HEIDELBERG
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05. Februar 2025

Neues vom amerikanischen Hämatologenkongress
Neues zur Therapie des Multiples Myelom

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Disclosures

- Honoraria
  - Amgen, BMS, Celgene, Chugai, GSK, Janssen, Novartis, Sanofi
- Consulting or advisory role
  - Adaptive Biotechnology, Amgen, BMS, Celgene, Millenium Pharmaceuticals Inc., Janssen, Sanofi, Takeda
- Research funding
  - Amgen, BMS, Celgene, Chugai, Janssen, Incyte, Merck Sharp and Dohme (MSD), Molecular Partners AG Zürich, Mundipharma, Novartis, Sanofi, Takeda
- Travel, accommodations, expenses
  - Amgen, BMS, Celgene, Chugai, GSK, Janssen, Novartis, Omnia Med Deutschland, Sanofi, Takeda

Revision der Responsekriterien

Fred Hutch Cancer Center

24-hour urine testing does not add value to multiple myeloma response assessments: a secondary analysis of BMT CTN 0702

Rahul Banerjee, MD; Amber R. Fritz, PhD; Othman S. Akhtar, MD; Ciara L. Freeman, MD, PhD, MSc; Andrew J. Cowan, MD; Nina Shah, MD; Heather J. Landau, MD; Shaji K. Kumar, MD; Dan T. Vogl, MD, MSCE; Yvonne A. Efebera, MD, MPH; Philip L. McCarthy, MD; David H. Vesole, MD, PhD; Adam Mendizabal, PhD; Amrita Y. Krishnan, MD; George Somlo, MD; Edward A. Stadtmauer, MD; Marcelo C. Pasquini, MD, MS

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Abstract #81: Presented at the 2024 ASH meeting on December 7, 2024.

BMT CTN Blood & Marrow Transplant Clinical Trials Network®

Do we even need urine for MM responses?

	Traditional responses	Proposed urine-free responses
CR	• <5% BMPCs, no EMD, negative serum and urine IFE • (Also: normal FLC ratio for light-chain-only disease)	• <5% BMPCs, no EMD, negative serum ~~and urine~~ IFE • (Also: normal FLC ratio for light-chain-only disease)
VGPR	• M-protein detectable only by serum/urine IFE; or, ≥90% reduction in serum M-protein and urine M-protein < 100mg/24hrs • (Or: ≥90% reduction in Δ serum FLC in light-chain-only disease)	• M-protein detectable only by serum~~/urine~~ IFE; or, ≥90% reduction in serum M-protein ~~and urine M-protein < 100mg/24hrs~~ • (Or: ≥90% reduction in Δ serum FLC in light-chain-only disease)
PR	• 50-89% reduction in serum M-protein; or, urine M-protein reduced by ≥90% or to <200mg/24hrs • (Or: 50-89% reduction in Δ serum FLC in light-chain-only disease) • (Or: ≥50% reduction in BMPCs & EMD for non-secretory disease)	• 50-89% reduction in serum M-protein~~; or, urine M-protein reduced by ≥90% or to < 200mg/24hrs~~ • (Or: 50-89% reduction in Δ serum FLC in light-chain-only disease) • (Or: ≥50% reduction in BMPCs & EMD for non-secretory disease)

Natsuhara KH et al. Leuk Lymph. 2023;64(6):1186-1193.

Abbreviations: ASCT, autologous stem cell transplantation; BMPC, bone marrow plasma cell; CR, complete response; EMD, extramedullary disease; FLC, free light chain; IFE, immunofixation electrophoresis; MM, multiple myeloma; PR, partial response; VGPR, very good partial response.

High concordance with traditional assessments

- Only **1.1% of 645 analyzed patients** (*n* = 7) had discordant responses between traditional and urine-free response criteria

- VGPR → urine-free CR (*n* = 2)
  - Met all other stringent CR criteria but still had positive urine paraprotein at Day +56 (faint UIFE+ in one case, UPEP 89 mg/24h in another)
- VGPR → urine-free PR (*n* = 1)
  - Negative serum paraprotein throughout, urine paraprotein had cleared, and BMPC not assessed; however, only 89% reduction in difference of serum FLC
- Non-evaluable → evaluable with urine-free criteria (*n* = 4)
  - Missing UPEP values no longer precluded achievement of VGPR (*n* = 3) or PR (*n* = 1) based on serum paraprotein reductions using urine-free criteria

Abbreviations: BMPC, bone marrow plasma cell burden; CR, complete response; FLC, free light chain; PR, partial response; UIFE, urine immunofixation; UPEP, urine protein electrophoresis; VGPR, very good partial response.

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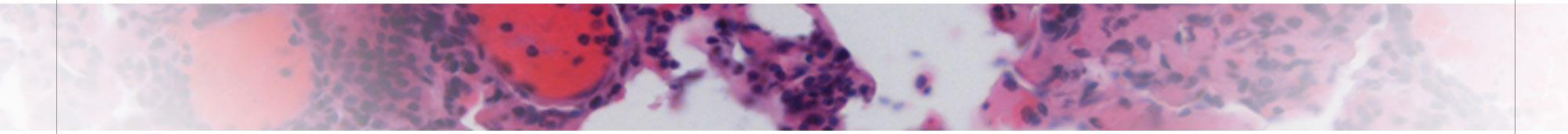


Reevaluating the IMWG Multiple Myeloma Complete Response Criterion in the Era of Mass Spectrometry: a Critical Analysis

N Puig, C Agulló, B Paiva, MT Cedena, L Rosiñol, T Contreras, J Martínez-López, A Oriol, MJ Blanchard, R Ríos-Tamayo, AM Sureda, MT Hernández, J de la Rubia, V Cabañas, F de Arriba, L Palomera, MB Iñigo, V González-Calle, EM Ocio, S Castro, J Bargay, J Bladé, JF San Miguel, JJ Lahuerta, MV Mateos

on behalf of the PETHEMA/GEM cooperative group

Aims

- To analyze the value of bone marrow examinations in MM patients with suspected CR based on negative IFE results in serum (sIFE)

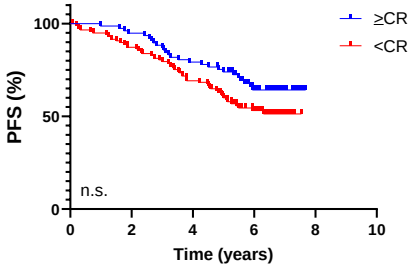
- To explore the utility of mass spectrometry as a marrow sparing, single serological marker to determine a potentially mass-spec based CR category

