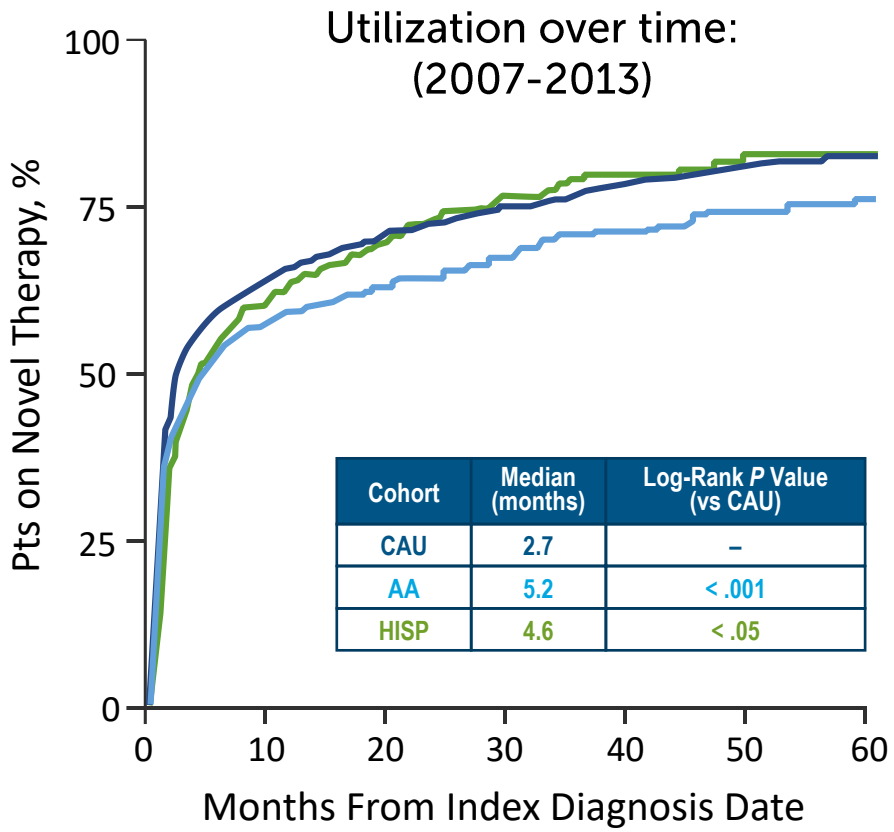
Racial Disparities in Access to Care: Novel Agents

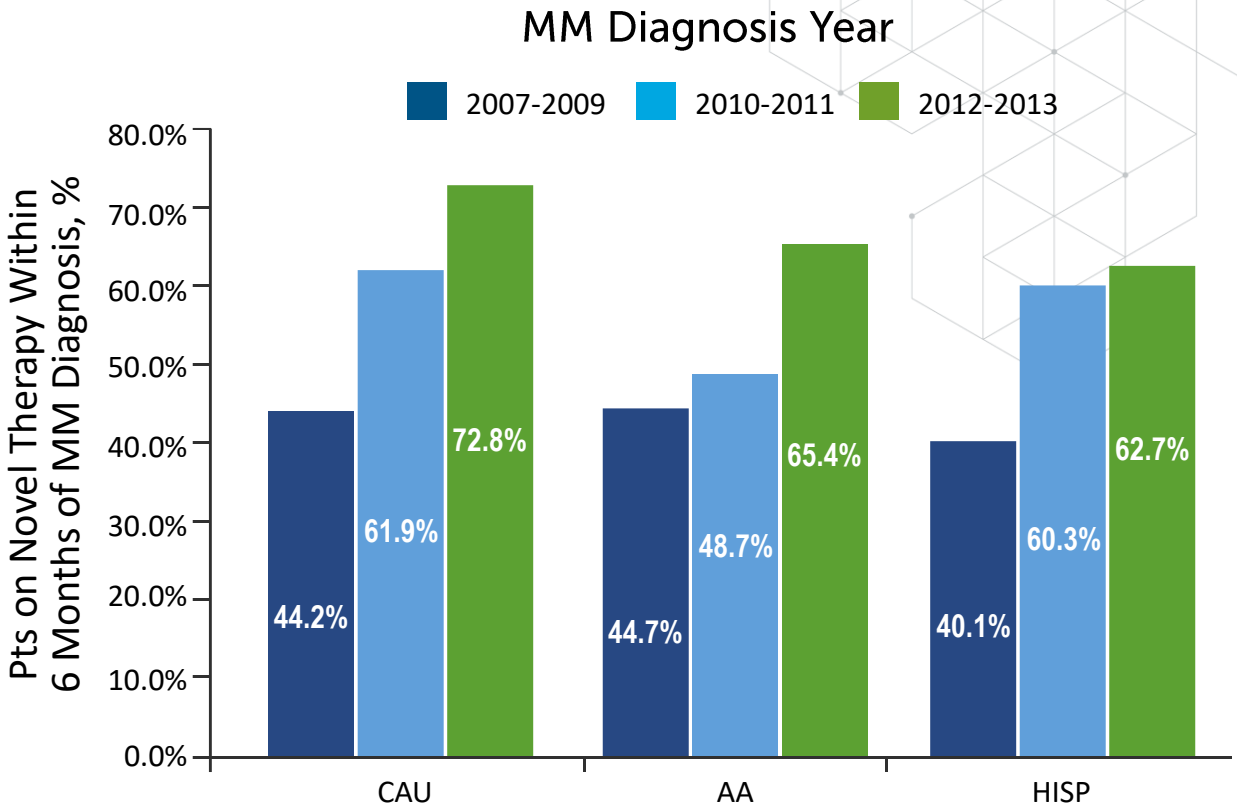
- Utilization over time: (2007, 2008, 2009)
- Significantly lower utilization of lenalidomide among AA
- Significantly lower bortezomib utilization among Asians
- Hispanics:
  - Highest number of median days (102) to first bortezomib dose



