ASH 2023 Multiple Myeloma Review

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3 February 2024
University of Nebraska

THE OHIO STATE UNIVERSITY
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Conflicts of Interest

Research support Sanofi
FDA ODAC Advisory Board
Consultancy Curio Science
Speaking ASH, ASTCT

Myeloma ASH 2023 Review

Objectives

1. Highlight ASH 2023 Myeloma practice ‘Changing’ or ‘Influencing’ abstracts.

American Society *of* Hematology

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Results of the Phase III Randomized Iskia Trial: Isatuximab-Carfilzomib-Lenalidomide-Dexamethasone vs Carfilzomib-Lenalidomide-Dexamethasone as Pre-Transplant Induction and Post-Transplant Consolidation in Newly Diagnosed Multiple Myeloma Patients

Francesca Gay, M.D., Ph.D.

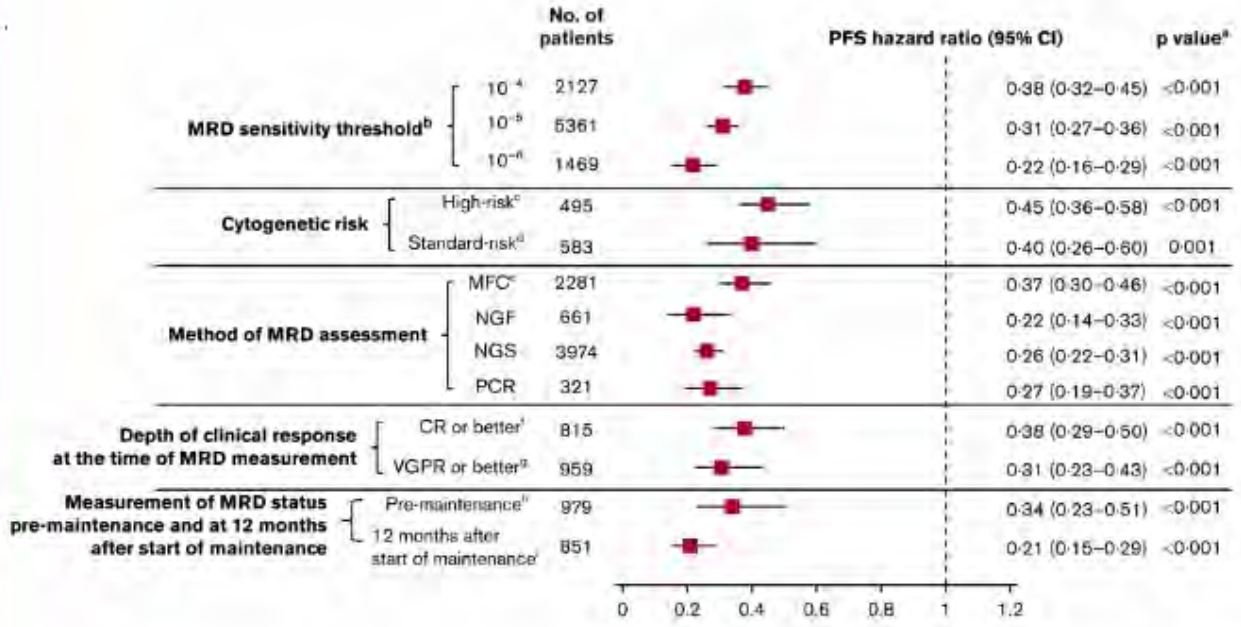
Peter Voorhees, M.D.

Levine Cancer Institute

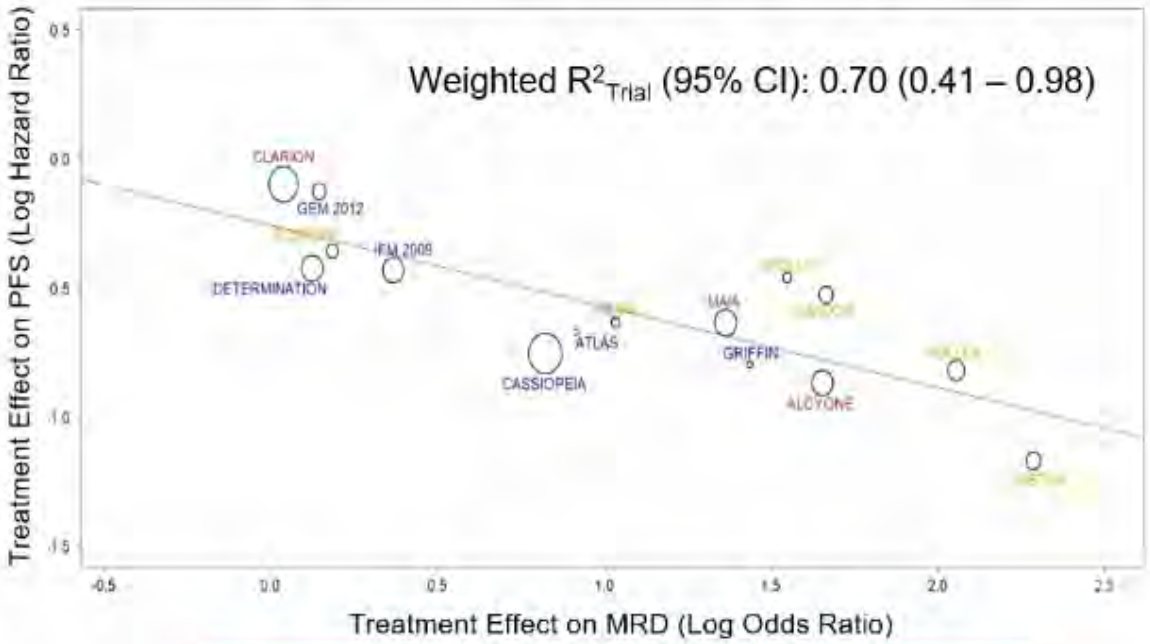
Atrium Health Wake Forest Baptist Comprehensive Cancer Center

Measurable Residual Disease as a Surrogate Endpoint for Studies in Patients with Newly Diagnosed Myeloma

- Meta-analysis of MRD in 8098 patients
- PFS HR 0.33 (95% CI 0.28 – 0.40), OS HR 0.50 (95% CI 0.42 – 0.59) in transplant eligible patients with newly diagnosed myeloma



Impact of Treatment Effect on MRD and PFS



i²TEAMM initiative: Meta-analysis of trial and patient level data

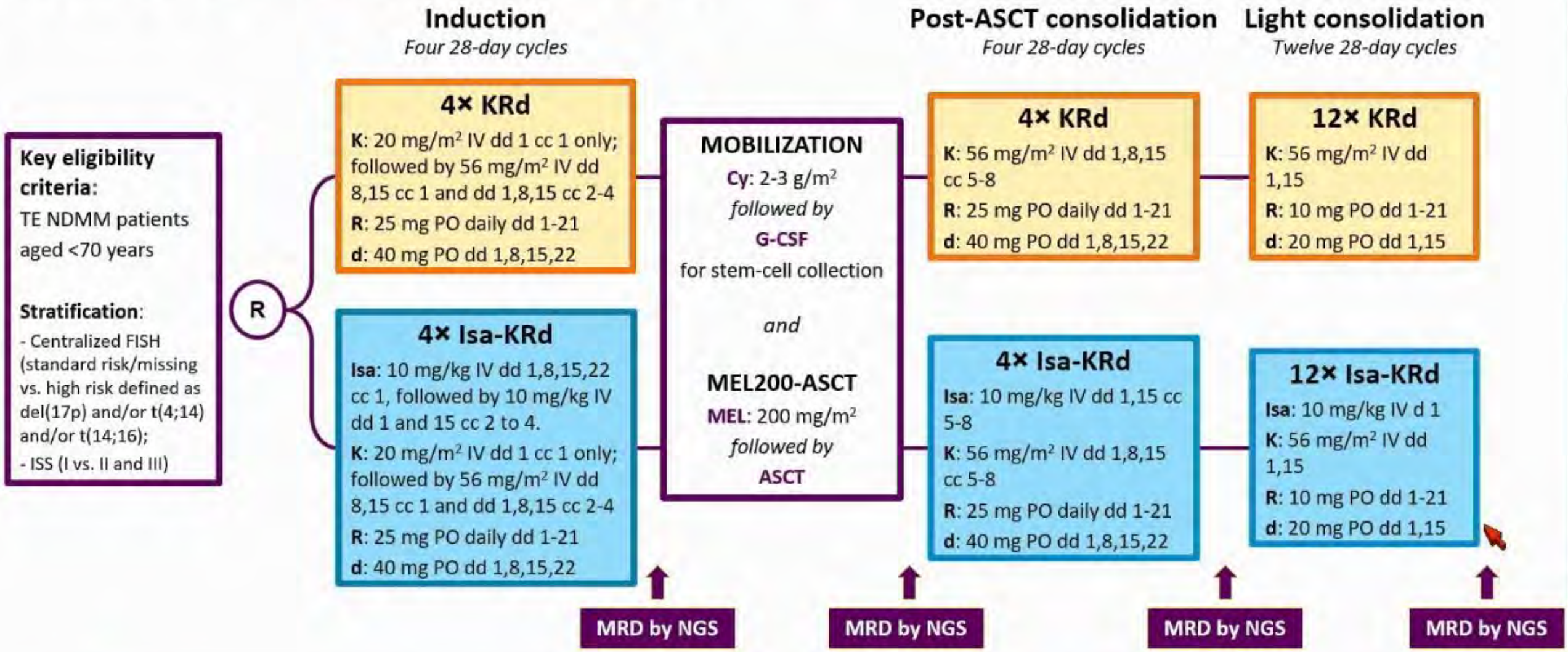
CI=Confidence interval; HR=Hazard ratio; MRD=Measurable residual disease; NGF=Next generation flow cytometry; NGS=Next generation sequencing; OS=Overall survival; PFS=Progression-free survival

Munshi NC et al. Blood Adv 2020;4:5988-5999

Paiva B et al. Blood Adv 2023 Aug:Online ahead of print

IsKia EMN24 Study Design

42 active sites; enrollment: Oct 7, 2020 – Nov 15, 2021



TE, transplant-eligible; NDMM, newly diagnosed multiple myeloma; FISH, fluorescence *in situ* hybridization; del, deletion; t, translocation; ISS, International Staging System stage; R, randomization; Isa, isatuximab; K, carfilzomib; R, lenalidomide; d, dexamethasone; IV, intravenous; dd, days; cc, cycles; PO, orally; Cy, cyclophosphamide; G-CSF, granulocyte colony-stimulating factor; MEL, melphalan; ASCT, autologous stem-cell transplantation; MRD, minimal residual disease; NGS, next-generation sequencing; PFS, progression-free survival.

Patient characteristics

		Isa-KRd n=151	KRd n=151
Age, years	Median (IQR)	61 (55–66)	60 (54–63)
Sex, n (%)	Female	72 (48)	67 (44)
	Male	79 (52)	84 (56)
Cytogenetic risk as per IMWG, n (%) *High risk: t(4;14), t(14;16), or del(17p)*	Standard risk	115 (82)	113 (81)
	High risk	25 (18)	26 (19)
	Missing	*11*	*12*
No. of HRCA risk: 0 vs. 1 vs. 2+ HRCA, n (%) *del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21)*	0 HRCA	78 (56)	75 (54)
	1 HRCA	49 (35)	49 (35)
	2+ HRCA	13 (9)	15 (11)
	Missing	*11*	*12*
R-ISS, n (%)	I	50 (35)	48 (34)
	II	82 (58)	85 (59)
	III	10 (7)	10 (7)
	Missing	*9*	*8*
R2-ISS, n (%)	I	34 (24)	35 (25)
	II	45 (32)	47 (34)
	III	52 (37)	51 (37)
	IV	8 (6)	6 (4)
	Missing	*12*	*12*

% are calculated on the number of patients whose data were available.; % may not total 100 because of rounding

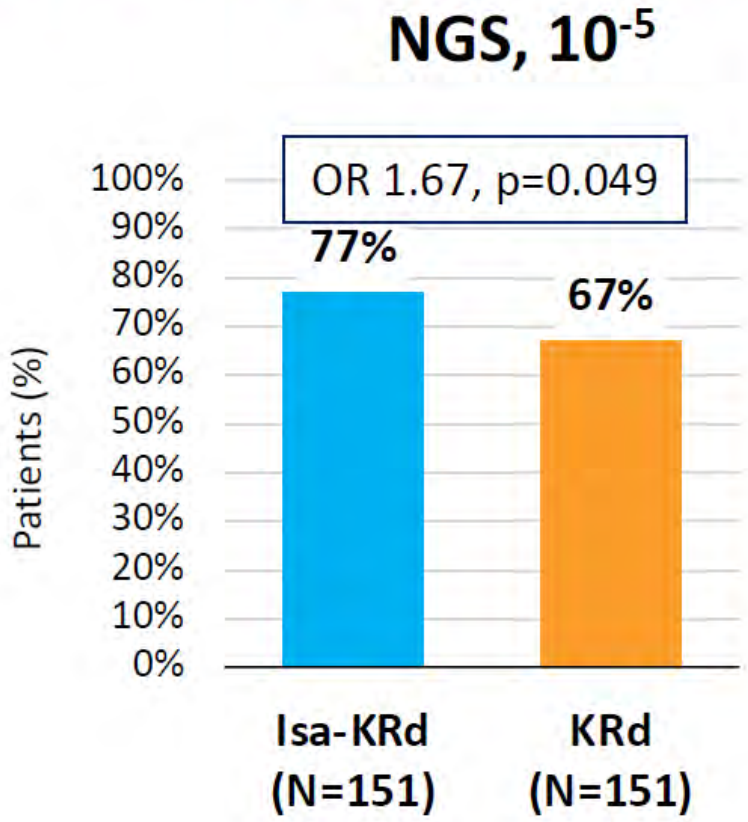
Sonneveld P, et al. Blood. 2016 Jun 16;127(24):2955-62. doi: 10.1182/blood-2016-01-631200.

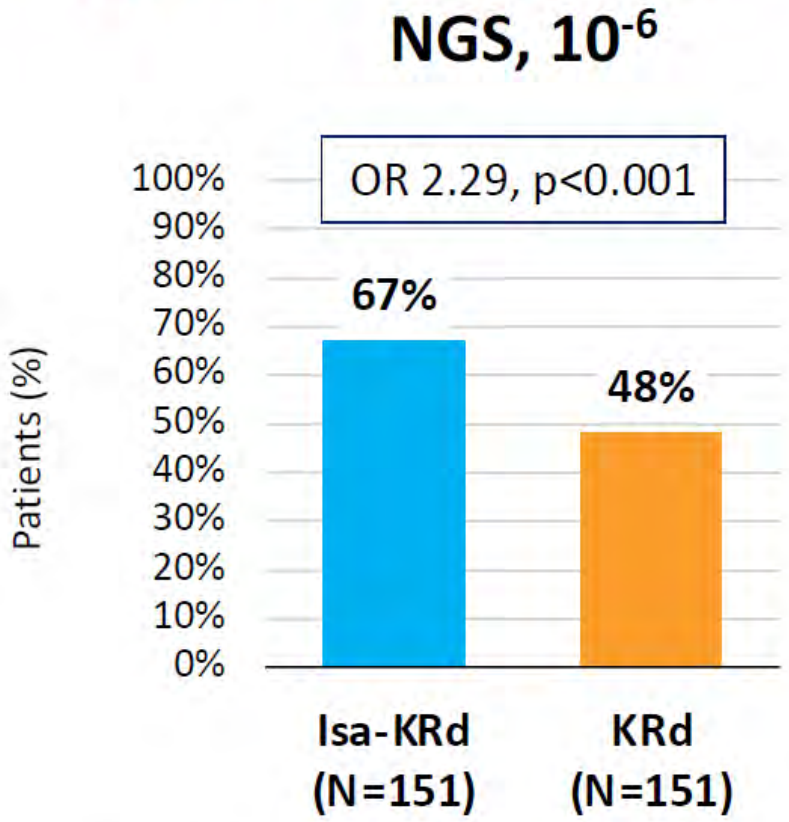
D'Agostino M et al. J Clin Oncol. 2022 Oct 10;40(29):3406-3418. doi: 10.1200/JCO.21.02614. Erratum in: J Clin Oncol. 2022 Dec 1;40(34):4032.

Palumbo A, et al. J Clin Oncol. 2015 Sep 10;33(26):2863-9. doi: 10.1200/JCO.2015.61.2267.

Isa, isatoximab; K, carfilzomib; R, lenalidomide; d, dexamethasone; IQR, interquartile range; IMWG, International Myeloma Working Group; t, translocation; del, deletion; No., number; HRCA, high-risk cytogenetic abnormalities; amp, amplification; R-ISS, Revised International Staging System stage; R2-ISS, Second Revision of the International Staging System stage.

Primary Endpoint: Post-consolidation MRD negativity (ITT analysis)





≥VGPR after consolidation was 94% in both arms; ≥CR 74% vs 72% and sCR 64% vs 67% in the IsaKRd vs KRd arms.