PFS in samples in ≥CR *vs* <CR at each pre-stablished time point

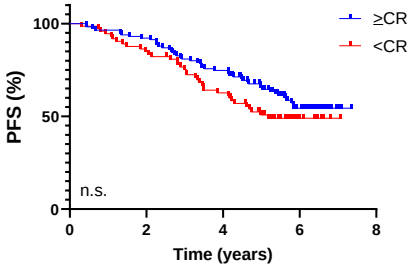
SPEP/IFE and morphology

GEM2012MENOS65 & GEM2014MAIN & GEMCESAR

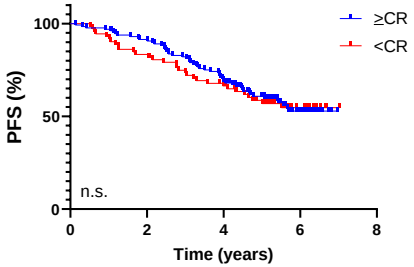
Post-Induction



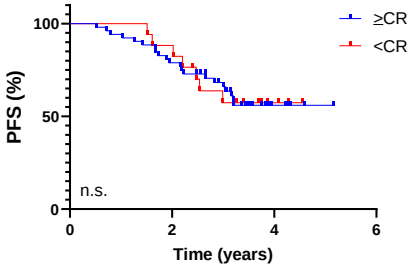
Post-ASCT



Post-Consolidation



After 2 ys of maintenance

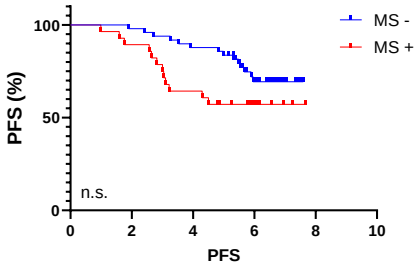


PFS in samples in ≥CR at each pre-stablished point according to MS

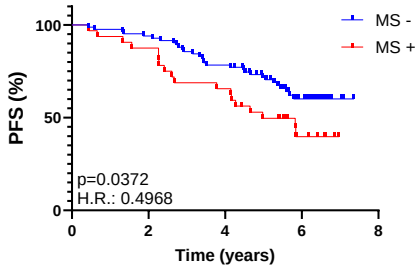
Mass-spec

GEM2012MENOS65 & GEM2014MAIN & GEMCESAR

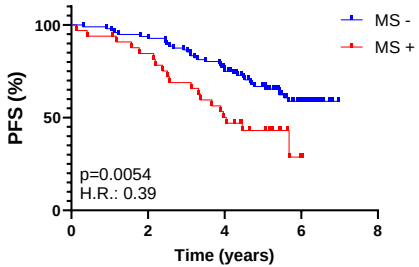
Post-Induction



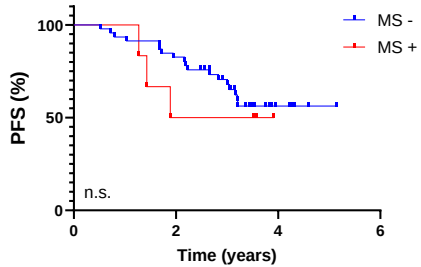
Post-ASCT



Post-Consolidation



After 2 ys of maintenance



Conclusions

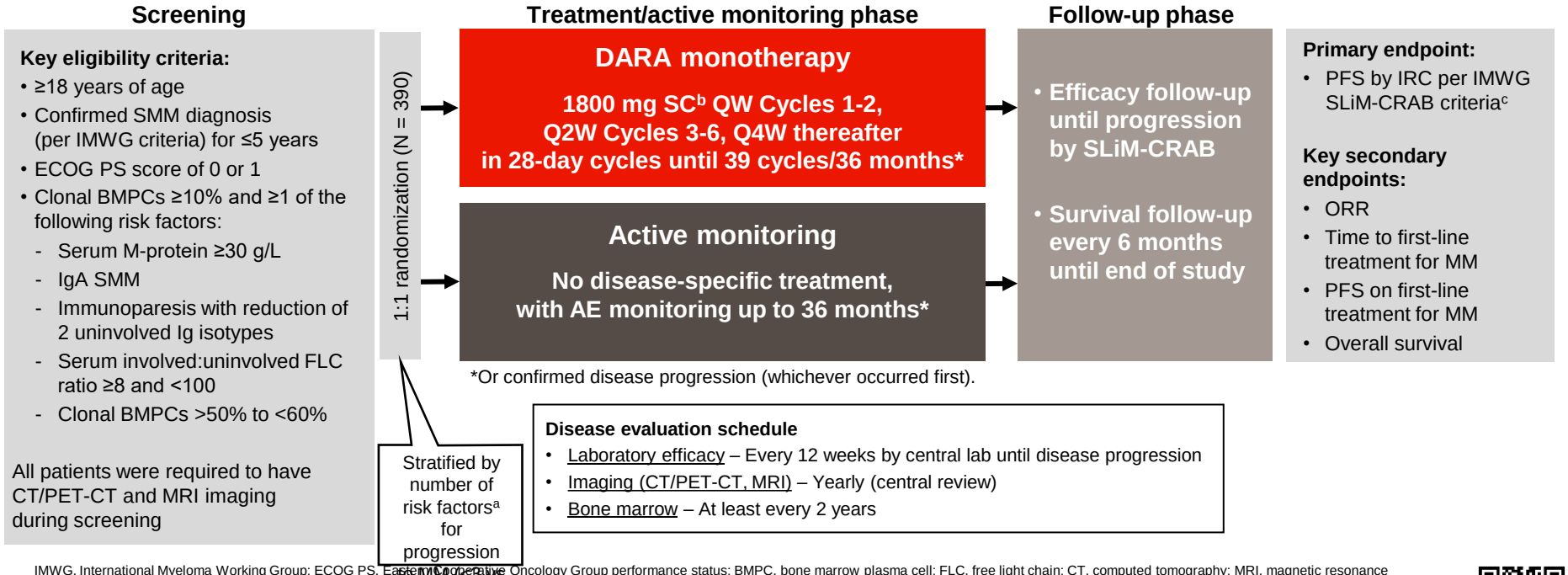
- Our study suggests that MS surpasses the clinical value of the CR category and the limitations of PC counting and sIFE, and thus supports the consideration of a new, MS-based, category of treatment response in pts with MM.

- Our results show that performing a BM aspiration in cases with “suspected CR” should be carried out with the intention of analyzing MRD, given the very limited added value of PC counting.

Smoldering Myelom

AQUILA: Study Design

AQUILA enrollment period: December 2017 to May 2019 at 124 sites in 23 countries



IMWG, International Myeloma Working Group; ECOG PS, Eastern Cooperative Oncology Group performance status; BMPC, bone marrow plasma cell; FLC, free light chain; CT, computed tomography; MRI, magnetic resonance imaging; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; AE, adverse event; IRC, independent review committee; ORR, overall response rate. [a]Risk factors included involved:uninvolved FLC ratio ≥8 (yes vs no), serum M-protein ≥30 g/L (yes vs no), IgA SMM (yes vs no), immunoparesis (reduction of 2 uninvolved immunoglobulins vs other), or clonal BMPCs (>50% to <60% vs ≤50%). [b]DARA SC (1800 mg co-formulated with recombinant human hyaluronidase PH20 [rHuPH20; 2,000 U/mL; ENHANZE® drug delivery technology; Halozyme, Inc.]). [c]PFS was defined as duration from randomization to initial documented progression to active MM or death due to any cause, whichever occurred first.

