ASH 2022 Update: Multiple Myeloma

Rebecca Silbermann, MD
silbermr@ohsu.edu

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Disease Biology

- MGUS (Iceland Studies)
- Disease variance by race and ethnicity

Smoldering Myeloma

- CURE trial updates

Older NDMM patients

- Dex sparing combinations

Bispecific Antibodies and other new things

- BCMA targets
- other targets

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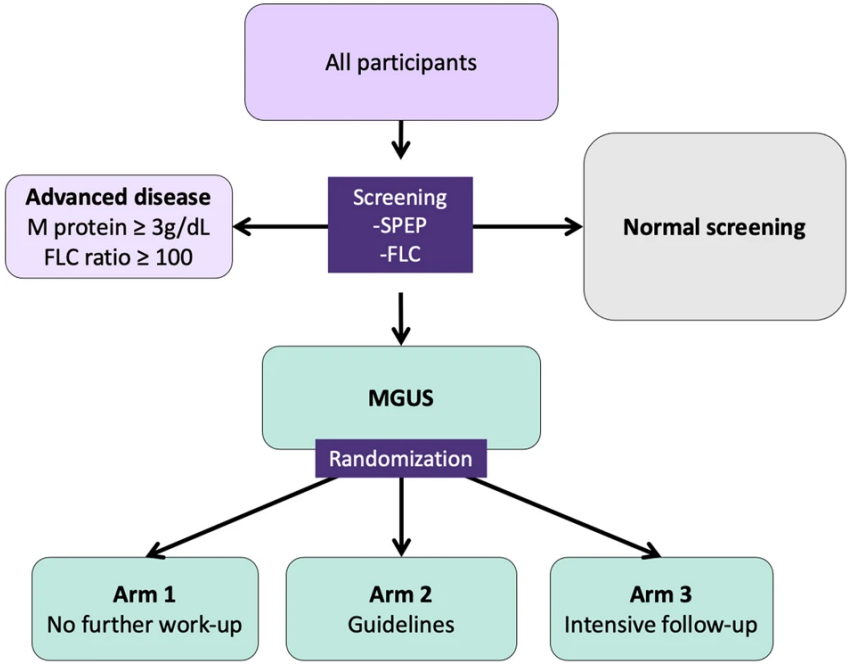
MGUS: iStopMM updates



- **All Iceland residents born before 1976**
- **54% (80,759) agreed to participate**
- **93% (75,422) screened**
- **4.9% (3,725) overall prevalence of MGUS**
  - **2.3% ages 40-59**
  - **6.2% ages 60 – 79**
  - **12.9% ages 80 - 103**

2022 Updates

- #103: Prevalence of MGUS is High in the iStopMM Study but the Prevalence of IgA MGUS Does Not Increase with Age in the Way other Immunoglobulin Subtypes Do
- #107: Predicting the Need for Upfront Bone Marrow Sampling in Individuals with MGUS
- #105: Sars-Cov-2 Vaccinations Do not Lead to Progression of MGUS
- #4507: Autoimmune Disease Are Not Associated with MGUS
- #4541: MGUS and Risk of Chronic Kidney Disease

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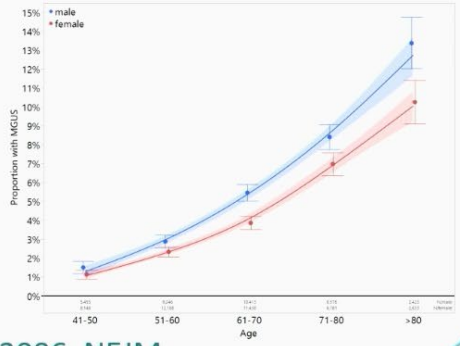
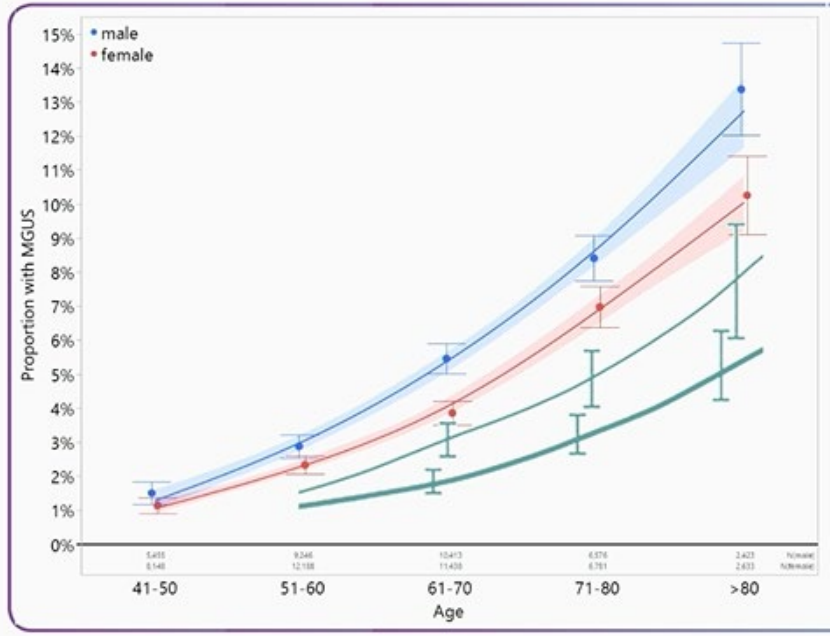
MGUS: iStopMM #103, IgA Prevalence

Age and sex standardized prevalence

- **Population invited to participate in 2016**
  - →Data from statistics Iceland, n=148,704
- **Over 40 years of age: 3.9%** (3.8%-4.0%)
- Over 50 years of age: 5.0% (4.9%-5.2%)

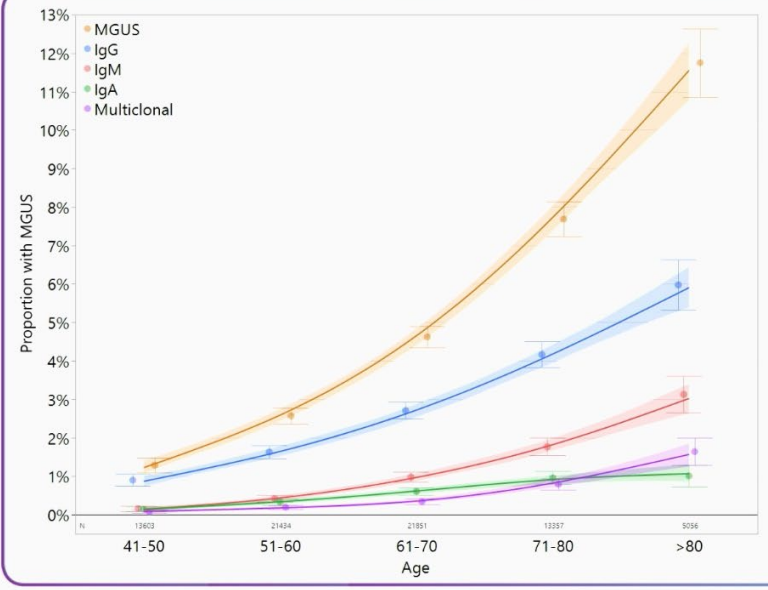


- **US population in 2000**
  - →Allows direct comparison to study by Kyle et al, 2006, NEJM
- Over 40 years of age: 3.8% (95%CI: 3.6%-3.9%)
- **Over 50 years of age: 5.2%** (95% CI: 5.0%-5.3%)



Population prevalence of MGUS by age and sex

overlay of data from Kyle et al



Population prevalence of MGUS by immunoglobulin subtype

Ig-type	iStopMM	Kyle et al
IgG	57.3%	68.9%
IgM	21.4%	17.2%
IgA	11.9%	10.8%
Biclonal	9.4%	3.0%

- Prevalence of IgA MGUS plateaus after age 70
  - →**IgA has been reported to be associated with more rapid progression**
  - →Future studies need to confirm and perhaps explain this phenomenon

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MGUS: iStopMM #107, When to get a marrow in MGUS?

Goal: Develop a multivariate model that incorporates common parameters to predict the probability of ≥ 10% clonal plasma cells on BMBx

Mayo Risk Stratification

1. Isotype subtype
2. Serum M protein size
3. Free light chain ratio

Absolute risk of progression at 20 years

Low-risk: (all of the following) — **5%**
- M protein ≤ 1.5g/dL
- IgG isotype
- Normal FLC ratio

Low-intermediate risk: any 1 factor abnormal — **21%**

High-intermediate risk: any 2 factors abnormal — **37%**

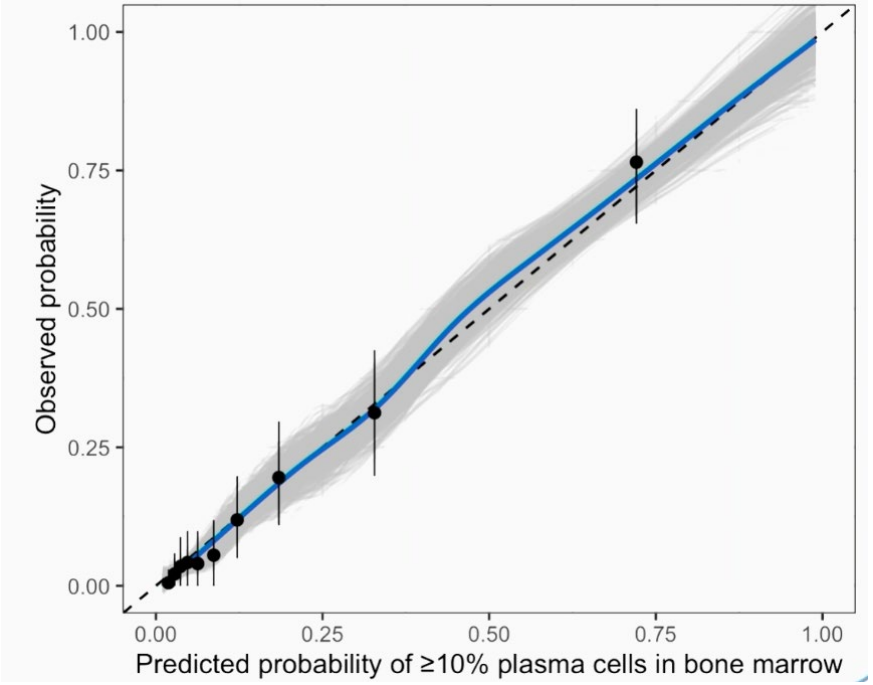
High risk: all 3 factors abnormal — **58%**

Skeletal imaging BMBx

Rajkumar Blood. 2005 Aug 1; 106(3):812-7

iStopMM Model

- Derived from 1,013 persons with IgG, IgA or biclonal MGUS
- Predictors: isotype, M protein, FLC ratio, total IgG, IgA, IgM



https://istopmm.com/riskmodel/

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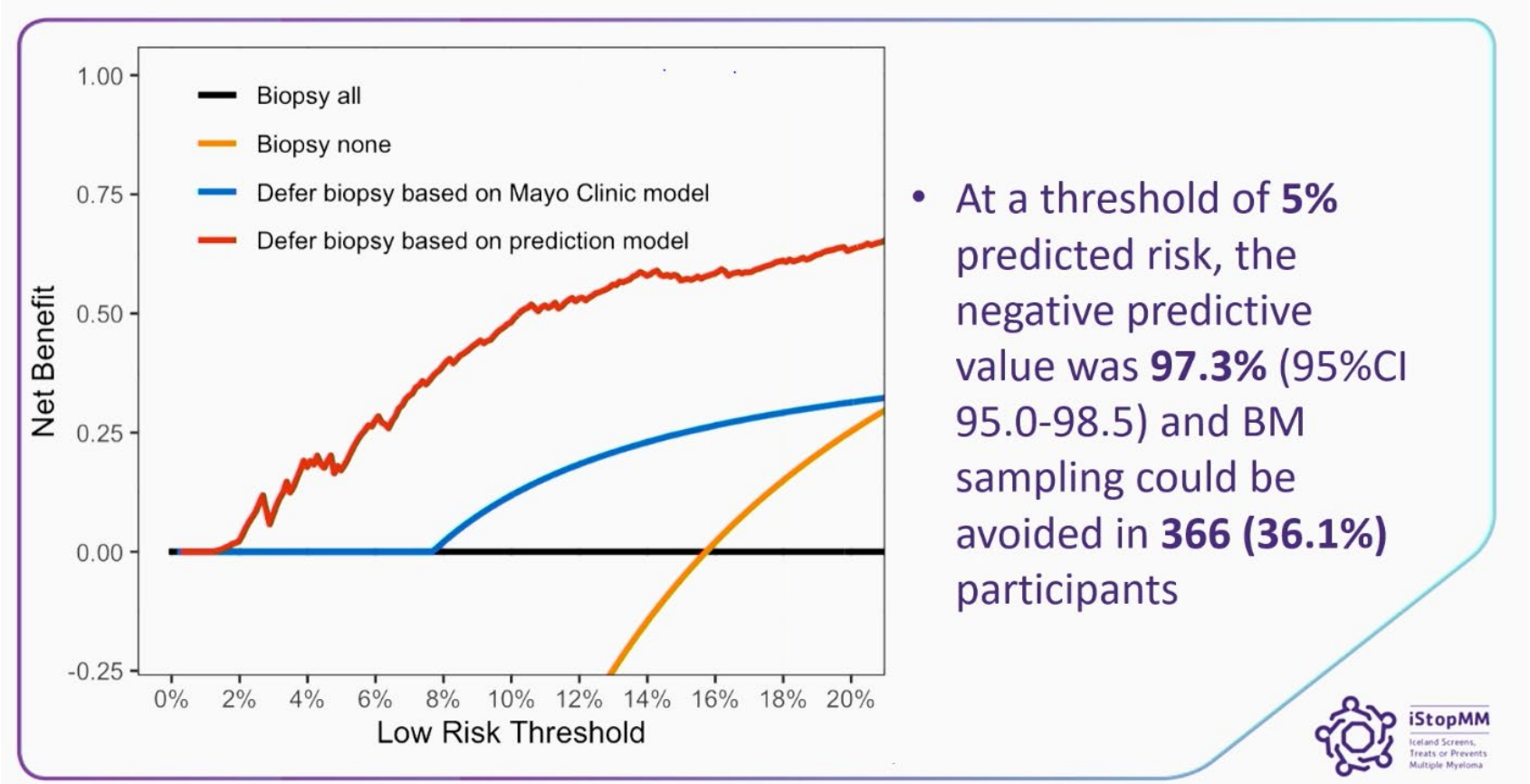
MGUS: iStopMM #107, Which MGUS patients should get a marrow?

Goal: Develop a multivariate model that incorporates common parameters to predict the probability of ≥ 10% clonal plasma cells on BMBx



- At a threshold of **5%** predicted risk, the negative predictive value was **97.3%** (95%CI 95.0-98.5) and BM sampling could be avoided in **366 (36.1%)** participants

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

https://istopmm.com/riskmodel/

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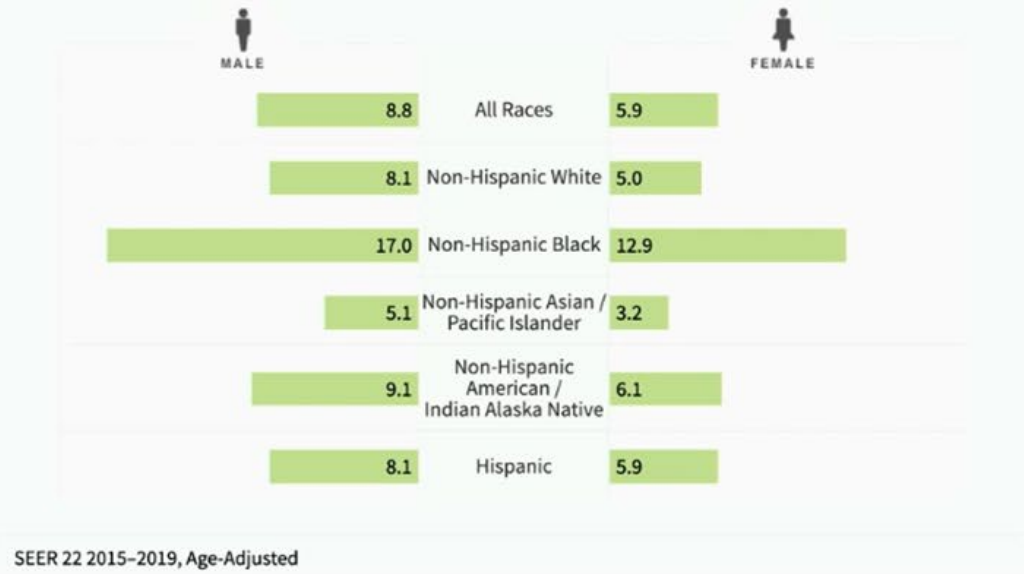
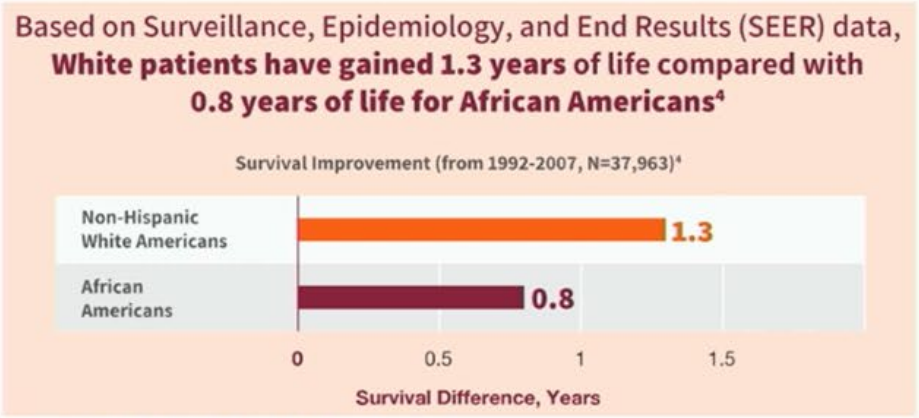
Race and Ethnicity:





Standing in the Gaap, Bristol Myers Squibb.

Compared to Non-Hispanic Whites, Non-Hispanic Black and Hispanic patients are:

- ***Less likely*** to receive transplant and novel therapies
- Have a ***longer time*** from diagnosis to treatment initiation
- ***Underrepresented*** in clinical trials

4

Schriber et al. (2017) *Cancer*; Ailawadhi et al., (2017) *Cancer Med*; Ailawadhi et al. (2019) *Blood Adv.*

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Race and Ethnicity: #3582: The Impact of Hispanic Ethnicity on Disease Characteristics in Multiple Myeloma

- Retrospective study of newly dx MM patients at Columbia 1/18 – 12/21 – to determine if Hispanic clinical characteristics and outcomes (Wash heights, predom Dominican)

Demographic and clinical characteristics of patients with newly diagnosed multiple myeloma at CUIMC from 2018-2021.

(n=number of patients with available data)	Hispanics (n=76)	Non-Hispanics (n=125)	p-value
Age at diagnosis, median (range)	68.8 (41.2-93.7)	66.8 (29.5-91.7)	0.274
Sex, male (%)	43.4	60.8	0.016*
Light-Chain Myeloma (%)	24	24.2	0.975
ISS stage (n=177)			
Stage I (%)	30.9	32.1	0.218
Stage II (%)	38.2	26.6	
Stage III (%)	30.9	41.3	
eGFR<60 at diagnosis (%) [n=196]	52	48.8	0.659
Hypercalcemia at diagnosis (%) [n=193]	14.9	16.8	0.719
Bone disease at diagnosis (%) [n=195]	84	79.2	0.398
Extramedullary Disease[a] (%) [n=121]	10.9	9.3	0.785
Hyperdiploidy (%) [n=167]	63.1	52.9	0.196
t(11;14) (%) [n=175]	16.9	30.0	0.049*
FISH High-Risk[b] (%) [n=130]	38.5	29.5	0.288
1q gain or amplification (%) [n=124]	52.2	47.4	0.610
del(1p) (%) [n=125]	25.5	10.3	0.026*
del(17p) (%) [n=162]	19.7	8.9	0.052
FISH Expanded High Risk[c] (%) [n=133]	73.6	55.0	0.028*
R-ISS stage [n=153]			
Stage I (%)	13.1	19.6	0.244
Stage II (%)	68.9	55.4	
Stage III (%)	18.0	25.0	
HDM-ASCT in 1st line (%)	35.7	40.7	0.466

[a]Extraosseous extramedullary disease
[b]Included t(4;14), t(14;16), t(14;20), del(17p), or amp(1q)-≥4 copies
[c]Included high-risk as above plus gain (1q) and del (1p)

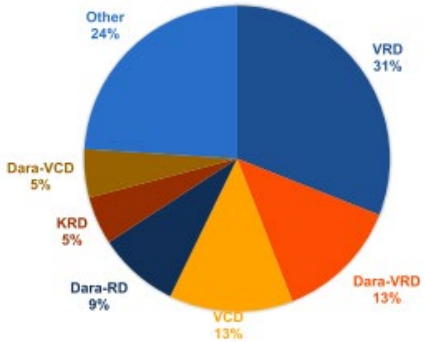

Figure 1. Induction Regimens. Other induction regimens were used in <5% of cases each.