Ailawadhi S, et al. *Cancer Med*. 2017;6(12):5501-5506.

Racial Disparity in Access to Care: Novel Agents

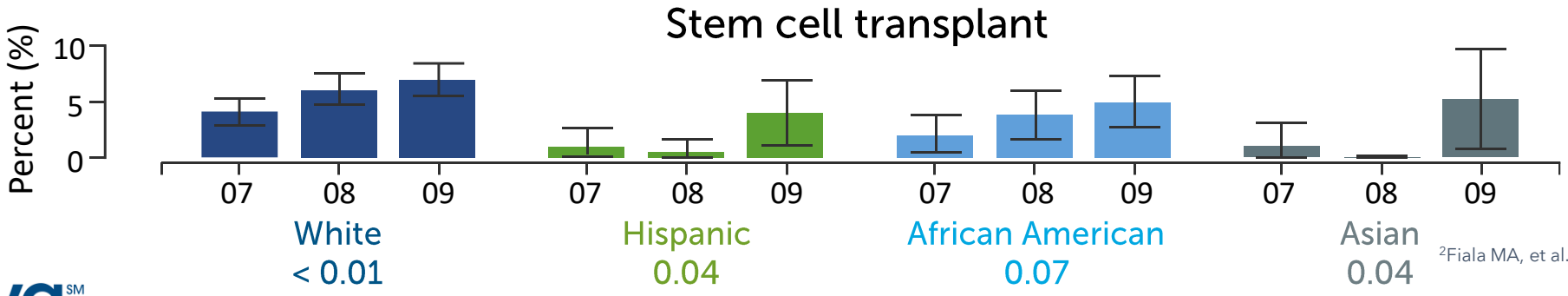




Ailawadhi S, et al. *Blood Adv*. 2019;3(20):2986-2994.