AQUILA: Baseline Demographics and Disease Characteristics

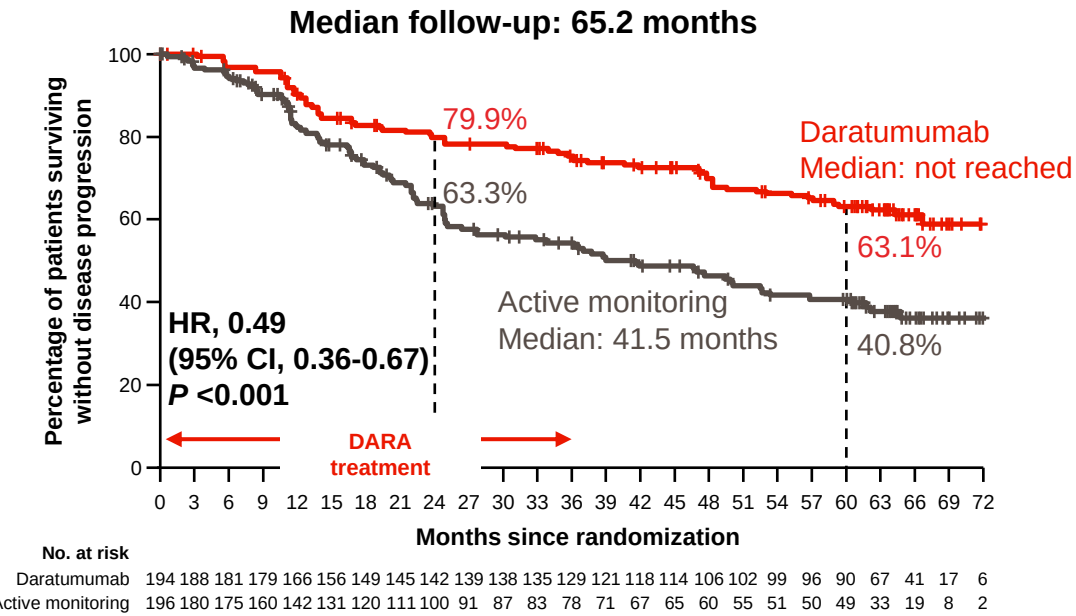
Characteristic	DARA (n = 194)	Active monitoring (n = 196)
Age		
Median (range), years	63.0 (31-86)	64.5 (36-83)
18 to <65 years, n (%)	106 (54.6)	98 (50.0)
65 to <75 years, n (%)	67 (34.5)	74 (37.8)
≥75 years, n (%)	21 (10.8)	24 (12.2)
Sex, n (%)		
Female	99 (51.0)	103 (52.6)
Male	95 (49.0)	93 (47.4)
ECOG PS score, n (%)		
0	165 (85.1)	160 (81.6)
1	29 (14.9)	36 (18.4)
Median time from diagnosis of SMM to randomization (range), years	0.80 (0-4.7)	0.67 (0-5.0)
Median BMPCs (range), %	20.0 (8.0-59.5)	20.0 (10.0-55.0)

Characteristic	DARA (n = 194)	Active monitoring (n = 196)
Type of SMM, n (%)		
IgG	127 (65.5)	138 (70.4)
IgA	55 (28.4)	42 (21.4)
Other	12 (6.2)	16 (8.2)
AQUILA risk factors for progression to MM, n (%)[a]		
<3	154 (79.4)	156 (79.6)
≥3	40 (20.6)	40 (20.4)
Cytogenetic risk profile[b]	n = 167	n = 170
≥1 of del(17p), t(4;14), and/or t(14;16), n (%)	29 (17.4)	22 (12.9)
Mayo 2018 risk criteria, n (%)[c]		
Low	45 (23.2)	34 (17.3)
Intermediate	77 (39.7)	76 (38.8)
High	72 (37.1)	86 (43.9)

Baseline characteristics were generally balanced between groups

[a]Risk factors: serum M-protein ≥30 g/L, IgA SMM, immunoparesis with reduction of 2 uninvolved immunoglobulin isotypes, serum involved:uninvolved FLC ratio ≥8 and <100, or clonal BMPCs >50% to <60% with measurable disease. [b]Cytogenetic risk was assessed by fluorescence in situ hybridization. [c]Mayo 2018 risk criteria: serum M-protein >2 g/L, involved:uninvolved FLC ratio >20, and clonal BMPCs >20%. Patients with 0 factors = low risk, 1 factor = intermediate risk, ≥2 factors = high risk (Lakshman A, et al. *Blood Cancer J*. 2018;8(6):59).

AQUILA: Progression to MM by IMWG SLiM-CRAB Criteria (IRC Assessment)



	DARA (n = 194)	Active monitoring (n = 196)
PFS event, n (%)	67 (34.5)	99 (50.5)
Death without disease progression	5 (2.6)	5 (2.6)
Disease progression[a]	62 (32.0)	94 (48.0)
CRAB criteria	12 (6.2)	34 (17.3)
Calcium elevation	0	2 (1.0)
Renal insufficiency[b]	0	0
Anemia	2 (1.0)	14 (7.1)
Bone disease	10 (5.2)	18 (9.2)
SLiM criteria	50 (25.8)	65 (33.2)
Clonal BMPCs	5 (2.6)	16 (8.2)
Serum FLC	33 (17.0)	33 (16.8)
Focal lesion by MRI	12 (6.2)	16 (8.2)

DARA significantly reduced the risk of progression to MM or death by 51% versus active monitoring; the benefit continued beyond 36 months

HR, hazard ratio; CI, confidence interval. [a]A patient may show disease progression based on ≥1 criterion. [b]Some patients met the CRAB criteria for renal insufficiency, but the investigator attributed this to a cause other than disease progression to MM. Adapted with permission © The *New England Journal of Medicine* (2024).

AQUILA: Conclusions

- In this large phase 3 study in a well-defined population with high-risk SMM, DARA SC monotherapy for 36 months demonstrated a statistically significant PFS benefit versus active monitoring (HR, 0.49 [95% CI, 0.36-0.67])
  - The greatest PFS benefit with DARA was observed among patients with high-risk SMM retrospectively identified by Mayo 2018 criteria (HR, 0.36 [95% CI, 0.23-0.58])
- DARA prolonged PFS on first-line treatment for MM (HR, 0.58 [95% CI, 0.35-0.96])
- DARA demonstrated a favorable safety profile, with a low rate of treatment discontinuation due to TEAEs
- Patients' health-related quality of life with DARA was maintained compared with active monitoring
- DARA extended overall survival (HR, 0.52 [95% CI, 0.27-0.98])

AQUILA strongly favored early intervention with DARA monotherapy in patients with high-risk SMM, representing an opportunity to delay or avoid end-organ damage and progression to MM and to extend overall survival

Neudiagnostiziertes MM

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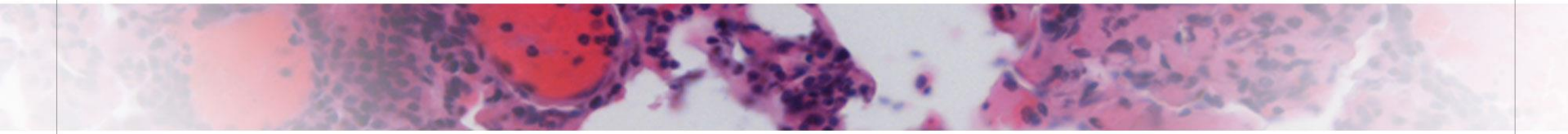