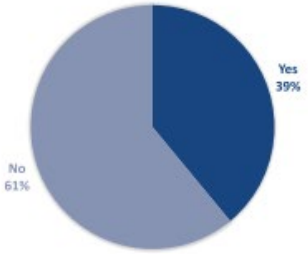

Figure 2. Upfront high-dose melphalan autologous stem cell transplant. **There was no significant difference in upfront transplant utilization between ethnicity.**

Clinical Outcomes

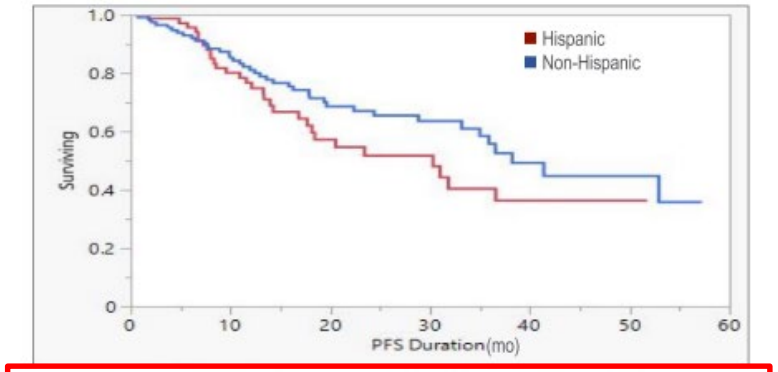

Figure 3. Progression free survival (PFS). **Median PFS of Hispanics was 30.3 months (95%CI 17.6-NR) compared to 38.2 months (95%CI 33.2-NR) in non-Hispanics (p=0.15)**

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Race and Ethnicity: #252: Racial and Ethnic Differences in Clinical Outcomes Among Multiple Myeloma Patients Treated with CAR T therapy

- **Pooled data for 215 RRMM treated with SOC ide-cel (US MM Cellular Therapy Consortium)**

Patient Characteristics	Hispanic N = 21	NH Black N = 36	NH White N = 150	P
Patient age, Median (Range)	57.0 (43.0, 78.0)	62.5 (42.0, 83.0)	65.0 (36.0, 81.0)	0.1
Male sex, n (%)	15 (71%)	15 (42%)	93 (62%)	0.04
Extramedullary disease, n (%)	13 (62%)	15 (42%)	64 (43%)	0.2
High marrow burden (>= 50%), n (%)	7 (35%)	12 (34%)	35 (26%)	0.5
Unknown	1	1	17	
ECOG performance status at LD, n (%)				0.7
0-1	17 (85%)	23 (79%)	125 (84%)	
2-4	3 (15%)	6 (21%)	23 (16%)	
Unknown	1	7	2	
R-ISS at CAR-T infusion, n (%)				0.9
I	6 (29%)	6 (19%)	21 (20%)	
II	10 (48%)	18 (56%)	53 (50%)	
III	5 (24%)	8 (25%)	31 (30%)	
Unknown	0	4	45	
High-risk cytogenetics, n (%)	4 (24%)	8 (24%)	51 (39%)	0.2
Unknown	4	3	19	
Bridging therapy, n (%)	15 (71%)	30 (86%)	114 (76%)	0.4
Unknown	0	1	0	
Number of prior lines of therapy, Median (Range)	6.0 (4.0, 11.0)	7.0 (4.0, 19.0)	6.0 (3.0, 18.0)	0.3
Prior BCMA therapy, n (%)	5 (24%)	9 (25%)	35 (23%)	>0.9

NH: Non-Hispanic, ECOG: Eastern Cooperative Oncology Group, LD: lymphodepletion, BCMA: B cell maturation antigen.

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Race and Ethnicity: #252: Racial and Ethnic Differences in Clinical Outcomes Among Multiple Myeloma Patients Treated with CAR T therapy

Patient characteristics	Hispanic, N = 21	NH Black, N = 36	NH White, N = 150	*P*
Prior auto SCT, n (%)	19 (90%)	29 (81%)	129 (86%)	0.6
Refractory status, n (%)				
Double refractory	18 (86%)	32 (89%)	131 (87%)	0.9
Triple refractory	15 (71%)	30 (83%)	125 (83%)	0.4
Penta refractory	7 (33%)	14 (39%)	66 (44%)	0.6
Cell dose (<400 vs. ≥400), n (%)				>0.9
< 400	10 (48%)	15 (43%)	64 (43%)	
≥ 400	11 (52%)	20 (57%)	85 (57%)	
Unknown	0	1	1	
Baseline Ferritin, Median (Range)	354.0 (20.0, 4,862.0)	721.5 (22.0, 8,537.0)	314.5 (9.0, 27,260.0)	0.06
Unknown	0	2	2	
Baseline CRP, Median (Range)	0.6 (0.0, 84.4)	3.5 (0.1, 286.0)	0.8 (0.0, 275.4)	0.03
Unknown	0	2	7	
Albumin pre-CAR T infusion, Median (Range)	3.8 (2.1, 4.4)	3.5 (2.1, 4.1)	3.7 (1.7, 4.8)	0.08
Unknown	0	1	0	
Met criteria for KarMMa1 pre-CAR T infusion, n (%)	5 (24%)	7 (19%)	38 (25%)	0.8

NH: Non-Hispanic, SCT: stem cell transplant, CRP: C-reactive protein.

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Race and Ethnicity: #252: Racial and Ethnic Differences in Clinical Outcomes Among Multiple Myeloma Patients Treated with CAR T therapy

Safety by race and ethnicity

Safety	Hispanic N = 21	NH Black N = 36	NH White N = 150	*P*
Any CRS, n (%)	16 (76%)	33 (97%)	125 (84%)	0.05
CRS grade, n (%)				0.2
No CRS	5 (24%)	1 (2.9%)	23 (16%)	
Grade 1 or 2	16 (76%)	32 (94%)	120 (81%)	
Grade ≥3	0 (0%)	1 (3%)	5 (3%)	
Any ICANS, n (%)	4 (20%)	5 (16%)	29 (21%)	0.9
ICANS grade, n (%)				0.6
No ICANS	16 (80%)	26 (84%)	108 (79%)	
Grade 1 or 2	2 (10%)	2 (7%)	21 (15%)	
Grade ≥3	2 (10%)	3 (10%)	8 (6%)	
Length of hospital stay in days*, Median (Range)	8.0 (6.0, 21.0)	12.5 (7.0, 68.0)	9.0 (5.0, 69.0)	0.01
ICU admission, n (%)	1 (5%)	2 (6%)	14 (10%)	0.8
Grade ≥ 3 cytopenia ≥ 30 days, n (%)	9 (56%)	26 (87%)	83 (72%)	0.07
Infection, n (%)	10 (48%)	16 (47%)	42 (28%)	0.04

*Total days of hospital stay including readmissions.

NH: Non-Hispanic, CRS: cytokine release syndrome, ICANS: immune effector cell-associated neurotoxicity syndrome, ICU: intensive care unit.

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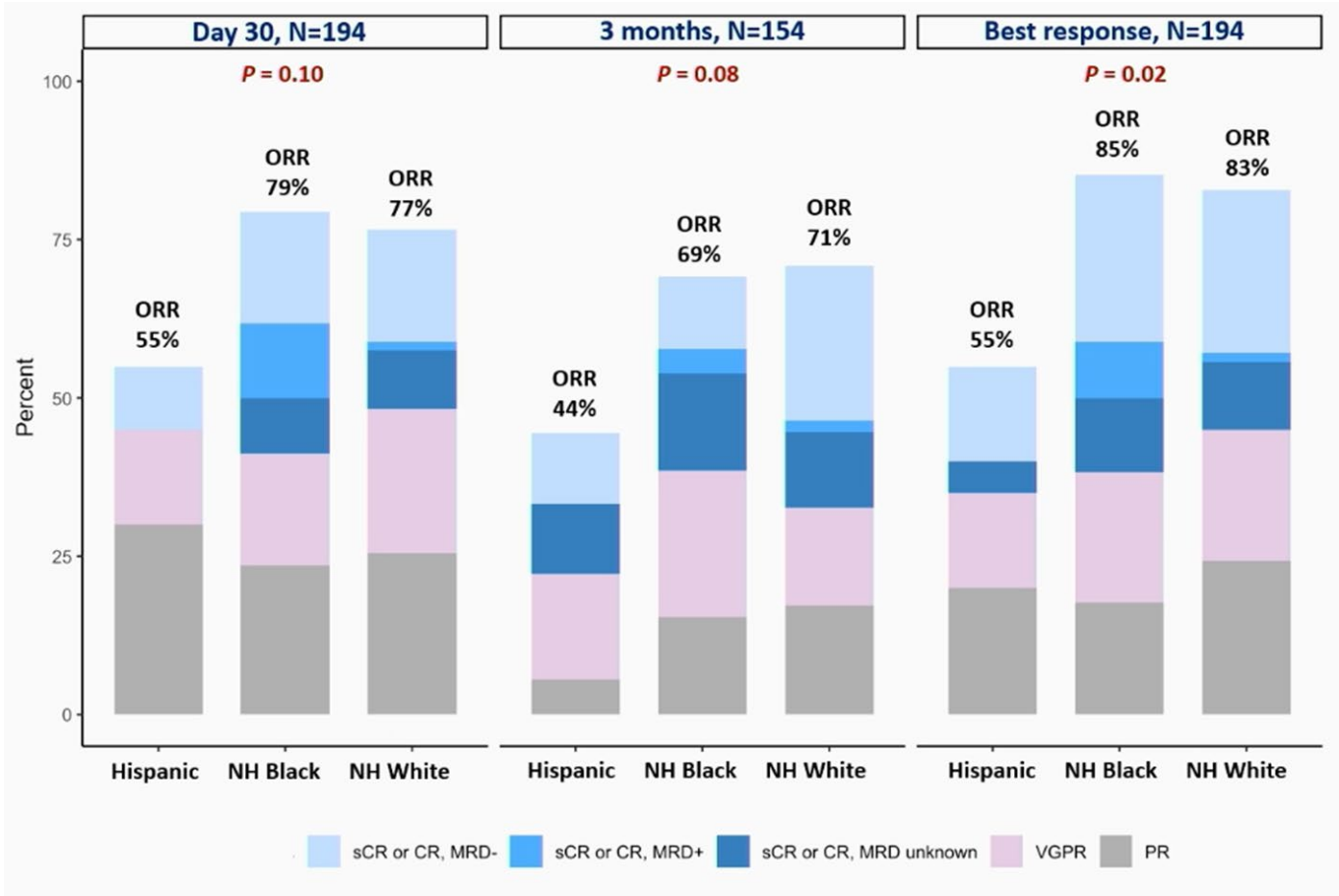
Race and Ethnicity: #252: Racial and Ethnic Differences in Clinical Outcomes Among Multiple Myeloma Patients Treated with CAR T therapy



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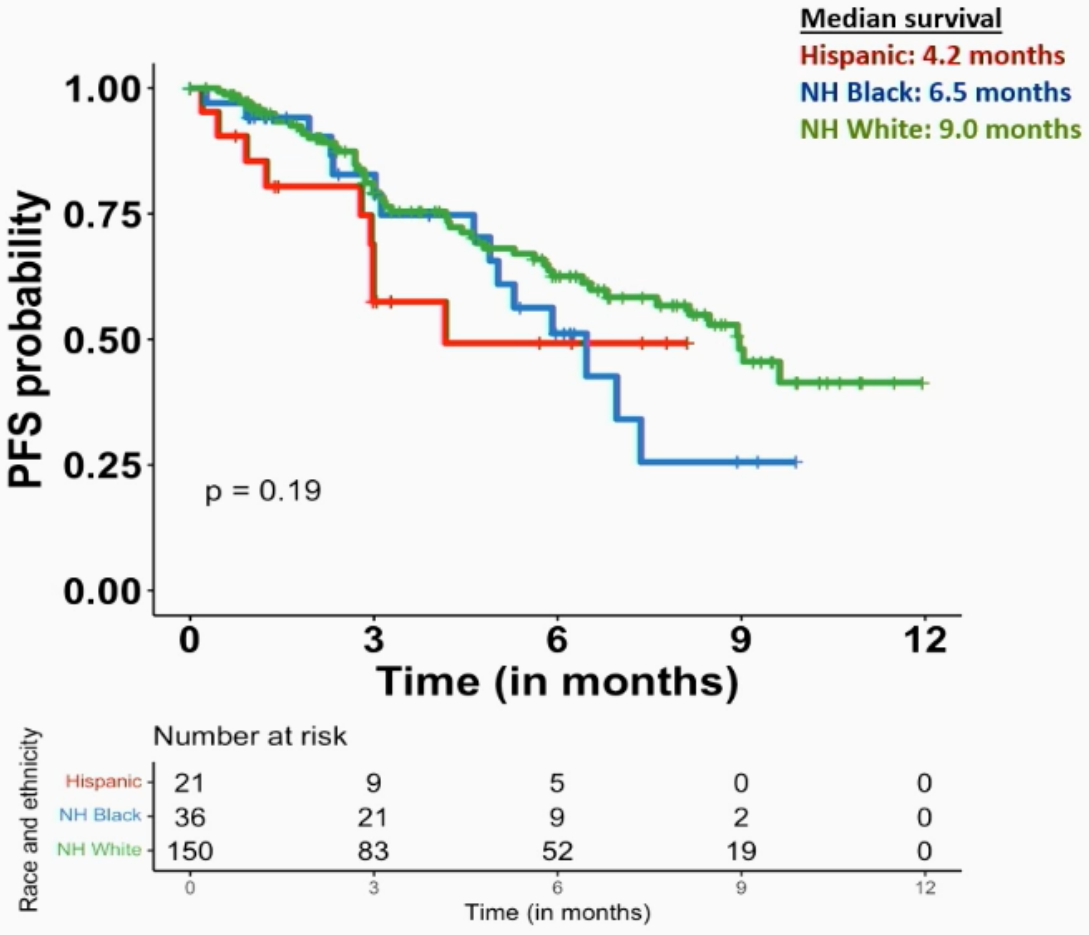

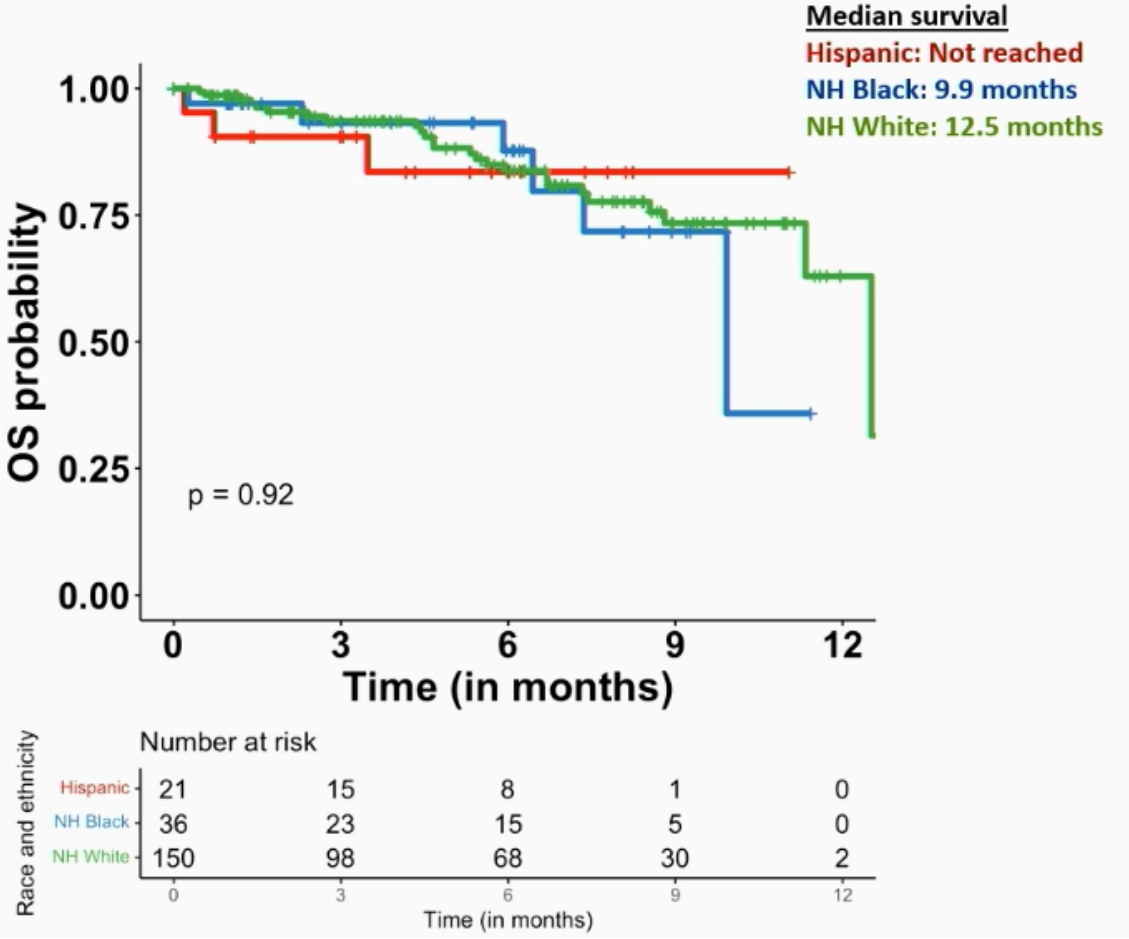

Author conclusions: There may be racial and ethnic differences in systemic inflammation, safety, and efficacy among RRMM patients treated with ide-cel in the real world setting.

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SMM: CURE trial updates

#757, ASCENT (daraKRd x2y for high-risk SMM)
#118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

Goal: Determine if intense therapy can provide a significant reduction in tumor burden and result in long term responses or cure

Patients with high-risk SMM are likely to progress to active MM within 2 yr

- Models can identify patients at high risk of progression to active MM (>50% risk within 2 yr)
  - Mayo model includes presence of both ≥3 g/dL serum M-protein and ≥10% PCs in BM
  - Spanish model includes ≥3 g/dL serum M-protein or ≥10% PCs in BM *and* ≥95% aberrant PCs within BM PC compartment by immunophenotyping and immunoparesis

- Early lenalidomide ± dexamethasone shown in 2 phase III trials to decrease risk of progression to active MM and delay TTP, with a signal of OS benefit.

1. Mateos. Eur J Cancer. 2022;174:243. 2. Mateos. NEJM. 2013;369:438. 3. Mateos. Lancet Oncol. 2016;17:1127.

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SMM: CURE trial updates

#757, ASCENT (daraKRd x2y for high-risk SMM)

Open-label phase II study: median f/u 26.2 mo

Patients with untreated, high-risk smoldering MM*; adequate marrow and organ function; no evidence of amyloidosis or significant comorbidities (N = 87)

→

Induction
Six 4-Wk Cycles

Carfilzomib 36 mg/m^2 twice weekly or 56 mg/m^2 weekly

Lenalidomide 25 mg daily x 3 wk per cycle

Daratumumab weekly for 8 wk; every other wk for 16 wk

Dexamethasone 40 mg weekly

→

Consolidation
Six 4-Wk Cycles

Carfilzomib 36 mg/m^2 twice weekly or 56 mg/m^2 weekly

Lenalidomide 25 mg daily x 3 wk per cycle

Daratumumab every 4 wk

Dexamethasone 20 mg weekly

→

Maintenance
Twelve 4-Wk Cycles

Lenalidomide 10 mg daily x 3 wk per cycle

Daratumumab every 8 wk

*Defined with IMWG updated risk stratification with any 2 of the following: serum M spike >2 g/dL *or* involved to uninvolved FLC ratio >20 *or* bone marrow PC % >20%, *or* score of ≥9 using risk scoring system of FLC ratio, serum M spike, marrow plasma cell %, and presence of high-risk FISH.