Racial Disparity in Access to Care: Stem Cell Transplant

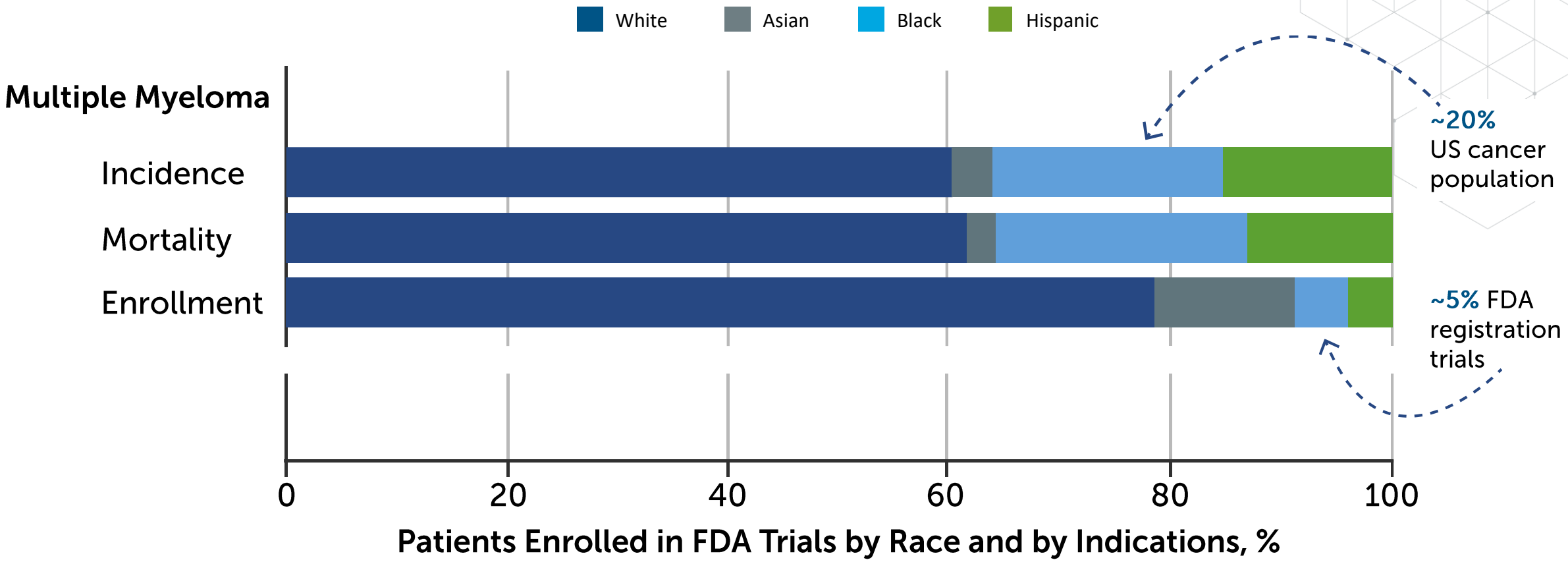
- Age-adjusted odds of receiving SCT for MM significantly higher for Caucasians as compared to AA (OR = 1.75; 95% CI, 1.64-1.86; $P < 0.01$)[1]
- AA less likely to receive SCT than White Americans even after controlling for age, sex, SES, insurance provider, and comorbidity score[2]
- SCT utilization rate (2008-2013) was lowest and had smallest increase over time for Hispanics[3]
- AA are referred for a SCT significantly later in their disease course than White patients[4]
- Overall SCT utilization (2007-2009) was lowest for Hispanics[5]



SCT, stem cell transplant; SES, socio-economic status.