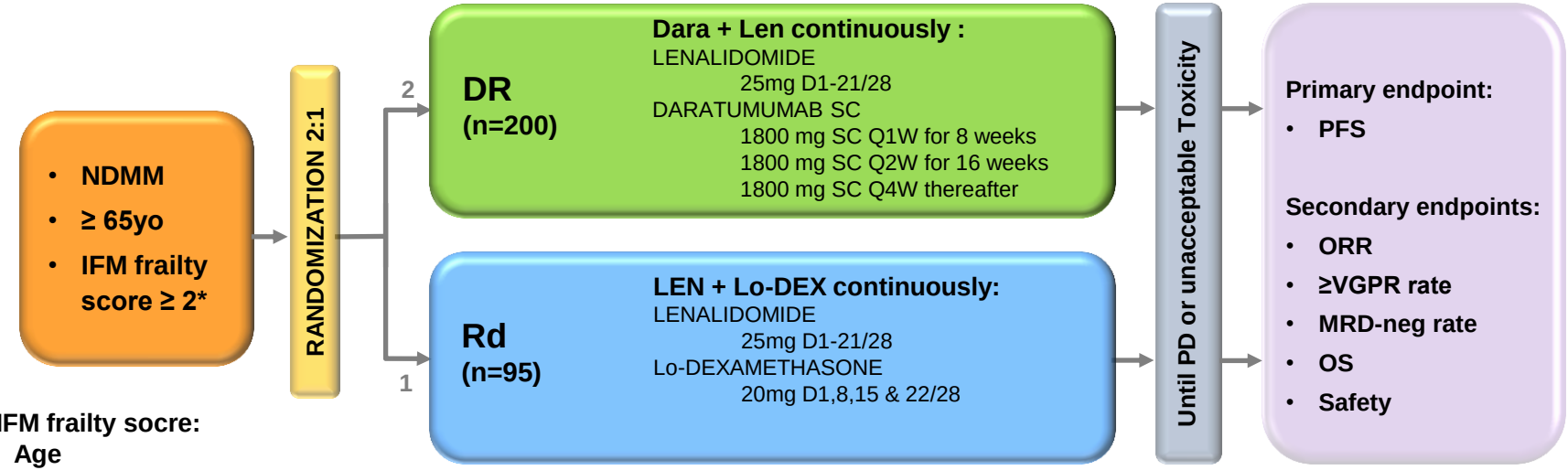
A Dexamethasone Sparing-Regimen with Daratumumab and Lenalidomide in Frail Patients with Newly-Diagnosed Multiple Myeloma: the Phase 3 IFM2017-03 Trial

S. Manier, J. Lambert, C. Hulin, M. Macro, K. Laribi, C. Araujo, G.M. Pica, C. Touzeau, P. Godmer, B. Slama, L. Karlin, F. Orsini Piocelle, M. Dib, L. Sanhes, N. Bigot, A. Perrot, J. Corre, J.Y. Mary, H. Avet-Loiseau, P. Moreau, X. Leleu, T. Facon

ASH 2024, San Diego

IFM 2017-03 - Study design

Phase 3 study of DR vs Rd in TNE frail NDMM (n = 295)



*IFM frailty socre:
Age
ECOG
Charlson

Randomization stratified by ISS (I vs II vs III) and age (<80 vs ≥80)
In Arm B low-dose dex (20mg/week) during Cycle 1 and 2 (with Dara)

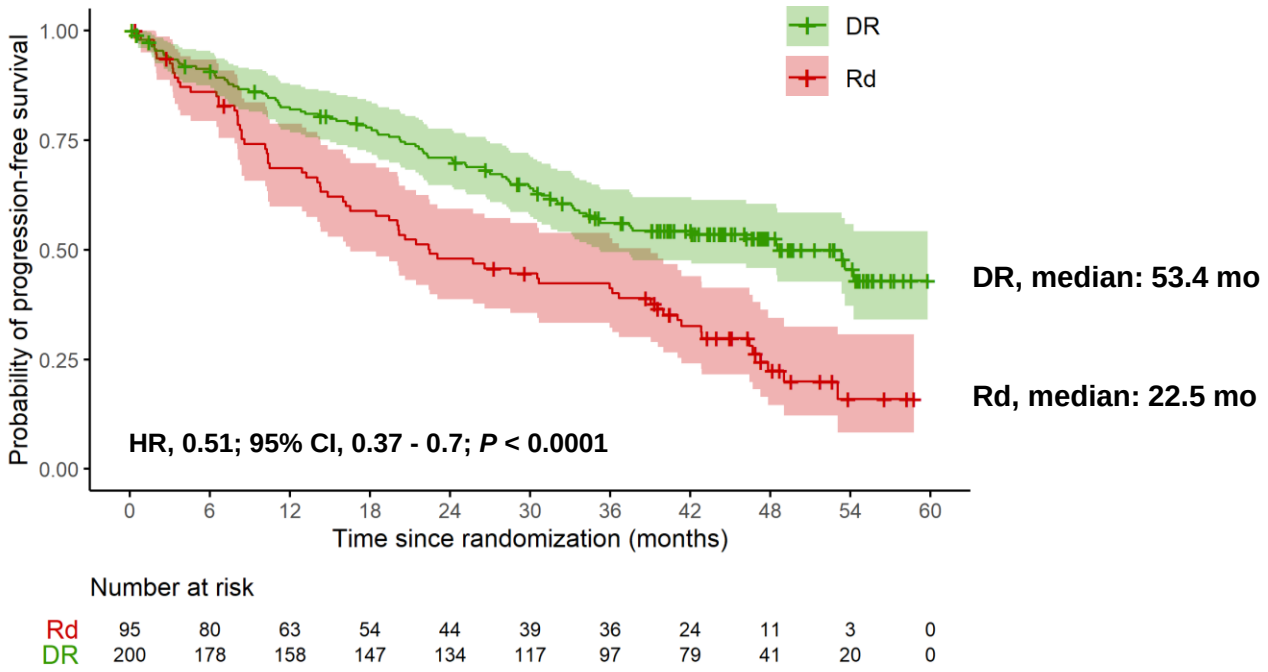
Interim analysis : 12-months data cut on response rates and safety