- **Primary endpoint:** rate of confirmed sCR
- **Secondary endpoints:** rate of MRD negativity (10^{-5} by flow cytometry), OS, PFS, safety, and toxicities

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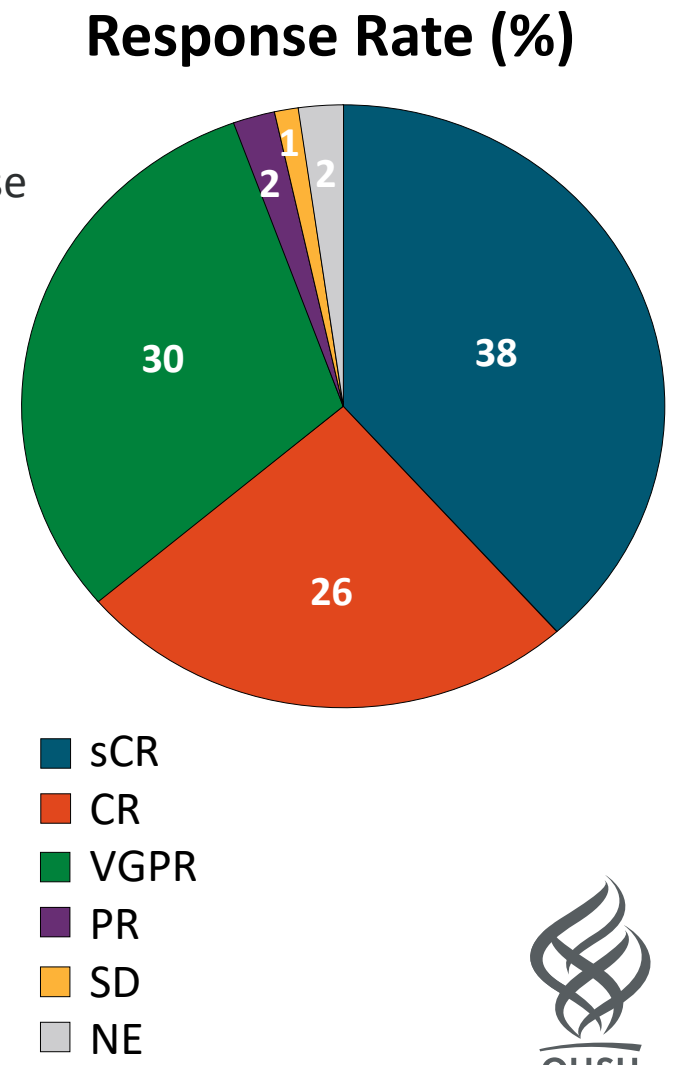
SMM: CURE trial updates

#757, ASCENT (daraKRd x2y for high-risk SMM)

- ORR 97% (92% ≥ VGPR)
  - 84% MRD neg (61% CR with MRD neg)
- Median time to MRD negativity: 6.6 mo, with patients continuing to deepen response over time
- Majority of patients remain in deep remission after completion of 2y of therapy
- 3y PFS rate: 89.9% (95% CI: 82.3% - 98.3%) – median PFS for cohort has not been reached

4 patients progressed: 3 biochemical progression
1 plasma cell leuk 6mo after completing rx



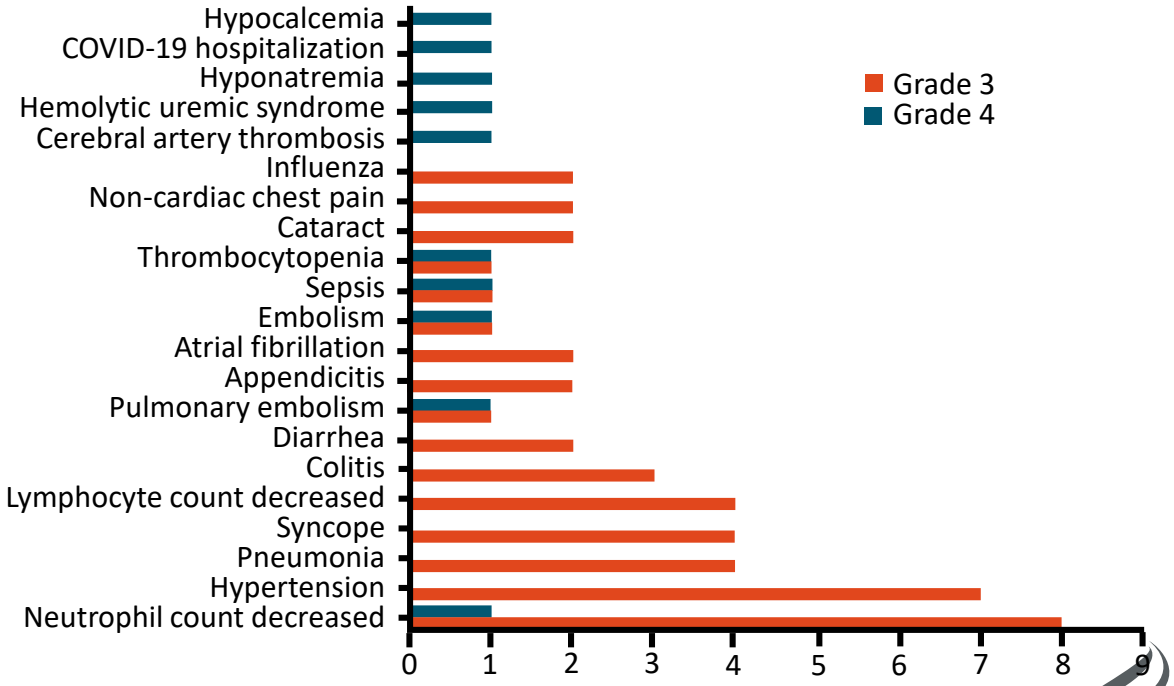
SMM: CURE trial updates

#757, ASCENT (daraKRd x2y for high-risk SMM)

- **No new toxicity signals observed**

Event	Patients (N = 87)
Any-grade AE possibly related to Tx, n (%)	81 (92)
Hematologic EA grade ≥3, n (%)	16 (18)
Nonhematologic AE grade ≥3, n (%)	44 (51)
Dose reductions, n	
▪ Carfilzomib	12
▪ Lenalidomide	12
▪ Dexamethasone	14
Median dose per cycle, mg	
▪ Daratumumab	1600
▪ Carfilzomib	312
▪ Lenalidomide	210
▪ Dexamethasone	80

Grade 3 AEs Observed in ≥2 Patients or Grade 4 AEs in ≥1 Patient

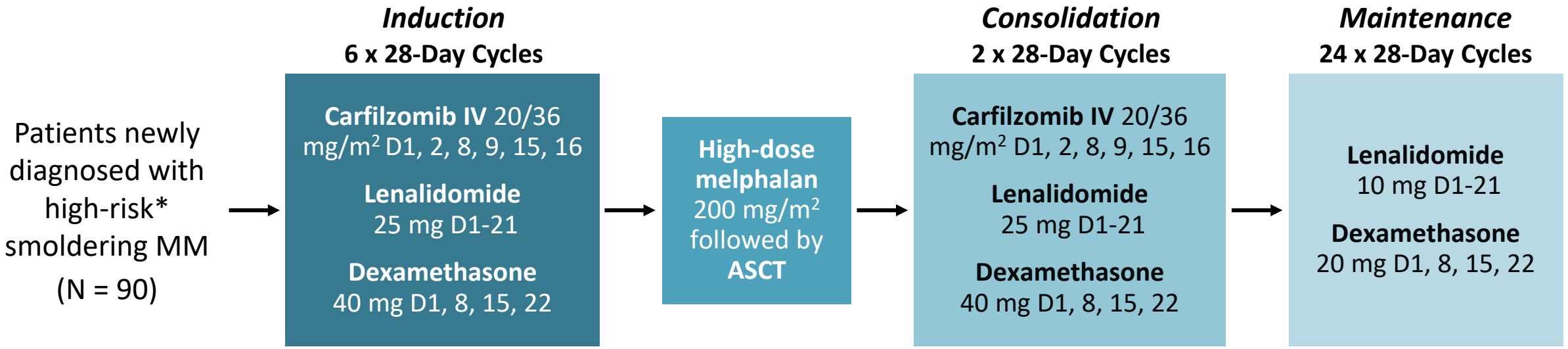


Deaths on trial: COVID-19 (n = 2), RSV (n = 1), PD (n = 1)

SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

- Multicenter, open-label phase II trial, Median follow-up: 70.1 mo



*Using Mayo and/or Spanish models (pre-2014 diagnostic criteria): ≥3 g/dL serum M-protein and ≥10% PCs in BM or either ≥3 g/dL serum M-protein or ≥10% PCs in BM and >95% of aberrant PCs within PCs in BM by immunophenotyping and immunoparesis.

- Patients included with ≥1 biomarker predictive for imminent risk of progression
- Patients with bone disease on CT or PET/CT at screening excluded

- **Primary endpoint:** MRD negativity (by flow cytometry) after HDT-ASCT and at 3 yr and 5 yr after HDT-ASCT
  - MRD assessment at 3 yr amended to 4 yr due to COVID-19 pandemic
- **Secondary endpoints:** response, TTP, PFS, OS, biochemical progression, safety

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SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

Characteristic	Patients (N = 90)
Median age, yr (range)	59 (33-70)
Median serum / urine M-protein, g/dL (range) / g/24 hr (range)	2.77 (0-8.6) / 0.43 (0-7.2)
Median PCs in bone marrow, % (range)	22 (10-80)
High-risk definition, n (%)	
▪ Mayo Clinic model only	19 (21)
▪ Spanish model only	47 (52)
▪ Both	24 (27)
Ultra high risk (≥1 biomarker), n (%)	30 (33)
▪ Serum FLC ratio >100	18 (20)
▪ >1 focal lesion on MRI	11 (12)
▪ ≥60% PCs in bone marrow	7 (8)
PET positive with no lytic lesions, n (%)	5 (6)
Cytogenetic abnormalities, n (%)	
▪ Standard risk	54 (60)
▪ High risk: t(4;14), t(14;16), del17, del1p	31 (34)
▪ Unknown risk	5 (6)

- Median follow-up: 70.1 mo (range: 6.2-88.8)
- 70 patients completed all treatment, including 2 yr of maintenance

Response Category, n (%)	Induction (N = 90)	HDT-ASCT (N = 90)	Consolidation (N = 90)	Maintenance (N = 90)
ORR, n (%)	85 (94)	82 (91)	85 (94)	80 (95)
▪ ≥ CR	37 (41)	54 (60)	64 (70)	58 (64)
▪ VGPR	35 (39)	17 (19)	14 (16)	9 (10)
▪ PR	13 (14)	11 (12)	7 (8)	3 (3)
Stable disease	1 (1)	1 (1)	--	--
Progressive disease	2 (3)*	--	--	7 (7)†
Not evaluable	2 (3)	7 (8)	5 (5)	13 (14)
MRD negative at 10^{-5}	36 (40)	56 (63)	51 (63)	47 (52)

SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

Undetectable MRD, n (%)	3 Mo After ASCT (n = 82)	4 Yr After ASCT (n = 58)
MRD neg at 10^{-5}	56 (68)	25 (43)
MRD neg at 10^{-6}	39 (48)	28 (48)

Evaluable patients included those that discontinued earlier than the specific time point due to biochemical progression or progressive disease.

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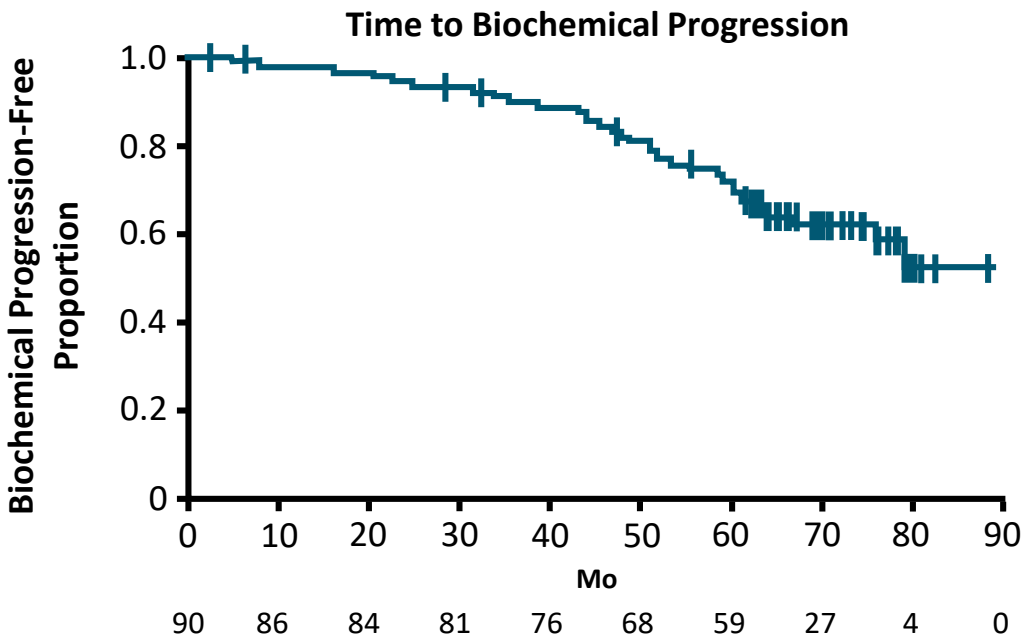
SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

- 34 patients had biochemical progression
  - 9 (26%) during treatment phase
  - 8 (24%) during first 4 yr after treatment
  - 17 (50%) between fourth and fifth yr post transplant
- Type of biochemical progression
  - Progressive disease: 8 (24%)
  - Relapse from CR: 19 (56%)
  - Ultrasensitive MRD relapse: 7 (21%)
    - Defined as confirmed conversion from MRD positive to negative with sensitivity ≥10^{-5} or >1-log increase between first and second determination (if sensitivity 10^{-6})

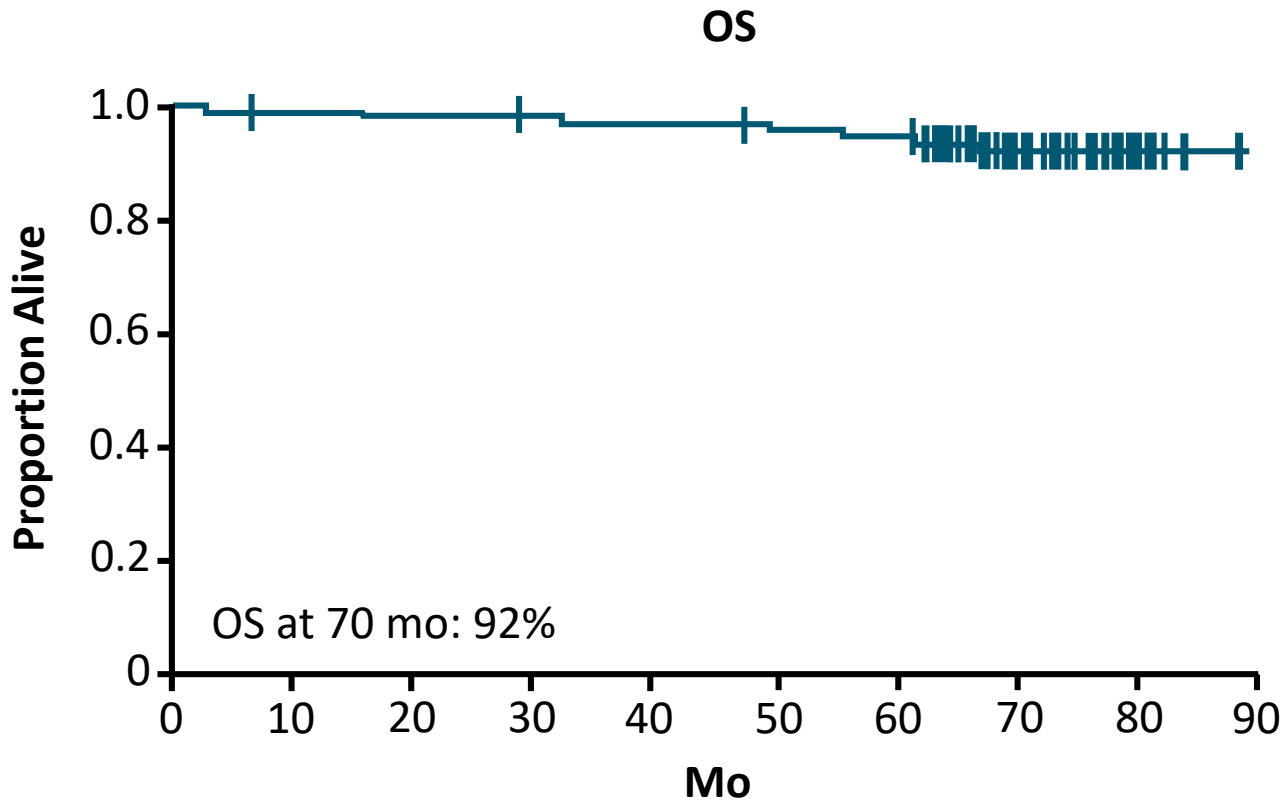


OHSU

SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

- 7 patients have died (OS at 70 mo: 92%)
  - 3 related to PD (1 after rescue therapy with DaraPd)
  - 1 cardiac arrest, not related to treatment
  - 1 massive ischemic stroke during induction
  - 1 related to lung cancer
  - 1 related to MDS



OHSU

SMM: CURE trial updates

118, GEM-CESAR (KRd + autoSCT) Post-Hoc Analysis of Sustained MRD

- 68% of evaluable patients were MRD negative at 3 mo after ASCT, and 43% remained negative at 4 yr post ASCT
- 94% of patients had not progressed to active MM at 70 mo
  - Presence of SLiM criteria and presence of MRD at end of maintenance predicted for progression to MM
- Although 48% of patients had biochemical progression at 70 mo, rescue therapy with DaraPd led to response in 79% of evaluable patients, allowing majority to continue with no myeloma-defining events

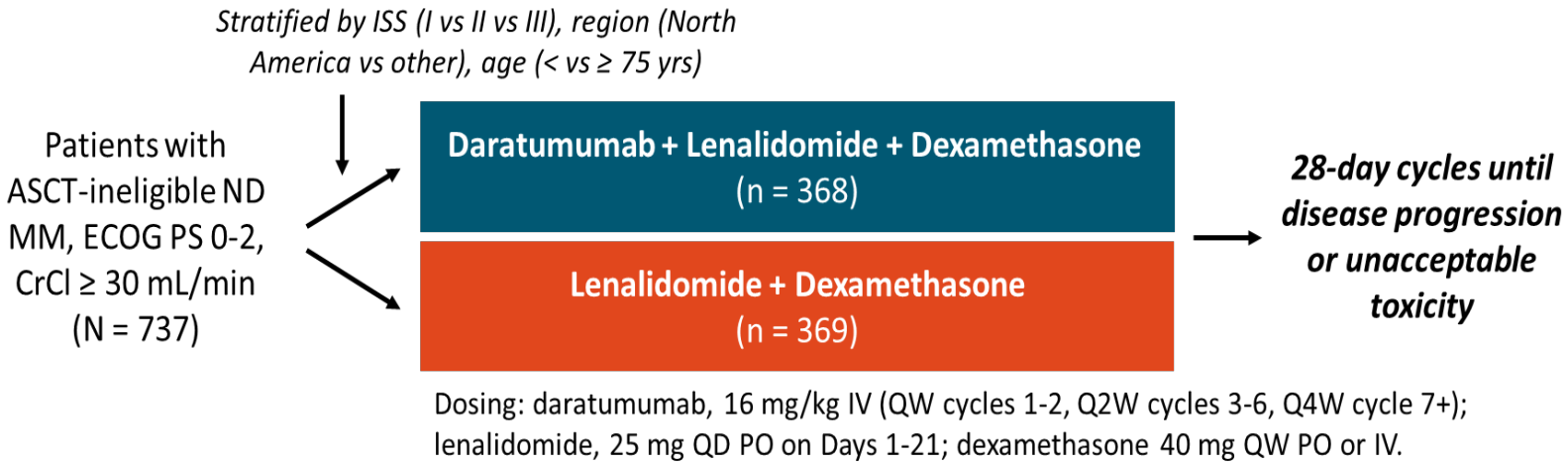
- MRD negativity after maintenance and sustained MRD negativity at 4 yr after ASCT were predictive of continued disease response (lack of biochemical progression)

OHSU

NDMM: Frail Patients

#3245: Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Transplant-Ineligible Patients (Pts) with Newly Diagnosed Multiple Myeloma (NDMM): Clinical Assessment of Key Subgroups of the Phase 3 Maia Study

- Multicenter, open-label, randomized phase III trial



Dosing: daratumumab, 16 mg/kg IV (QW cycles 1-2, Q2W cycles 3-6, Q4W cycle 7+); lenalidomide, 25 mg QD PO on Days 1-21; dexamethasone 40 mg QW PO or IV.

- Primary endpoint: PFS
- Secondary endpoints: TTP, CR/sCR, MRD by NGS (10^{-5}), PFS2, OS, ORR, safety

*64.5 mo median follow-up

Subgroups Evaluated*

- Age ≥ 75y
- ISS III
- Renal insufficiency
- Extramedullary plasmacytomas
- High cytogenetic risk (≥1 of t(4;14), t(4:16), del 17p, 1q gain or amp)

Manier. ASH 2022. Abstr 569.

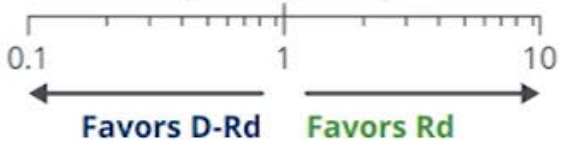
OHSU

NDMM: Frail Patients

#3245: MAIA Subgroups

FIGURE 1: Subgroup analysis of PFS in the ITT population

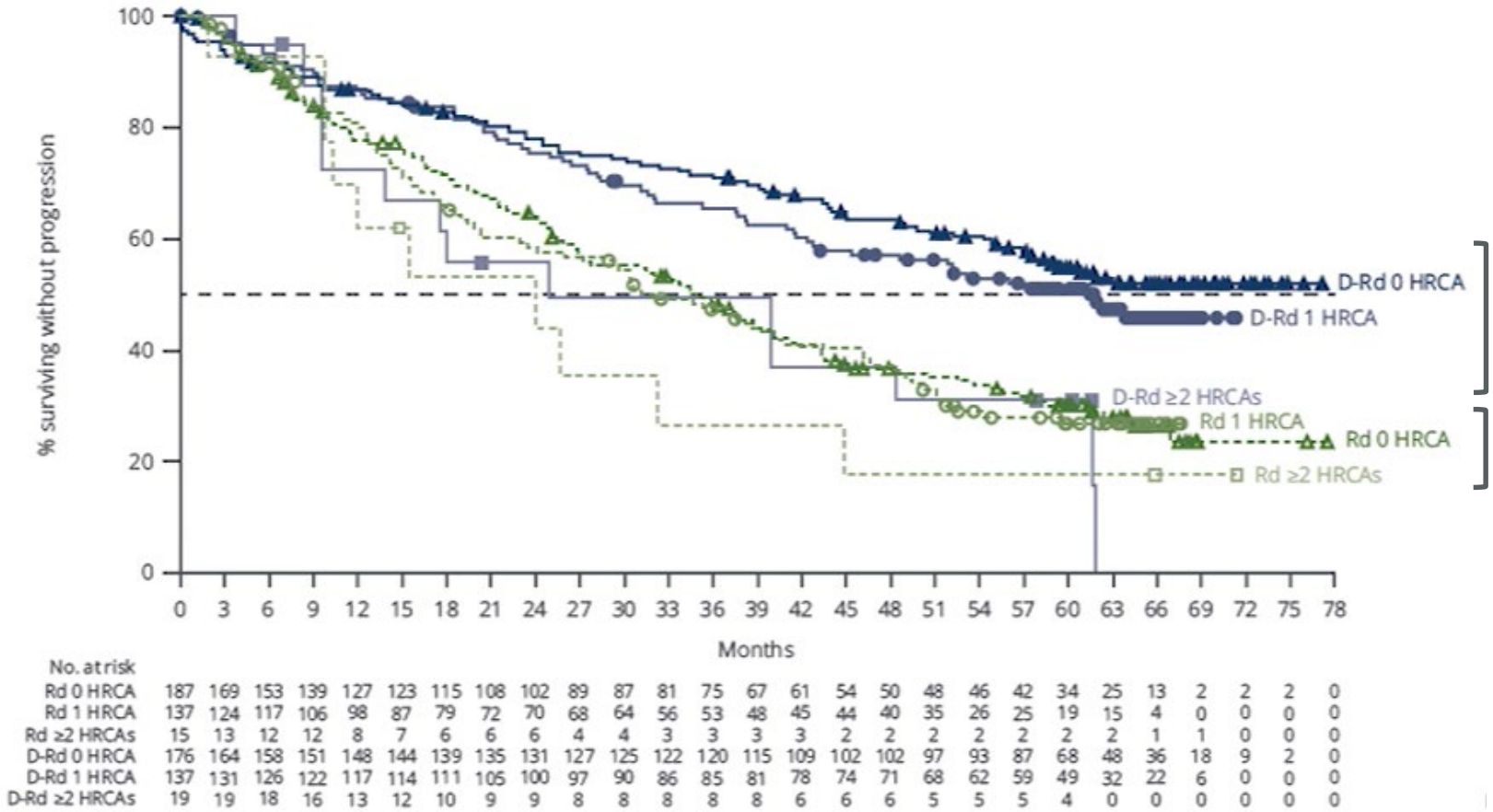
	D-Rd		Rd		
	n/N	*Median PFS (mo)*	*n/N*	*Median PFS (mo)*	HR (95% CI)[a]
ITT (overall)	176/368	61.9	228/369	34.4	0.55 (0.45-0.67)
Baseline characteristic					
Age ≥75 years	87/160	54.3	106/161	31.4	0.59 (0.44-0.79)
ISS stage III	61/107	42.4	73/110	24.2	0.61 (0.43-0.86)
Renal insufficiency	82/162	56.7	92/142	29.7	0.55 (0.41-0.75)
Extramedullary plasmacytomas	7/15	57.5	5/9	19.4	0.47 (0.15-1.50)
Cytogenetic risk					
Standard cytogenetic risk	126/271	63.8	174/279	34.4	0.51 (0.41-0.64)
High cytogenetic risk	28/48	45.3	31/44	29.6	0.57 (0.34-0.96)
Revised standard cytogenetic risk	78/176	NR	115/187	35.1	0.50 (0.37-0.66)
Revised high cytogenetic risk	82/156	56.0	96/152	30.7	0.59 (0.44-0.80)
Gain(1q21)	20/53	NR	28/44	37.8	0.43 (0.24-0.76)
Amp(1q21)	48/74	40.0	45/76	26.1	0.81 (0.54-1.21)
Gain(1q21) or amp(1q21)	68/127	53.2	73/120	32.3	0.63 (0.46-0.88)
1 HRCA	68/137	61.4	86/137	31.2	0.55 (0.40-0.76)
≥2 HRCAs	14/19	24.9	10/15	24.0	0.92 (0.40-2.10)
Isolated gain(1q21)	16/47	NR	27/42	37.8	0.36 (0.19-0.67)
Isolated amp(1q21)	38/61	42.8	38/65	28.9	0.78 (0.50-1.22)
Isolated gain(1q21) or amp(1q21)	54/108	61.4	65/107	37.1	0.58 (0.40-0.83)
Gain(1q21) or amp(1q21) plus ≥1 HRCA	14/19	24.9	8/13	24.0	1.03 (0.42-2.48)