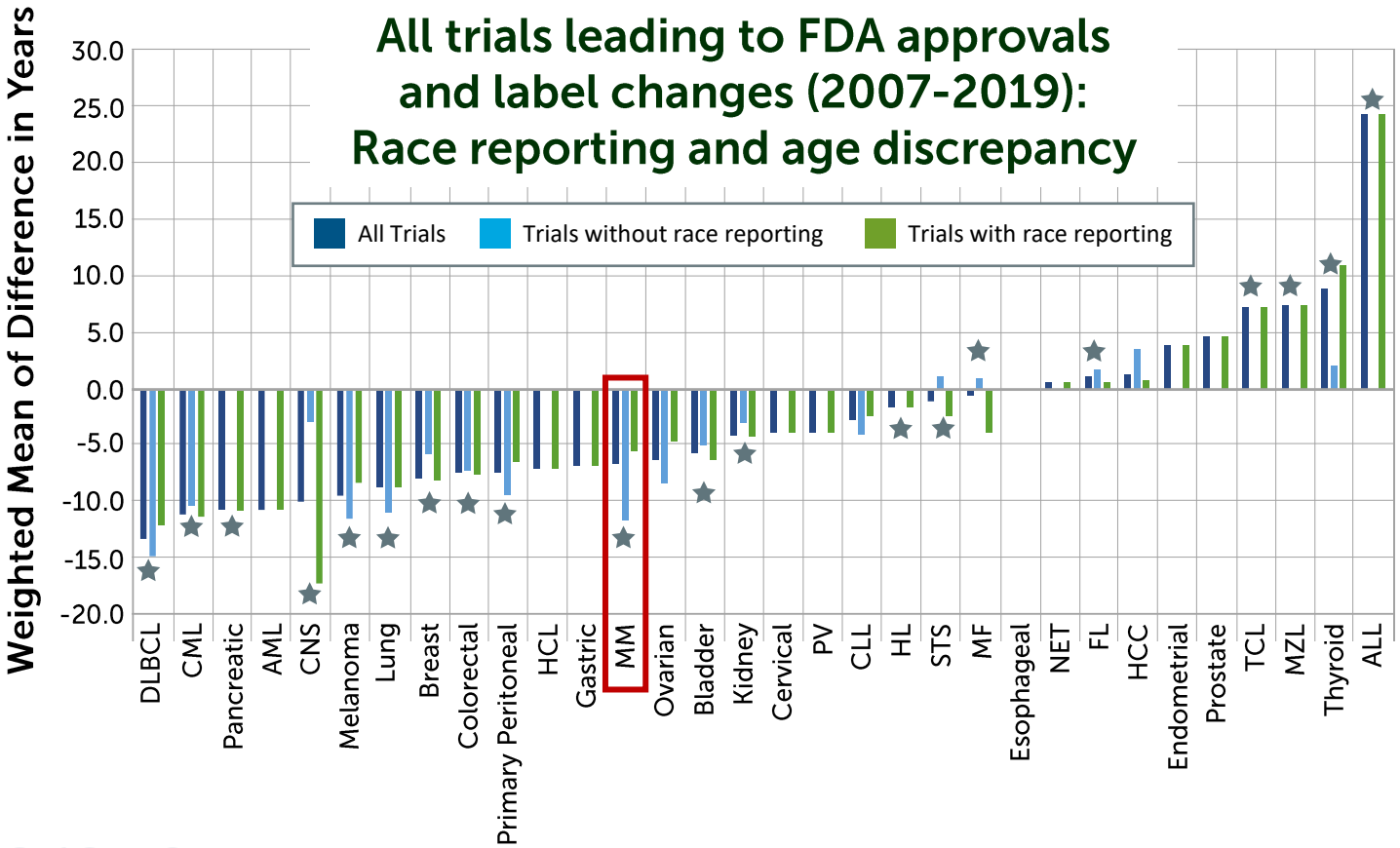
[1]Joshua TV, et al. *Cancer*. 2010;116(14):3469-3476.
[2]Fiala MA, et al. *Biol Blood Marrow Transplant*. 2015;21(7):1153-1154.
[3]Schriber JR, et al. *Cancer*. 2017;123(16):3141-3149.
[4]Bhatnagar V, et al. *Cancer*. 2015;121(7):1064-1070.
[5]Ailawadhi S, et al. *Cancer Med*. 2017;6(12):2876-2885.

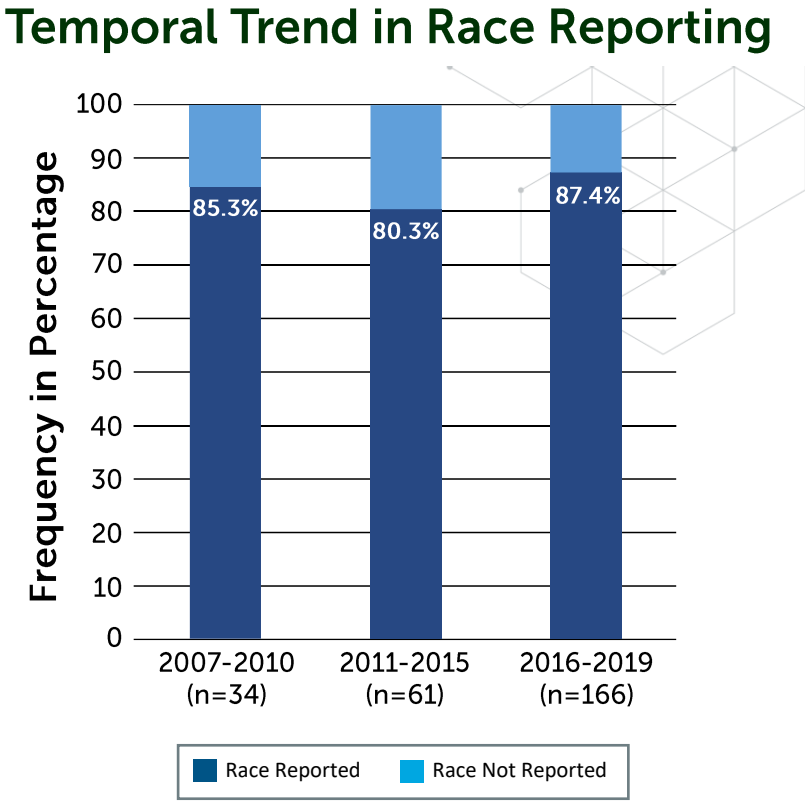
Racial Disparity in Access to Care: Clinical Trials



Loree JM, et al. *JAMA Oncol.* 2019;5(10):e191870.