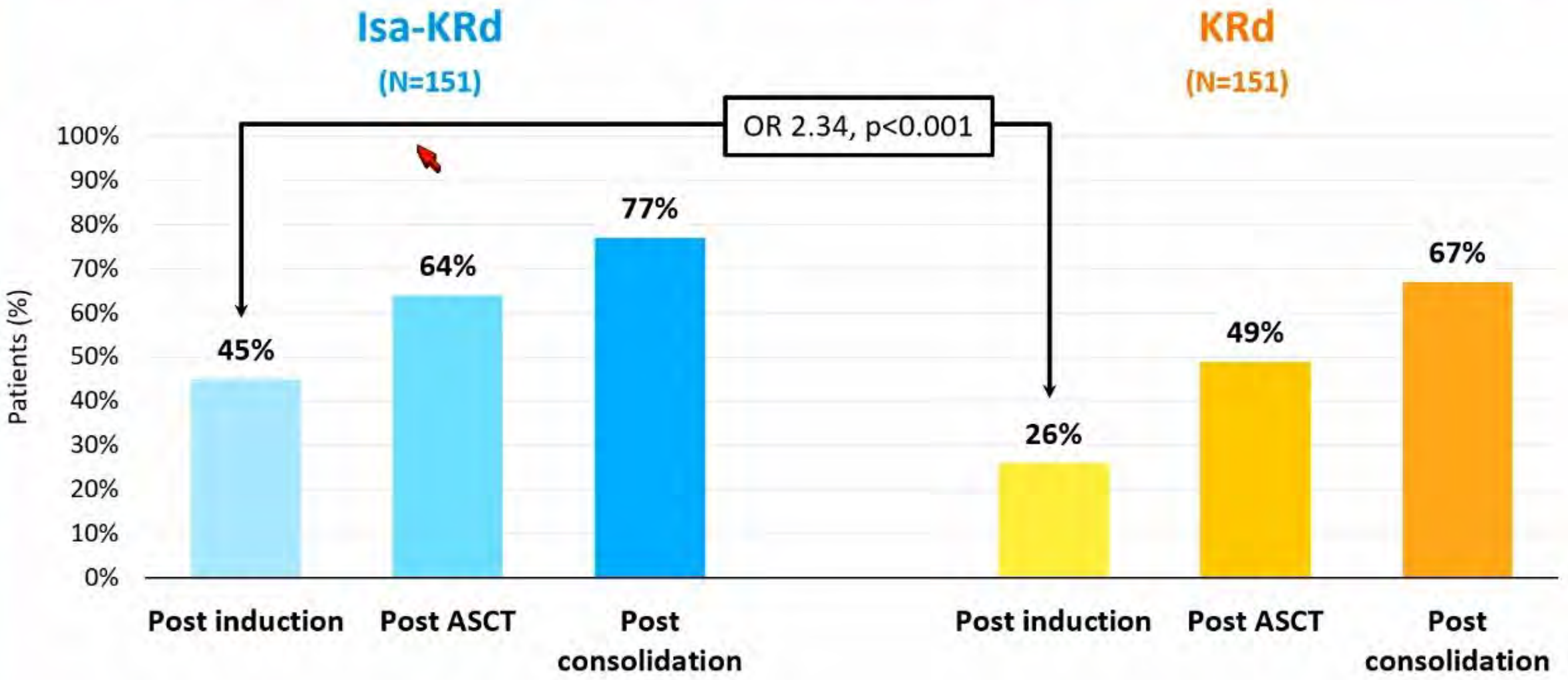
High MRD compliance and sample quality (97-100% of sample evaluable at 10^{-5} and 10^{-6} cut off.

Consistent MRD results were detected by next-generation flow

In the logistic regression analysis, ORs, 95% CIs, and p-values were adjusted for stratification factor.

MRD, minimal residual disease; ITT, intention to treat; NGS, next-generation sequencing; OR, odds ratio; p, p-value; Isa, isatuximab; K, carfilzomib; R, lenalidomide; d, dexamethasone; CI, confidence interval.

MRD negativity rates improved over time (10^{-5})



MRD, minimal residual disease; p, p-value; ASCT, autologous stem-cell transplantation.

Safety analysis: treatment-related adverse events

	Isa-KRd (n=151)		KRd (n=151)	
	Any grade, n (%)	Grade 3-4, n (%)	Any grade, n(%)	Grade 3-4, n (%)
Pts with ≥1 hematologic toxicity	83 (55)	61 (40)	67 (44)	46 (30)
Anemia	32 (21)	5 (3)	28 (19)	5 (3)
Neutropenia	62 (41)	55 (36)*	39 (26)	33 (22)*
Thrombocytopenia	51 (34)	22 (15)	38 (25)	25 (17)
Pts with ≥1 Non-Hematologic toxicity	136 (90)	61 (41)	129 (85)	56 (37)
Infections (excluding COVID19)	55 (36)	23 (15)	49 (32)	17 (11)
Asthenia/fatigue	37 (25)	5 (3)	40 (26)	3 (2)
Dyspnea	20 (13)	2 (1)	9 (6)	1 (<1)
Rash	33 (22)	5 (3)	40 (26)	5 (3)
Peripheral neuropathy	22 (15)	0	25 (17)	0
Infusion-related reactions	30 (20)	5 (3)	2 (1)	0
Cardiac disorders	11 (7)	1 (<1)	19 (13)	5 (3)
Vascular disorders	29 (19)	7 (5)	33 (22)	15 (10)
Hypertension	5 (3)	2 (1)	6 (4)	3 (2)
Thromboembolism	12 (8)	4 (3)	16 (11)	9 (6)
Gastrointestinal disorders	79 (52)	10 (7)	73 (48)	8 (5)
Nausea	36 (24)	4 (3)	31 (21)	2 (1)
Vomiting	18 (12)	2 (1)	12 (8)	1 (<1)
Diarrhea	41 (27)	6 (4)	37 (25)	5 (3)

Key Points

- Isa-KRD unlikely to supplant D-VRD ENDURANCE
- MRD primary endpoint?

*p-value =0.008

Isa, isatuximab; K, carfilzomib; R, lenalidomide; d, dexamethasone.

Phase 3 Randomized Study of Daratumumab + Bortezomib, Lenalidomide, and Dexamethasone (VRd) Versus VRd Alone in Patients With Newly Diagnosed Multiple Myeloma Who Are Eligible for Autologous Stem Cell Transplantation: Primary Results of the PERSEUS Trial*

*ClinicalTrials.gov Identifier: NCT03710603; sponsored by EMN in collaboration with Janssen Research & Development, LLC.

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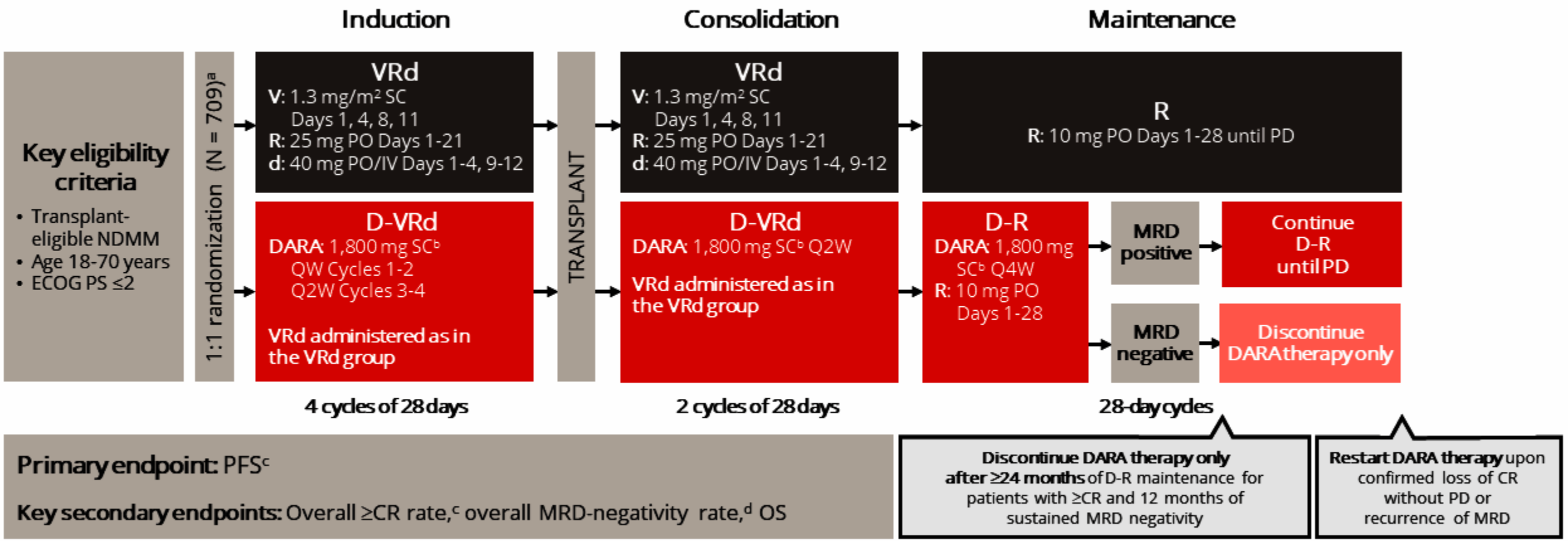
Presented by P Sonneveld at the 65th American Society of Hematology (ASH) Annual Meeting; December 9-12, 2023; San Diego, CA, USA

PERSEUS: Study Design



Primary endpoint: PFS[c]

Key secondary endpoints: Overall ≥CR rate,[c] overall MRD-negativity rate,[d] OS

Discontinue DARA therapy only after ≥24 months of D-R maintenance for patients with ≥CR and 12 months of sustained MRD negativity

Restart DARA therapy upon confirmed loss of CR without PD or recurrence of MRD

ECOG PS, Eastern Cooperative Oncology Group performance status; V, bortezomib; SC, subcutaneous; PO, oral; d, dexamethasone; IV, intravenous; QW, weekly; Q2W, every 2 weeks; PD, progressive disease; Q4W, every 4 weeks; MRD, minimal residual disease; OS, overall survival; ISS, International Staging System; rHuPH20, recombinant human hyaluronidase PH20; IMWG, International Myeloma Working Group; VGPR, very good partial response. [a]Stratified by ISS stage and cytogenetic risk. [b]DARA 1,800 mg co-formulated with rHuPH20 (2,000 U/mL; ENHANZE® drug delivery technology, Halozyme, Inc., San Diego, CA, USA). [c]Response and disease progression were assessed using a computerized algorithm based on IMWG response criteria. [d]MRD was assessed using the clonoSEQ assay (v.2.0; Adaptive Biotechnologies, Seattle, WA, USA) in patients with ≥VGPR post-consolidation and at the time of suspected ≥CR. Overall, the MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity (10^{-5} threshold) and ≥CR at any time.

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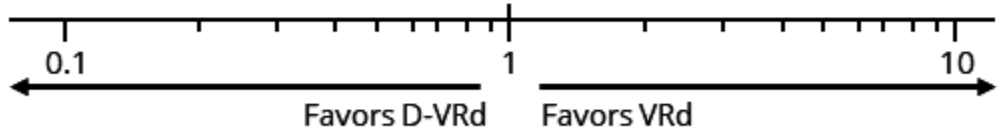
PERSEUS: PFS in Prespecified Subgroups

Subgroup	D-VRd no. of progression events or deaths/total no.	VRd no. of progression events or deaths/total no.	HR (95% CI)
Sex			
Male	36/211	61/205	0.51 (0.34-0.77)
Female	14/144	42/149	0.29 (0.16-0.53)
Age			
<65 y	30/261	84/267	0.30 (0.20-0.46)
≥65 y	20/94	19/87	0.97 (0.52-1.81)
Race			
White	47/330	95/323	0.42 (0.30-0.60)
Other	3/25	8/31	0.40 (0.11-1.50)
ISS stage			
I	18/186	35/178	0.46 (0.26-0.81)
II	19/114	43/125	0.37 (0.22-0.64)
III	13/55	25/50	0.42 (0.22-0.83)
Type of MM			
IgG	28/204	58/185	0.36 (0.23-0.57)
Non-IgG	13/78	31/96	0.46 (0.24-0.88)
Cytogenetic risk			
Standard risk	25/264	62/266	0.35 (0.22-0.56)
High risk	24/76	38/78	0.59 (0.36-0.99)
Indeterminate	1/15	3/10	0.16 (0.02-1.56)
ECOG PS			
0	28/221	60/230	0.42 (0.27-0.66)
≥1	22/134	43/124	0.41 (0.25-0.69)



- PFS was improved with D-VRd versus VRd across clinically relevant subgroups

The subgroup analysis for type of MM was performed on data from patients who had measurable disease in serum. Cytogenetic risk was assessed by fluorescence in situ hybridization; high risk was defined as the presence of del(17p), t(4;14), and/or t(14;16).

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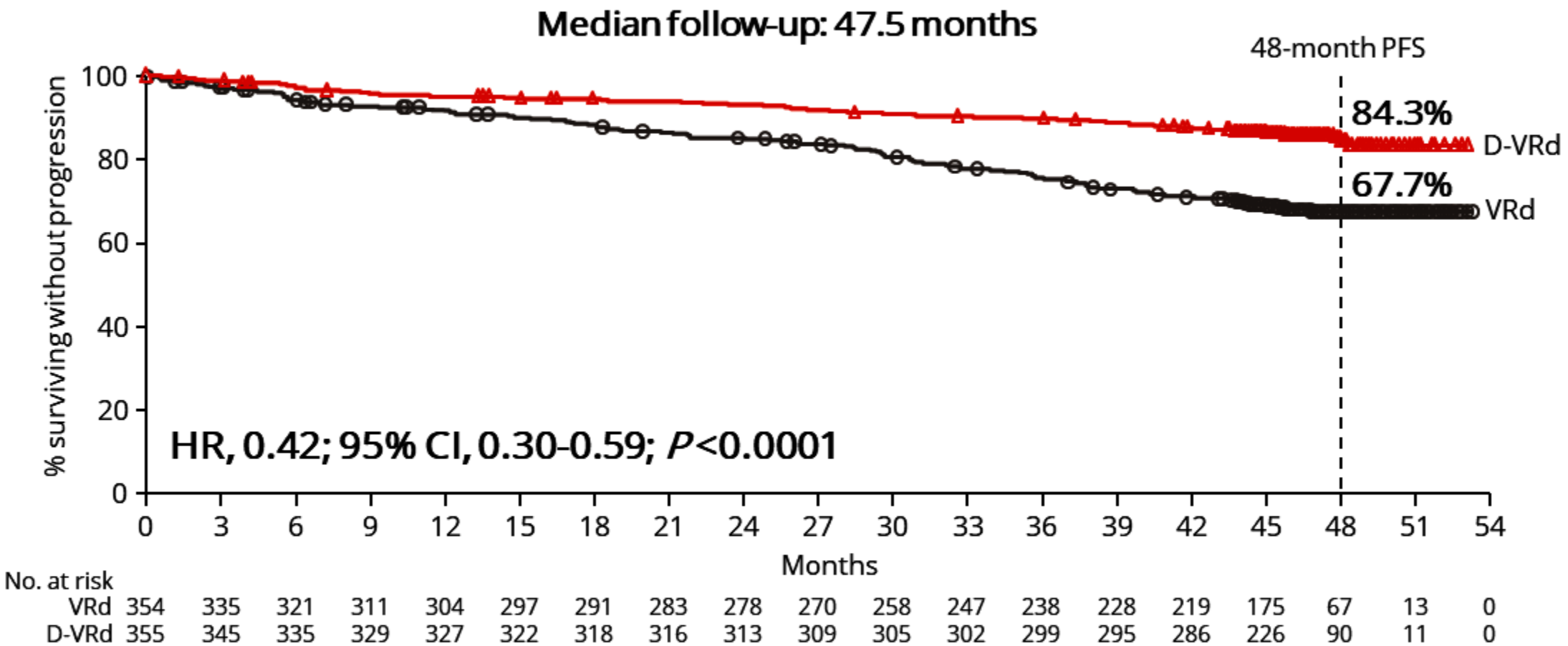
PERSEUS: Progression-free Survival



- 58% reduction in the risk of progression or death in patients receiving D-VRd

HR, hazard ratio; CI, confidence interval.

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PERSEUS: Safety

Event, n (%)[a]	D-VRd (n = 351)		VRd (n = 347)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
HEMATOLOGIC				
Neutropenia	**243 (69.2)**	**218 (62.1)**	**204 (58.8)**	**177 (51.0)**
Thrombocytopenia	**170 (48.4)**	**102 (29.1)**	**119 (34.3)**	**60 (17.3)**
Anemia	78 (22.2)	21 (6.0)	72 (20.7)	22 (6.3)
Febrile neutropenia	34 (9.7)	33 (9.4)	38 (11.0)	35 (10.1)
NON-HEMATOLOGIC				
Diarrhea	214 (61.0)	37 (10.5)	188 (54.2)	27 (7.8)
Peripheral sensory neuropathy	**188 (53.6)**	**15 (4.3)**	**179 (51.6)**	**14 (4.0)**
Constipation	119 (33.9)	8 (2.3)	118 (34.0)	6 (1.7)
Pyrexia	111 (31.6)	8 (2.3)	109 (31.4)	9 (2.6)
Insomnia	95 (27.1)	8 (2.3)	61 (17.6)	6 (1.7)
Asthenia	94 (26.8)	12 (3.4)	89 (25.6)	9 (2.6)
Cough	85 (24.2)	1 (0.3)	51 (14.7)	0
Fatigue	84 (23.9)	10 (2.8)	92 (26.5)	18 (5.2)
Rash	82 (23.4)	9 (2.6)	94 (27.1)	17 (4.9)
Back pain	80 (22.8)	2 (0.6)	66 (19.0)	1 (0.3)
Peripheral edema	72 (20.5)	4 (1.1)	74 (21.3)	1 (0.3)
Nausea	71 (20.2)	2 (0.6)	58 (16.7)	2 (0.6)
Infections	**305 (86.9)**	**124 (35.3)**	**266 (76.7)**	**95 (27.4)**
COVID-19	123 (35.0)	12 (3.4)	83 (23.9)	4 (1.2)
Upper respiratory tract infection	111 (31.6)	2 (0.6)	87 (25.1)	6 (1.7)
Pneumonia	64 (18.2)	37 (10.5)	38 (11.0)	21 (6.1)

TEAE, treatment-emergent adverse event. [a]TEAEs of any grade reported in ≥20% of patients in either treatment group and grade 3 or 4 TEAEs reported in ≥10% of patients in either treatment group.

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Table S6. Overview of Adverse Events by Age Subgroup in the Safety Population.*

	D-VRd				VRd			
	<50 y (n = 53)	50–<65 y (n = 205)	≥65 y (n = 93)	Total (n = 351)	<50 y (n = 53)	50–<65 y (n = 207)	≥65 y (n = 87)	Total (n = 347)
Treatment-emergent adverse event – no. (%)								
Any grade	52 (98.1)	204 (99.5)	93 (100.0)	349 (99.4)	52 (98.1)	205 (99.0)	87 (100.0)	344 (99.1)
Grade 3	30 (56.6)	116 (56.6)	47 (50.5)	193 (55.0)	29 (54.7)	122 (58.9)	48 (55.2)	199 (57.3)
Grade 4	15 (28.3)	64 (31.2)	38 (40.9)	117 (33.3)	11 (20.8)	46 (22.2)	26 (29.9)	83 (23.9)
Treatment-emergent adverse event leading to treatment discontinuation – no. (%)	2 (3.8)	17 (8.3)	12 (12.9)	31 (8.8)	6 (11.3)	33 (15.9)	[illegible]	[illegible]
Treatment-emergent adverse event leading to death – no. (%)	0	8 (3.9)	5 (5.4)	13 (3.7)	2 (3.8)	10 (4.8)	4 (4.6)	16 (4.6)

D-VRd denotes subcutaneous daratumumab plus bortezomib/lenalidomide/dexamethasone. VRd denotes bortezomib/lenalidomide/dexamethasone.

*The safety population included patients who received at least one dose of study treatment.