NDMM: Frail Patients

#3245: MAIA Subgroups

PFS subgroup analysis among patients with:
0 HRCA (standard cytogenetic risk), 1 HRCA, or ≥ 2 HRCA



No. at risk																									
Rd 0 HRCA	187	169	153	139	127	123	115	108	102	89	87	81	75	67	61	54	50	48	46	42	34	25	13	2	2	2	0
Rd 1 HRCA	137	124	117	106	98	87	79	72	70	68	64	56	53	48	45	44	40	35	26	25	19	15	4	0	0	0	0
Rd ≥2 HRCAs	15	13	12	12	8	7	6	6	6	4	4	3	3	3	3	2	2	2	2	2	2	2	1	1	0	0	0
D-Rd 0 HRCA	176	164	158	151	148	144	139	135	131	127	125	122	120	115	109	102	102	97	93	87	68	48	36	18	9	2	0
D-Rd 1 HRCA	137	131	126	122	117	114	111	105	100	97	90	86	85	81	78	74	71	68	62	59	49	32	22	6	0	0	0
D-Rd ≥2 HRCAs	19	19	18	16	13	12	10	9	9	8	8	8	8	8	6	6	6	5	5	5	4	0	0	0	0	0	0

- PFS improved with D-Rd vs RD in patients with 0 or 1 HRCA
- PFS was similar with D-Rd vs Rd in patients with ≥ 2 HRCA (though this sample size was small)

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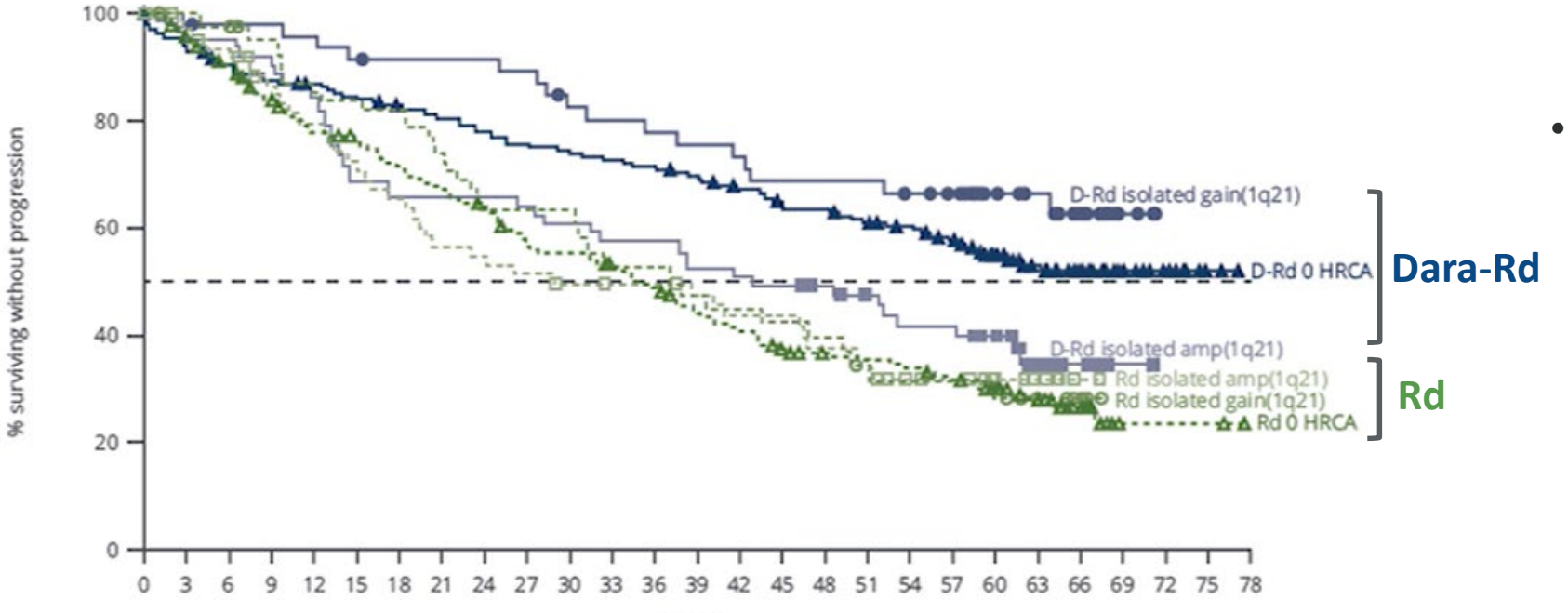
NDMM: Frail Patients

#3245: MAIA Subgroups

PFS subgroup analysis among patients with:
0 HRCA (standard cytogenetic risk), isolated gain (1q21), isolated amp(1q21)



No. at risk																									
Rd 0 HRCA	187	169	153	139	127	123	115	108	102	89	87	81	75	67	61	54	50	48	46	42	34	25	13	2	2	2	0
Rd isolated gain(1q21)	42	40	39	36	32	26	25	25	24	24	24	20	20	18	17	16	15	12	10	10	9	7	3	0	0	0	0
Rd isolated amp(1q21)	65	59	56	49	45	40	37	32	31	29	27	26	26	24	22	22	19	18	13	12	8	6	1	0	0	0	0
D-Rd 0 HRCA	176	164	158	151	148	144	139	135	131	127	125	122	120	115	109	102	102	97	93	87	68	48	36	18	9	2	0
D-Rd isolated gain(1q21)	47	46	45	45	44	42	41	41	41	40	36	35	34	33	32	30	30	30	28	26	21	17	12	3	0	0	0
D-Rd isolated amp(1q21)	61	59	58	56	52	51	50	45	40	39	37	35	35	32	31	30	28	25	22	22	18	9	6	2	0	0	0

- PFS was improved with D-Rd vs RD in patients isolated gain(1q21) or isolated amp(1q21)

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NDMM: Frail Patients

#3245: MAIA Subgroups

FIGURE 4: Subgroup analysis of MRD-negativity (10^{-5}) rates in the ITT population

	D-Rd *n/N (%)*	Rd *n/N (%)*	OR (95% CI)[a]
ITT (overall)	118/368 (32.1)	41/369 (11.1)	3.78 (2.55-5.59)
Baseline characteristic			
Age ≥75 years	43/160 (26.9)	16/161 (9.9)	3.33 (1.79-6.21)
ISS stage III	29/107 (27.1)	12/110 (10.9)	3.04 (1.46-6.34)
Renal insufficiency	48/162 (29.6)	11/142 (7.7)	5.01 (2.49-10.11)
Extramedullary plasmacytomas	5/15 (33.3)	0/9	NE (NE-NE)
Cytogenetic risk			
Standard cytogenetic risk	93/271 (34.3)	33/279 (11.8)	3.89 (2.50-6.06)
High cytogenetic risk	12/48 (25.0)	1/44 (2.3)	14.33 (1.78-115.59)
Revised standard cytogenetic risk	60/176 (34.1)	21/187 (11.2)	4.09 (2.36-7.09)
Revised high cytogenetic risk	49/156 (31.4)	15/152 (9.9)	4.18 (2.22-7.86)
Gain(1q21)	19/53 (35.8)	6/44 (13.6)	3.54 (1.27-9.89)
Amp(1q21)	23/74 (31.1)	8/76 (10.5)	3.83 (1.59-9.27)
Gain(1q21) or amp(1q21)	42/127 (33.1)	14/120 (11.7)	3.74 (1.92-7.30)
1 HRCA	44/137 (32.1)	15/137 (10.9)	3.85 (2.02-7.34)
≥2 HRCAs	5/19 (26.3)	0/15	NE (NE-NE)
Isolated gain(1q21)	17/47 (36.2)	6/42 (14.3)	3.40 (1.19-9.71)
Isolated amp(1q21)	20/61 (32.8)	8/65 (12.3)	3.48 (1.39-8.66)
Isolated gain(1q21) or amp(1q21)	37/108 (34.3)	14/107 (13.1)	3.46 (1.74-6.89)
Gain(1q21) or amp(1q21) plus ≥1 HRCA	5/19 (26.3)	0/13	NE (NE-NE)

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NDMM: Frail Patients

#3245: MAIA Subgroups

Safety (patients > 75 years)

Grade 3/ 4 TEAEs: **95.5% of D-Rd, 95% of Rd patients**

- **Most common:** **neutropenia (D-Rd 62.4%; Rd 41.5%)**
  lymphopenia (D-Rd 21%; Rd 12.6%)
  anemia (D-Rd 20.4%; Rd 25.2%)
  pneumonia (D-Rd 20.4%, Rd 14.5%)

TEAEs leading to study discontinuation: D-Rd 15.3%, Rd 27.7%
TEAEs leading to death: D-Rd 11.5%, Rd 13.2%

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NDMM: Frail Patients

#3245: MAIA Subgroups

Conclusions

- In this subgroup analysis of MAIA, D-Rd generally improved PFS, ORR, and MRD-negativity rates versus Rd across clinically important subgroups, including patients aged ≥75 years; patients with ISS stage III disease; patients with renal insufficiency; patients with extramedullary plasmacytomas; patients with high cytogenetic risk; and patients with revised high cytogenetic risk, including patients with gain(1q21) or amp(1q21)
  - Results from this subgroup analysis were consistent with efficacy results for the ITT population (*Poster #4559*)
  - Additional evidence is needed for patients with extramedullary plasmacytomas and with ultra high–risk disease (≥2 HRCAs)
- In patients aged ≥75 years, the rates of grade 3/4 TEAEs and serious TEAEs were similar for D-Rd and Rd, and the rate of discontinuation due to TEAEs was lower for D-Rd versus Rd

Key Takeaway

- Results of this subgroup analysis at a median follow-up of 64.5 months support the use of D-Rd for patients with high-risk baseline characteristics, including patients with high cytogenetic risk, supporting D-Rd as a standard of care for transplant-ineligible patients with NDMM

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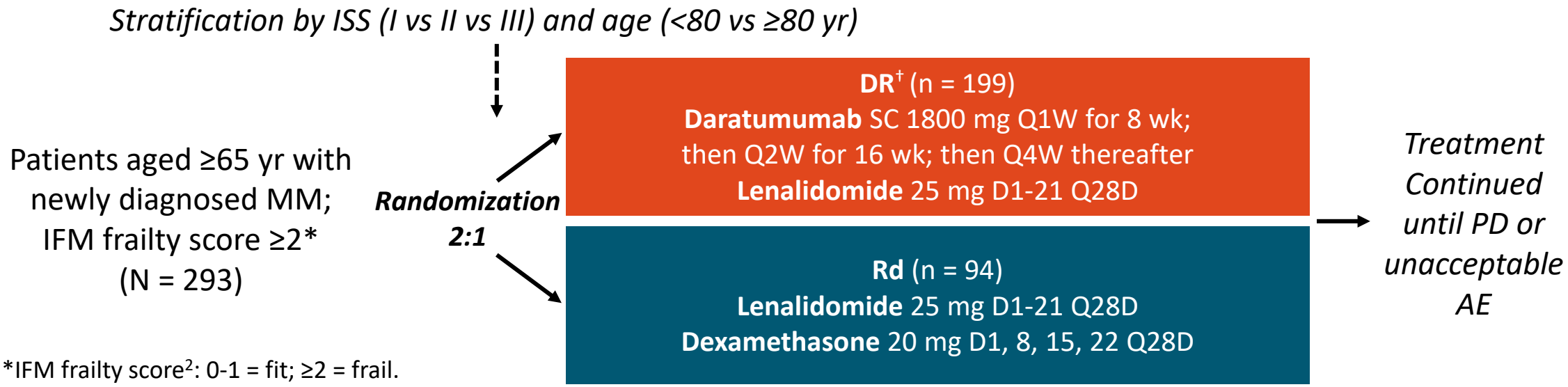
NDMM: Frail Patients

#569: A Dexamethasone Sparing-Regimen with Daratumumab and Lenalidomide in Frail Patients with Newly-Diagnosed Multiple Myeloma: Efficacy and Safety Analysis of the Phase 3 IFM2017-03 Trial

Randomized, open-label, multicenter phase III trial[1] 12 mo interim analysis

Hypothesis: Dexamethasone-sparing regimens will be effective and will limit toxicity in a frail population of patients



*IFM frailty score[2]: 0-1 = fit; ≥2 = frail.

†DR included low-dose dexamethasone 20 mg/wk during cycles 1,2, along with SC daratumumab dosing.

- **Primary endpoint:** PFS (not yet reported)
- **Interim analysis at 12 mo of therapy:** ORR, ≥ VGPR, MRD rate, grade ≥3 AEs

1. Broome. ASH 2022. Abstr 3. 2. Facon. Leukemia. 2020;34:224.

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IFM 2017-03 – Patients characteristics

Characteristics	DR group (N=199)	Rd group (N=94)
Median age (range) - yr	81 (68-92)	81 (68-90)
Age category – no. (%)		
65 to < 70 yr	2 (1%)	2 (2%)
70 to < 75 yr	30 (15%)	13 (14%)
75 to < 80 yr	49 (25%)	19 (20%)
≥ 80 yr	118 (59%)	61(65%)
Sex - no. (%)		
Female	101 (51%)	48 (51%)
Male	98 (49%)	46 (49%)
ECOG – no. (%)		
0	21 (10%)	9 (10%)
1	93 (46%)	47 (50%)
2	86 (44%)	38 (40%)
Charlson – no. (%)		
≤ 1	113 (58%)	57 (61%)
> 1	87 (42%)	37 (39%)
IFM frailty score – no. (%)		
≤ 1	0	0
2	57 (29%)	35 (37%)
3	81 (41%)	26 (28%)
4	44 (22%)	24 (26%)
5	17 (9%)	9 (10%)

Characteristics	DR group (N=199)	Rd group (N=94)
ISS disease stage – no. (%)		
I	33 (17%)	18 (19%)
II	102 (51%)	49 (53%)
III	64 (32%)	26 (28%)
NA	0	1
Type of measurable disease – no (%)		
IgG	113 (57%)	49 (52%)
IgA	38 (19%)	20 (21%)
PBJ only	21 (11%)	10 (11%)
SFLC only	27 (14%)	15 (16%)
Cytogenetics profile* – no (%)		
Standard risk	148 (83%)	60 (78%)
High risk	31 (17%)	17 (22%)
NA	20	17
del17p	16 (9%)	11 (14%)
t(4;14)	9 (5%)	5 (6%)
t(14;16)	6 (3%)	3 (3%)
Creatinine clearance – no. (%)		
< 30mL/min	1 (1%)	3 (3%)
30 to < 60mL/min	119 (60%)	50 (53%)
≥ 60 mL/min	79 (40%)	41 (44%)

* del17p, t(4;14), t(14;16)

NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)

Response	DR (n = 199)	Rd (n = 94)	*P* Value
ORR, %	96	85	.001
▪ CR	17	10	
▪ VGPR	47	33	
▪ PR	32	42	
≥ VGPR	64	43	
MRD at 10^{-5} by NGS,* %	10	3	.012

Rate of Response Over Time	Proportion of Patients With ≥ VGPR, %	
	DR (n = 199)	Rd (n = 94)
Mo 4	41	26
Mo 8	68	48
Mo 12	71	55

*In ITT analysis. MRD was assessed in patients with ≥ VGPR at 12 mo and was not assessable or missing for 20.6% of patients in DR arm and 14.1% of patients in Rd arm. Patients with missing data were considered MRD positive.

- Similar improvement in rate of ≥ VGPR with DR across all subgroups analyzed, including IFM frailty score (*P* = .87) and cytogenetic risk (*P* = .29)
- Fewer discontinuations in DR arm vs Rd arm (32% vs 45%)

Manier. ASH 2022. Abstr 569.

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NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)

IMWG frailty score[1]

Score assessment		Score
Age (year)	≤75	0
	76-80	1
	>80	2
Activity of Daily Living	>4	0
	≥4	1
Instrumental Activity of Daily Living	>5	0
	≤5	1
Charlson Comorbidity Index	≤1	0
	≥2	1

Score assessment	Total score
Fit	0
Intermediate	1
Frail	≥2

Simplified IFM frailty score[2]

Score assessment		Score
Age (year)	≤75	0
	76-80	1
	>80	2
Charlson Comorbidity Index	≤1	0
	≥2	1
ECOG	0	0
	1	1
	≥2	2

Score assessment	Total score
Fit	0-1
Frail	≥2

[1]Palumbo et al. *Blood* 2015, [2]Facon et al. *Leukemia* 2020

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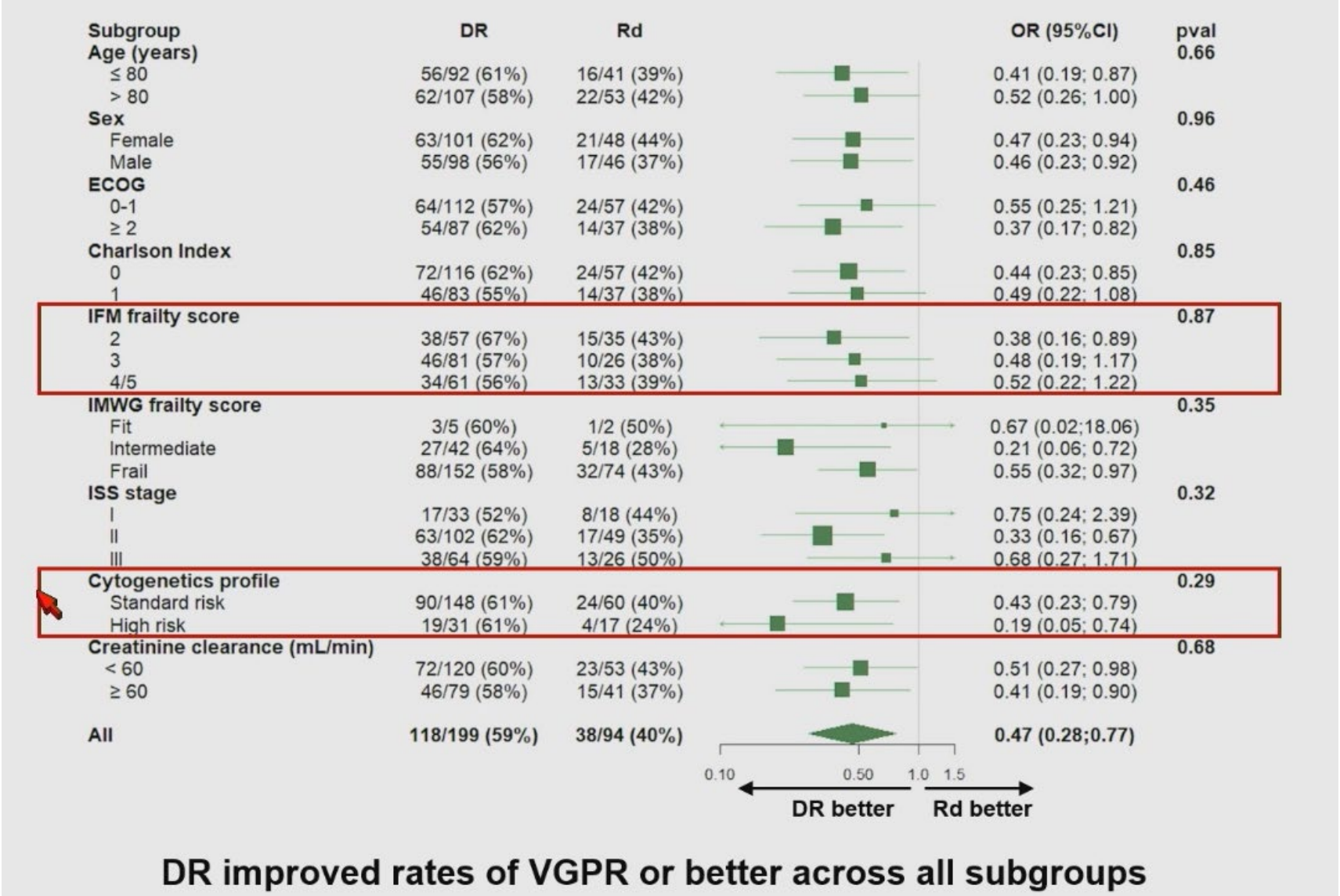
NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)



DR improved rates of VGPR or better across all subgroups

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NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)

Most Common Grade ≥3 AEs	DR (n = 199)	Rd (n = 94)	*P* Value
Any grade ≥3 AE, n (%)	164 (82)	64 (68)	.010
SAE, n (%)	109 (55)	59 (63)	.21
Grade ≥3 hematologic AEs, n (%)	109 (55)	24 (26)	<.0001
▪ Anemia	21 (11)	2 (2)	.010
▪ Neutropenia	91 (46)	17 (18)	<.0001
▪ Thrombocytopenia	18 (9)	3 (3)	.089
Grade ≥3 infection, n (%)	26 (13)	17 (18)	.29
▪ Non–COVID-19 infections	17 (9)	13 (14)	.21
▪ Pneumonia	5 (3)	7 (7)	.060
▪ COVID-19	9 (5)	4 (4)	1
Treatment discontinuation for AE, n (%)	27 (14)	15 (16)	.65

Manier. ASH 2022. Abstr 569.