Racial Disparity in Access to Care: Clinical Trials

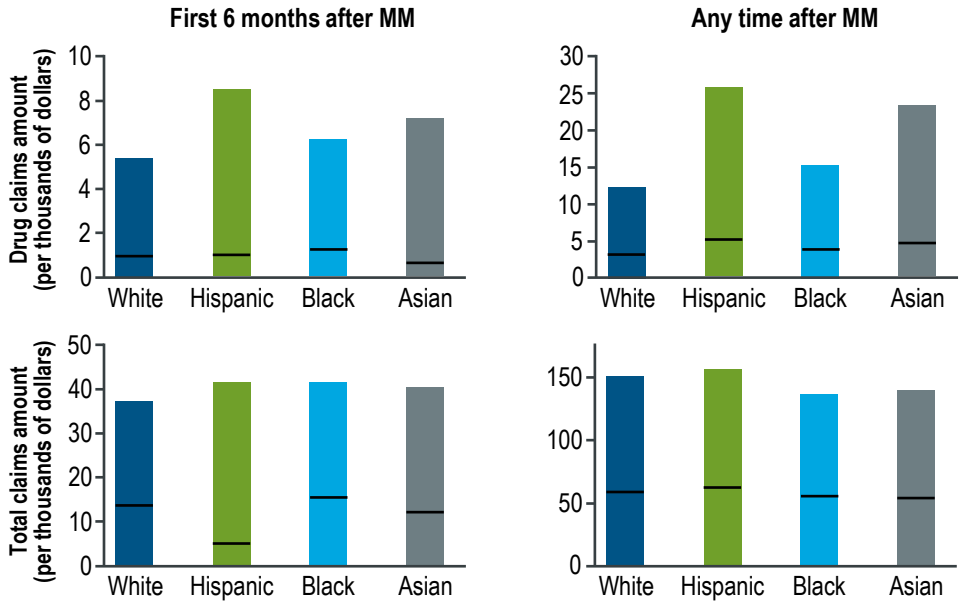




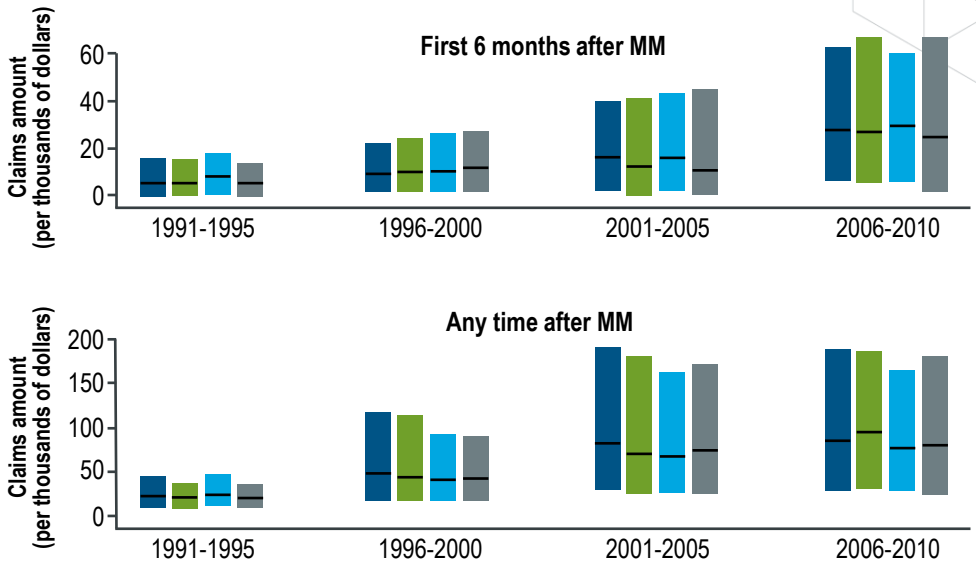
Jayakrishnan T, et al. *Cancers*. 2021;13(22):5770.