Key Points

- D-VRD SOC
- Nuances: practice vs trials (velcade, consolidation)

Sonneveld et al. NEJM 12 Dec 2023

GEM-2017FIT: Induction therapy with VMP/Rd vs KRd or Dara-KRd 18c followed by consolidation and maintenance therapy with Dara and Len: phase III, multicenter, randomized trial for elderly FIT NDMM aged between 65 and 80 years

María-Victoria Mateos, Bruno Paiva, Teresa Cedena, Noemí Puig, Anna Sureda, Albert Oriol, Enrique-M Ocio, Laura Rosiñol, Yolanda González, Joan Bargay, Esther González, Miguel Teodoro Hernández, Angel Payer, Alexia Suarez, María-Jesús Blanchard, Sebastián Garzón, Felipe Casado, Valentín Cabañas, Jaime Pérez de Oteyza, Mercedes Gironella, Joaquín Martínez, Ana Isabel Teruel, Pilar Delgado, Elena Prieto, Juan-José Lahuerta, Joan Bladé, Jesús San Miguel

GEM2017FIT phase 3 trial: VMP-Rd 18c vs KRd or D-KRd 18c in NDMM-TIE and up to 80 years

Induction

VMP 9c

Bortezomib: 1.3 mg/m² SC twice per week C1 and weekly C2-C9

Melphalan 9mg/m² PO D1-4 C1-C9

Prednisone 60mg/m² PO D1-4 C1-C9

Rd 9c

Lenalidomide 25 mg PO D1-21 every 28 days C1-C9

Dexamethasone 40 mg PO weekly C1-C9

KRD 18c

Carfilzomib: 36 mg/m² IV twice per week C1-C2 and 56 mg/m² weekly C3-C18

Lenalidomide 25 mg PO D1-21 every 28 days C1-C9

Dexamethasone 40 mg PO weekly C1-C9

Dara-KRD 18c

Daratumumab 1800 mg SC QW C1-C2, Q2W C3-C6 and Q4W C7-C18

Carfilzomib: 36 mg/m² IV twice per week C1-C2 and 56 mg/m² weekly C3-C18

Lenalidomide 25 mg PO D1-21 every 28 days C1-C9

Dexamethasone 40 mg PO weekly C1-C9

- VMP-Rd in patients younger than 80 years resulted in a MRD-ve rate of 20%
- Hypothesis was to increase the MRD-ve rate up to 35% in the two experimental arms
- Sample size required was 462 patients

Primary end-point: MRD-ve by NGF at 10^{-5} after 18 cycles comparing VMP-Rd with KRd and VMP-Rd with D-KRd

Dexamethasone 20 mg in patients older than 75 years

GEM2017 phase 3 trial in NDMM TIE FIT

Fitness was evaluated based on the chronological age (up to 80 years) and the Geriatric Assessment in Hematology (GAH) score

Table 2. Dimensions used for the development of the GAH scale

Dimension	Measurement	Range of score	Cut-off point	Coefficients
No. of drugs	Medication count of drugs of current use.	Continuous	≥ 5	2
Gait speed	Double determination of gait speed at usual pace over a 4 meter course	Continuous	< 0.8 m/s	13
Mood	*In the last week, did you feel depressed?* (CES-D)	Never, rarely, or occasionally (no more than 2 days); frequently, most of the time or all time (3-7 days)	Frequently, most of the time or all time (3-7 days)	4
ADL	Item no. 4 of the VES-13 Instrument: *Do you have any difficulty in...? Do you need any help in your daily living? Do you have a caregiver?*	Yes / No	Needs help in at least one area	22
Subjective Health Status	*Compared to other people your age, would you say your health is...?* (VES-13 Instrument:)	Poor, fair, good, very good, or excellent	Poor and fair	6
Nutrition	MNA-SF	0-10	≤ 8	40
Mental Status	SPMSQ	Right / Wrong	≥ 3 errors	5
Comorbidities	Prognostic Index for 4-year Mortality in Older Adults	0-10	≥ 3	5

ADL activities of daily living, *CES-D* centre for epidemiological studies depression scale, *DM* diabetes mellitus, *MNA-SF* mini-nutritional assessment questionnaire, *SPMSQ* short portable mental status questionnaire, *VES-13* 13-item vulnerable elders survey.

Table 3. Diagnosis accuracy of the GAH scale

AUC (95% CI)	Cut-off point	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
0.625 (0.512 – 0.739)	3.2	96.3% (87.5-98.98%)	9.3% (3.7-21.6%)	57.1% (46.3-67.5%)	66.7% (22.3-95.7%)
	41.6	68.5% (55.3-79.3%)	55.8% (41.1-69.6%)	66.1% (52.2-87.2%)	55.8% (41.1-69.6%)
	84.6	3.7% (1.0-12.5%)	95.3% (84.5-98.7%)	50.0% (6.8-93.2%)	44.1% (33.8-54.8%)

Data are expressed as n, unless otherwise stated. *AUC* area under the curve, *CI* confidence interval, *NPV* negative predictive value, *PPV* positive predictive value.

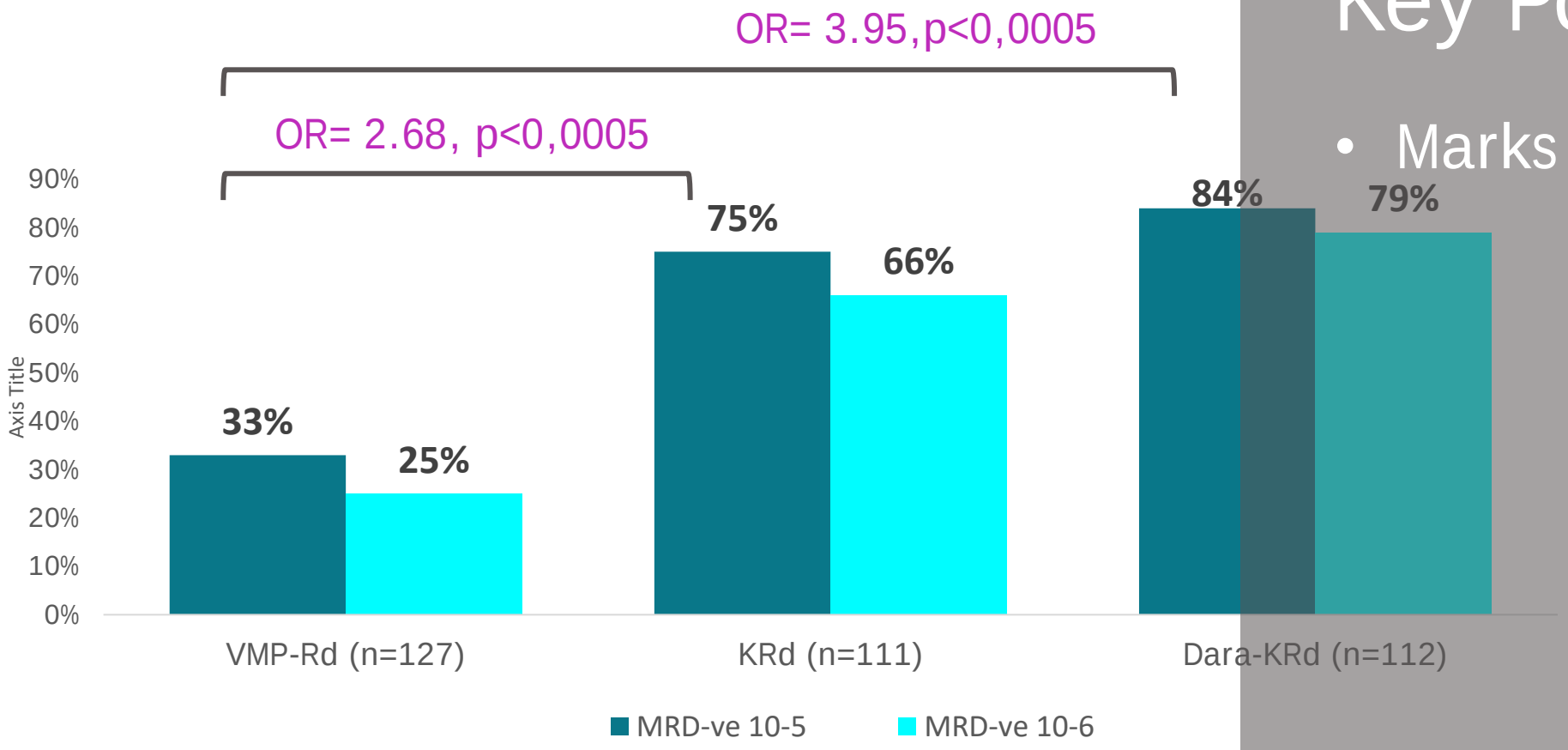
- The sum of the GAH scale score ranges from 0 to 94, with a cut-off point set at 42 (Figure 1).

Figure 1. GAH scale score for predicting treatment-related toxicity

30 ítems in 10-12 minutes. Lower score → Better status

Bonanad S, et al. JGO. 2015; Jentoft AJ, et al. JGO. 2017; de la Rubia J, et al. JGO. 2023.

GEM2017 phase 3 trial in NDMM TIE FIT: MRD-ve rate at 10^{-5} after 18 induction cycles in the evaluable population: Primary endpoint



Key Points

- Marks the end of VMP

Evaluable population included all patients who have completed the 18 induction cycles as well as those who discontinued early because of progressive disease and the MRD was considered as positive

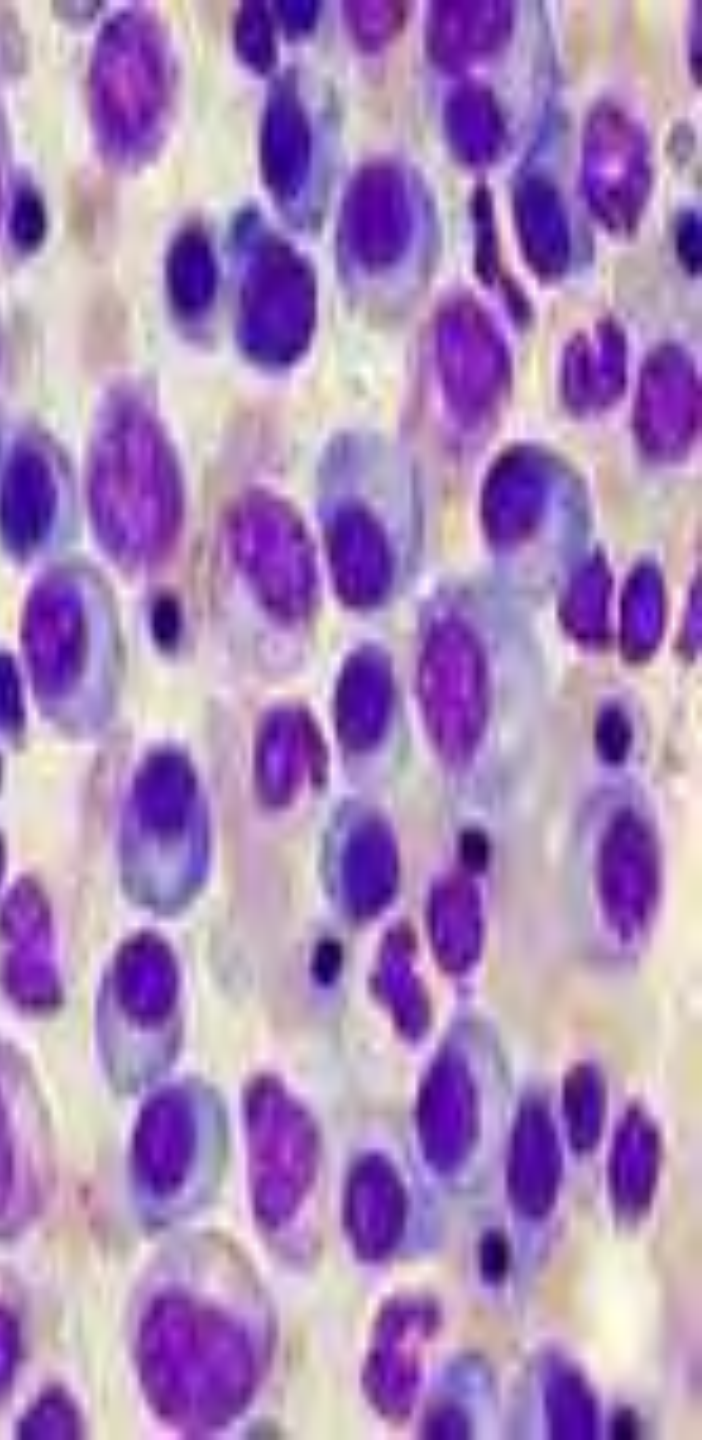
GEM2017 phase 3 trial in NDMM TIE FIT: Early discontinuations

Discontinuation during induction	VMP-Rd (n=49)	Toxicity leading to discontinuation	KRD (n=43)	Toxicity leading to discontinuation	D-KRd (n=48)	Toxicity leading to discontinuation
Time to early discontinuation	9.9 (0.5-18.9)		8.4 (0.3-18.4)		4.0 (0.03-18.8)	
Toxicity	8 (16%)	PN G3 (1), cardiac tox (1), GI tox (2), renal tox (1),cytopenias (1), pulmonar tox (1), len intolerance (1)	14 (32%) OR. 2.47, p=0.06	Cardiac tox (3), Thrombotic events (2), rash (2), renal tox (3), hepatitis (1), respiratory infection (1), thrombopenia (1),TLS (1)	7 (14%) OR: 1.1, p=0.8	Sepsis (1), Hepatitis (2), Rash (1), Len-related pneumonitis (1), renal toxicity (1)
Toxicity-related death	7 (14%)	Cardiac arrest (2) Sepsis (2) Respiratory infection (3)	5 (12%) OR: 0.78, p=0.7	Sepsis (2), Covid-19 (1), Infection (1), Guillen Barre síndrome (1)	13 (33%) OR: 2.88 P=0.04	Cardiac arrest (2) Sepsis (4), Respiratory infection (3), Covid-19 (4)
GAH ≥ 20	25 (51%)		17 (40%) OR: 0.62, p=0.2		26 (67%) OR: 1.92, p=0.1	

- Toxicity in the KRd arm leading to discontinuation was higher tan VMP—Rd but there was not any trend to specific toxicity
- Toxicity in the D-KRd arm leading to discontinuation was similar to VMP-Rd with not any trend to specific toxicity
- Toxicity-related deaths in the three arms were because of infections as the most frequent reason
- There is a trend for patients with GAH ≥ 20 to discontinue because of toxicity or toxicity-related death and especifically, higher scores concentrated on gait speed and nutrition.

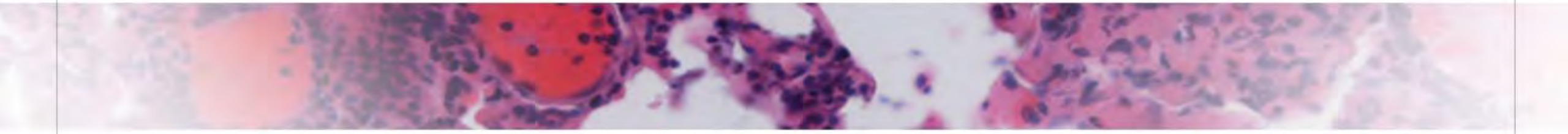
Key Points

- 4- drug induction
- Toxicity and toxicity related death
- GMMG-CONCEPT trial
- Primary endpoint MRD



Relapsed Multiple Myeloma

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



Randomized Phase 3 Study of Pomalidomide Cyclophosphamide Dexamethasone (PCD) Versus Pomalidomide Dexamethasone (PD) in Relapse or Refractory Myeloma: An Asian Myeloma Network (AMN) Study

Yang Song[1*], Jin Seok Kim[2*], CS Chim,[3*], Je-Jung Lee[4*], Sung-Soo Yoon[5], Soo Chin Ng, FRCP[6], Gin Gin Gan[7*], Hiroshi Handa[8], Wei-Ying Jen,[1*], Xinhua Li[9*], Yogesh Mahadev Pokharkar[9*], Brian GM Durie[10] and **Wee-Joo Chng[1]**

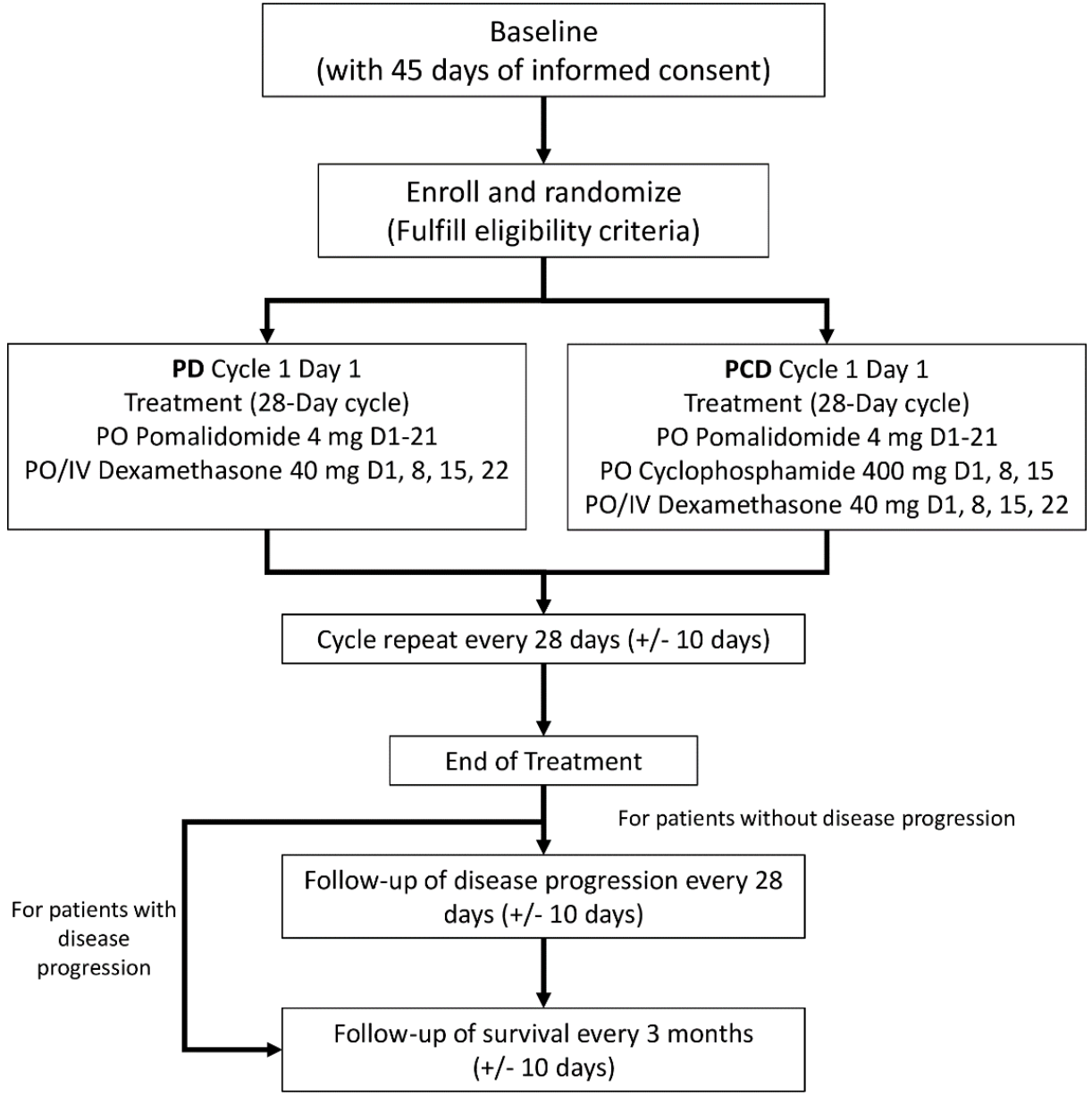
[1]Department of Haematology-Oncology, National University Cancer Institute, Singapore, Singapore; [2]Severance Hospital, Yonsei University Health System, Seoul, Korea, Republic of (South); [3]Comprehensive Oncology Centre, 3/F, Li Shu Fan Block, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong, China; [4]Chonnam National University Hwasun Hospital, Hwasun, Korea, Republic of (South); [5]Department of Hemato-Oncology, Seoul National University Hospital, Seoul, Korea, Republic of (South); [6]Subang Jaya Medical Center, Petaling Jaya, Malaysia; [7]University of Malaya, Kuala Lumpur, Malaysia; [8]Department of Hematology, Gunma University Hospital, Maebashi, Gunma, Japan; [9]Singapore Clinical Research Institute, Singapore, Singapore; [10]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Outpatient Cancer Center, Los Angeles, CA