Final analysis with primary endpoint: PFS

NCT03993912

IFM 2017-03 – Progression free survival

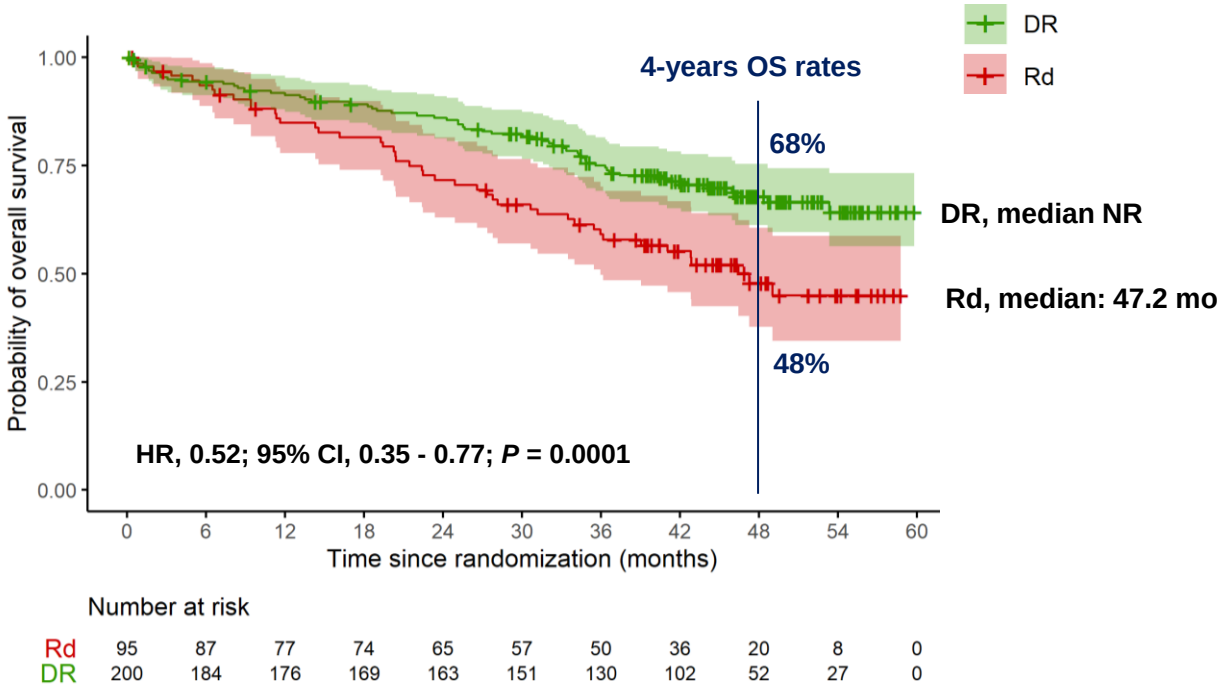
Median follow up time = 46.3 months



49% reduction in the risk of progression or death in patients receiving DR

IFM 2017-03 – Overall Survival

Median follow up time = 46.3 months



48% reduction in the risk of death in patients receiving DR

IFM 2017-03 – Most common grade ≥3 AEs

	DR group (n=200) Grade ≥ 3	Rd group (n=95) Grade ≥ 3
Median treatment duration	31.6 months	14.3 months
All grade ≥ 3 AEs, n (%)	178 (89%)	75 (79%)
All grade 5, n (%)	23 (12%)	12 (13%)
Hematologic, n (%)	123 (62%)	32 (34%)
neutropenia	110 (55%)	23 (24%)
anemia	24 (12%)	3 (3%)
thrombocytopenia	19 (10%)	5 (5%)
Non-hematologic AEs, n (%)	132 (66%)	68 (72%)
Infection, n (%)	38 (19%)	20 (21%)
pneumonia	11 (6%)	8 (8%)
Infection rate per patient-year	0.07	0.09

	DR group (n=200)	Rd group (n=95)
Treatment discontinuation due to AE, n (%)	60 (30%)	32 (34%)

No increased rates of infection or treatment discontinuation in patients receiving DR

IFM 2017-03 – Conclusions

- IFM2017-03 is the first randomized phase 3 trial dedicated to frail patients
- Daratumumab-lenalidomide (DR) let to a significant reduction in the risk of progression or death by 49% (mPFS 53.4 [DR] vs. 22.5 months [Rd]; HR, 0.51)
- Overall survival of frail patients was significantly improved with DR (mOS NR [DR] vs. 47 months [Rd]; HR, 0.52)
- Safety profile was favorable without increased infection or pneumonia rates with DR *vs*. Rd and with similar rates of treatment discontinuation
- A dexamethasone-sparing strategy is effective and safe for treating frail patients with multiple myeloma

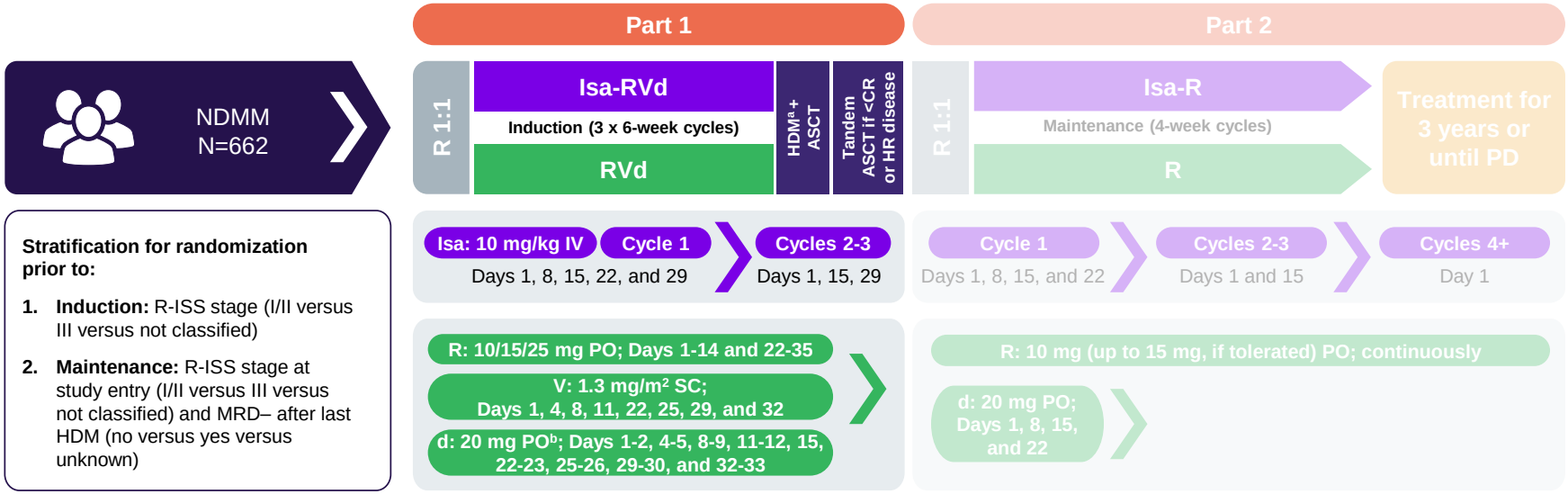
Isatuximab, Lenalidomide, Bortezomib and Dexamethasone Induction Therapy for Transplant-Eligible Patients With Newly Diagnosed Multiple Myeloma: Final Progression-Free Survival Analysis of Part 1 of an Open-label, Multicenter, Randomized, Phase 3 Trial (GMMG-HD7)

Hartmut Goldschmidt[1,2], Uta Bertsch[1,2], Ema Pozek[3], Axel Benner[3], Roland Fenk[4], Britta Besemer[5], Christine Hanoun[6], Roland Schroers[7], Ivana von Metzler[8], Mathias Hänel[9], Christoph Mann[10], Lisa B. Leypoldt[11], Bernhard Heilmeier[12], Stefanie Huhn[1], Sabine K. Vogel[1], Michael Hundemer[1], Christof Scheid[13], Igor W. Blau[14], Steffen Luntz[15], Tobias A. W. Holderried[16], Karolin Trautmann-Grill[17], Deniz Gezer[18], Maika Klaiber-Hakimi[19], Martin Müller[20], Evgenii Shumilov[21], Wolfgang Knauf[22], Christian S. Michel[23], Thomas Geer[24], Hendrik Riesenberg[25], Christoph Lutz[26], Marc S. Raab[1,2], Martin Hoffmann[27], Katja C. Weisel[11], Hans J. Salwender[28], and Elias K. Mai[1] for the German-speaking Myeloma Multicenter Group (GMMG) HD7 investigators