Racial Disparity in Cost of Care: Financial Toxicity

Drug-only claims and total claims for patients with MM in Medicare by patient race



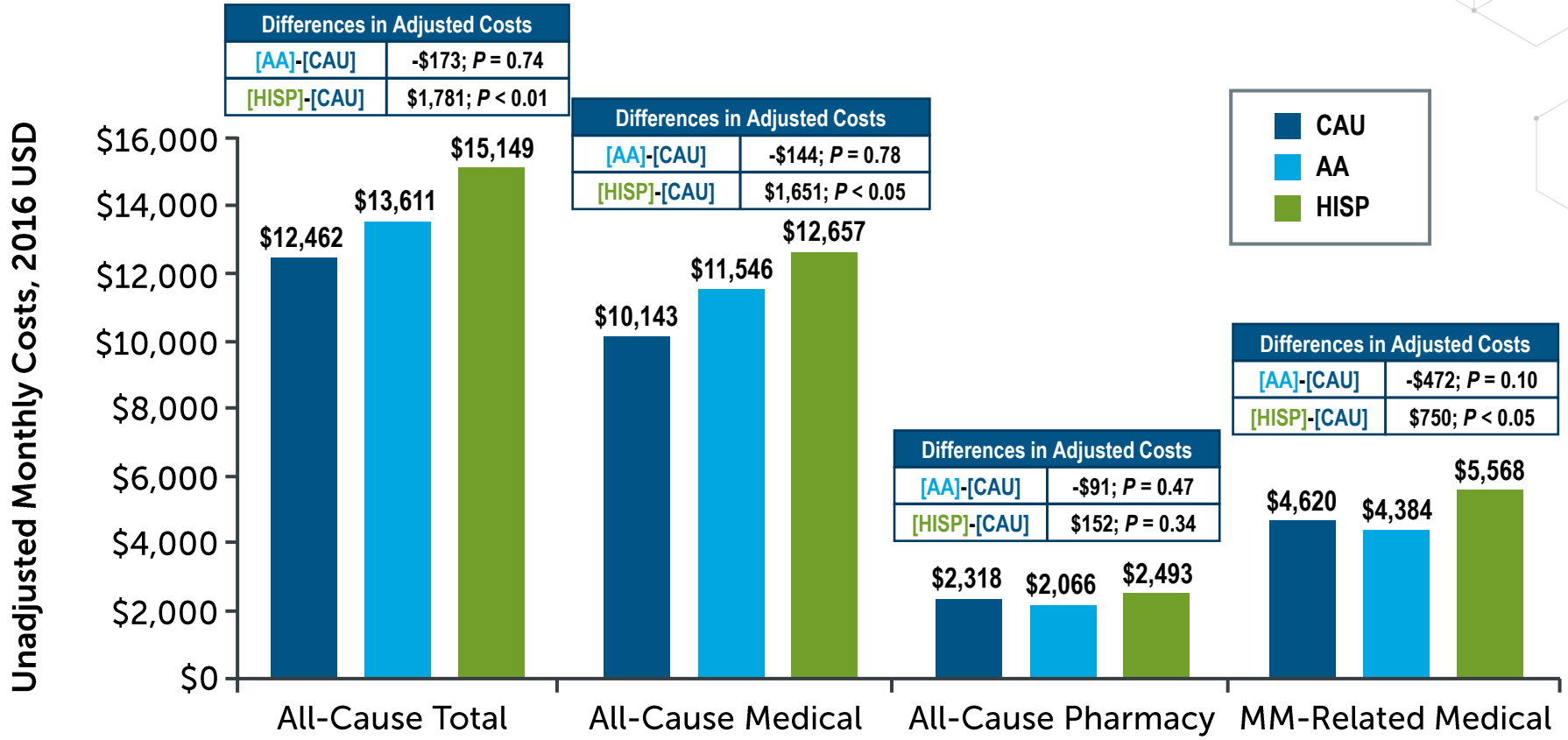
Total claims for patients with MM in Medicare by race and year of diagnosis



Ailawadhi S, et al. *Cancer*. 2018;124(8):1710-1721.

Racial Disparity in Cost of Care: Financial Toxicity

Healthcare cost over time by patient race-ethnicity:



Ailawadhi S, et al. *Blood Adv*. 2019;3(20):2986-2994.