Prior Therapies

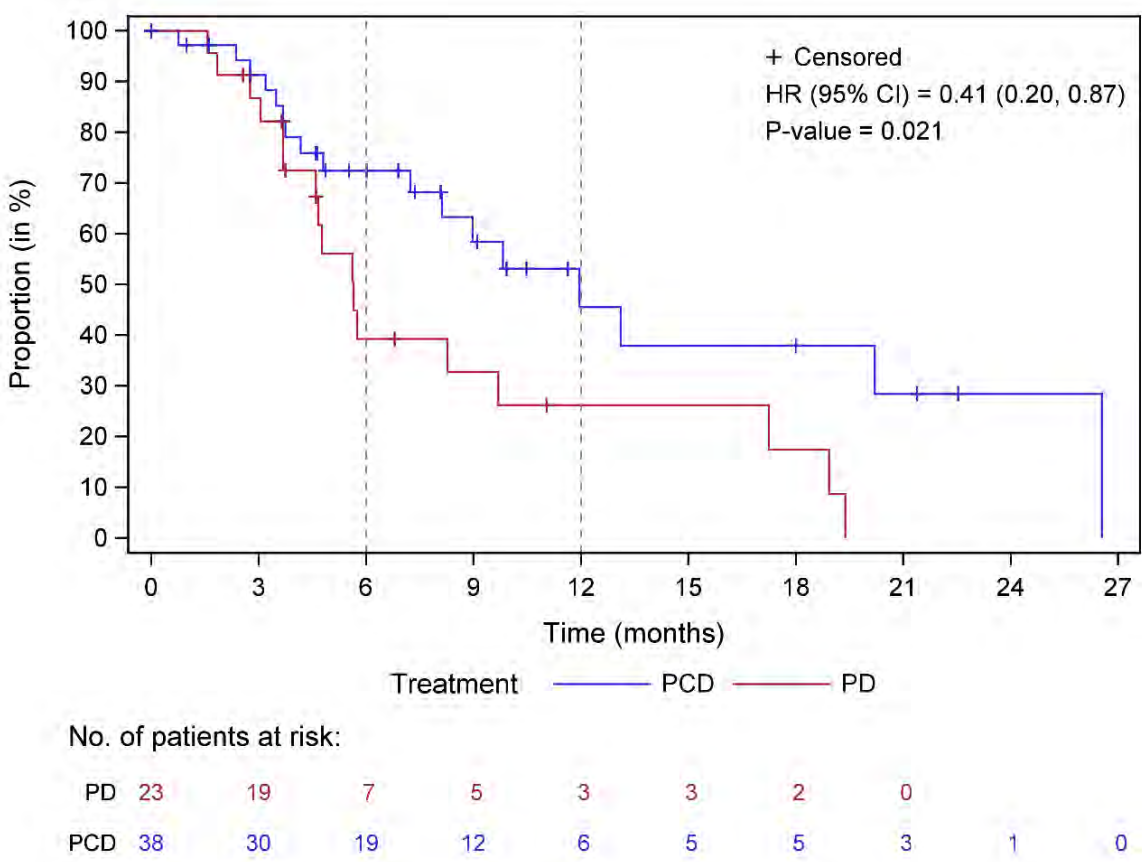
Parameters, N(%) / Median [range]	PCD (N=62)	PD (N=60)
No. of lines of prior treatment	3 [1-6]	3 [1-6]
Previously received therapies		
(i) Bortezomib	47 (75.8)	46 (76.7)
(ii) Carfilzomib	24 (38.7)	18 (30.0)
(iii) Ixazomib	7 (11.3)	8 (13.3)
(iv) Lenalidomide	61 (98.4)	60 (100)
(v) Thalidomide	34 (54.8)	28 (46.7)
(vi) Cyclophosphamide	29 (46.8)	19 (31.7)
Prior Autologous Stem Cell Transplant	27 (43.5)	24 (40.0)

Methods

- Patients randomised in a 1:1 ratio to receive PCD or PD
- Dosing schedule for PCD
  - 4-weekly: pom 4mg day 1 – 21, dexamethasone 40mg once a week, cyclophosphamide 400mg weekly for 3 weeks.
- Dosing schedule for PD
  - 4-weekly: pom 4mg day 1 – 21, dexamethasone 40mg once a week.

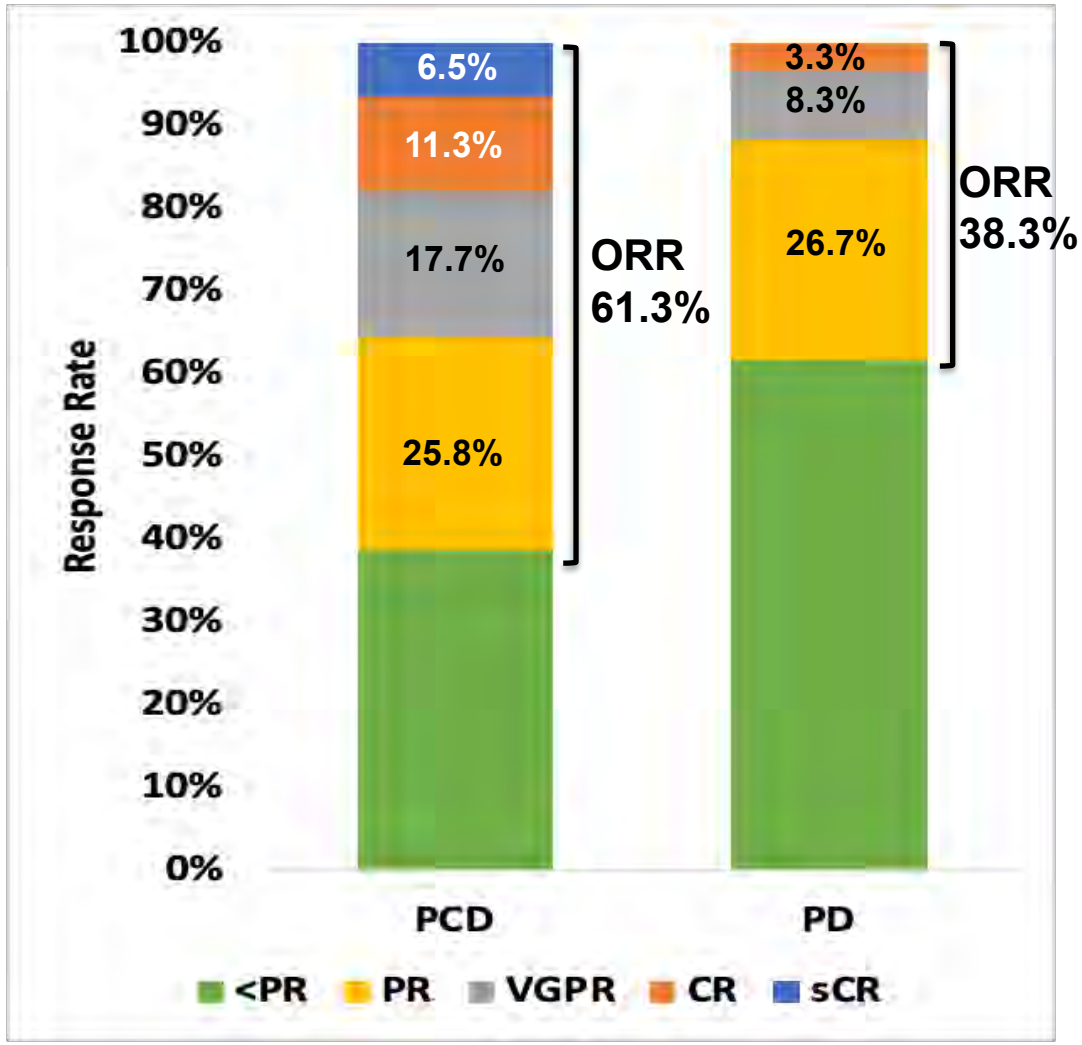


PCD has longer Duration of Response (DOR)



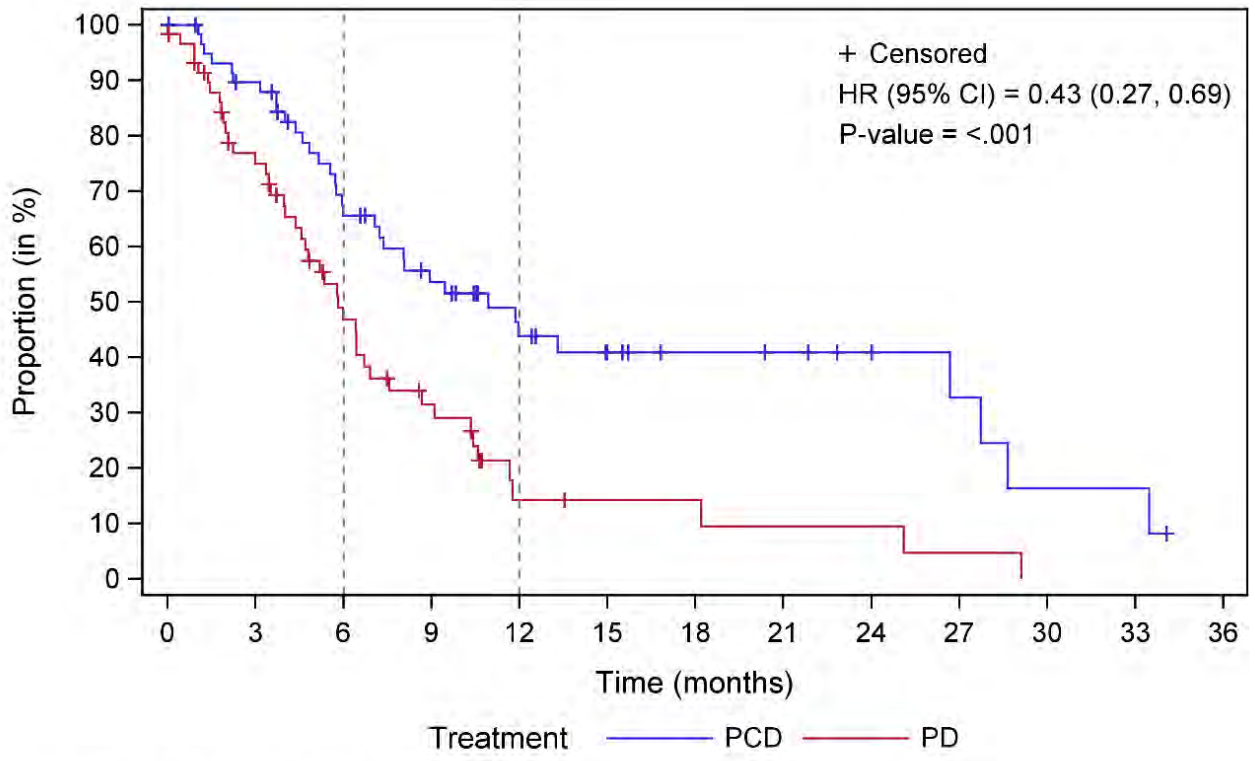
- Median DOR was 12.0 months (95% CI, 7.2 – not reached, NR) in the PCD arm and 5.7 months (95% CI, 3.7 – 9.7) in the PD arm (HR 0.41, 95% CI, 0.20 – 0.87).

PCD produce better and deeper response



- ORR was 61.3% (95% CI, 41.0 – 69.7) in the PCD arm and 38.3% (95% CI, 19.5 – 44.5) in the PD arm
- Difference 23% (95% CI, 6.5 – 40.2, p = 0.007)

PFS is significantly improved by PCD



Kaplan-Meier plot – progression free survival (PFS)
Efficacy Evaluable Population

Key Points

- Median follow-up of 13.5 (IQR, 8.7 – 24.0) months
- Median PFS was 10.9 (95% CI, 7.1 – 27.7) months for PCD compared to 5.8 (95% CI, 4.4 – 6.9) months for PD
- Hazard ratio (HR) 0.43 (95% CI, 0.27-0.69); p < 0.001)

- All oral PCD
- DOR 1 year
- Practical

HEIDELBERG UNIVERSITY HOSPITAL

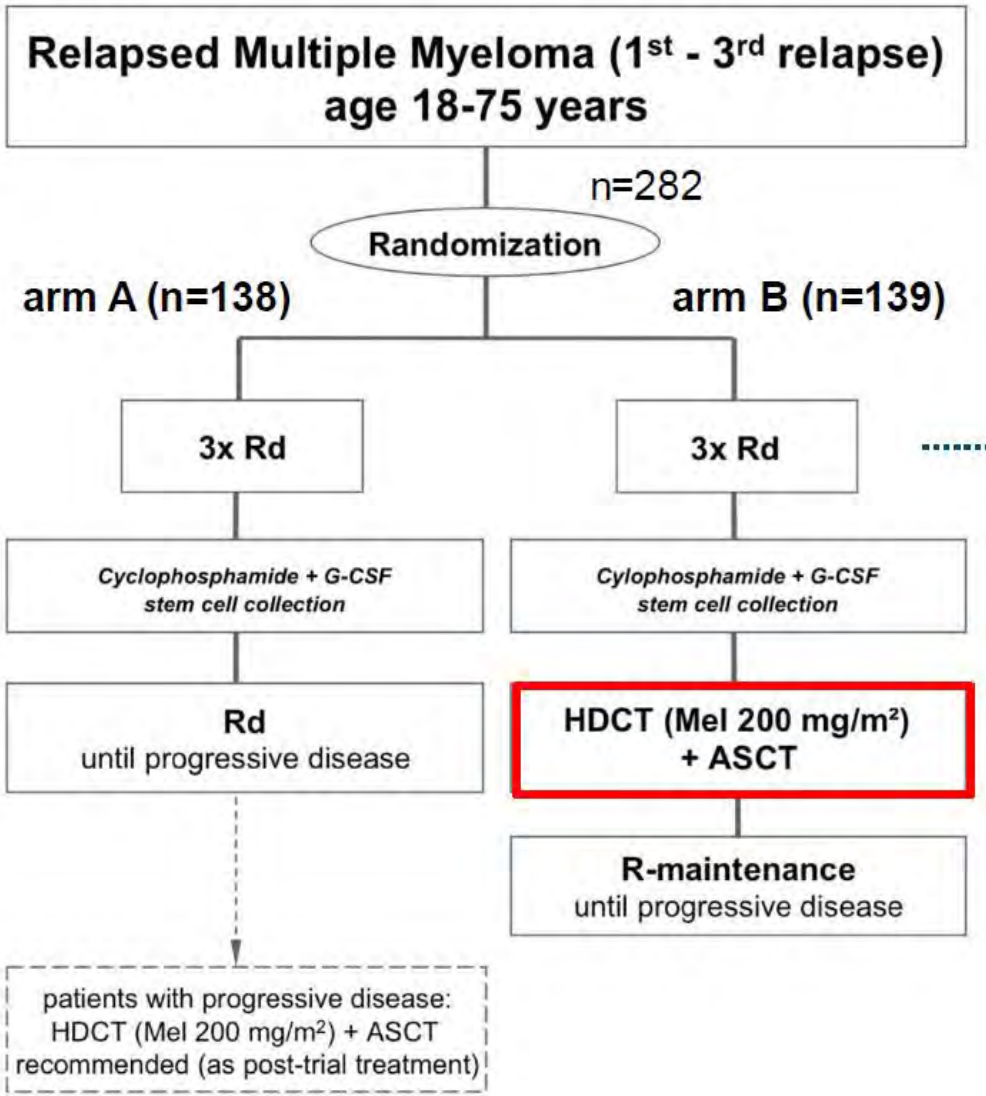
Salvage Autologous Transplant and Lenalidomide Maintenance Versus Continuous Lenalidomide/Dexamethasone for Relapsed Multiple Myeloma: Long term follow Up results of the Randomized GMMG Phase III Multicenter Trial ReLApsE

Marc-Andrea Baertsch, MD[1,2], Jana Schlenzka, MD[1], Thomas Hielscher[3], Marc-Steffen Raab, MD[1,2,4], Sandra Sauer[1], MD, Maximilian Merz, MD[5], Elias Karl Mai, MD[1], Carsten Müller-Tidow, MD[1,4], Steffen Luntz, MD[6], Anna Jauch, PhD[7], Peter Brossart, MD[8], Martin Goerner, MD[9], Stefan Klein, MD[10], Bertram Glass, MD[11], Peter Reimer, MD[12], Ullrich Graeven, MD[13], Roland Fenk, MD PhD[14], Mathias Haenel, MD[15], Ivana von Metzler, MD[16], Hans W. Lindemann, MD[17], Christof Scheid, MD[18], Axel Nogai, MD[19], Hans Salwender, MD[20], Richard Noppeney, MD[21], Britta Besemer, MD[22], Katja Weisel, MD[23], Hartmut Goldschmidt, MD[1,4]