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NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)

Most Common Grade ≥3 AEs	IFM Frailty Score 2 + 3 (n = 199)			IFM Frailty Score 4 + 5 (n = 94)		
	DR (n = 138)	Rd (n = 61)	*P* Value	DR (n = 61)	Rd (n = 33)	*P* Value
SAE, n (%)	74 (54)	35 (57)	.65	35 (57)	24 (73)	.18
Infection, n (%)	13 (9)	8 (13)	.46	13 (21)	9 (27)	.61
▪ Non–COVID-19 infections	10 (7)	6 (10)	.58	7 (11)	7 (21)	.23
▪ Pneumonia	2 (1)	3 (5)	.17	3 (5)	4 (12)	.24
▪ COVID-19	3 (2)	2 (3)	.64	6 (10)	2 (6)	.71

Manier. ASH 2022. Abstr 569.

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NDMM: Frail Patients

#569: DaraRev vs RevDex in Frail NDMM patients (IFM2017-03)

- DR was associated with higher response rates vs Rd
  - ORR: 96% with DR vs 85% with Rd
  - Higher MRD negativity rates (10% vs 3%, respectively) and rapid responses

- DR associated with favorable safety profile and no increased risk of infection or pneumonia vs Rd
  - Treatment discontinuation rates were similar between arms

- Investigators concluded that results of this trial are encouraging regarding potential for dexamethasone-sparing strategy in frail patients, but longer follow-up is needed. PFS analysis is ongoing

Manier. ASH 2022. Abstr 569.

OHSU

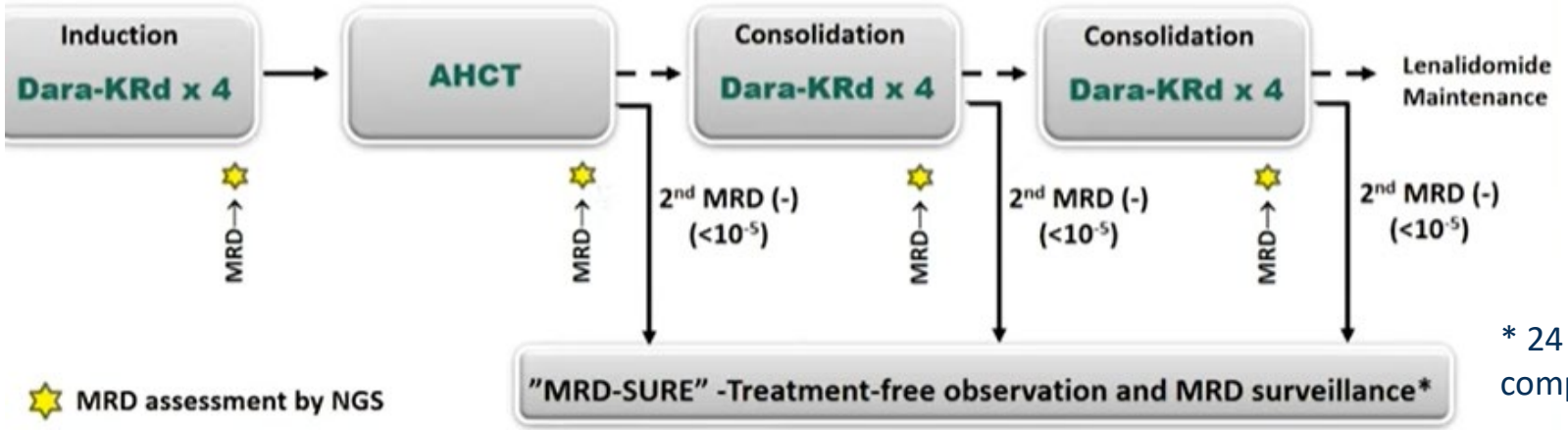
NDMM: Frail Patients

#1930: Quadruplet Induction, Autologous Transplantation and Minimal Residual Disease Adapted Consolidation and Treatment Cessation in Older Adults ≥70y with Newly Diagnosed Multiple Myeloma: A Subgroup Analysis of the Master Trial

Exploratory (unplanned) secondary analysis of MASTER (Ph II)

Dara-KRd

- Daratumumab 16 mg/m^2 days 1,8,15,22 (days 1,15 C 3-6; day 1 C >6)
- Carfilzomib (20) 56 mg/m^2 Days 1,8,15
- Lenalidomide 25 mg Days 1-21
- Dexamethasone 40mg PO Days 1,8,15,22



* 24 and 72 weeks after completing therapy

- **86% of patients achieved a CR or better**
- **80% of patients achieved MRD negativity (10x^-5), 66% achieved MRD negativity at 10x^-6**
- **Responses deepened with each phase of treatment and were similar in patients with 0, 1, or 2+ high-risk genetic abnormalities**
- **ASCT increased the rates of MRD negativity following induction therapy, benefitting patients with highest-risk disease features**

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NDMM: Frail Patients

#1930: MASTER subset analysis (older adults ≥70y)

Variable	≥ 70 years	<70 years	P value
N	24 (23 MRD trackable)	99 (95 MRD trackable)	
Median age (range),y	72.5 (70-79)	59 (35-69)	N/A
Female sex	9 (38%)	44 (44%)	0.54
Racial-ethnic minority	6 (25%)	23 (23%)	0.85
No.of High-risk chromosomal abnormalities*			0.30
0	12 (50%)	41 (41%)	
1	10 (42%)	36 (36%)	
2+	2 (8%)	22 (22%)	
High LDH	5 (21%)	21 (21%)	0.97
R-ISS Stage			0.18
1	6 (25%)	30 (30%)	
2	16 (67%)	47 (47%)	
3	2 (8%)	22 (22%)	
ECOG PS			0.45
0-1	18 (75%)	81 (82%)	
2	6 (25%)	18 (18%)	

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NDMM: Frail Patients

#1930: MASTER subset analysis (older adults ≥70y)

- Similar rates of MRD negativity post induction (36% vs 41%; p=0.66)
- Similar rates of MRD-SURE (61% vs 74%; p=0.18).
- However, lower rates of overall MRD negativity (65% vs 84%; p=0.03) and CR (71% vs 93%; p=0.002).

Variable	≥ 70 years	<70 years	P value
N	24 (23 MRD trackable)	99 (95 MRD trackable)	
MRD negativity ($<10^{-5}$) post induction	8 (35%)	39 (41%)	0.58
MRD negativity at any point ($<10^{-5}$)	15 (65%)	81 (85%)	0.03
MRD $<10^{-6}$ at any point	13 (57%)	71 (75%)	0.08
Response ≥CR	17 (71%)	91 (93%)	0.002
Achievement MRD-SURE	14 (61%)	71 (74%)	0.18
3-year PFS	86.3%	80.3%	0.75
3-year OS	95.8%	88.7%	0.53

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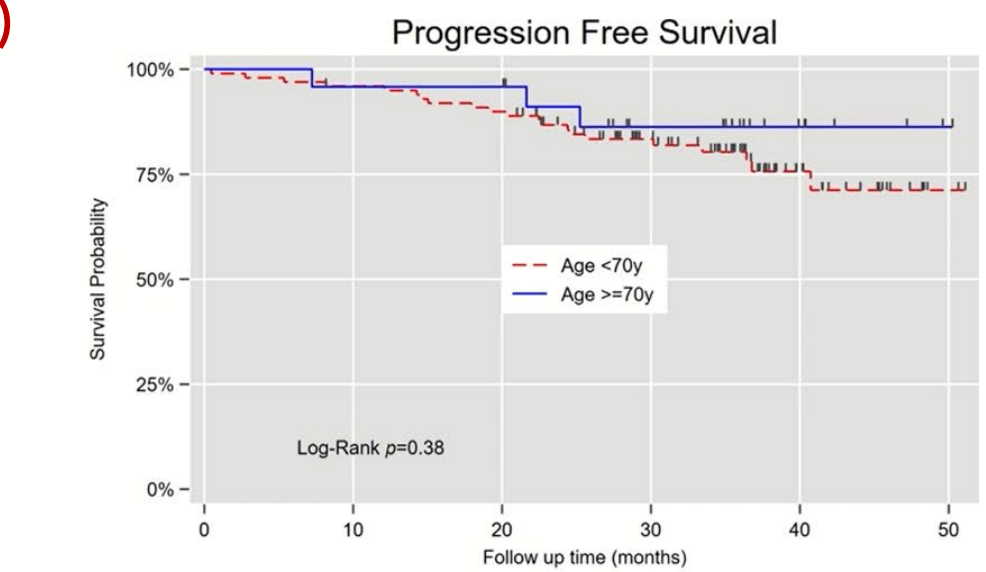
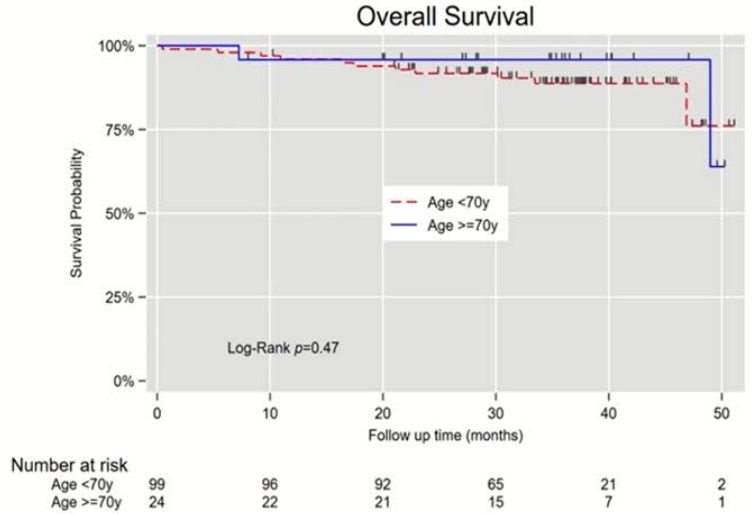
NDMM: Frail Patients

#1930: MASTER subset analysis (older adults ≥70y)

PFS/OS and toxicity outcomes

- At a median follow up of 36 m, older vs younger pts had similar 3y PFS (86.3% vs 80.3%; log rank p=0.74) and 3y OS (96% vs 89%; p=0.53).
- Similar rates of grade ≥3 AEs (79% vs 69%; p=0.31). No pts in the age ≥70y discontinued therapy due to toxicity.
- Three deaths during study period in overall population (1 pt ≥70y, unwitnessed sudden death 2 m post-ASCT but, before consolidation).





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NDMM: Frail Patients

#1930: MASTER subset analysis (older adults ≥70y)

Conclusions:

- **Older adults can be candidates for quadruplet induction, ASCT and MRD adapted consolidation therapy**
- **Chronologic age alone should not be an eligibility criteria for trials that use higher intensity regimens.**

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Bispecific Antibodies for RRMM

	MagnetisMM	MajesTEC	Ph1	Ph1	MonumenTAL
Agent	**Elranatamab**	**Teclistamab**	**REGN5458**	**Cevostamab**	**Talquetemab**
Target	BCMA x CD3	BCMA x CD3	BCMA x CD3	FcRH5 x CD3	GPRC5D x CD3
Dosing	sc weekly	sc weekly	iv q2w	iv q3w	sc weekly

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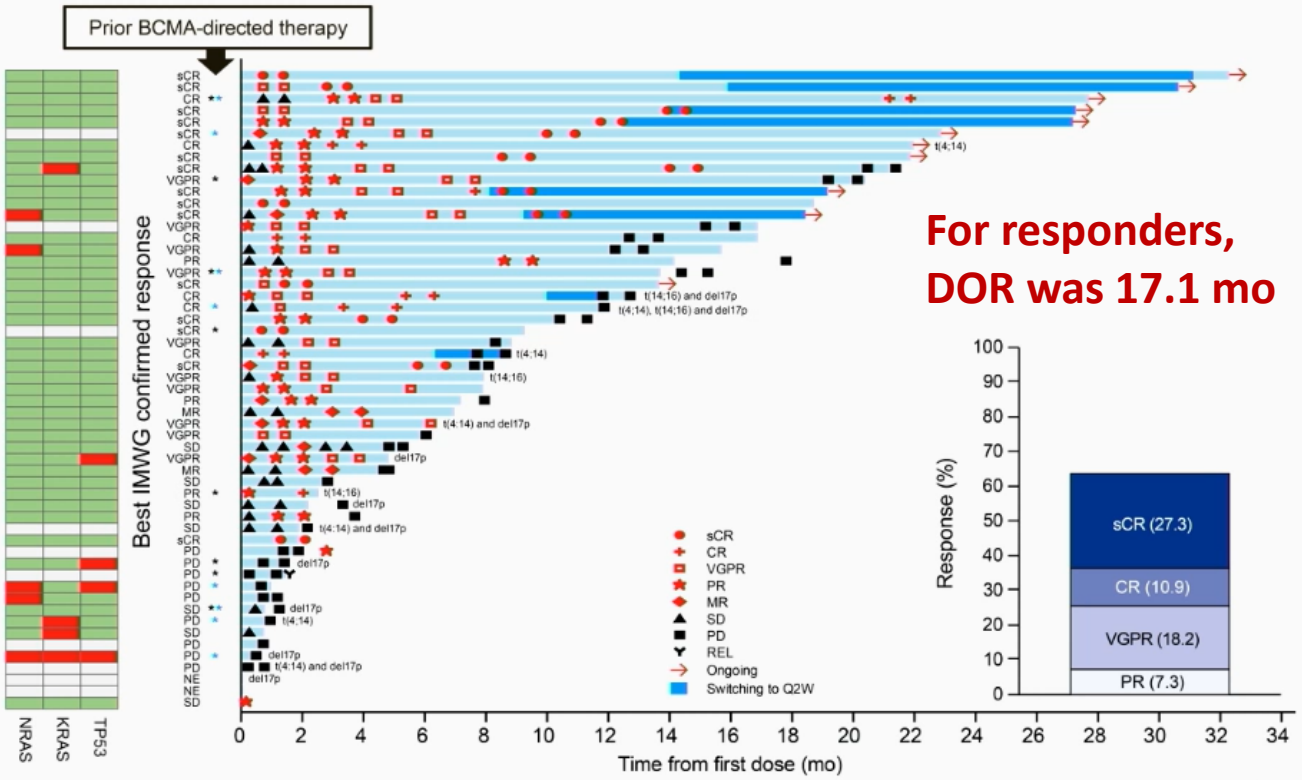
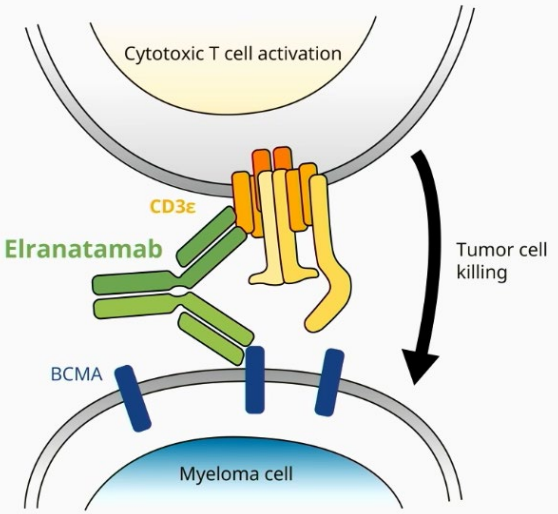
BCMA Targets:

158, Elranatamab, a BCMA Targeted T-Cell Engaging Bispecific Antibody (MagnetisMM-1) – Ph 1
159, Efficacy and Safety of Elranatamab in Patients with R/R MM (MagnetisMM-3, Cohort A) – Ph 2
3192, Dose Optimization to Mitigate the Risk of CRS with Elranatamab
1921, Elranatamab in Combination with Dara (MagnetisMM-5)

- Elranatamab (PF-06863135), a humanized bispecific antibody targeting BCMA on myeloma cells and CD3 on T cells, induces a selective cytotoxic T-cell response against myeloma cells[2]



For responders, DOR was 17.1 mo

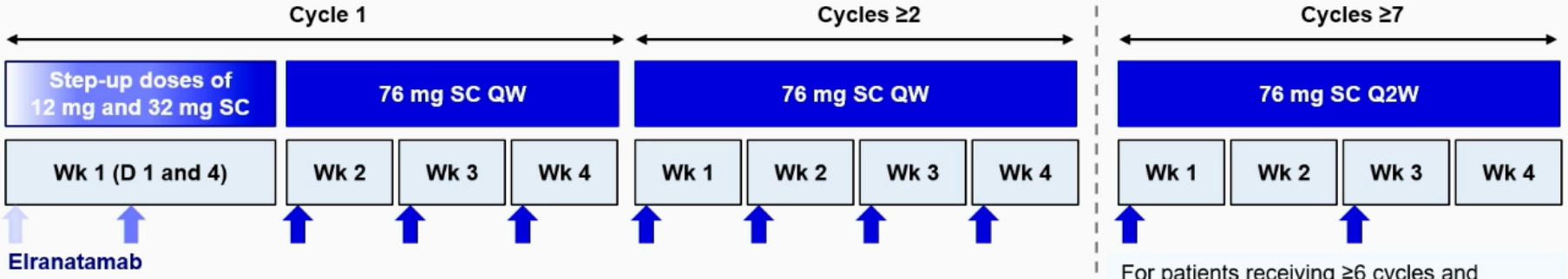


MagnetisMM-1

- Median duration of follow-up was 12.0 months (range 0.3–32.3)
- ORR was 64% (95% CI, 50–75) and CR/sCR rate was 38% (21/55)
- 54% (7/13) of patients with prior BCMA-directed therapy achieved response
- For responders (N=35), median time to response was 36 days (range 7–262)

- 13 patients with confirmed CR or sCR were MRD evaluable
- 100% (13/13) achieved MRD negativity
- 62% (8/13) had documented MRD negativity at >6 months
- 31% (4/13) had documented MRD negativity at >12 months

BCMA Targets: Elranatamb Safety (MagnetisMM-3 cohort A – naïve to BCMA directed therapy)



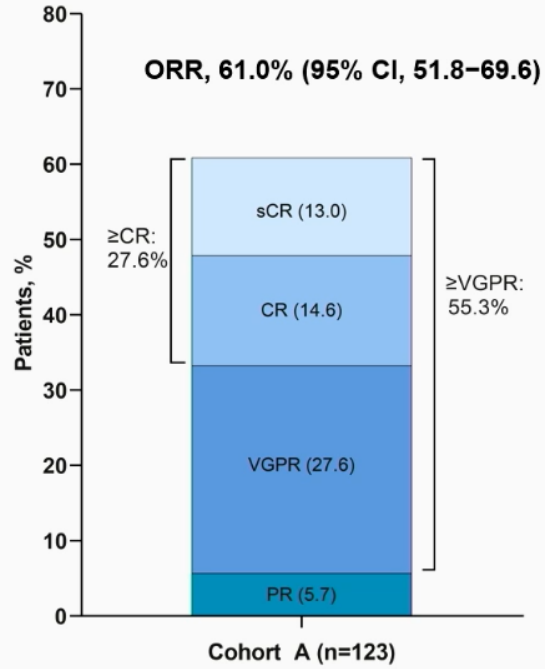
Premedication:

60 min (±15 min) prior to the first 3 doses of elranatamab

- Acetaminophen 650 mg (or paracetamol 500 mg)
- Diphenhydramine 25 mg (or equivalent), oral or IV
- Dexamethasone 20 mg (or equivalent), oral or IV

	Cohort A (N=123)[a]
Extramedullary disease by BICR, n (%)[d]	39 (31.7)
Bone marrow plasma cells, n (%)	
<50%	89 (72.4)
≥50%	26 (21.1)
Missing	8 (6.5)
Prior lines of therapy, median (range)	5 (2–22)
Prior stem cell transplant, n (%)	87 (70.7)
Exposure status, n (%)	
Triple-class[e]	123 (100)
Penta-drug[f]	87 (70.7)
Refractory status, n (%)	
Triple-class[e]	119 (96.7)
Penta-drug[f]	52 (42.3)
Refractory to last line of therapy, n (%)	118 (95.9)

- Confirmed ORR per BICR was 61.0% (95% CI, 51.8−69.6)
- Among patients who achieved an objective response (n=75), median time to response was 1.2 (range, 0.9−7.4) mo
- MRD-negativity at the threshold of 10^{-5} was achieved by 90.9% of evaluable patients (n=22)



BCMA Targets: Elranatamb Safety (MagnetisMM-3 cohort A – naïve to BCMA directed therapy)