[1]Internal Medicine V, Hematology, Oncology and Rheumatology, Heidelberg University Hospital, Heidelberg, Germany; [2]National Center for Tumor Diseases Heidelberg, Heidelberg, Germany; [3]Division of Biostatistics, German Cancer Research Center (DKFZ) Heidelberg, Heidelberg, Germany; [4]Department of Hematology, Oncology and Clinical Immunology, University Hospital Düsseldorf, Düsseldorf, Germany; [5]Department of Internal Medicine II, University Hospital Tübingen, Tübingen, Germany; [6]Department for Hematology and Stem Cell Transplantation, University Hospital Essen, Essen, Germany; [7]Medical Clinic II, Ruhr-University Bochum, Bochum, Germany; [8]Department of Medicine II – Hematology and Oncology, Goethe-University Frankfurt, University Hospital, Frankfurt am Main, Germany; [9]Department of Internal Medicine III, Klinikum Chemnitz, Chemnitz, Germany; [10]Department for Hematology, Oncology and Immunology, University Hospital Gießen and Marburg, Marburg, Germany; [11]Department of Oncology, Hematology and BMT, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [12]Clinic for Oncology and Hematology, Hospital Barmherzige Brueder Regensburg, Regensburg, Germany; [13]Department of Internal Medicine I, University Hospital Cologne, Cologne, Germany; [14]Medical Clinic, Charité University Medicine Berlin, Berlin, Germany; [15]Coordination Centre for Clinical Trials (KKS) Heidelberg, Heidelberg, Germany; [16]Department of Hematology, Oncology, Stem Cell Transplantation, Immune and Cell Therapy, Clinical Immunology and Rheumatology, University Hospital Bonn, Bonn, Germany; [17]Department of Internal Medicine I, University Hospital Dresden, Dresden, Germany; [18]Department of Hematology, Oncology, Hemostaseology, and Stem Cell Transplantation, Faculty of Medicine, RWTH Aachen University, Aachen, Germany; [19]Clinic for Hematology, Oncology and Palliative Care, Marien Hospital Düsseldorf, Düsseldorf, Germany; [20]Clinic for Hematology, Oncology and Immunology, Klinikum Siloah Hannover, Hannover, Germany; [21]Department of Medicine A, Hematology, Oncology and Pneumology, University Hospital Münster, Münster, Germany; [22]Center for Hematology and Oncology Bethanien, Frankfurt am Main, Germany; [23]Department of Internal Medicine III, University Hospital Mainz, Mainz, Germany; [24]Department of Internal Medicine III, Diakoneo Clinic Schwäbisch-Hall, Schwäbisch-Hall, Germany; [25]Hematology/Oncology Center, Bielefeld, Germany; [26]Hematology/Oncology Center, Koblenz, Germany; [27]Medical Clinic A, Clinic Ludwigshafen, Ludwigshafen, Germany; [28]Asklepios Tumorzentrum Hamburg, AK Altona and AK St. Georg, Hamburg, Germany

ASH 2024; Final Abstract Code: 769

Study design – Part 1



Stratification for randomization prior to:

1. **Induction:** R-ISS stage (I/II versus III versus not classified)
2. **Maintenance:** R-ISS stage at study entry (I/II versus III versus not classified) and MRD– after last HDM (no versus yes versus unknown)

Primary end points[c]: Post-induction MRD– (NGF, 10^{-5}); PFS after second randomization

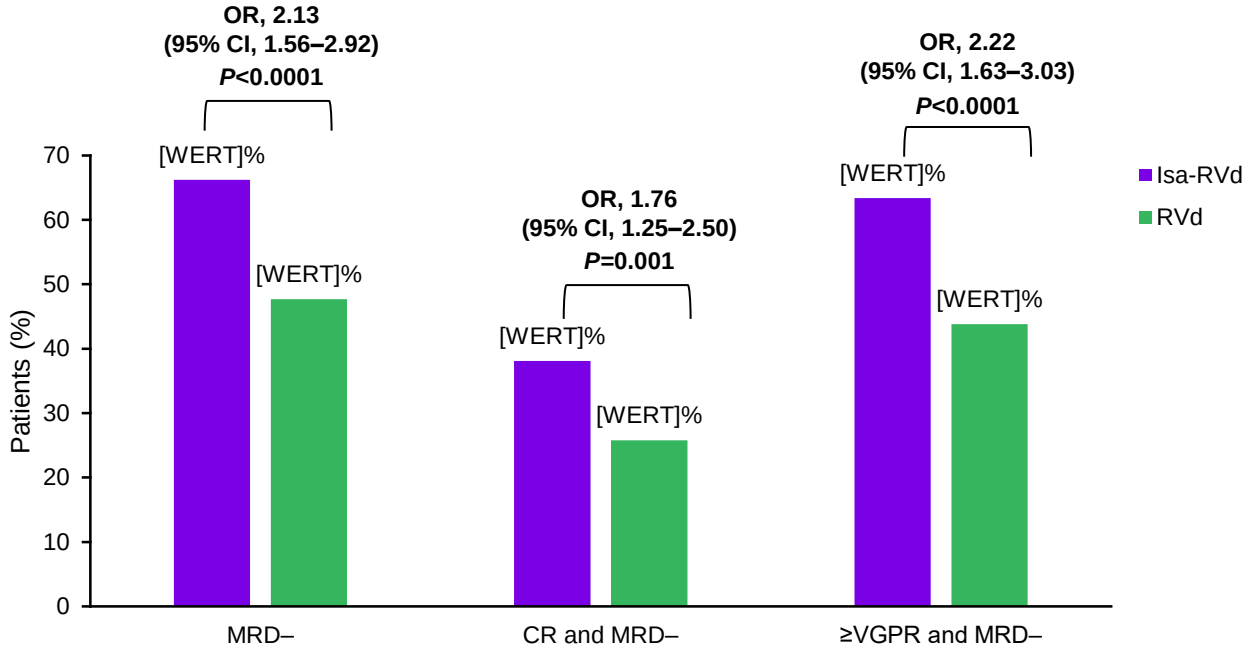
Key secondary end points: PFS (whole study); OS (whole study and from second randomization); post-induction CR; CR and MRD– after HDM and during and after maintenance therapy

Selected secondary end point: PFS after first randomization

Here, we present the PFS from first randomization comparing Isa-RVd and RVd induction therapies

[a]Melphalan 200 mg/m². [b]On days of isatuximab infusion, dexamethasone will be administered intravenously as part of the premedication.
ASCT, autologous stem cell transplant; CR, complete response; d, dexamethasone; HDM, high-dose melphalan; HR, high-risk; Isa, isatuximab; IV, intravenous; MRD–, minimal residual disease negativity; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PO, oral; R, lenalidomide; R-ISS, Revised International Staging System; SC, subcutaneous; V, bortezomib.