65th ASH Annual Meeting, San Diego, December 11 2023

UK HD

GMMG ReLApsE trial - Flow chart



Rd (arm A+B)
- **Lenalidomide** 25 mg, d1-21
- **Dexamethasone** 40 mg, d1,8,15,22
- 4 week cycles

R-maintenance (arm B)
- **Lenalidomide** 10 mg daily

Goldschmidt H*, Baertsch MA* et al., Leukemia, 2021

ReLApsE - Baseline characteristics

	arm A (n=138) n (%)	arm B (n=139) n (%)
Age [years]	62.2 (41.9; 74.5)	61.3 (29.9; 74.7)
Sex		
Female	54 (39)	60 (43)
WHO PS		
0	105 (76)	96 (69)
1	32 (23)	43 (31)
2	1 (1)	0
ISS stage		
I	77/129 (60)	82/131 (63)
II	40/129 (31)	32/131 (24)
III	12/129 (9)	17/131 (13)
Cytogenetics		
t(4;14)	10/99 (10)	19/94 (20)
t(14;16)	0/97 (0)	2/90 (2)
del13q14	45/104 (43)	59/97 (61)
del17p13	15/107 (14)	14/98 (14)
gain1q (>3 copies)	12/105 (11)	11/97 (11)
High risk*	31/98 (32)	39/91 (43)

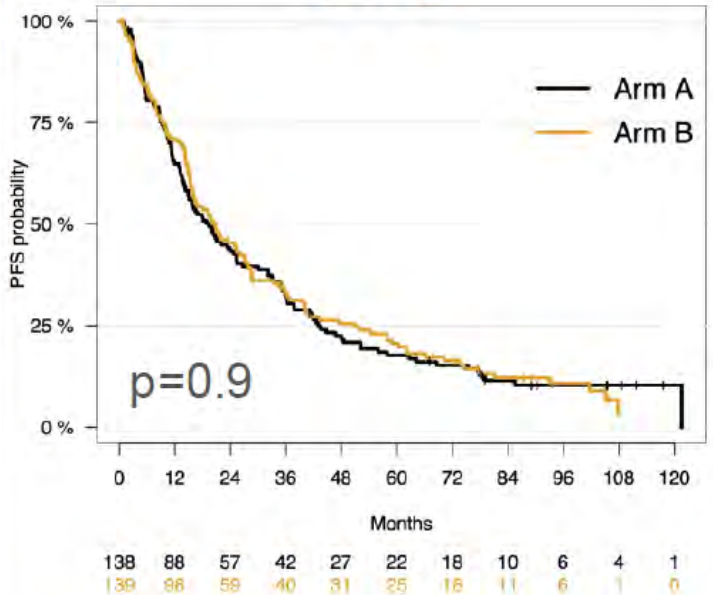
	arm A (n=138) n (%)	arm B (n=139) n (%)
Interval diagnosis to randomization [years]	4.1 (0.7-16.5)	3.9 (0.2-19.4)
Prior lines of therapy		
1	129 (94)	131 (94)
2	8 (6)	5 (4)
3	1 (1)	3 (2)
Frontline HDCT/ASCT	130 (94)	129 (93)
Single	71 (55)	83 (64)
Tandem	59 (45)	46 (36)
Prior therapy		
Bortezomib	106 (77)	107 (77)
Thalidomide	25 (18)	31 (22)
Lenalidomide	18 (13)	12 (9)
Interferone	9 (7)	9 (6)
Chemoth. only	10 (7)	14 (10)

*High risk cytogenetic aberrations: t(4;14), t(14;16), del17p13, gain1q (>3 copies)

Goldschmidt H*, Baertsch MA* et al., Leukemia, 2021

ReLApsE - Survival - LTFU analysis

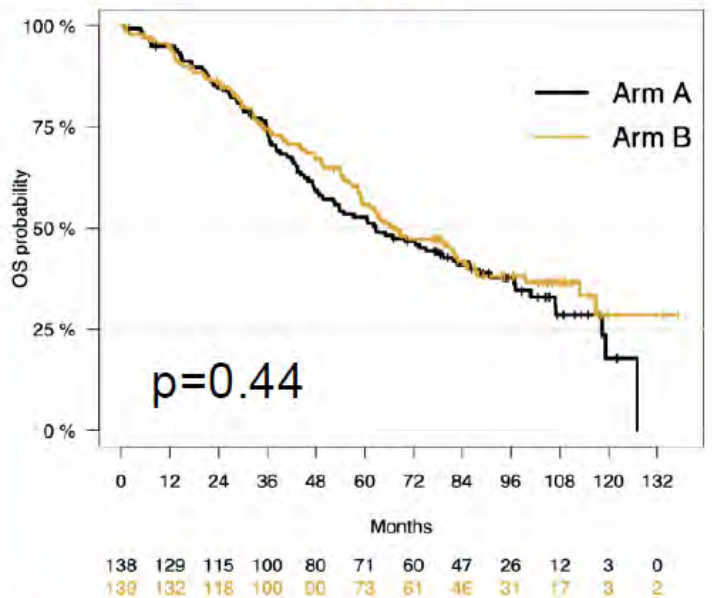
PFS



Median PFS

- Arm A: 19.3 months
- Arm B: 20.5 months
- HR 0.98 (95% CI 0.76-1.27)

OS

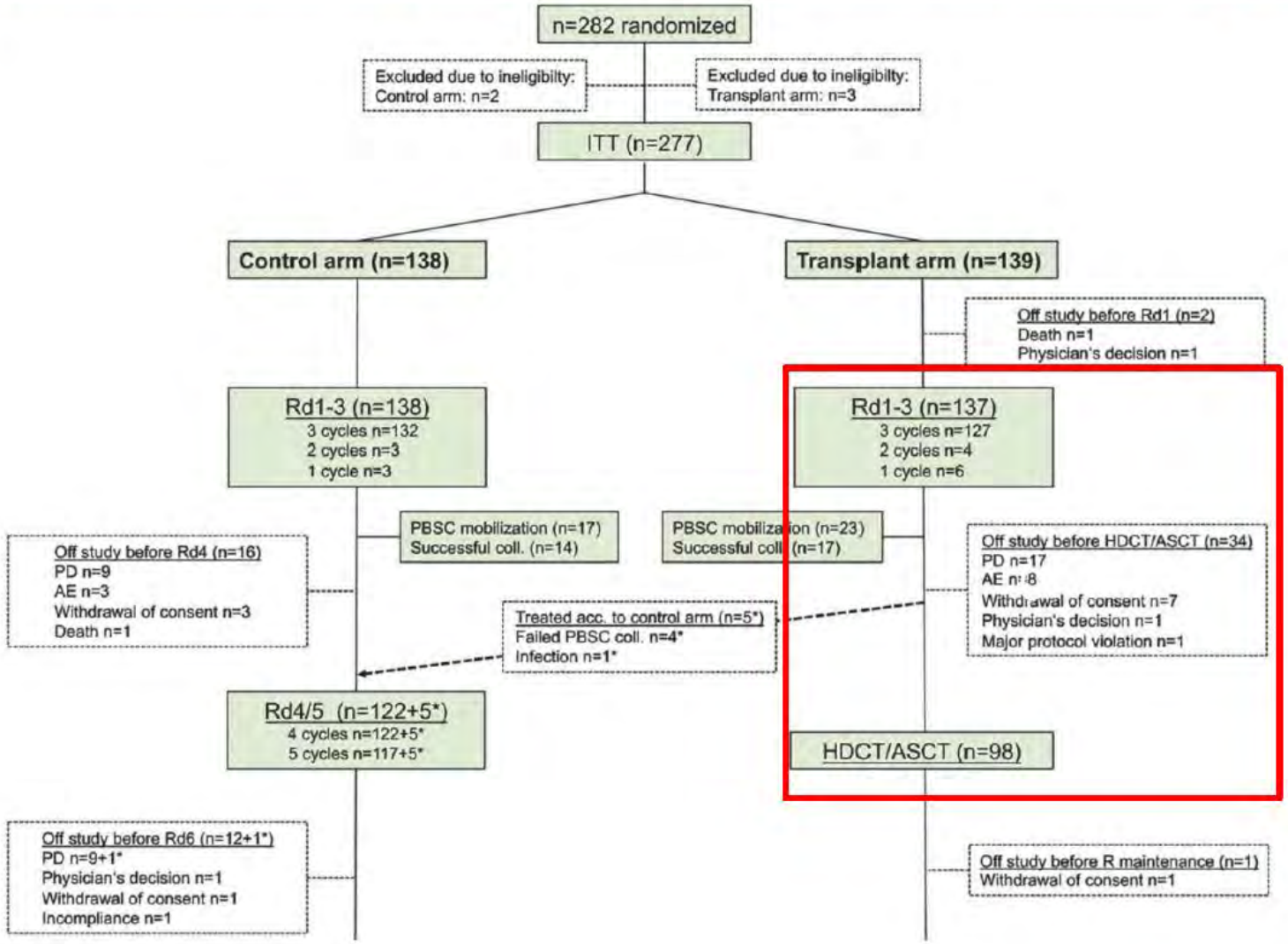


Median OS

- Arm A: 62.7 months
- Arm B: 67.1 months
- HR 0.89 (95% CI 0.66-1.20)

No survival benefit in long term follow up analysis from randomization

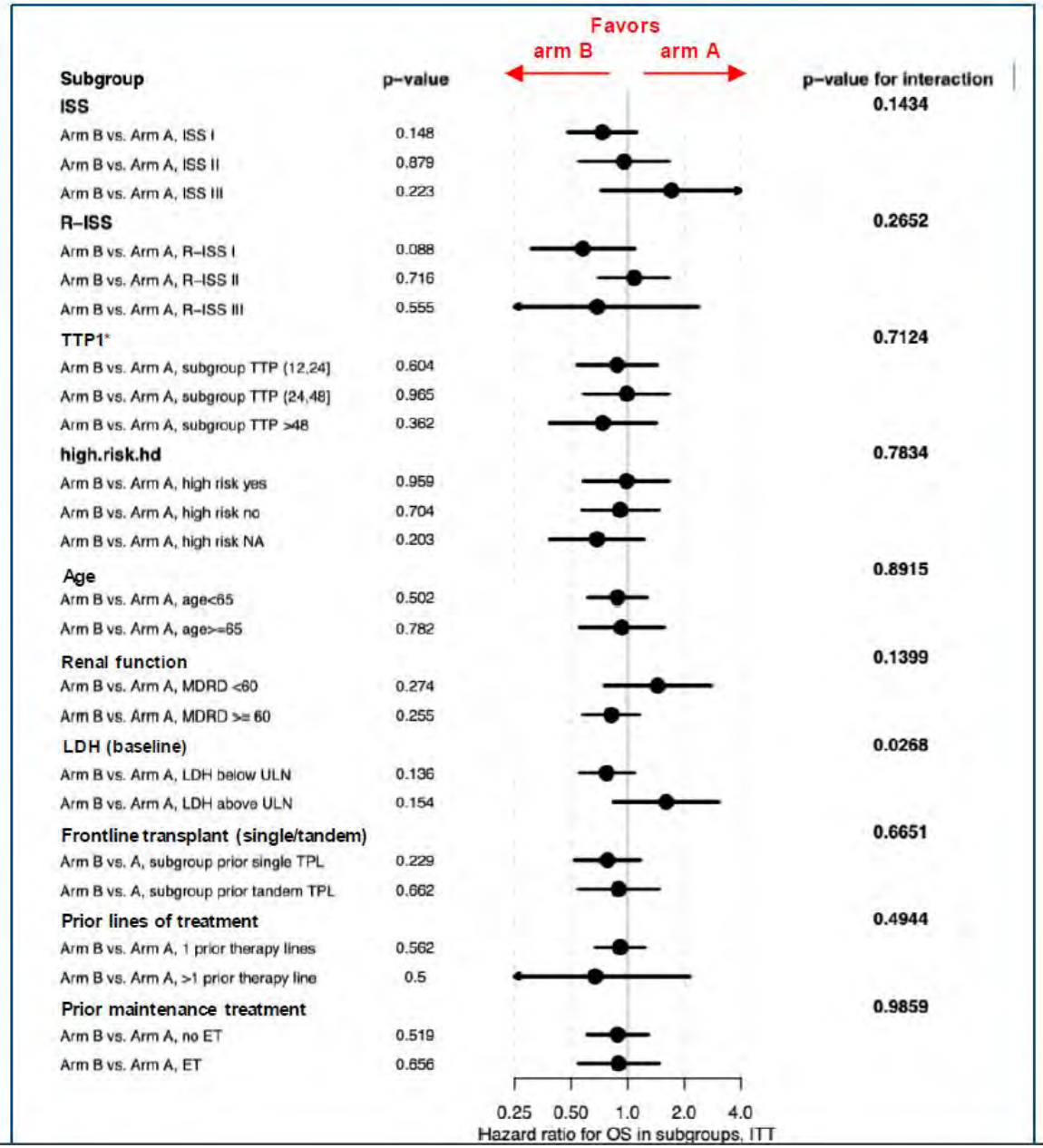
ReLApsE - Drop outs before salvage ASCT



29% of patients (41/139) did not receive salvage transplant

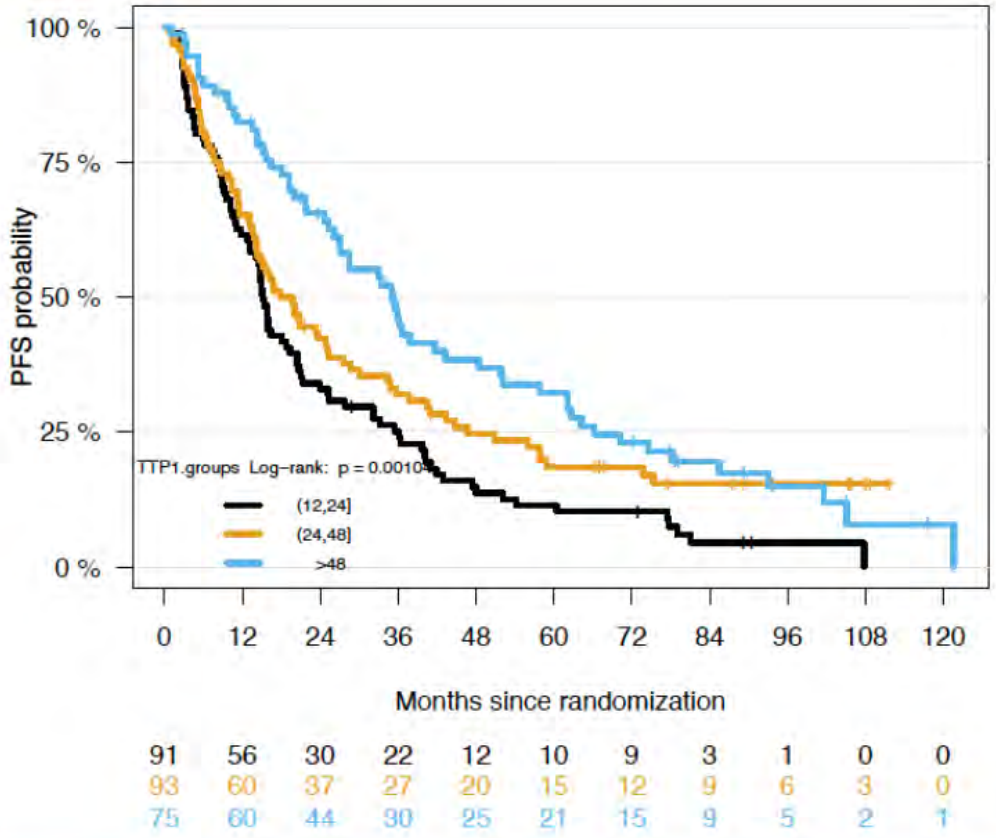
Subgroups OS

Absence of OS benefit is consistent across key patient subgroups



TTP1: Time to progression after frontline HDCT/ASCT

TTP1 – prognostic impact



Arm A	12 to 24 mo	24 to 48 mo
24 to 48 mo	p=0.19	
>48 mo	p=0.01	p=0.27

Arm B	12 to 24 mo	24 to 48 mo
24 to 48 mo	p=0.16	
>48 mo	p=0.011	p=25

Arm A+B	12 to 24 mo	24 to 48 mo
24 to 48 mo	p=0.054	
>48 mo	p=0.0001	p=0.10

Key Points

- No to salvage transplant (in frontline)
- No PFS or OS benefit

Time to progression after frontline transplant is a prognostic factor for survival in both treatment arms

Patient-Reported Outcomes in the Phase 3 CARTITUDE-4 Study of Ciltacabtagene Autoleucel vs Standard of Care in Patients With Lenalidomide-Refractory Multiple Myeloma After 1–3 Lines of Therapy

Roberto Mina[1], Anne K Mylin[2], Hisayuki Yokoyama[3], Hila Magen[4], Winfried Alsdorf[5], Monique C Minnema[6], Leyla Shune[7], Iris Isufi[8], Simon J Harrison[9-11], Urvi A Shah[12], Jordan M Schecter[13], Nikoletta Lendvai[13], Katharine S Gries[14], Eva G Katz[14], Ana Slaughter[15], Carolina Lonardi[16], Jane Gilbert[17], Quanlin Li[18], William Deraedt[19], Octavio Costa Filho[20], Nitin Patel[20], Lionel Karlin[21], Katja Weisel[5]