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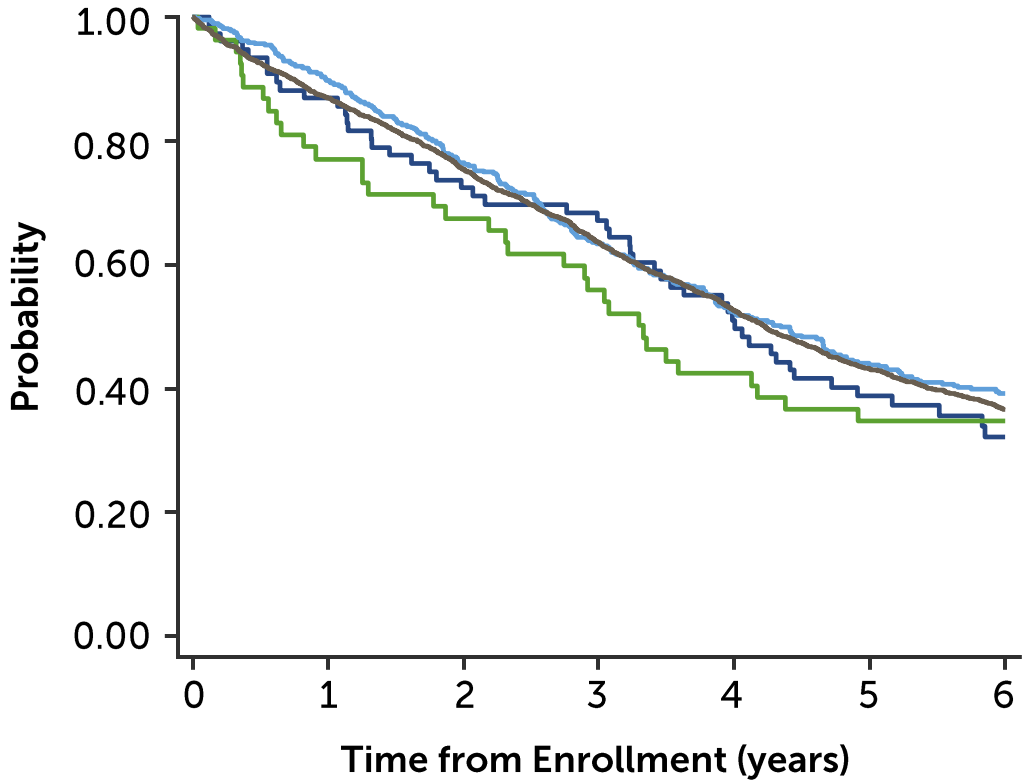
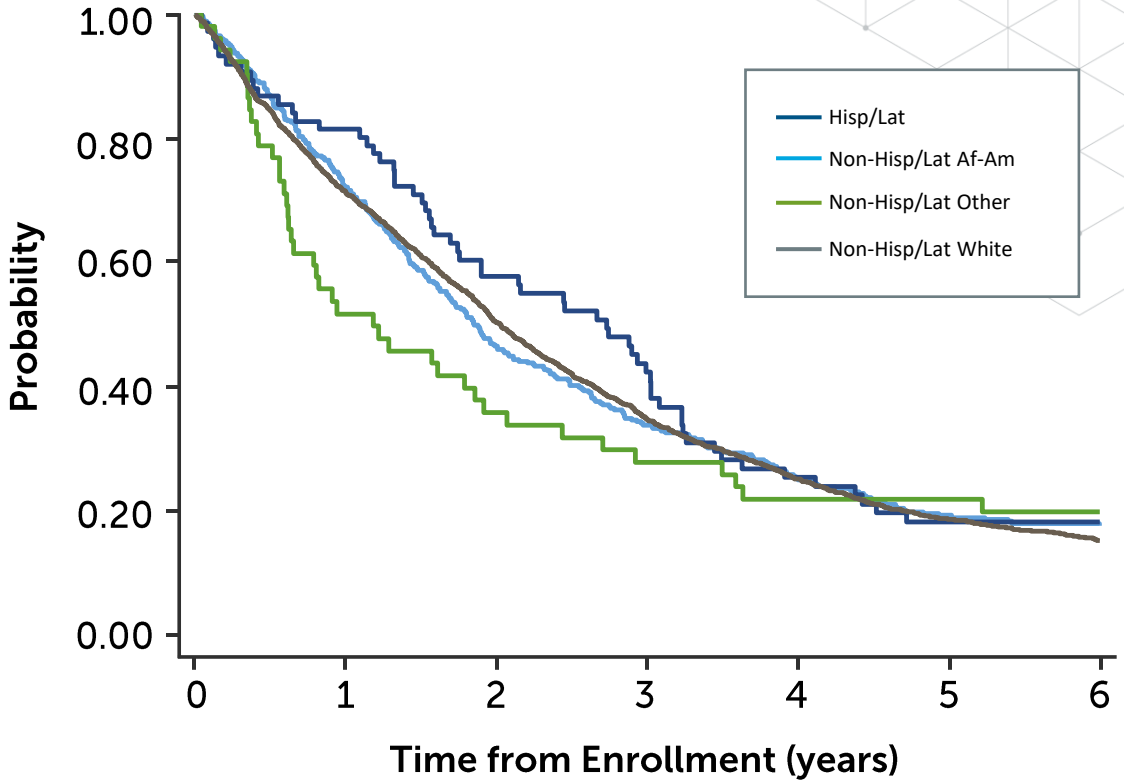
Cooperative Group Trials