TEAEs in ≥20% of patients, n (%)	Cohort A (N=123)	
	Any grade	Grade 3/4
Hematologic		
Anemia	59 (48.0)	45 (36.6)
Neutropenia	59 (48.0)	59 (48.0)
Thrombocytopenia	37 (30.1)	27 (22.0)
Lymphopenia	32 (26.0)	30 (24.4)
Non-hematologic		
CRS	71 (57.7)	0
Diarrhea	48 (39.0)	2 (1.6)
Fatigue	42 (34.1)	4 (3.3)
Decreased appetite	40 (32.5)	1 (0.8)
Injection site reaction	32 (26.0)	0
Nausea	32 (26.0)	0
COVID-19 related[a]	31 (25.2)	14 (11.4)
Hypokalemia	29 (23.6)	12 (9.8)
Pyrexia	29 (23.6)	4 (3.3)
Cough	27 (22.0)	0
Headache	27 (22.0)	0

- The most common Grade 3/4 TEAEs were hematologic events; non-hematologic events were predominantly Grade 1/2
- All CRS and ICANS events were Grade 1/2
- No fatal neurotoxicity events were observed
- TEAEs led to permanent elranatamab discontinuation in 19 (15.4%) patients
- TEAEs led to death in 21 patients (11 due to progressive disease); 2 considered treatment-related by investigator[b]
  - 1 grade 5 pseudomonal pneumonia
  - 1 grade 5 failure to thrive

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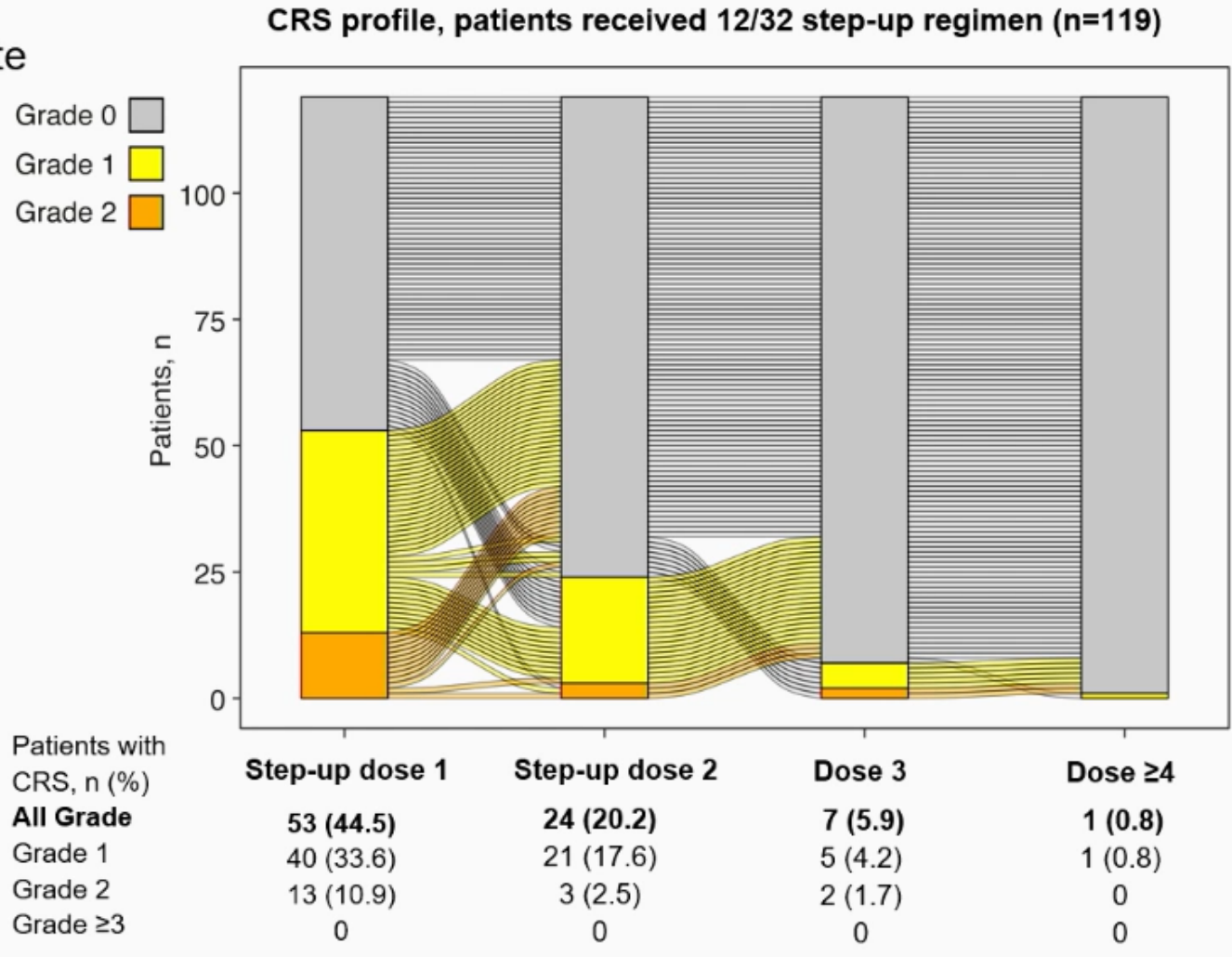
BCMA Targets: Elranatamb Safety (MagnetisMM-3 cohort A – naïve to BCMA directed therapy)

AEs of Special Interest: CRS and ICANS

- The step-up priming regimen successfully mitigated the rate and severity of CRS, and the CRS profile was predictable

TEAE of special interest	12/32 mg step-up regimen (n=119)[a] CRS	ICANS
Patients with TEAE, n (%)	67 (56.3)	4 (3.4)
Maximum Grade 1	50 (42.0)	1 (0.8)
Maximum Grade 2	17 (14.3)	3 (2.5)
Maximum Grade ≥3	0	0
Patients with >1 TEAE, n (%)	18 (15.1)	1 (0.8)
Median time to onset of TEAE, d (range)	2.0 (1.0–9.0)	2.5 (1.0–4.0)
Median time to resolution of TEAE, d (range)	2.0 (1.0–19.0)	2.0 (1.0–6.0)
Patients who received tocilizumab[b] or steroids, n (%)		
Tocilizumab	27 (22.7)	2 (1.7)
Steroids	10 (8.4)	2 (1.7)
Permanent discontinuation due to AE, n (%)	0	0



BCMA Targets: 766, Ide-cel in patients with R/R disease following prior BCMA-Targeted Therapy (BCMA-TT)

- Retrospective analysis of patient-level data at 11 US academic centers

Characteristic	SOC Ide-cel with prior BCMA-TT (N=50)	SOC Ide-cel without prior BCMA-TT (N=153)	KarMMa (N=128)
Median age (range)	66 (43-79)	63 (36-83)	61 (33-78)
Male Sex, n (%)	33 (66)	89 (58)	76 (59)
ECOG PS, n (%)			
0-1	39 (81)	123 (83)	125 (98)
2-4	9 (19)	25 (17)	3 (2)
R-ISS stage, n (%)			
I	4 (11)	28 (24)	14 (11)
II	23 (62)	57 (48)	90 (70)
III	10 (27)	33 (28)	21 (16)
Extramedullary disease, n (%)	25 (50)	85 (56)	50 (39)
High tumor burden, n (%)	13 (30)	42 (29)	65 (51)
High-risk cytogenetics, n (%)			
Any high-risk	17 (36)	42 (31)	45 (35)
del(17p)	10 (21)	30 (22)	23 (18)
t(4;14)	11 (23)	10 (8)	23 (18)
t(14;16)	1 (2)	6 (5)	6 (5)
Bridging therapy, n (%)	43 (86)	113 (74)	112 (88)
Median prior lines of therapy (range)	9 (4-18)	6 (4-19)	6 (3-16)
Prior autologous HSCT, n (%)	44 (88)	128 (84)	120 (94)
Refractory status, n (%)			
Triple-refractory	45 (90)	125 (82)	108 (84)
Penta-refractory	31 (62)	57 (37)	33 (26)

Type of prior BCMA-TT	n, (%)
Antibody-Drug Conjugate (ADC)	38 (76%)
Bispecific	7 (14%)
CAR T	5 (10%)
Timing of prior BCMA-TT (continuous)	**Median (Range) in days**
Duration of prior BCMA-TT	30 (1 – 370)
Time from last BCMA-TT to apheresis	160 (1 – 1066)
Time from last BCMA-TT to infusion	202.5 (16 – 1118)
Timing of prior BCMA-TT (categorical)	**n, (%)**
< 3 months from infusion	9 (18%)
< 6 months from infusion	20 (40%)

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BCMA Targets: 766, Ide-cel in patients with R/R disease following prior BCMA-Targeted Therapy (BCMA-TT)

Response outcome	n, (%)
ORR to prior BCMA-TT	
All (N=48)	10 (21%)
ADC (N=36)	6 (17%)
Bispecific (N=7)	0 (0%)
CAR T (N=5)	4 (80%)
Best response to prior BCMA-TT	
≥ CR	3 (6%)
VGPR	3 (6%)
PR	4 (8%)
SD/MR	14 (29%)
PD	24 (50%)

- For the prior bispecific T-cell redirecting antibody cohort: 5/7 patients (71%) received a suboptimal dose, or a dose level lower than that chosen for expansion on the respective clinical trial
- Non-responder to prior CAR T received autologous product on a phase 1 study for which phase 2 was not pursued

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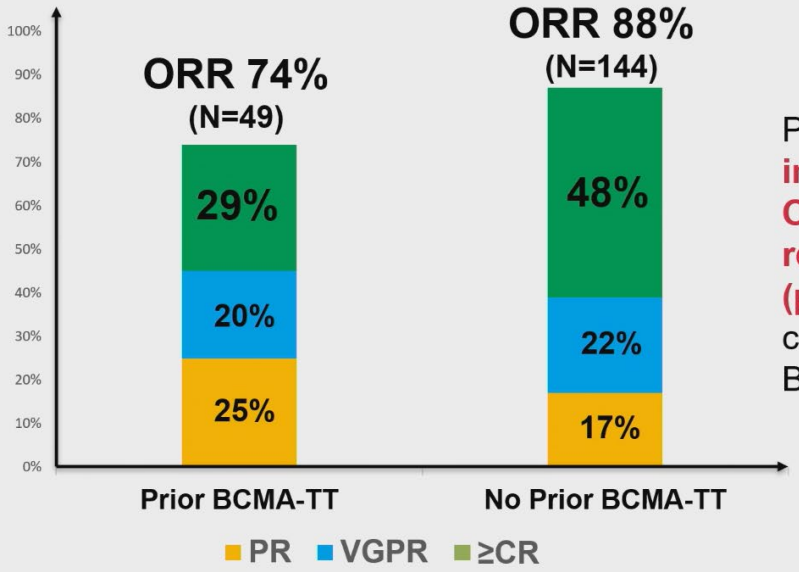
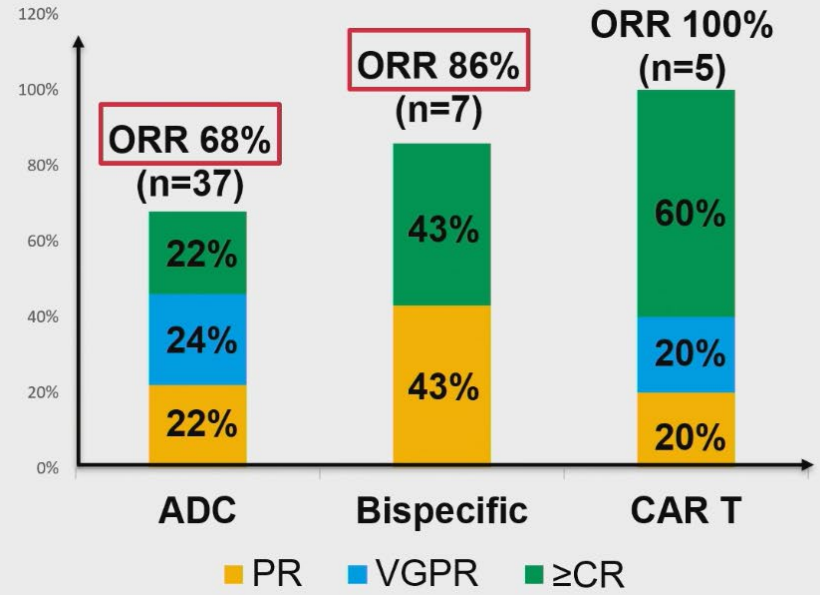
BCMA Targets: 766, Ide-cel in patients with R/R disease following prior BCMA-Targeted Therapy (BCMA-TT)

Efficacy Outcomes with Ide-Cel: Response



Prior BCMA-TT cohort had **inferior outcomes** for **ORR (p = 0.021) and best response of ≥ CR (p = 0.018)** compared to cohort with no prior BCMA-TT



Response outcome	n, (%)
ORR to prior BCMA-TT	
All (N=48)	10 (21%)
Prior ADC (n=36)	6 (17%)
Prior Bispecific (n=7)	0 (0%)
Prior CAR T (n=5)	4 (80%)

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BCMA Targets: 766, Ide-cel in patients with R/R disease following prior BCMA-Targeted Therapy (BCMA-TT)

Efficacy Outcomes: Timing of Prior BCMA-TT

Timing Characteristic	Responders (n=36)	Non-responders (n=13)	
Duration of prior BCMA-TT in days, median (range)	23 (1-208)	63 (1-370)	p = 0.025*
Time from last BCMA-TT to apheresis in days, median (range)	169.5 (30-1066)	84 (1-286)	p = 0.017*
Time from last BCMA-TT to ide-cel infusion in days, median (range)	209 (16-1118)	128 (32-362)	p = 0.052*

*P values by Wilcoxon rank sum test

Timing Characteristic	Prior BCMA-TT > 6 months (n=29)	Prior BCMA-TT < 6 months (n=20)	
Overall Response Rate, n (%)	24 (83%)	12 (60%)	p = 0.076 by Chi-square
≥ CR	10 (35%)	4 (20%)	

BCMA Targets: 766, Ide-cel in patients with R/R disease following prior BCMA-Targeted Therapy (BCMA-TT)

In a multivariate efficacy analysis among all patients, prior BCMA-TT was associated with significantly inferior:

- Best response of ≥ CR with OR: 0.29 (95% CI: 0.13-0.66; *P* = .003)
- PFS with HR: 2.91 (95% CI: 1.68-5.04; *P* <.0001)
- OS with HR: 2.94 (95% CI: 1.27-6.82; *P* = .012)
- Timing of idecabtagene vicleucel administration relative to last exposure of prior BCMA-TT may be predictive of response

- Investigators concluded that the inferior PFS outcomes in patients who received previous BCMA-TT suggest further investigation of different treatment strategies is warranted for this patient population

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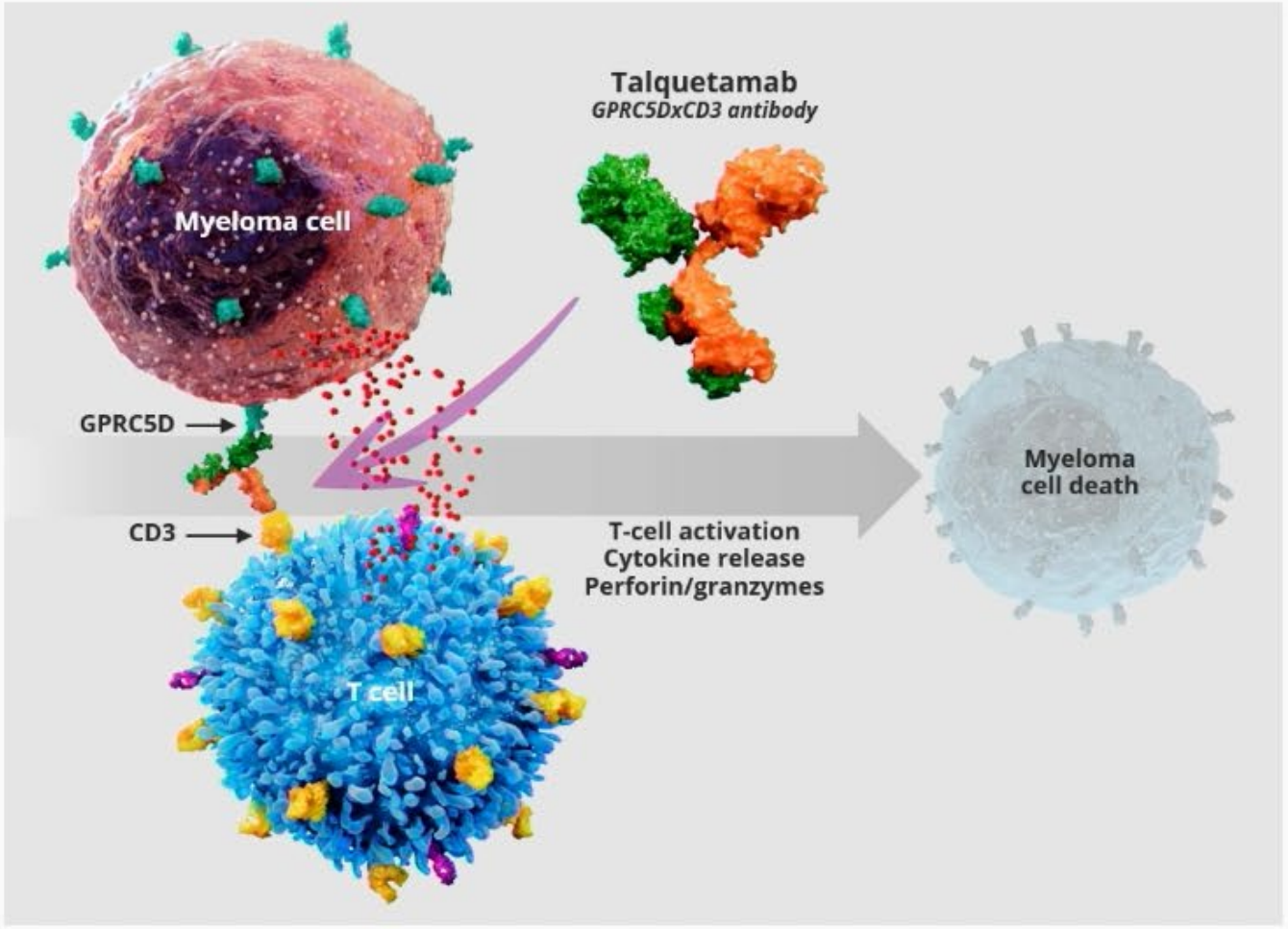
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

- **Talquetamab is a novel first-in-class, off-the-shelf, T-cell redirecting bispecific antibody** directed against a new antigen target called GPRC5D[1,2]
- **GPRC5D is a novel antigen target in myeloma** that is highly expressed on malignant plasma cells with limited expression in normal human tissues,[3-6] including hematopoietic stem cells[7]
- **Talquetamab has shown an ORR of 64–70%** with QW and Q2W dosing in the phase 1 MonumenTAL-1 study (NCT03399799)[8]



GPRC5D, G protein-coupled receptor family C group 5 member D; ORR, overall response rate; RP2D, recommended phase 2 dose; Q2W, every other week; QW, weekly.

1. Verkleij CPM, et al. *Blood Adv* 2021; 5(8):2196. 2. Pillarisetti K, et al. *Blood* 2020; 135:123. 3. Atamaniuk J, et al. *Eur J Clin Invest* 2012; 42:953. 4. Inoue S, et al. *J Invest Dermatol* 2004; 122:565. 5. Smith EL, et al. *Sci Transl Med* 2019; 11. 6. Goldsmith R, et al. Presented at IMW; September 8–11, 2021; Vienna, Austria. Poster P095. 7. Kodema T, et al. *Mol Cancer Ther* 2019; 18:15555. 8. Minnema M, et al. Presented at ASCO; June 3–7, 2022; Chicago, IL. Poster 8015.

Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

Key objectives

- Describe the efficacy and safety at the RP2Ds

Key eligibility criteria

- Adults with measurable MM
- Phase 1: Progression on or intolerance to all established therapies, ECOG PS 0–1
- Phase 2: ≥3 prior lines of therapy that included a PI, an IMiD, and an anti-CD38 antibody, ECOG PS 0–2

RP2D 0.4 mg/kg QW SC
Prior anti-BCMA ADC treatment allowed
T-cell redirection therapy naive

(Phase 1 [n=21] + **Phase 2 [n=122]**: N=143)

RP2D 0.8 mg/kg Q2W SC
Prior anti-BCMA ADC treatment allowed
T-cell redirection therapy naive

(Phase 1 [n=36] + **Phase 2 [n=109]**: N=145)

Prior T-cell redirection (QW and Q2W)
Previously exposed to T-cell redirection therapies
Dosed with either 0.4 mg/kg weekly SC or 0.8 mg/kg Q2W SC

(Phase 1 [n=17] + **Phase 2 [n=34]**: N=51)

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Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

Characteristic	0.4 mg/kg SC QW[a]	0.8 mg/kg SC Q2W[a]
	n=143	n=145
Age (years), median (range)	67.0 (46–86)	67.0 (38–84)
Male, n (%)	78 (54.5)	83 (57.2)
Race, n (%)		
White	128 (89.5)	125 (86.2)
Black/African American	12 (8.4)	9 (6.2)
Asian	1 (0.7)	6 (4.1)
Not reported	2 (1.4)	2 (1.4)
Bone marrow plasma cells ≥60%,[b] n (%)	17 (12.3)	32 (22.7)
Extramedullary plasmacytomas ≥1,[c] n (%)	33 (23.1)	39 (26.9)
High-risk cytogenetics,[d] n (%)	41 (31.1)	37 (28.9)
ISS stage, n (%)[e]		
I	62 (43.4)	64 (44.4)
II	53 (37.1)	45 (31.3)
III	28 (19.6)	35 (24.3)

Characteristic	0.4 mg/kg SC QW[a]	0.8 mg/kg SC Q2W[a]
	n=143	n=145
Time since diagnosis (years), median (range)	6.7 (1.4–20.8)	6.4 (0.8–25.4)
Prior lines of therapy, median (range)	5 (2–13)	5 (2–17)
Prior stem cell transplantation, n (%)	113 (79.0)	114 (78.6)
Exposure status, n (%)		
Triple-class[f]	143 (100)	145 (100)
Penta-drug[g]	105 (73.4)	101 (69.7)
Belantamab	22 (15.4)	16 (11.0)
Refractory status, n (%)		
PI[h]	114 (79.7)	120 (82.8)
IMiD[i]	133 (93.0)	130 (89.7)
Anti-CD38 mAb[j]	**133 (93.0)**	**134 (92.4)**
Triple-class[f]	**106 (74.1)**	**100 (69.0)**
Penta-drug[g]	42 (29.4)	34 (23.4)
Belantamab	18 (12.6)	13 (9.0)
To last line of therapy	134 (93.7)	137 (94.5)

- Approx 60% of patients were ISS III, extramedullary disease AND high-risk disease
- Approx 40% of patients were ISS III or extramedullary disease

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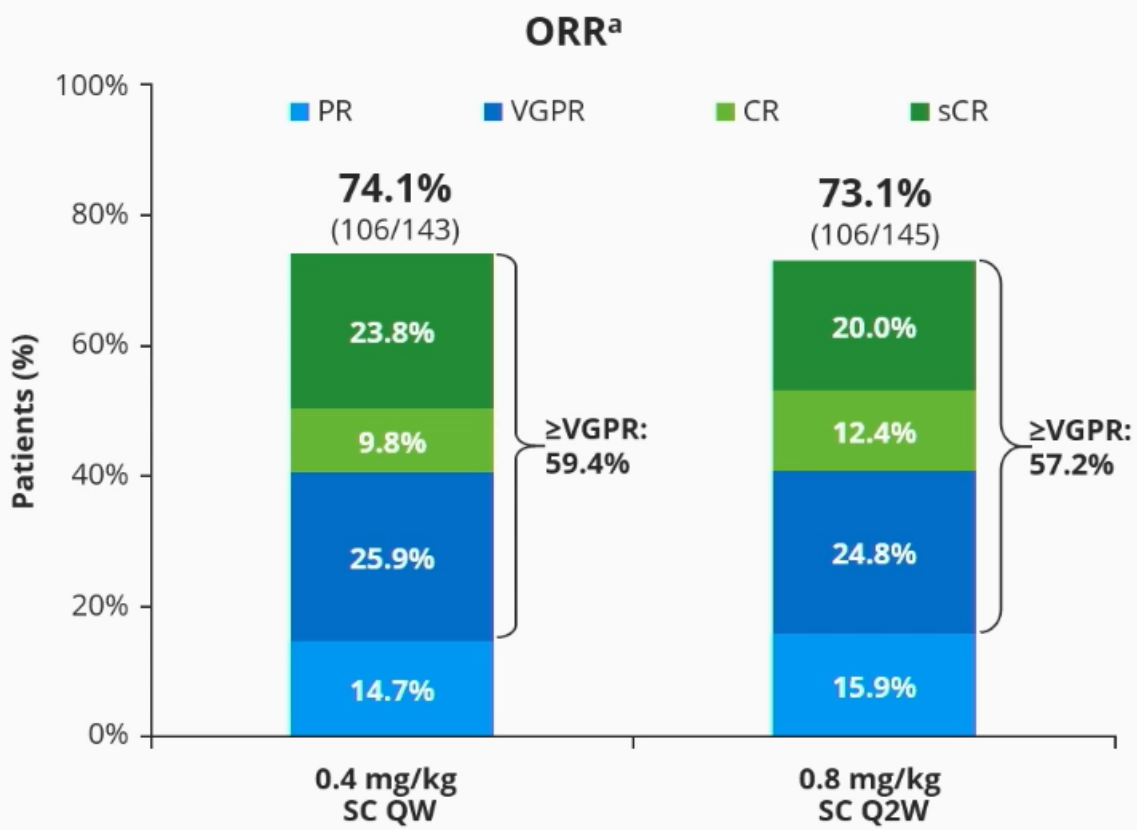
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment



- ORR was similar for QW and Q2W schedules
  - **Triple-class refractory: 72.6%** and **71.0%**
  - **Penta-drug refractory: 71.4%** and **70.6%**
  - **ORR was consistent across subgroups** including baseline ISS stage III disease, baseline cytogenetic risk, number of prior therapies, and belantamab exposure, except among patients with baseline plasmacytomas

Timing, months	0.4 mg/kg SC QW[b] n=143	0.8 mg/kg SC Q2W[c] n=145
Median (range) time to first response[d]	1.2 (0.2–10.9)	1.3 (0.2–9.2)
Median (range) time to best response[d]	2.2 (0.8–12.7)	2.7 (0.3–12.5)

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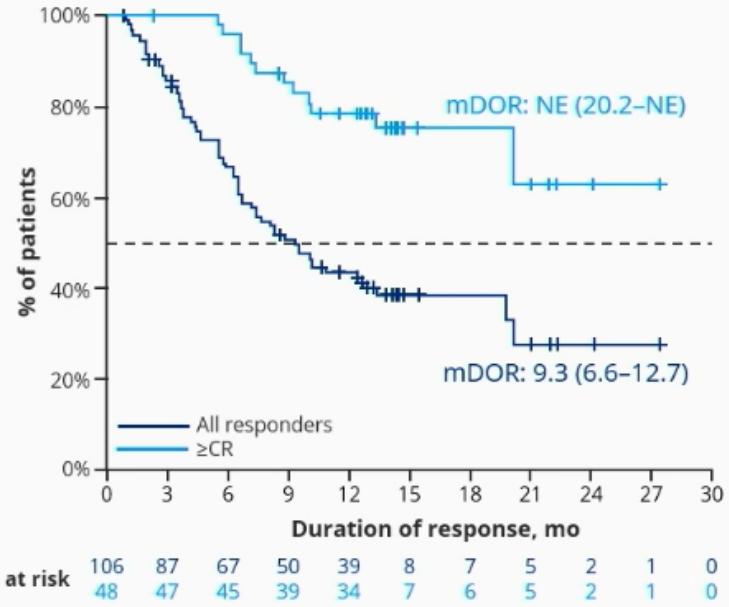
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

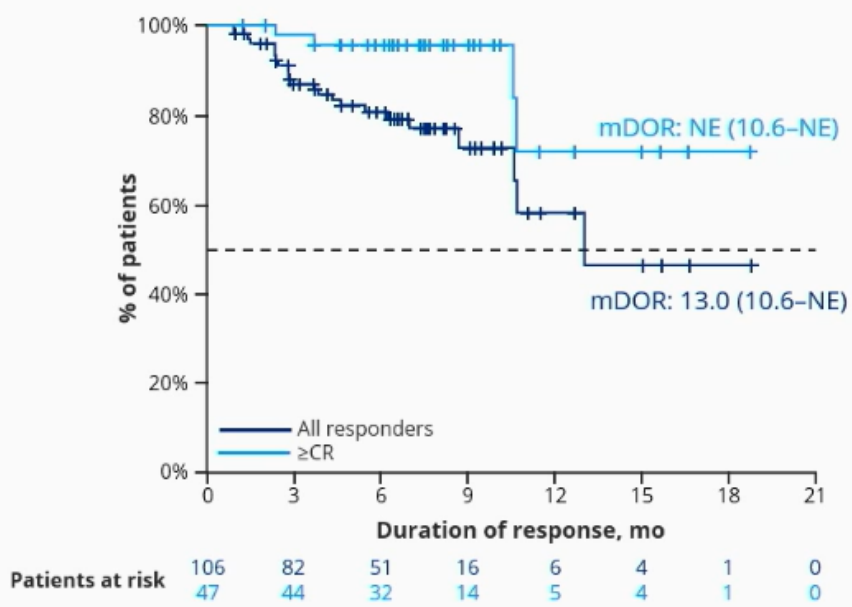
- Treatment at both doses led to durable responses
  - Median DOR not reached for those patients who achieved ≥CR

DOR, 0.4 mg/kg SC QW
mFU: 14.9 months (range, 0.5[a]–29.0)



mPFS: 7.5 months (95% CI: 5.7–9.4; 33% censored)

DOR, 0.8 mg/kg SC Q2W
mFU: 8.6 (range, 0.2[a]–22.5)



11.9 months (95% CI: 8.4–NE; 61% censored)

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Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

Hematologic adverse events

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW[a] (n=143) mFU, 11.0 months[b]		0.8 mg/kg SC Q2W[a] (n=145) mFU, 5.1 months[c]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Anemia	64 (44.8)	45 (31.5)	57 (39.3)	36 (24.8)
Neutropenia	49 (34.3)	44 (30.8)	41 (28.3)	32 (22.1)
Lymphopenia	40 (28.0)	37 (25.9)	38 (26.2)	37 (25.5)
Thrombocytopenia	39 (27.3)	29 (20.3)	39 (26.9)	24 (16.6)

- Most high-grade AEs were cytopenias
- Cytopenias were generally limited to the first few cycles

Infections

- At 0.4 mg/kg QW and 0.8 mg/kg Q2W:
  - Infections occurred in 57.3% and 50.3%
    - Grade 3/4 in 16.8% and 11.7%
  - 5 (3.5%)[d] and 4 (2.8%)[e] patients had opportunistic infections
  - 13 (9.1%) and 16 (11.0%) patients had COVID-19
    - Grade 3/4 in 0.7% and 2.1%
    - 2 patients died from COVID-19
- 13.3% and 9.7% of patients received IVIg, respectively

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Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW[a] (n=143) mFU, 11.0 months[b]		0.8 mg/kg SC Q2W[a] (n=145) mFU, 5.1 months[c]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	113 (79.0)	3 (2.1)	105 (72.4)	1 (0.7)
Skin-related AEs[d]	80 (55.9)	0	98 (67.6)	1 (0.7)
Nail-related AEs[e]	74 (51.7)	0	63 (43.4)	0
Dysgeusia[f]	69 (48.3)	NA	67 (46.2)	NA
Rash-related AEs[g]	56 (39.2)	2 (1.4)	39 (26.9)	8 (5.5)
Weight decreased	57 (39.9)	3 (2.1)	47 (32.4)	2 (1.4)
Pyrexia	53 (37.1)	4 (2.8)	35 (24.1)	1 (0.7)
Asthenia	37 (25.9)	3 (2.1)	13 (9.0)	2 (1.4)
Dry mouth	36 (25.2)	0	53 (36.6)	0
Diarrhea	34 (23.8)	3 (2.1)	32 (22.1)	0
Dysphagia	34 (23.8)	0	33 (22.8)	3 (2.1)
Fatigue	32 (22.4)	5 (3.5)	29 (20.0)	1 (0.7)
Decreased appetite	25 (17.5)	2 (1.4)	29 (20.0)	2 (1.4)

- **Low rates of grade 3/4 nonhematologic AEs** were observed
- **Low rates of discontinuation due to AEs** were observed with QW (4.9%) and Q2W (6.2%) schedules
- **Most common AEs were CRS, skin-related events, nail-related events, and dysgeusia**
  - Rates of high-grade skin, nail, and rash-related events were low
  - Dysgeusia was managed with supportive care, and at times with dose reduction
- At 0.4 mg/kg QW and at 0.8 mg/kg Q2W,
  - 8.4% and 13.8% had dose delays due to AEs
  - 14.7% and 6.2% had dose reductions due to AEs
- At time of data cut-off, no patients in these cohorts died due to drug-related AEs

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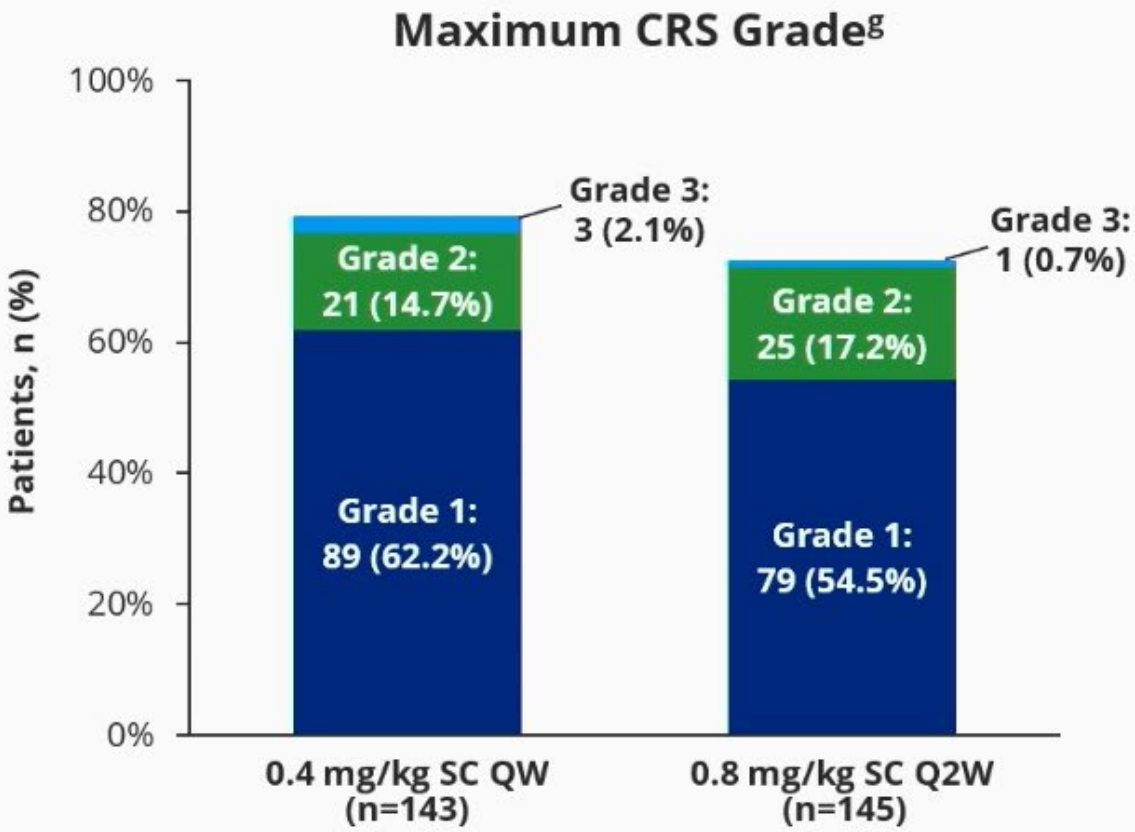
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

Parameter	0.4 mg/kg SC QW[a] (n=143)	0.8 mg/kg SC Q2W[a] (n=145)
Patients with CRS, n (%)	113 (79.0)	105 (72.4)
Time to onset (days),[b] median (range)	2.0 (1–8)	2.0 (1–8)
Duration (days), median (range)	2 (1–13)	2 (1–29)
Patients with CRS up to 1st full dose, n (%)		
1st step-up dose	48 (34)	38 (26)
2nd step-up dose	70 (49)	58 (40)[c]
1st full dose	38 (27)	19 (13)
Patients with CRS after 1st full dose,[d] n (%)	19 (13.3)	13 (9.0)
Patients who received supportive measures,[e] n (%)	106 (74.1)	100 (69.0)
Tocilizumab[f]	50 (35.0)	53 (36.6)
Steroids	5 (3.5)	4 (2.8)
Oxygen	8 (5.6)	10 (6.9)
Vasopressor	2 (1.4)	1 (0.7)
Patients with >1 CRS event, n (%)	46 (32.2)	46 (31.7)



- Most CRS events were grade 1/2 and largely confined to the step-up doses and first full dose

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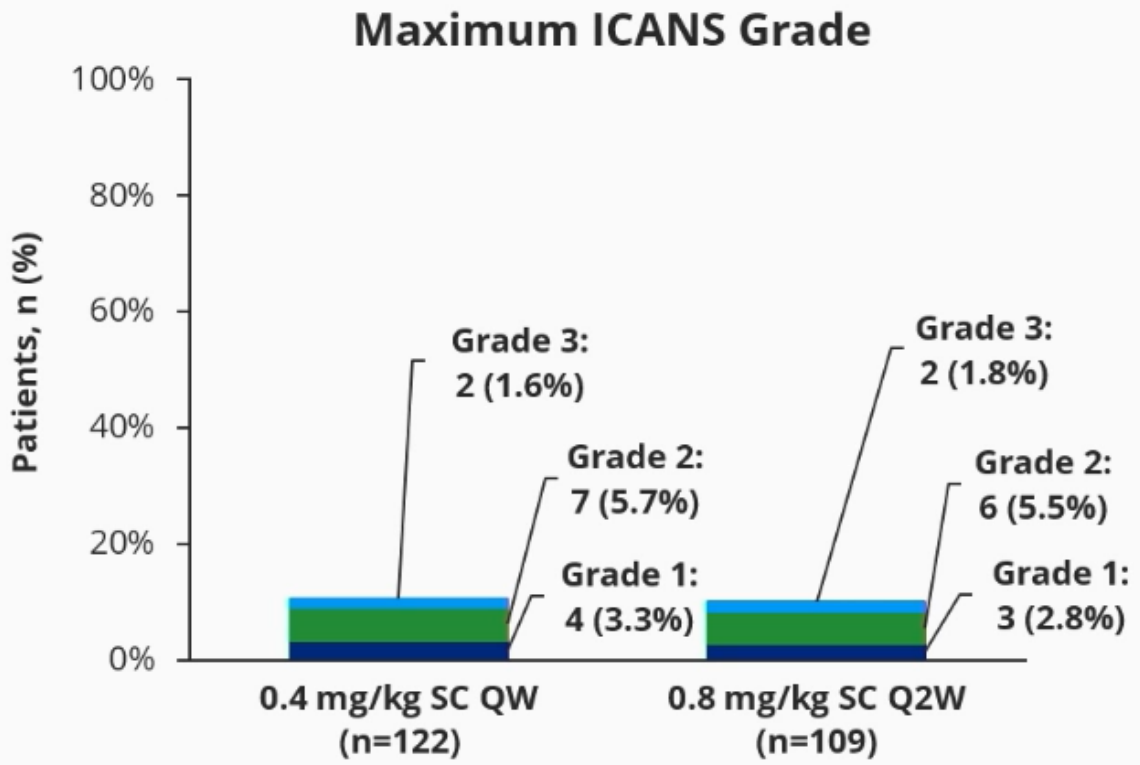
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

Parameter	0.4 mg/kg SC QW[a] (n=122[b])	0.8 mg/kg SC Q2W[a] (n=109[b])
Patients with ICANS, n (%)	13 (10.7)	11 (10.1)
Time to onset (days),[c] median (range)	2.0 (1–9)	3.0 (2–16)
Duration (days), median (range)	2 (1–22)	1 (1–15)
Outcome of ICANS, n (%)		
Number of ICANS events, n[d]	21	14
Recovered/resolved	18 (85.7)	11 (78.6)
Not recovered/not resolved	2 (9.5)	2 (14.3)
Fatal	0	0
Concurrent CRS[e]		
Yes	14 (66.7)	8 (57.1)
No	7 (33.3)	6 (42.9)



- ICANS occurred in 10–11% of patients across RP2D groups
- Most ICANS events were grade 1 or 2
- 7–8% of patients received supportive measures for ICANS across RP2D groups, including tocilizumab and corticosteroids

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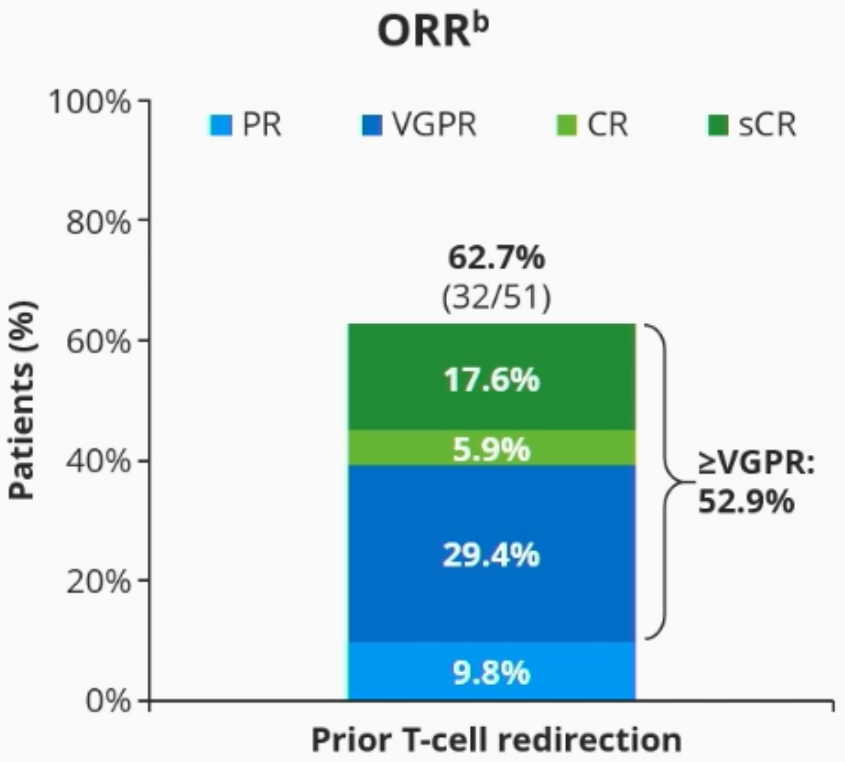
Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

- **Patients enrolled in cohort of prior T-cell redirection therapy:**
  - **Were younger** and had a **higher prevalence of high-risk cytogenetics**
  - **Median of 6 prior lines of therapy** (range, 3–15)
  - 70.6% (n=36) received prior CAR-T cell therapy and 35.3% (n=18) prior bispecific antibody therapy; 3 patients received both
  - 7.8% (n=4) were refractory to belantamab
  - Most patients received QW (n=43) vs Q2W (n=8) talquetamab dosing
- **ORR was 62.7%**
  - **72.2% ORR** (26/36) in patients with **prior CAR-T therapy**
  - **44.4% ORR** (8/18) in patients with **prior bispecific antibody treatment**
- Median DOR was 12.7 months (range, 3.7–NE) at a median follow-up of 11.8 months (range, 1.0[a]–25.4)
  - Data are still immature, with 56.3% of patients censored
- Safety profile comparable in patients with and without prior T-cell redirection therapy