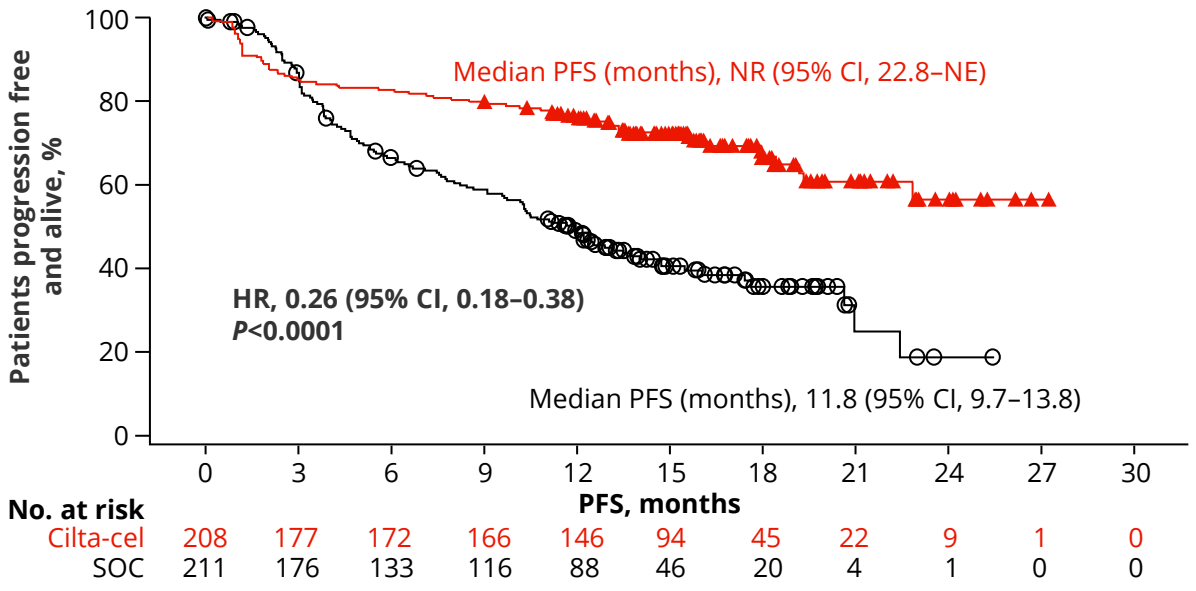
[1]University of Turin, Turin, Italy; [2]Rigshospitalet, Copenhagen, Denmark; [3]Tohoku University Graduate School of Medicine, Sendai, Japan; [4]Chaim Sheba Medical Center, Ramat-Gan, Sackler Faculty of Medicine, Tel Aviv University, Israel; [5]University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [6]University Medical Center Utrecht, Utrecht, Netherlands; [7]The University of Kansas Medical Center, Kansas City, KS, USA; [8]Yale School of Medicine, Yale University, New Haven, CT, USA; [9]Peter MacCallum Cancer Centre, Melbourne, Australia; [10]Royal Melbourne Hospital, Melbourne, Australia; [11]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, Australia; [12]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA; [13]Janssen Research & Development, Raritan, NJ, USA; [14]Janssen Global Services, LLC, Raritan, NJ, USA; [15]Cilag GmbH International, Zug, Switzerland; [16]Janssen, Buenos Aires, Argentina; [17]Janssen Research & Development, High Wycombe, UK; [18]Janssen Research & Development, Apex, NC, USA; [19]Janssen Research & Development, Beerse, Belgium; [20]Legend Biotech USA Inc., Somerset, NJ, USA; [21]Centre Hospitalier Lyon Sud, Pierre-Bénite, France

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

CARTITUDE-4: Introduction

- Cilta-cel is a CAR-T cell therapy approved for the treatment of RRMM after ≥4 LOT in the US (≥3 LOT in the EU)[1,2]
- In the phase 1b/2 CARTITUDE-1 trial, a single cilta-cel infusion in heavily pretreated patients:
  - Led to deep and durable responses alongside a manageable safety profile[3]
  - Improved HRQoL, including emotional and physical functioning, and reduced MM-related symptoms[4]
- The phase 3 CARTITUDE-4 trial compared cilta-cel with SOC in patients with lenalidomide-refractory MM after 1–3 LOT[5,6]
  - A single cilta-cel infusion significantly improved PFS and increased the rate and depth of response vs SOC[5,6]

PFS in CARTITUDE-4: Cilta-cel vs SOC[6,a]



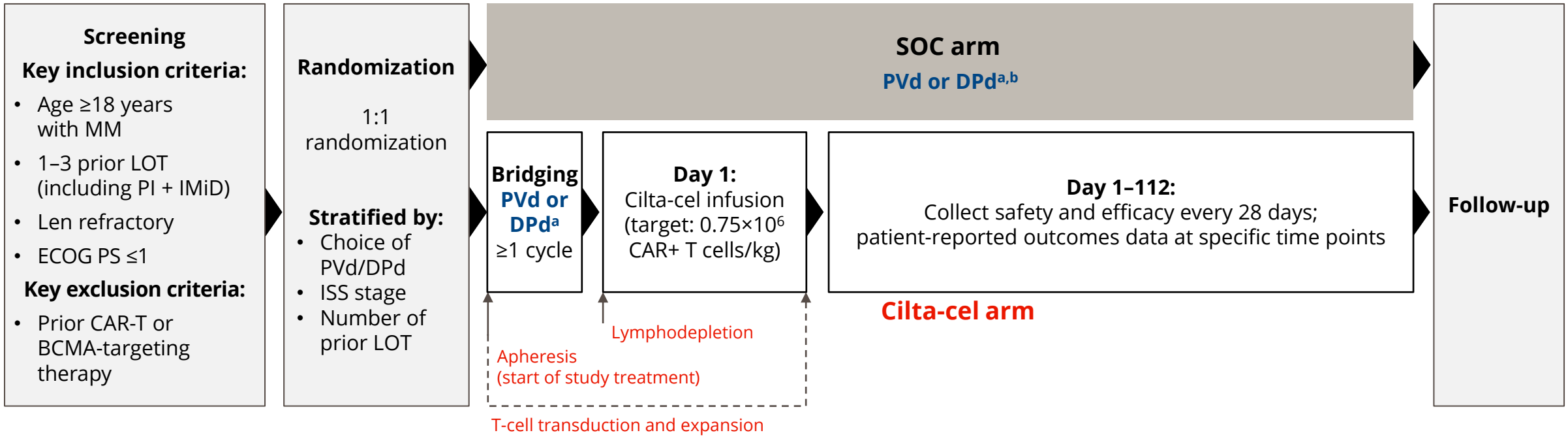
Here, we present patient-reported outcomes from patients randomized to cilta-cel vs SOC in CARTITUDE-4 at 15.9-month median follow-up

[a]At the clinical cut-off of November 1, 2022, median follow-up from randomization was 15.9 months. cilta-cel, ciltacabtagene autoleucel; EU, European Union; HR, hazard ratio; HRQoL, health-related quality of life; LOT, line of therapy; MM, multiple myeloma; NE, not estimable; NR, not reached; PFS, progression-free survival; RRMM, relapsed refractory MM; SOC, standard of care.

1. CARVYKTI® (ciltacabtagene autoleucel). Prescribing information. Janssen Biotech, Inc.; 2023. Accessed November 27, 2023. https://www.fda.gov/media/156560/download. 2. CARVYKTI® (ciltacabtagene autoleucel). European Medicines Agency. Orphan maintenance assessment report. June 7, 2022. Accessed November 27, 2023. https://www.ema.europa.eu/en/documents/product-information/carvykti-epar-product-information_en.pdf. 3. Martin T, et al. *J Clin Oncol* 2023;41:1265-74. 4. Martin T, et al. *Lancet Haematol* 2022;9:e897-905. 5. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47. 6. Dhakal B, et al. *J Clin Oncol* 2023;41(suppl 17):LBA106.

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

CARTITUDE-4: Study Design and Endpoints[1,2]



Primary endpoint

- PFS[c]

Secondary endpoints

- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- **Patient-reported outcomes**

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death. BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

1. San-Miguel J, et al. *N Engl J Med* 2023;389:335-47. 2. Dhakal B, et al. *J Clin Oncol* 2023;41(suppl 17):LBA106.

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

CARTITUDE-4: PRO Assessments

- PRO assessments were administered at baseline[a] and at months 3, 6, 9, 12, 18, and 24 in both arms
  - Change from baseline[a] was calculated for patients with assessments at baseline[a] and at the given time point
- EORTC QLQ-C30, EQ-5D-5L, and MySIm-Q questionnaires were administered to all patients until disease progression[b]

EORTC QLQ-C30[1,c]

- **Cancer-specific questionnaire**
  - Scores range from 0–100
- **Global health status scale**
- **3 symptom scales**
  - Fatigue
  - Nausea and vomiting
  - Pain
- **5 functional scales**
  - Physical
  - Role
  - Emotional
  - Cognitive
  - Social

EQ-5D-5L[2]

- **Generic measurement of health**
- **Visual analogue scale**
  - Patients' self-rated health between 100 (best imaginable health) and 0 (worst imaginable health)

MySIm-Q[3,d]

- **MM-specific questionnaire**
  - Assesses 17 single items across 8 domains on a 5-point verbal scale
- **Symptom subscale**
  - Assesses pain, neuropathy, fatigue, digestive, and cognitive symptom domains
- **Impact subscale**
  - Assesses activity, social, and emotional impact domains

[a]Baseline is defined as apheresis for cilta-cel arm and cycle 1 day 1 for SOC arm. [b]EQ-5D-5L collected post disease progression every 16 weeks until end of study. [c]Higher scores represent better health-related quality of life and better functioning (global health status and functional scales) or more/worse symptoms (symptom scales and single items). [d]Higher scores represent more/worse symptoms and impact. cilta-cel, ciltacabtagene autoleucel; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30-item; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; MM, multiple myeloma; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; PRO, patient-reported outcome.

1. Aaronson NK, et al. *J Natl Cancer Inst* 1993;85:365-76. 2. Herdman M, et al. *Qual Life Res* 2011;20:1727-36. 3. Gries KS, et al. *Value Health* 2021;24:1807-19.

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

CARTITUDE-4: Baseline PRO Scores Were Generally Similar in Both Treatment Arms

- Global health status scores at baseline for both treatment arms were lower than benchmark scores for the general population,[1,a] suggesting worse overall health
- Physical, role, and social functioning, as well as pain and fatigue symptoms, showed that most MM-relevant scores at baseline were worse in CARTITUDE-4 than in the general population[1,a]

	Cilta-cel (n=191)	SOC (n=100)	Benchmark general population[1,a]
EORTC QLQ-C30,[b] mean (SD)			
Global health status	60.7 (22.4)	62.4 (21.6)[c]	66.1 (21.7)
Functional scales			
Cognitive functioning	83.4 (19.9)	83.6 (18.7)	84.8 (21.3)
Emotional functioning	74.6 (20.2)	74.7 (20.6)	74.2 (24.7)
Physical functioning	74.2 (23.2)	70.7 (19.4)	85.1 (18.9)
Role functioning	66.4 (30.1)	70.6 (26.2)	84.3 (24.6)
Social functioning	72.1 (28.1)[d]	72.0 (24.0)	86.2 (24.1)
Symptom scales/items			
Fatigue	37.3 (26.2)[d]	35.9 (24.3)[e]	29.5 (25.5)
Nausea and vomiting	6.3 (13.6)[e]	4.1 (9.8)[c]	5.9 (16.0)
Pain	37.2 (29.9)	29.7 (27.8)	23.5 (27.1)
EQ-5D-5L,[b] mean (SD)			
Visual analogue scale	65.3 (19.9)	67.1 (20.2)[f]	NR
MySIm-Q,[g] mean (SD)			
Total symptom subscale	1.06 (0.69)	0.97 (0.60)[h]	NA
Total impact subscale	1.31 (0.93)	1.16 (0.82)[h]	NA

Key Points

- MM patients report some of the worse HRQoL scores across malignancies

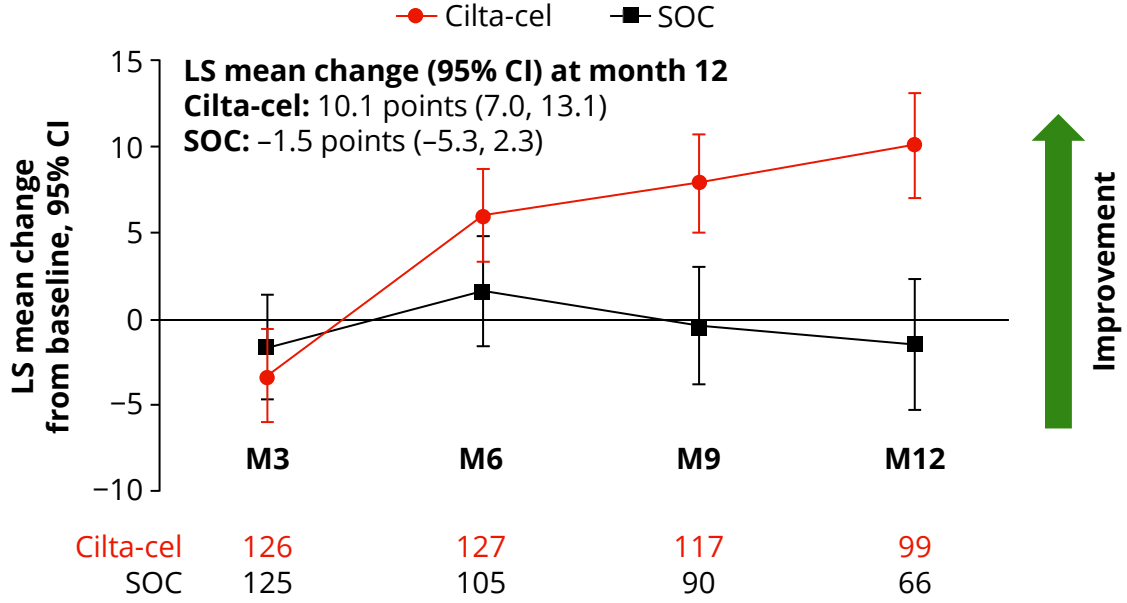
[a]General population ≥18 years of age from 11 European countries. [b]Scores range from 0–100; higher scores represent better health-related quality of life and better functioning (global health status, functional scales, and visual analogue scale) or more/worse symptoms (symptom scales). [c]n=189. [d]n=190. [e]n=188. [f]n=182. [g]5-point scale; higher scores represent more/worse symptoms or impacts. [h]n=183. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30-item; EQ-5D-5L, EuroQoL 5-Dimension 5-Level; MM, multiple myeloma; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; NA, not assessed; NR, not reported; PRO, patient-reported outcome; SOC, standard of care. 1. Nolte, S. et al. *Eur J Cancer* 2019;107:153-63.

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

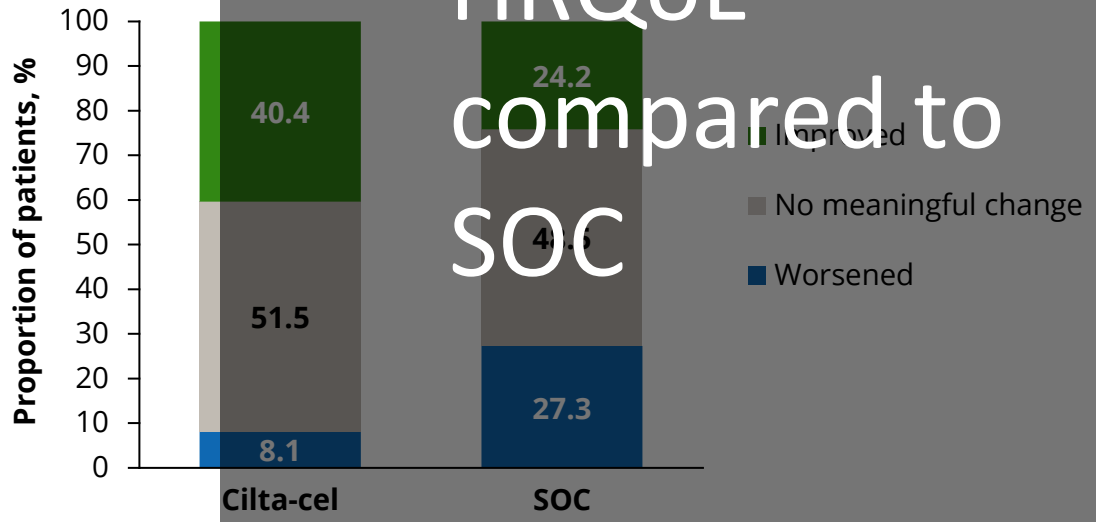
CARTITUDE-4: Clinically Meaningful Improvements in Global Health Status Score With Cilta-cel

- Global health status score improved over time in the cilta-cel arm but not the SOC arm
- At month 12, 40% of patients in the cilta-cel arm and 24% in the SOC arm achieved a clinically meaningful improvement[1,2,a]

LS mean change from baseline in global health status[b]



Clinically meaningful change[1,2,a] in global health status at month 12



Key Points

- CAR-T sustained improvement in HRQoL compared to SOC

[a]Change from baseline ≥10 points. [b]Mixed-model for repeated measures analyses were conducted using data from patients with assessments at both baseline and the given time point. Baseline patient-reported outcome score and prognostic characteristics were included as covariates to balance arms and to adjust for confounders. Assessments after the start of subsequent therapy were excluded. cilta-cel, ciltacabtagene autoleucel; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30-item; LS, least squares; M, month; SOC, standard of care.

1. King MT, *Qual Life Res* 1996;5:555–67. 2. Osoba D, et al. *J Clin Oncol* 1998;16:139–44.

Presented by R Mina at the 65th American Society of Hematology (ASH) Annual Meeting; December 9–12, 2023; San Diego, CA, USA

Effects of idecabtagene vicleucel versus standard regimens on health-related quality of life in patients with relapsed/refractory multiple myeloma who had received 2-4 prior regimens: updated results from the phase 3 KarMMa-3 trial

Michel Delforge,[1] Krina K. Patel,[2] Laurie Eliason,[3] Devender Dhanda,[3] Ling Shi,[4] Shien Guo,[4] Thomas S. Marshall,[3] Bertrand Arnulf,[5] Michele Cavo,[6] Ajay K. Nooka,[7] Salomon Manier,[8] Natalie S. Callander,[9] Sergio A. Giralt,[10] Hermann Einsele,[11] Sikander Ailawadhi,[12] Mihaela Popa-McKiver,[3] Mark Cook,[13] Paula Rodríguez-Otero[14]

[1]University Hospital Leuven, Leuven, Belgium; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Bristol Myers Squibb, Princeton, NJ, USA; [4]Evidera, Bethesda, MD, USA; [5]Hôpital Saint-Louis, Paris, France; [6]Seràgnoli Institute of Hematology, Bologna University School of Medicine, Bologna, Italy; [7]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [8]Centre Hospitalier Universitaire de Lille, Lille, France; [9]University of Wisconsin Health Carbone Cancer Center, Madison, WI, USA; [10]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [11]Medizinische Klinik und Poliklinik II, Uniklinikum Würzburg, Würzburg, Germany; [12]Mayo Clinic, Jacksonville, FL, USA; [13]Celgene International Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [14]Clínica Universidad de Navarra, Pamplona, Spain

ASH 2023, Presentation 96

PRO instruments

	EORTC QLQ-C30 (15 domains)	EORTC QLQ-MY20 (4 domains)	EQ-5D-5L (2 domains)
Prespecified primary domains	GHS/QoL, physical and cognitive functioning, fatigue, pain	Disease symptoms and treatment AEs	VAS
Exploratory domains	Role, social, and emotional functioning, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties	Future perspectives Body image	UI; derived based on scores for 5 dimensions
Scale range	0-100	0-100	VAS: 0-100 UI: 0-1
Interpretation	↑ GHS and functioning domain scores = ↑ HRQoL ↑ Symptom domain scores = ↑ symptomatology or problems	↑ Future perspectives/body image domain scores = ↑ HRQoL ↑ Symptom/side effects domain scores = ↑ symptomatology or problems	VAS: 0 = worst imaginable health; 100 = best imaginable health UI: 0 (death) - 1 (full health); negative = state perceived to be worse than death

AE, adverse event; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-MY20, European Organisation for Research and Treatment of Cancer Quality of Life Multiple Myeloma Questionnaire; EQ-5D-5L, EuroQol 5 dimensions 5 levels; GHS, global health status; QoL, quality of life; UI, utility index; VAS, visual analogue scale.