MRD– rates post transplant in the ITT population[1]

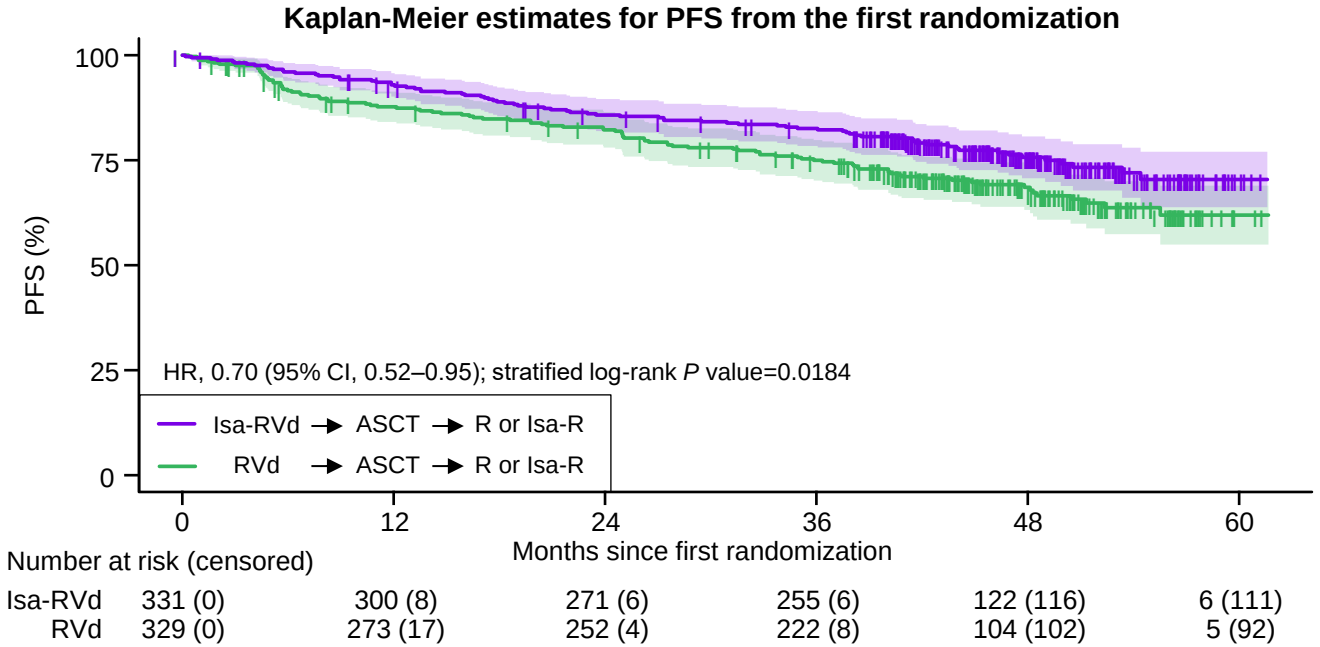


Compared with RVd alone, Isa-RVd led to deeper MRD– response post transplant

CI, confidence interval; CR, complete response; d, dexamethasone; Isa, isatuximab; ITT, intent-to-treat; MRD–, minimal residual disease negativity; OR, odds ratio; R, lenalidomide; V, bortezomib; VGPR, very good partial response.

1. Mai E., et al. Abstract 364. Presented at American Society of Hematology 2024.

Secondary end point of Part 1: PFS from first randomization



At a median follow-up of 48 months, 18 weeks of Isa-RVd induction without consolidation resulted in a 30% reduction in risk of progression or death compared with RVd regardless of maintenance therapy received

ASCT, autologous stem cell transplant; CI, confidence interval; d, dexamethasone; HR, hazard ratio; Isa, isatuximab; PFS, progression-free survival; R, lenalidomide; V, bortezomib.

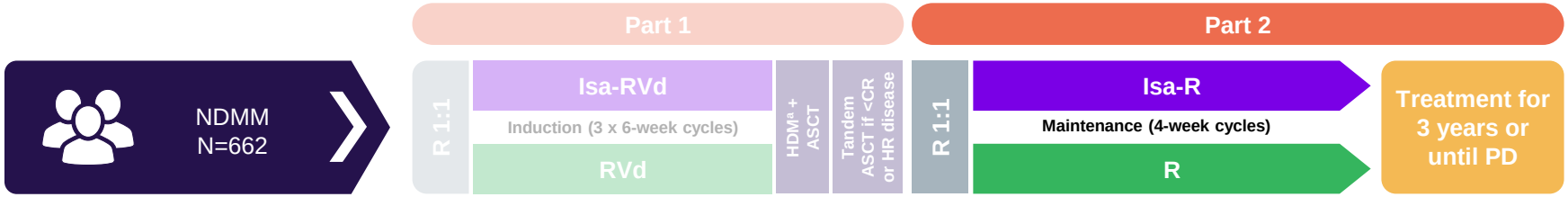
Summary

- Addition of Isa to RVd during an 18-week induction followed by ASCT without consolidation and regardless of second randomization resulted in an impressive 30% reduction in risk of progression or death compared with standard of care RVd
- Weighted risk set estimator analyses accounting for second randomization with lenalidomide only confirmed the significant benefit for Isa-RVd vs. RVd induction
- The PFS benefit was observed across clinically relevant subgroups
- Isa-RVd is the first regimen to demonstrate a deep and rapid response reflected by a statistically significant MRD– benefit at the end of induction and post-transplant in a Phase 3 trial, which translated to a PFS benefit vs RVd
- ASCT was feasible after induction therapy, as a similar proportion of patients in both treatment arms proceeded to ASCT, and hematologic recovery was comparable between the Isa-RVd and RVd groups

GMMG-HD7 is the first Phase 3 study to show that an 18-week initial quadruplet regimen with Isa, without consolidation, allows for significant long-term benefits regardless of subsequent maintenance therapy

ASCT, autologous stem cell transplant; d, dexamethasone; Isa, isatuximab; MRD–, minimal residual disease negativity; PFS, progression-free survival; R, lenalidomide; V, bortezomib.

Future perspectives



- Follow-up of the GMMG-HD7 trial is ongoing
- The next readout from the GMMG-HD7 trial will be the primary end point for part 2: PFS from second randomization comparing maintenance therapy with Isa-lenalidomide or lenalidomide alone

GMMG-HD7 is the only Phase 3 study with a second randomization before maintenance incorporating SOC lenalidomide, which allows the effects of isatuximab in induction and maintenance to be isolated and evaluated separately

[a]Melphalan 200 mg/m². ASCT, autologous stem cell transplant; CR, complete response; d, dexamethasone; HDM, high-dose melphalan; HR, high-risk; Isa, isatuximab; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PFS, progression-free survival; R, lenalidomide; SOC, standard of care;
V, bortezomib.