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Beyond BCMA: 157, Talquetamab, a GPRC5D x CD3 Bispecific Antibody MonumenTAL-1: Phase 2 Results, including a cohort of patients with prior CAR-T or bispecific Ab treatment

- Talquetamab, a novel agent directed against a new antigen target in myeloma, demonstrated an ORR of 73–74% with QW and Q2W schedules in a heavily pretreated group of patients
  - In those with prior T-cell redirection therapy, a 63% ORR was observed
  - Safety and PK/PD activity were consistent between QW and Q2W dosing schedules
- Median DOR was ≥9 months in all groups, with longer DOR in those achieving ≥CR
- Overall, a low rate of discontinuations due to AEs was observed; the most common AEs included CRS, skin-related events, nail-related events, and dysgeusia
- An ongoing phase 3 study (NCT05455320) is evaluating talquetamab vs approved therapies; additional phase 1 studies[a] are evaluating combinations with other agents, including teclistamab, daratumumab, IMiDs, and/or a checkpoint inhibitor

>70% ORR with talquetamab in patients with heavily pretreated myeloma

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Beyond BCMA:

1924, Enduring Responses after 1-year, fixed duration Cevostamab

- FcRH5 cell surface receptor expressed exclusively within B-cell lineage
  - Expression close to 100% on myeloma cells[1]
  - Greater expression on myeloma and plasma cells compared with normal B-cells[1]
  - Attractive target for MM therapy
- Cevostamab (BFCR4350A), is a novel, humanized T-cell–engaging bispecific IgG antibody[1]
  - Targets CD3 on T-cells and FcRH5 on myeloma cells to encourage immunologic synapse formation, leading to myeloma cell death

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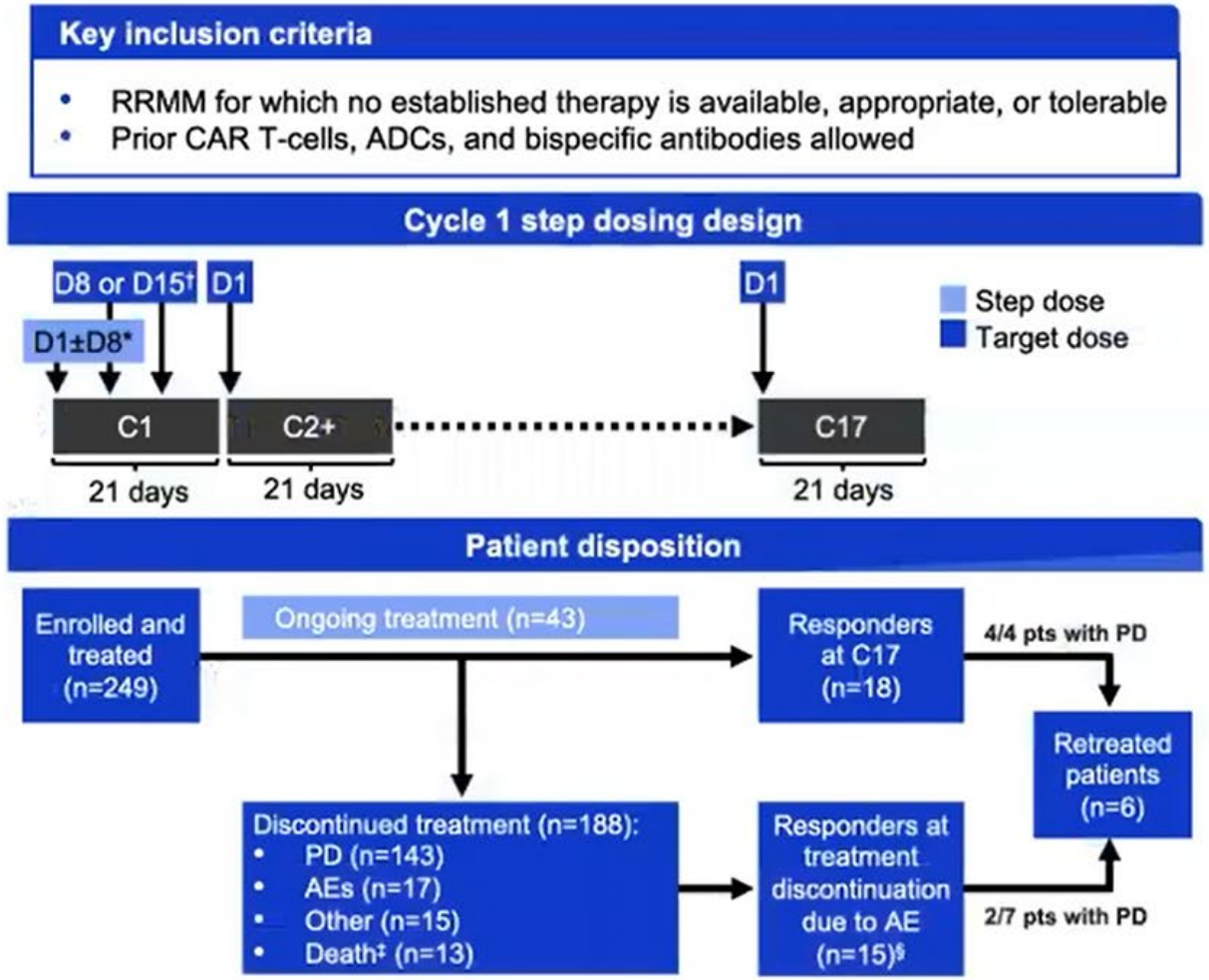
Beyond BCMA:

1924, Enduring Responses after 1-year, fixed duration Cevostamab

- Cevostamab was given as a fixed-duration treatment for up to 17 cycles or until unacceptable toxicity or PD
- Patients were eligible for retreatment if they:
  - Progressed after completion of C17
  - Were in response but discontinued cevostamab due to AE(s)
- Response was evaluated per International Myeloma Working Group criteria
- AEs were reported up to 90 days following the last dose of cevostamab
- SAEs were reported throughout follow-up



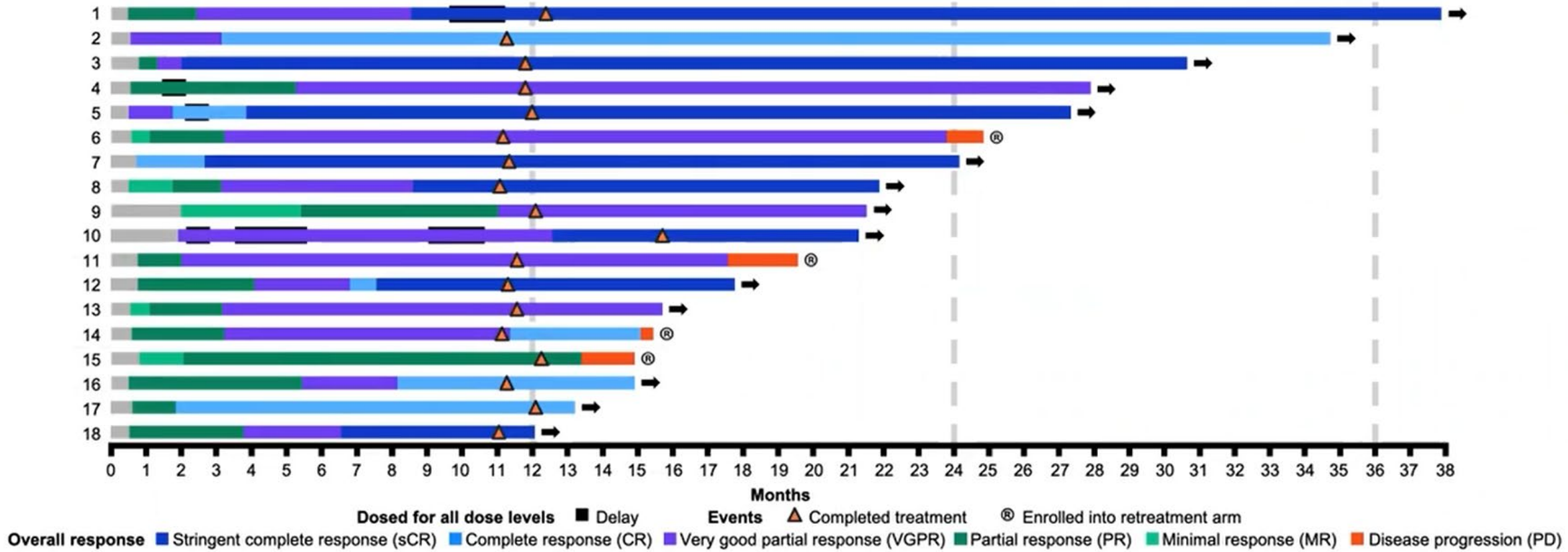
*Step dose consisted of either a single step on D1 or a double step on D1 and D8; †first target dose was given on D8 for patients with single-step or on D15 for patients with double-step dosing; ‡includes death due to disease progression (n=4); §a total of 17 patients discontinued due to AEs, but two patients were not responsive at discontinuation and thus have not been included in this subset of patients

ADC, antibody–drug conjugate; C, cycle; CAR, chimeric antigen receptor; D, Day; SAE, serious adverse event

Beyond BCMA:

1924, Enduring Responses after 1-year, fixed duration Cevostamab

- As of August 22, 2022, median follow-up post treatment was 9.6 months (range:1.2–26.2). Target cevostamab doses ranged from 40–160mg
- At data cut-off, 14/18 (78%) patients treated for 17 cycles of therapy remain in response

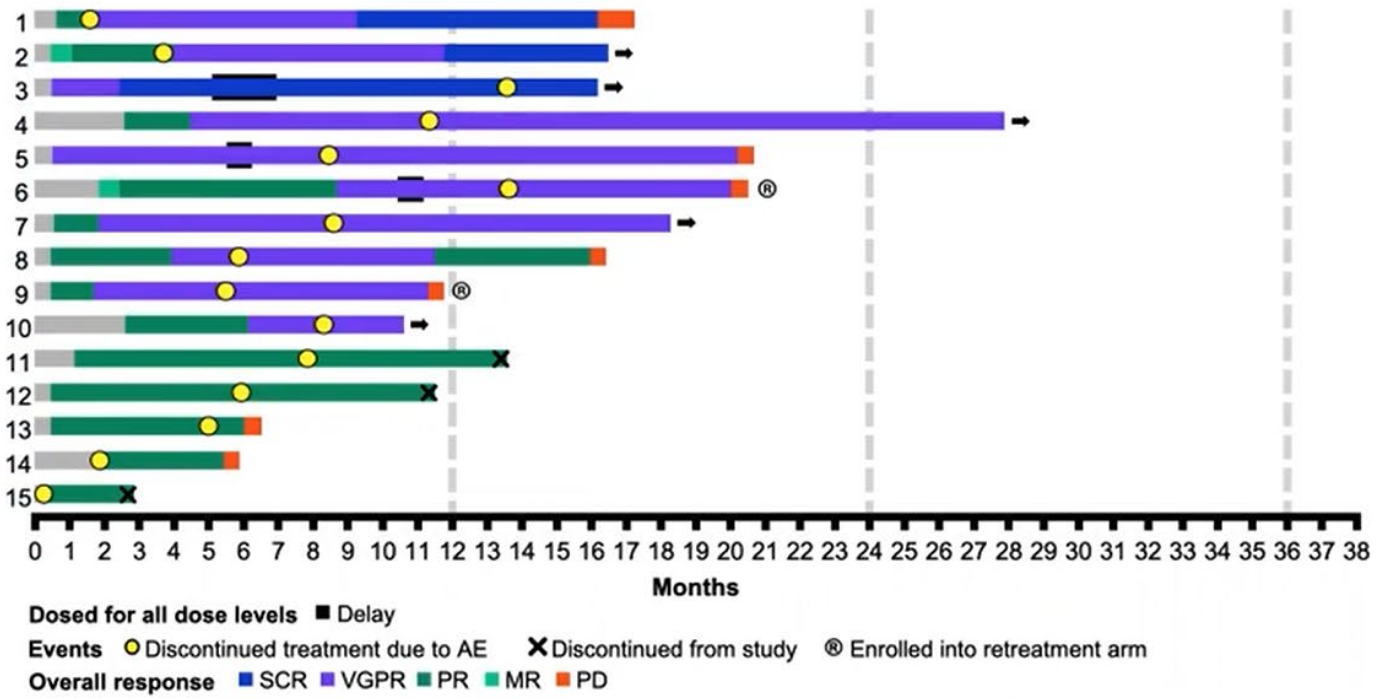


Beyond BCMA:

1924, Enduring Responses after 1-year, fixed duration Cevostamab

15 patients discontinued treatment due to AEs prior to C17 and continued in response:

- As of data cut-off, median follow-up for patients who remained in response upon discontinuation due to AEs was 11.0 months (range: 2.4–33.6)
- Target cevostamab doses ranged from 40–198mg with a median of 8 (range: 1–16) cycles of cevostamab therapy
- Median time on treatment was 6.0 months (range: 0.2–13.6) and median time on study was 19.3 months (range: 2.7–35.2)
- The median duration of response after treatment discontinuation was 9.2 months (95% CI: 6.3–14.9)



- The data presented are an encouraging indicator that a fixed treatment duration can be efficacious and offer patients a treatment-free period

Beyond BCMA:
568, Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD) with Dex

- Mezigdomide: oral cereblon E3 ligase modulator with improved tumor-killing and immune-stimulatory effects in R/R MM compared with traditional immunomodulatory drugs[1]
  - In preclinical studies, mezigdomide showed synergy with dexamethasone, proteasome inhibitors, and anti-CD38 antibodies[2]
- CC-92480-MM-001 is phase I/II trial evaluating mezigdomide ± dexamethasone in R/R MM[3]
  - In phase I, 54.5% ORR at RP2D of mezigdomide + dexamethasone
- Current analysis reported results from dose-expansion cohort of CC-92480-MM-001 with mezigdomide + dexamethasone in R/R MM[4]

1. Hansen. J Med Chem. 2020;63:6648. 2. Wong. ASH 2019. Abstr 1815.
3. Richardson. ASCO 2020. Abstr 8500. 4. Richardson. ASH 2022. Abstr 568.

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Beyond BCMA:
568, Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD) with Dex

- Phase I/II dose-escalation and dose-expansion trial (current analysis: dose-expansion cohort)

- **Primary endpoint:** ORR
- **Secondary endpoints:** safety, TTR, DoR, PFS
- **Exploratory:** pharmacodynamics

Prior Therapy	Patients (N = 101)
Median prior lines of therapy, n (range)	6 (3-15)
Stem cell transplantation, n (%)	78 (77.2)
IMiD agents, n (%) ▪ Pomalidomide ▪ Lenalidomide	101 (100) 101 (100) 101 (100)
PI, n (%)	101 (100)
Anti-CD38 mAb, n (%)	101 (100)
Anti-BCMA therapy, n (%) ▪ ADC ▪ Bispecific antibody ▪ CAR T-cell therapy	30 (29.7) 22 (21.8) 8 (7.9) 3 (3.0)
IMiD refractory, n (%) ▪ Pomalidomide ▪ Lenalidomide	101 (100) 97 (96.0) 89 (88.1)
PI refractory, n (%)	101 (100)
Anti-CD38 mAb refractory, n (%)	101 (100)
Triple-class refractory, n (%)	101 (100)

Richardson. ASH 2022. Abstr 568.

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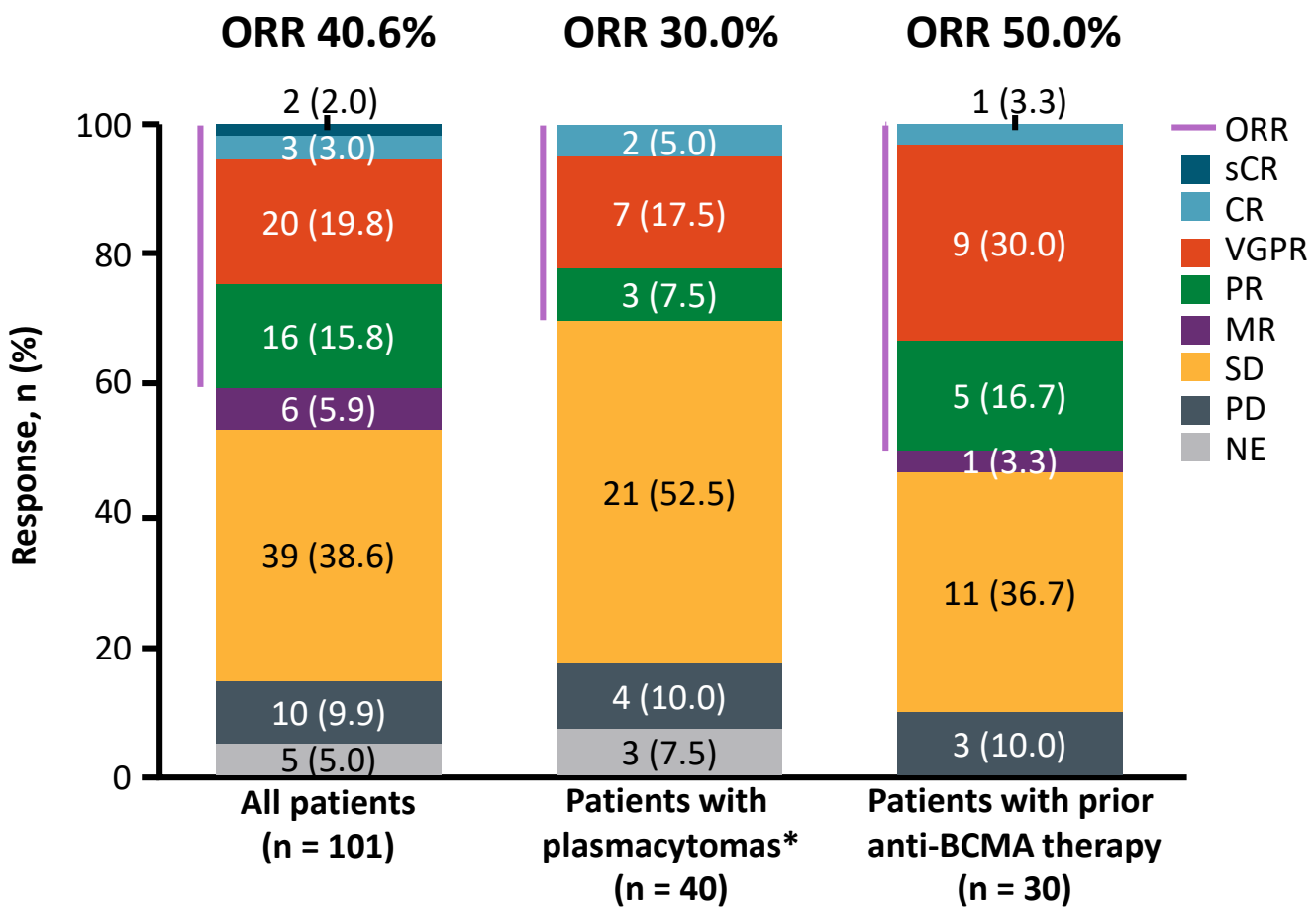
Beyond BCMA:
568, Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD) with Dex



Median Time to First Response, Mo (Range)	
All patients	0.95 (0.89-12.952)
Patients with plasmacytomas	2.17 (0.92-5.26)
Patients with previous BCMA-targeted tx	2.10 (0.89-10.16)

Median Follow-up, Mo (Range)	
All patients	5.46 (0.03-17.49)
Patients with plasmacytomas	6.10 (0.03-15.98)
Patients with previous BCMA-targeted tx	5.46 (0.03-15.98)

*Extramedullary soft tissue–only disease and soft tissue bone-related plasmacytomas

Richardson. ASH 2022. Abstr 568. Reproduced with permission.

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Beyond BCMA:

568, Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD) with Dex

- Mezigdomide + dexamethasone resulted in promising efficacy (ORR: 40.6%) in triple-class–refractory R/R MM
  - Activity was seen in patients with prior BCMA-targeted therapies and patients with plasmacytoma
- Safety profile of mezigdomide + dexamethasone was manageable
- Mezigdomide being investigated in combination with standard MM backbone therapies as part of large phase I/II trial (NCT03989414)
- 2 phase III trials evaluating mezigdomide with Vd and Kd are currently enrolling patients with R/R MM (SUCCESSOR-1 and SUCCESSOR-2)

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MM / AL Amyloid Trials at OHSU

OHSU Myeloma Clinical Research Team:
myelomaRT@ohsu.edu

Smoldering

- ECOG EAA173: Daratumumab / Len / Dex vs Len / Dex

Newly Diagnosed

- ECOG EAA181 (Transplant ineligible): Daratumumab / Len / Dex x9, then Dara / Len / Dex vs Dara / Len / Dex + Velcade consolidation

Relapsed / Refractory

- OHSU IIT: Isatuximab / Carfilzomib / Pomalidomide (1st relapse)
- HPN217 (Harpoon): T-cell activating construct (BCMA target)
- CC-99712 (Celgene): IV CC-99712 (BCMA ADC)
- DREAMM 12: Belantamab in renal failure (HD)
- Magrolimab Combinations: CD47 moAb

Maintenance

- MMY3021 (Janssen): MRD+ patients only: SC Dara + Len vs Len
- SWOG S1803: MRD+ or MRD- patients: SC Dara + Len vs Len

AL Amyloidosis

- CAEL 101-301/302: Newly dx AL amyloid, Mayo Stage IIIa and IIIb cardiac disease

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Please join us for Multiple Myeloma Rounds
https://www.mmrounds.com/
Feb 23, 2023, 6:15p

Thank You

(My favorite recent MyChart messages.)

Dr. Silberman , Sorry to bother you with this but this morning an owl stealth attacked my head. I never heard or saw it but Judge it was owl by force of impact. No evidence that it broke the skin but area still sensitive. My nurse daughter thought I might need antibiotics. As I do not have a primary care doctor I am asking you if you think as a precaution I should take antibiotics(owl talons carry all sorts of nasty bacteria) and if so what should I take and can you prescribe?

I got the message below [redacted]. I saw [redacted] today. I have no idea what to do. I don't even know what the CAR T thinks of my eligibility. I'm dubious that I can achieve clarity by Monday. Help!

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