Delforge M, et al. ASH 2023 [Abstract #96]

Changes in overall HRQoL from baseline[a]

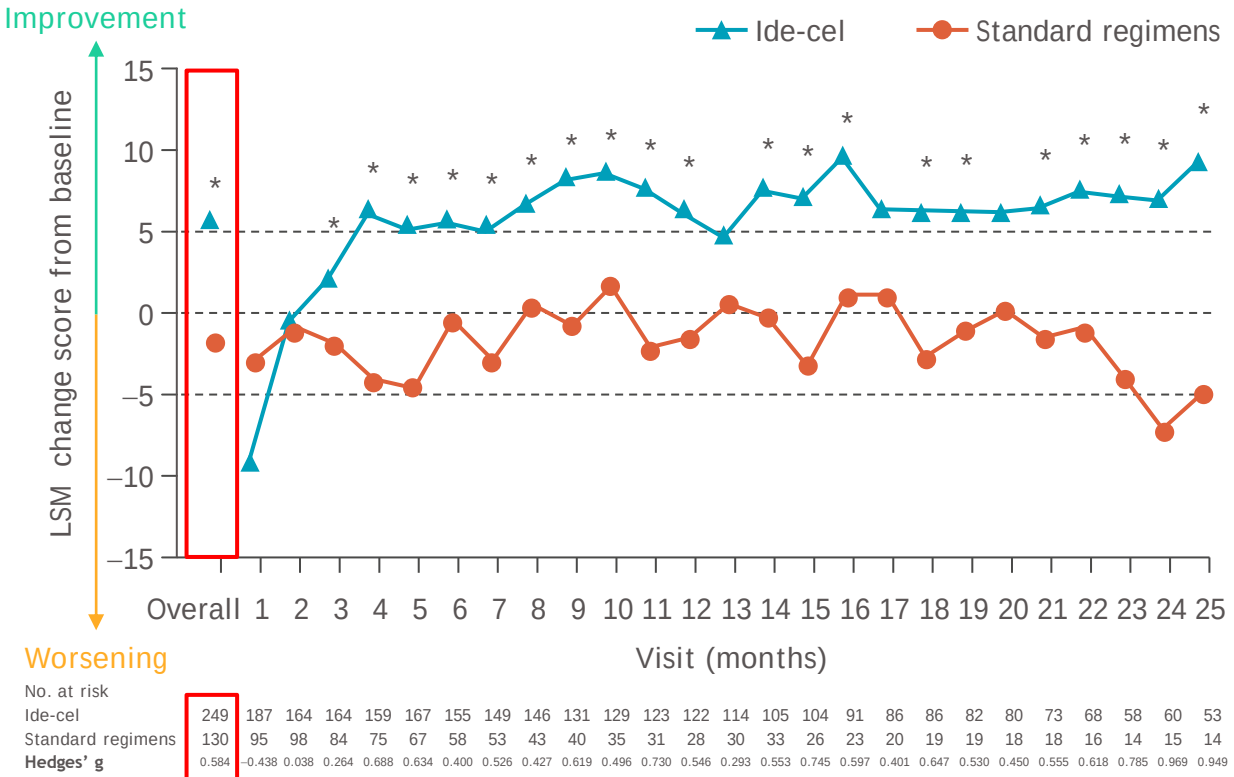
EORTC QLQ-C30 domains - GHS/QoL and EQ-5D-5L domain - VAS

Ide-cel showed significant and meaningful improvements in GHS/QoL and VAS compared with standard regimens

Key Points

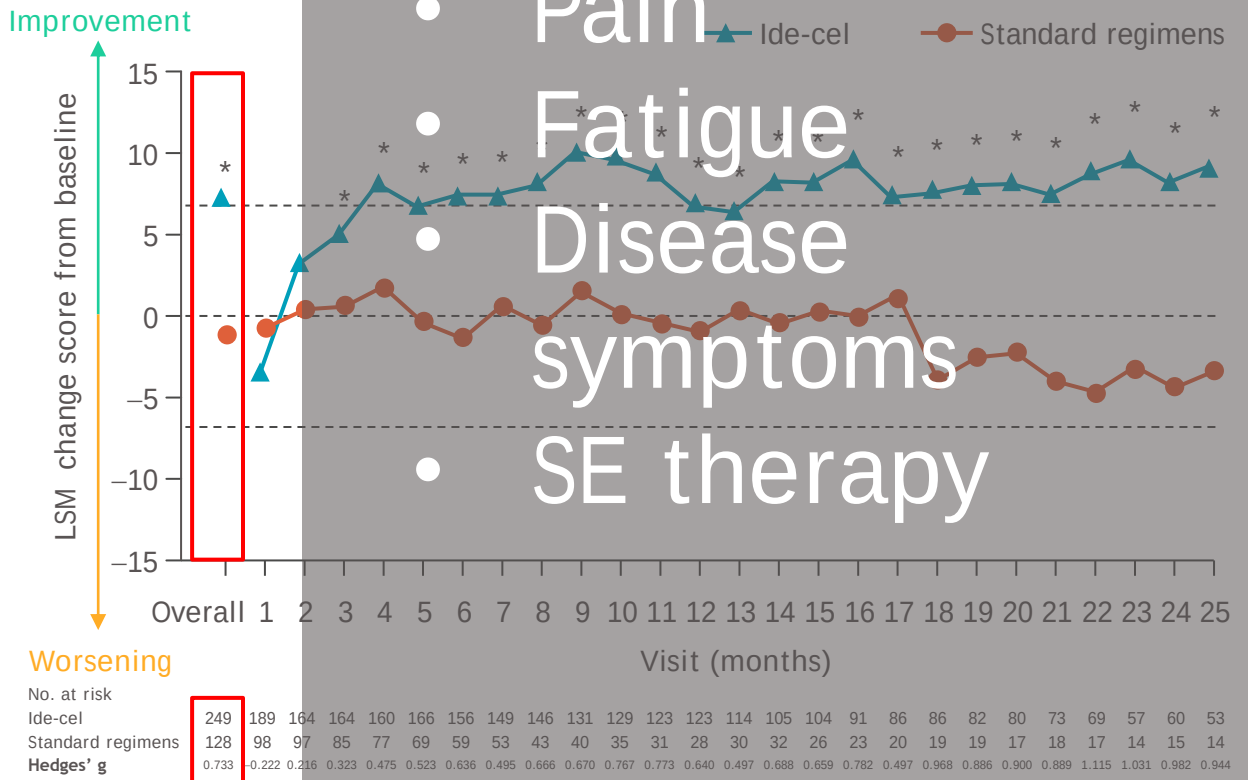
- HRQoL improved
- Pain
- Fatigue
- Disease symptoms
- SE therapy

EORTC QLQ-C30 GHS/QoL



No. at risk																									
Ide-cel	249	187	164	164	159	167	155	149	146	131	129	123	122	114	105	104	91	86	86	82	80	73	68	58	60	53
Standard regimens	130	95	98	84	75	67	58	53	43	40	35	31	28	30	33	26	23	20	19	19	18	18	16	14	15	14
Hedges' g	0.584	−0.438	0.038	0.264	0.688	0.634	0.400	0.526	0.427	0.619	0.496	0.730	0.546	0.293	0.553	0.745	0.597	0.401	0.647	0.530	0.450	0.555	0.618	0.785	0.969	0.949

EQ-5D-5L EQ-VAS



No. at risk																									
Ide-cel	249	189	164	164	160	166	156	149	146	131	129	123	123	114	105	104	91	86	86	82	80	73	69	57	60	53
Standard regimens	128	98	97	85	77	69	59	53	43	40	35	31	28	30	32	26	23	20	19	19	17	18	17	14	15	14
Hedges' g	0.733	−0.222	0.216	0.323	0.475	0.523	0.636	0.495	0.666	0.670	0.767	0.773	0.640	0.497	0.688	0.659	0.782	0.497	0.968	0.886	0.900	0.889	1.115	1.031	0.982	0.944

[a]Based on cLDA analysis until month 25.

Middle dashed line represents baseline (change = 0); top and bottom dashed lines represent MID (Cocks K, et al. *Eur J Cancer* 2012;48:1713–1721; Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70). *Indicates significant differences in LSM change from baseline between treatment arms at a specific post-baseline visit. Month 1 is day 1 of infusion for ide-cel and day 1 of the first cycle of treatment for standard regimens.

MID, minimally important difference.

Delforge M, et al. ASH 2023 [Abstract #96]

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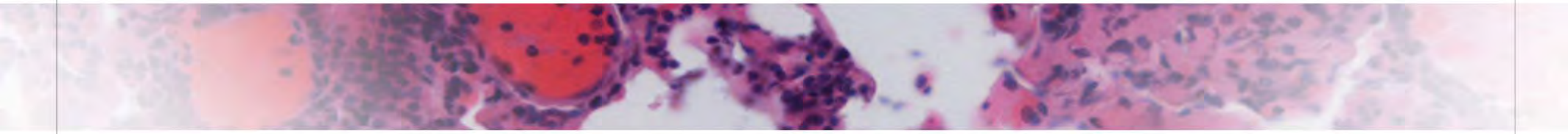

Real-World Safety and Efficacy of Teclistamab for Patients with Heavily Pretreated Relapsed-Refractory Multiple Myeloma

Danai Dima, James A. Davis, Nausheen Ahmed, Xuefei Jia, Aishwarya Sannareddy, Hira Shaikh, Leyla Shune, Gurbakhash Kaur, Jack Khouri, Aimaz Afrough, Christopher Strouse, Jonathan Lochner, Zahra Mahmoudjafari, Shahzad Raza, Jason Valent, Larry D. Anderson, Jr, Faiz Anwer, Al-Ola Abdallah, **Hamza Hashmi**

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Department of Hematology-Oncology, Cleveland Clinic, Taussig Cancer Center, Cleveland OH, USA
Department of Hematology-Oncology, Medical University of South Carolina, Charleston, SC, USA
Division of Hematologic Malignancies & Cellular Therapeutics, University of Kansas Medical Center, Westwood, KS, USA
Hematologic Malignancies and Cellular Therapy Program, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA
Division of Hematology, Oncology and Blood & Marrow Transplantation, University of Iowa Hospitals and Clinics, Iowa City, IA,USA

Results: Response to Teclistamab

Response (Full Cohort) N (%)	RWE cohort N=104	MajesTec-1 N=165
Overall response rate	70 (66)	104 (63)
Complete response or better	31 (29)	65 (39.4)
Very good partial response	18 (17)	32 (19.4)
Partial response	21 (20)	7 (4.2)
Minimal response	0	2 (1.2)
Stable disease	10 (9.5)	27 (16.4)
Progressive disease	26 (24.5)	24 (14.5)
Not evaluable	0	8 (4.8)

Subgroups of Interest	ORR, N (%)
Age>70 (n=34)	24 (71)
Non-Hispanic Black (n=28)	20 (71)
Pts ineligible for MajestEC-1 trial (n=88)	53 (60)
High-risk cytogenetics (n=56)	35 (63)
Triple Refractory (n=97)	62 (64)
Penta refractory (n=68)	46 (68)
Prior BCMA therapy	33 (59)
R-ISS III (n=25)	13 (52)
EMD (n=45)	21 (47)
Four or less prior LOT (n=26)	21 (81)
>4 lines of prior therapy (n=80)	49 (61)

Safety: Infections

No. of patients who developed infection	N=33 (31)
Total Number of Infections	39
Severe infections	18 (46)
Infections of the respiratory system	27 (69)
Bacterial infections	16 (41)
Viral infections	20 (51)
Fungal Infections	3 (3)
Onset, days, median	46 (1-218)

Subsequent Hospitalizations while on Teclistamab:

Cause of Hospitalization	Total Hospital Admissions = 28
Infection	16
Cytopenia	3
Symptom control	6
Neurotoxicity	2
Acute Kidney Injury	1

Severe Infections	Total =18
Unspecified bacterial pneumonia	2
Unspecified bacterial colitis	1
Unspecified bacterial sepsis	1
Enterobacter cloacae bacteremia	1
Parainfluenza	1
Respiratory syncytial virus	2
Metapneumovirus	2
Rhino & adenovirus pneumonia	1
Covid-19 infection	4
Unspecified viral respiratory infection	1
Aspergillus pneumonia	1
Candida guilliermondii fungemia	1

Three pts died from severe infection while on TEC:
1 from COVID-19 pneumonia, 1 from rhino/adenovirus pneumonia and 1 from sepsis

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Cumulative incidence and characteristics of infections requiring treatment, delay in treatment administration or hospitalisation in patients with relapsed or refractory multiple myeloma treated with anti BCMA or anti GPRC5D bispecific antibodies.

Elise Cellerin [*] *and Aurélie Jourdes* [*], *Xavier Brousse, Nicolas Vallet, Tom Cartau, Blandine Denis, Stephanie Harel, Simon Jamard, Alexis Redor, Titouan Cazaubiel, Virginie Roland, Carine Caleteix, Morgane Charles, Pierre Berger, Guillaume Escure, Aude Collignon, Emmanuel Faure, Clarisse Cazelles, Fanny Lanternier, Clementine de La Porte Des Vaux, Laurent Frenzel, Mathieu Blot, Francois Danion, Cécile Sonntag, Cyrille Touzeau, Andrea Pieragostini, Florence Ader, Lionel Karlin, Margaret Macro, Guillaume Martin-Blondel, Thomas Chalopin, Aurore Perrot – IFM study*

Method

Intergroupe Francophone du Myélome centers (n=14)

↓

All Relapsed/Refractory Multiple Myeloma treated with bispecific antibodies

From Dec 1st,2020 to Feb 1st, 2023

↓

n=229

↓

BCMA-targeting n=200

GPRC5D-targeting n=29

↓

teclistamab n=153

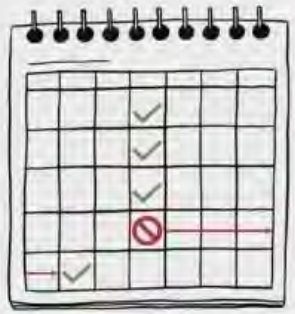
elranatamab n=47

talquetamab n=29

Infections impacting patient management

Hospitalization

Specific treatment



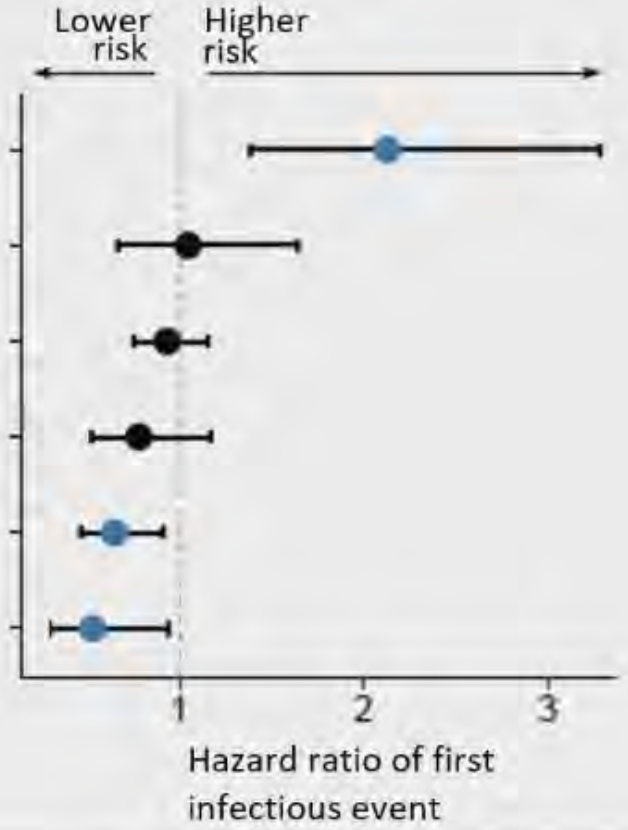
Adaptation in BsAb administration

Results

3 Identify associated variables – First infections

Univariate exploratory analysis

Variables	HR (95%CI)
Corticosteroids for CRS or ICANS	2.13 (1.38-3.28) p=0.001
Gammaglobuline > 4 g/L	1.05 (0.67-1.64) p=0.84
Number of weeks of neutropenia	0.93 (0.75-1.16) p=0.53
Immunoglobuline replacement	0.78 (0.52-1.17) p=0.23
Antibacterial Prophylaxis	0.65 (0.46-0.9) p=0.011
GPRC5D BsAb	0.53 (0.3-0.94) p=0.03



Competing risk model

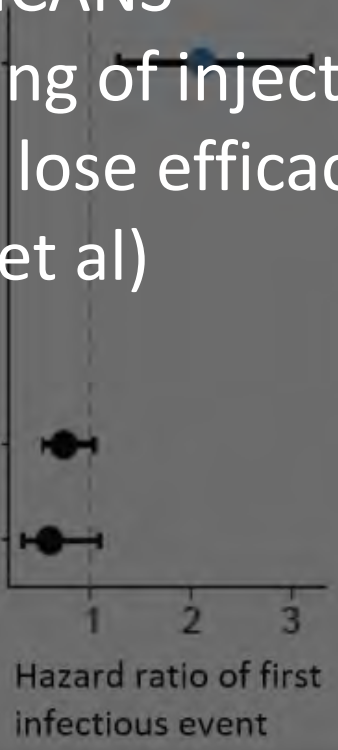
Adjustement [illegible]

HR (95%CI)

2.01 (1.27-3.19) p=0.0[illegible]