Survival was related to clinical characteristics including age, performance status, kidney function, disease stage: **No effect of race/ethnicity on OS or PFS**

OS by Race/Ethnicity

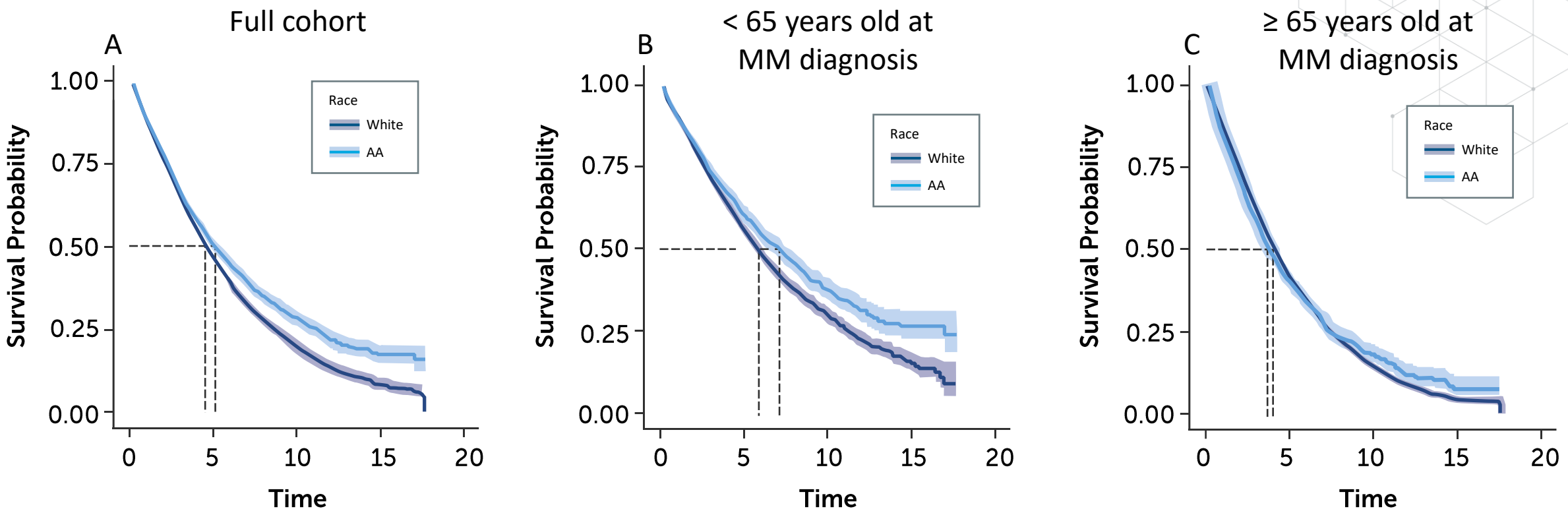


PFS by Race/Ethnicity



Ailawadhi S, et al. *Blood Cancer J.* 2018;8(7):67-74.

Survival by Race/Ethnicity: AA Can Have Better Survival



Fillmore NR, et al. *Blood*. 2019;133(24):2615-2618.

Strategies to Improve Access to Care

Moderated Panel Discussion

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Discussion Points: Improving Access to Care

- Strategies to discuss SDOH and address barriers to care
- Given the disparity in simply getting some patient populations SOC anti-myeloma treatment, how to we improve access to these new therapies?
- Strategies to engage community HCPs in improving access to care
- Improving enrollment of under-represented patients in clinical trials
- Resources, training, and current initiatives
- Culturally sensitive healthcare access and delivery

Audience Question

In which of the following racial/ethnic populations is stem cell transplant utilized the least for patients with multiple myeloma?

1. African American
2. Asian
3. Caucasian
4. Hispanic/Latino

Question and Answer Session

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Audience Question

How confident are your right now in your ability to interpret results from clinical trials evaluating the safety and efficacy of T-cell redirecting therapies as treatment for patients with multiple myeloma?

1. Not at all confident
2. Slightly confident
3. Somewhat confident
4. Fairly confident
5. Highly confident

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