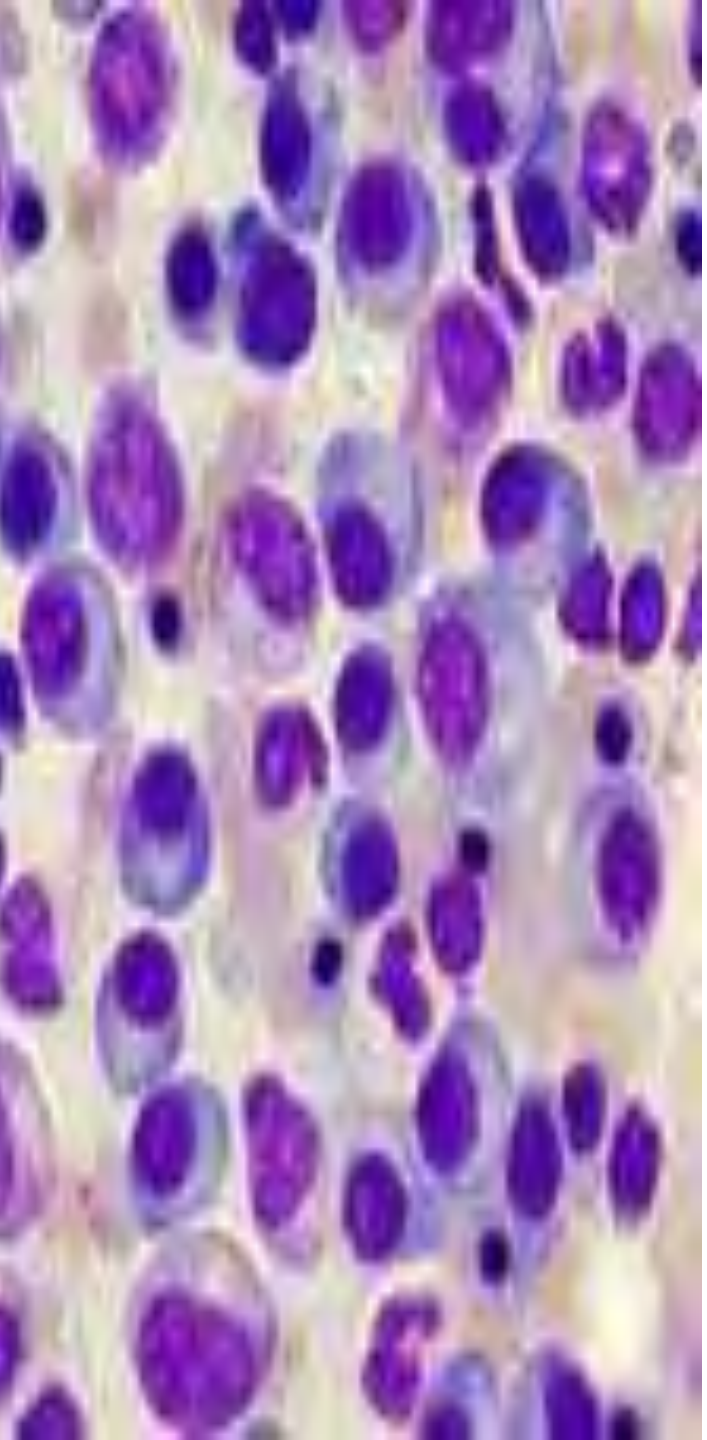
0.73 (0.52-1.03) p=0.071

0.59 (0.32-1.08) p=0.087



Key Points

- Higher risk of infections with steroids for CRS/ICANS
- Spacing of injections Does not lose efficacy (Usmani et al)



MGUS

Revised Definition of Free Light Chains in Serum and Light Chain Monoclonal Gammopathy of Undetermined Significance: Results of the iStopMM Study

Thorir Einarsson Long, Saemundur Rognvaldsson, Sigrun Thorsteinsdottir, Ingigerdur Solveig Sverrisdottir, Elias Eythorsson, Olafur Skuli Indridason, Runolfur Palsson, Thor Aspelund, Brynjar Vidarsson, Pall Torfi Onundarson, Bjarni Agnar Agnarsson, Margret Sigurdardottir, Ingunn Thorsteinsdottir, Isleifur Olafsson, Asdis Rosa Thordardottir, Asbjorn Jonsson, Gauti Gislason, Andri Olafsson, Malin Hultcrantz, Brian G.M. Durie, Stephen Harding, Thorvardur Jon Love, Ola Landgren, and Sigurdur Yngvi Kristinsson

University of Iceland, Reykjavik, Iceland; Skane University Hospital, Lund, Sweden; Lund University, Lund, Sweden; Rigshospitalet, Copenhagen, Denmark; Sahlgrenska University Hospital, Gothenburg, Sweden; Landspitali – The National University Hospital of Iceland, Reykjavik, Iceland; Akureyri Hospital, Akureyri, Iceland; Memorial Sloan Kettering Cancer Center, New York, NY; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Outpatient Cancer Center, Los Angeles, CA; Binding Site Group Ltd., Birmingham, United Kingdom; University of Miami, Sylvester Comprehensive Cancer Center, Miami.

iStopMM – Renal reference intervals

	New reference intervals		
Kidney function (mL/min/1.73 m^2)	Kappa (mg/L)	Lambda (mg/L)	FLC ratio
eGFR 45– 59 N=4612	7.8 – 83.6	7.3 – 65.1	0.46 – 2.62
eGFR 30–44 N=1465	8.8 – 103.3	8.2 – 73.2	0.48 – 3.38
eGFR < 30 N=384	11.7 – 265.1	12.6 – 150.9	0.54 – 3.30

Long et al. Blood Cancer J, 2022, ”Defining new reference intervals for serum free light chains in individuals with chronic kidney disease: Results of the iStopMM study”
”

Aims

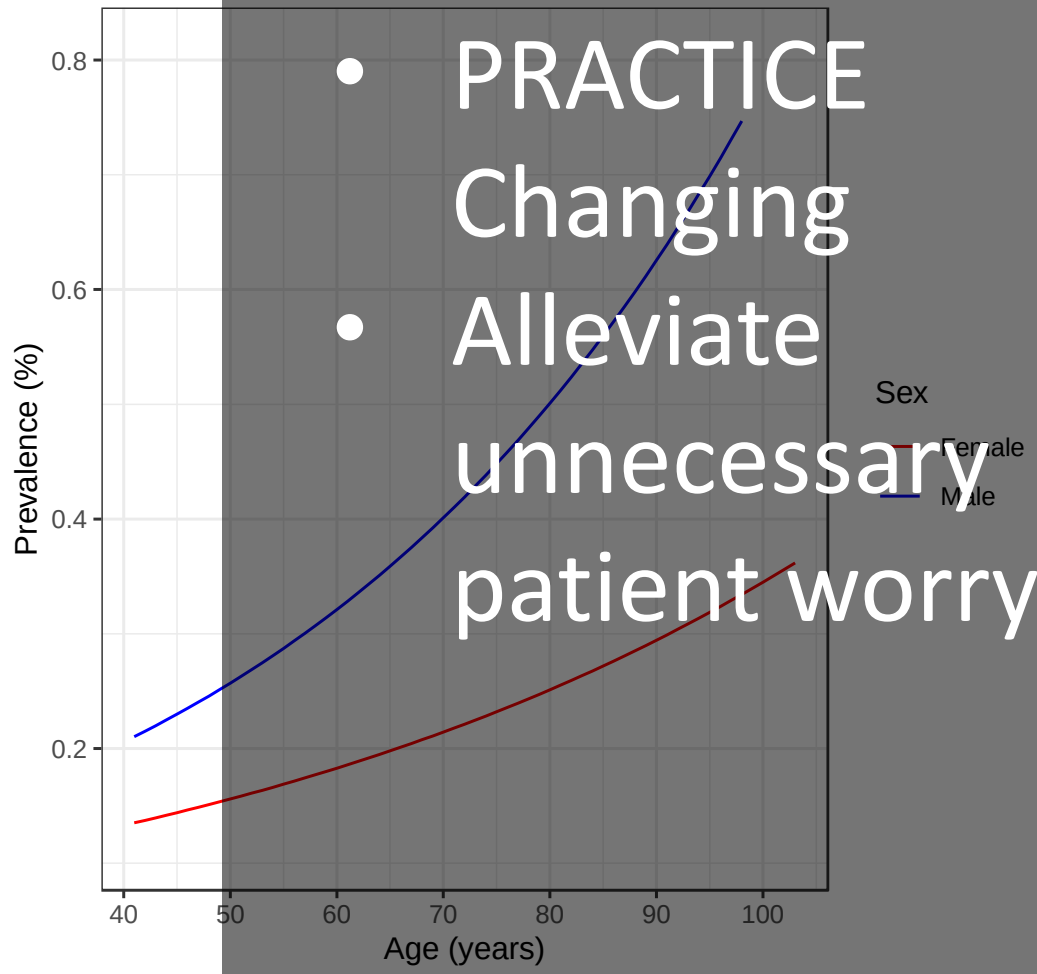
Assess the distribution of kappa, lambda, and the FLC ratio in terms of standard reference intervals. Revise FLC reference intervals in individuals with preserved kidney function (eGFR >60 mL/min/1.73 m^2) and propose a new definition of light chain MGUS.

Revised reference intervals for persons with preserved kidney function (eGFR ≥60 mL/min/1.73m^2)

	New reference intervals		
Age category	Kappa (mg/L)	Lambda (mg/L)	FLC ratio
Age < 70 years **N=33,181**	6.3 – 39.0	5.9 – 36.7	0.44 – 2.16
Age 70 years and above **N=8,701**	7.0 – 55.8	6.4 – 48.0	0.46 – 2.59

Prevalence of LC MGUS

- Prevalence of LC MGUS in the iStopMM cohort (N=75,422) based on novel definition was **0.26%** (95%CI: 0.23-0.30%).
- Prevalence using the standard definition was 1.54% (95%CI: 1.46-1.63%).
- Relative decrease of 83%, of whom none progressed to lymphoproliferative disorder after a median 3.5 year follow-up.



Key Points

- PRACTICE Changing
- Alleviate unnecessary patient worry

Light chain MGUS calculator

Serum free kappa, mg/L

63

Serum free lambda, mg/L

15

Age, years

73

eGFR* mL/min/1.73m2

62

Scan me!

FLC (free light chain ratio) is 4.2

Based on the information provided **this person has light chain monoclonal gammopathy of undetermined significance (LC-MGUS)**

https://istopmm.com/lcmgus/

* Serum creatinine based CKD-EPI eGFR equation (2009) was used in the study where these reference intervals were determined. This calculator was developed based on measurments using the Freelite assay.

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Primary Care Management Pathways to Reduce Wait Times in Hematology: Monoclonal Gammopathy of Undetermined Significance

P. Ganguli MD, **J. Dyba MD, A. E. Hay MB ChB**, L. Zhang PhD, S.A. Silver MD, MSc, Y. Huang PhD, **K. Loughlin MD**, E. Eisenhauer MD, **B. Monteith MD, MSc**

Queen's University, Canada

- **Red Flag Features Include Any of the Following:**
- Hemoglobin <100g/L
- Calcium > 2.75 mmol/L
- eGFR < 45 ml/min/1.72/m^2
- Lytic bone lesions
- Urine M-protein > 500mg/24hours
- sFLC ratio > 8 or <0.125

Referral Contact Details

Details provided to contact attending Hematologist for **emergency referrals** of a pathway patient

Do you have a question regarding a patient on the pathway?

Details provided to contact attending Hematologist for **non-urgent questions** regarding a pathway patient

Instructions provided to consider eConsult if there are questions about patients who do not meet pathway criteria for a referral.

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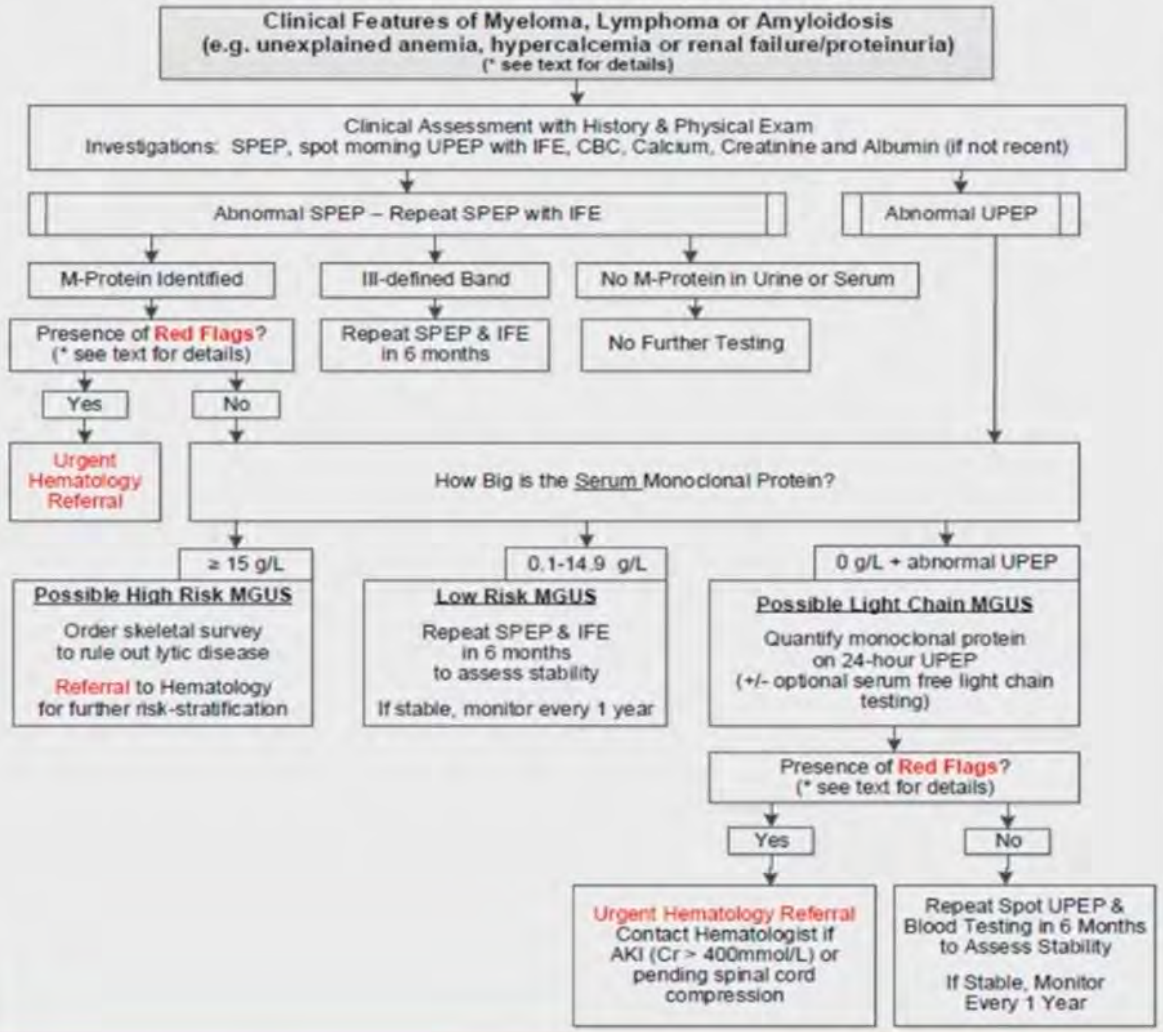
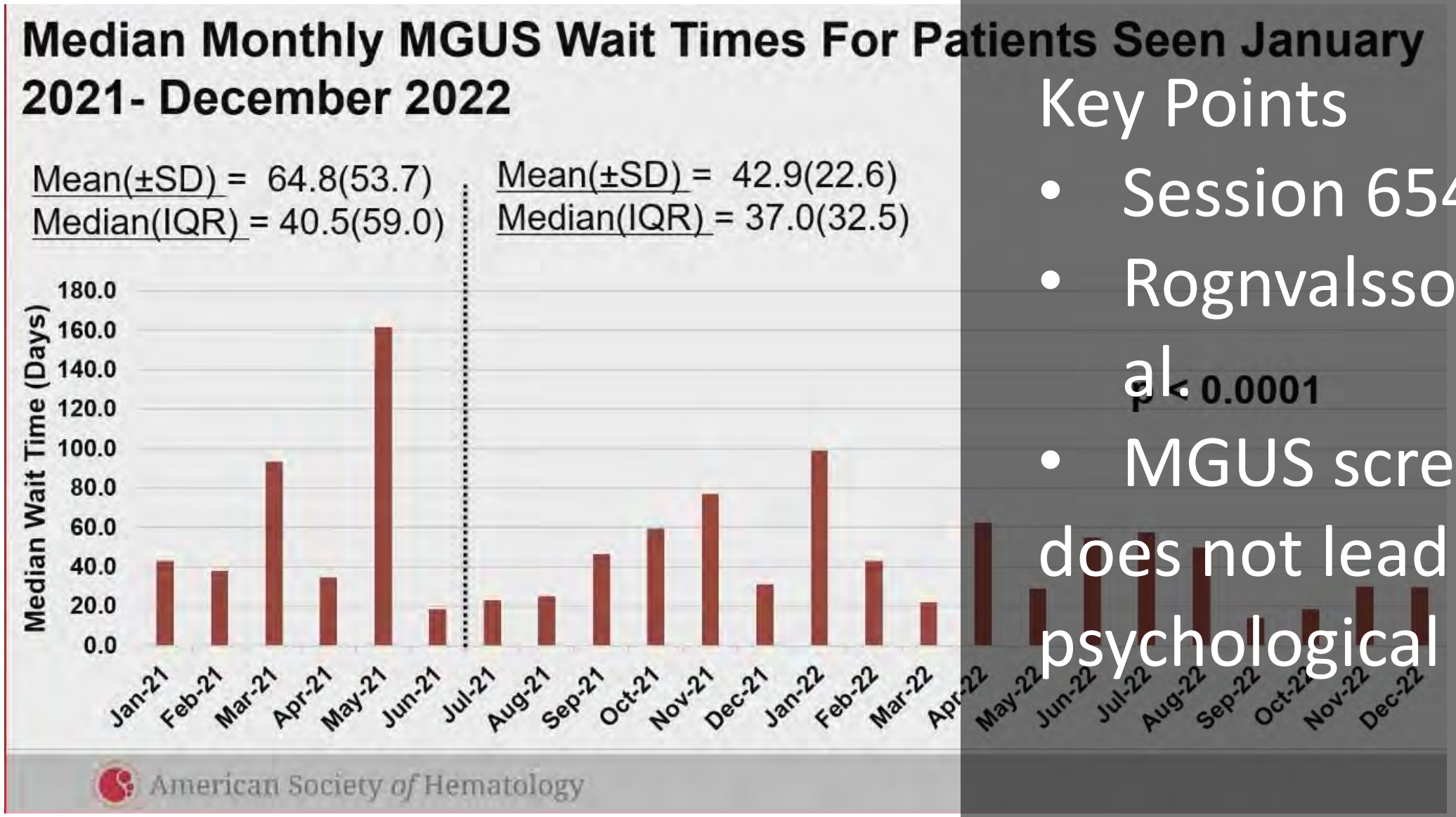
Primary Care Management Pathway – Clinical Flow Diagram
Monoclonal Gammopathy of Underdetermined Significance (MGUS)





Key Points

- Session 654
- Rognvalsson et al.
- MGUS screening does not lead to psychological harm

Thank you
Questions?

@Ashley_Rosko1

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