Phase 2 Study of Teclistamab-based Induction Regimens in Patients With Transplant-eligible Newly Diagnosed Multiple Myeloma: Results From the GMMG-HD10/DSMM-XX (MajesTEC-5) Trial*

deutsche studiengruppe multiples myelom

dsmm

doing studies on multiple myeloma

*ClinicalTrials.gov Identifier: NCT05695508; sponsored by the University of Heidelberg Medical Center and is in collaboration with Janssen Research & Development, LLC

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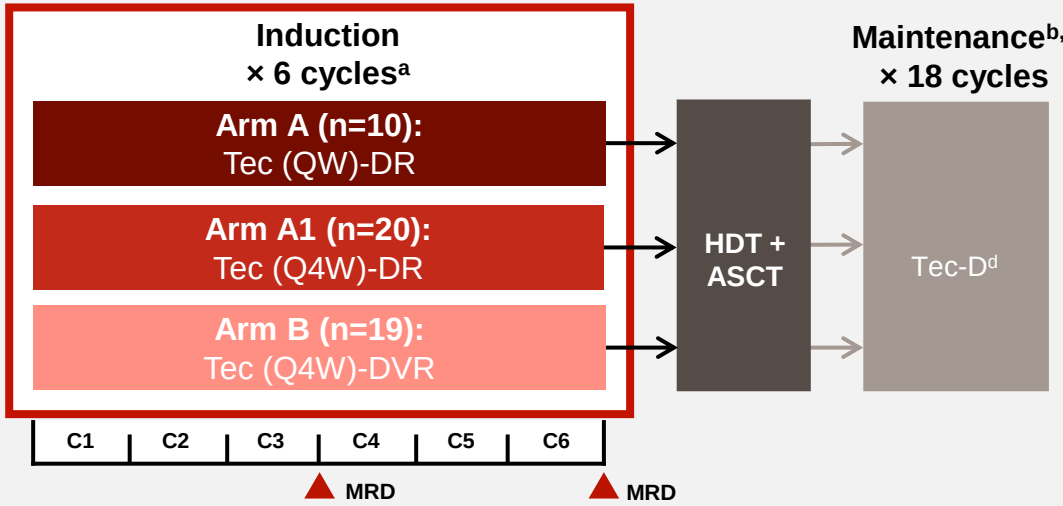
https://www.congresshub.com/ASH2024/Oncology/Teclistamab/Raab

Presented by MS Raab at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

GMMG-HD10/DSMM-XX/MajesTEC-5: Study Design

Key eligibility criteria:

- TE NDMM
- ECOG PS score of 0-2
- Aged 18-70 years



Primary endpoint:

- AEs, SAEs

Select secondary endpoints:

- MRD negativity (10^{-5})
- ORR
- ≥CR
- ≥VGPR
- Stem cell yield

- Per protocol, MRD assessments by NGF were planned following completion of C3 and C6 in all patients
- Additional cohorts evaluating Tal and Tec/Tal combinations are also being investigated as part of this study

[a]Each cycle is 28 days. Dexamethasone was also administered in C1 and C2. Stem cell collection was planned after 3 cycles of induction. [b]Following maintenance therapy, patients could receive additional SoC maintenance treatment per institutional standard and local investigator decision. [c]Maintenance treatment can be discontinued when 12 months of sustained MRD negativity (10^{-5}) have been observed, beginning in induction. [d]Planned maintenance treatment in Arm A was Tec-DR. A protocol amendment permitted patients initially assigned to Tec-DR maintenance to receive Tec-D maintenance per investigator's choice (patients who started Tec-DR may have discontinued Len to receive Tec-D per investigator's choice).

AE, adverse event; ASCT, autologous stem cell transplant; C, Cycle; CR, complete response; D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; HDT, high-dose therapy; Len, lenalidomide; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow cytometry; ORR, overall response rate; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; SAE, serious adverse event; SoC, standard-of-care; Tal, talquetamab; TE, transplant-eligible; Tec, teclistamab; V, bortezomib; VGPR, very good partial response.

GMMG-HD10/DSMM-XX/MajesTEC-5: Hematologic TEAEs

TEAEs, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Hematologic								
Neutropenia	4 (40)	3 (30)	13 (65)	13 (65)	14 (73.7)	12 (63.2)	31 (63.3)	28 (57.1)
Lymphopenia	8 (80)	7 (70)	7 (35)	7 (35)	7 (36.8)	7 (36.8)	22 (44.9)	21 (42.9)
Thrombocytopenia	3 (30)	1 (10)	7 (35)	2 (10)	7 (36.8)	1 (5.3)	17 (34.7)	4 (8.2)
Anemia	5 (50)	0	6 (30)	4 (20)	5 (26.3)	0	16 (32.7)	4 (8.2)
Leukopenia	5 (50)	2 (20)	3 (15)	2 (10)	6 (31.6)	5 (26.3)	14 (28.6)	9 (18.4)

- The most common hematologic TEAE was neutropenia
- Weekly bortezomib did not increase the frequency of thrombocytopenia

Data cutoff: September 30, 2024. [a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0.
AE, adverse event; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; V, bortezomib.

Presented by MS Raab at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

GMMG-HD10/DSMM-XX/MajesTEC-5: Nonhematologic TEAEs

TEAEs, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Nonhematologic[b]								
CRS	6 (60)	0	14 (70)	0	12 (63.2)	0	32 (65.3)	0
Pyrexia	6 (60)	1 (10)	9 (45)	2 (10)	7 (36.8)	0	22 (44.9)	3 (6.1)
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
Rash	5 (50)	2 (20)	5 (25)	0	7 (36.8)	0	17 (34.7)	2 (4.1)
GGT increased	3 (30)	0	6 (30)	3 (15)	5 (26.3)	3 (15.8)	14 (28.6)	6 (12.2)
Diarrhea	6 (60)	0	4 (20)	1 (5)	4 (21.1)	0	14 (28.6)	1 (2)
Hypokalemia	1 (10)	0	8 (40)	2 (10)	4 (21.1)	0	13 (26.5)	2 (4.1)
Nausea	1 (10)	0	4 (20)	0	7 (36.8)	0	12 (24.5)	0
Peripheral sensory neuropathy	1 (10)	0	5 (25)	0	4 (21.1)	0	10 (20.4)	0
BAP increased	4 (40)	0	1 (5)	0	3 (15.8)	1 (5.3)	8 (16.3)	1 (2)
ALT increased	3 (30)	0	2 (10)	1 (5)	2 (10.5)	2 (10.5)	7 (14.3)	3 (6.1)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Lipase increased	1 (10)	1 (10)	5 (25)	3 (15)	1 (5.3)	1 (5.3)	7 (14.3)	5 (10.2)
Hyperglycemia	3 (30)	0	3 (15)	1 (5)	0	0	6 (12.2)	1 (2)
Constipation	0	0	1 (5)	0	5 (26.3)	0	6 (12.2)	0

- Among the most common nonhematologic TEAEs, rates of grade 3/4 events were low
- All CRS events were grade 1/2
  - Most occurred in C1
  - All resolved; no discontinuations due to CRS
- No ICANS
- No grade 5 TEAEs

Data cutoff: September 30, 2024. [a]TEAEs reported in ≥25% of patients in any arm. AEs are graded according to the NCI-CTCAE Version 5.0. [b]Hypogammaglobulinemia based on TEAE reporting also met the ≥25% threshold and is reported separately.
AE, adverse event; ALT, alanine aminotransferase; BAP, blood alkaline phosphatase; CRS, cytokine release syndrome; D, daratumumab; GGT, gamma-glutamyltransferase; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; ICANS, immune effector cell–associated neurotoxicity syndrome; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection; V, bortezomib.

GMMG-HD10/DSMM-XX/MajesTEC-5: Infections

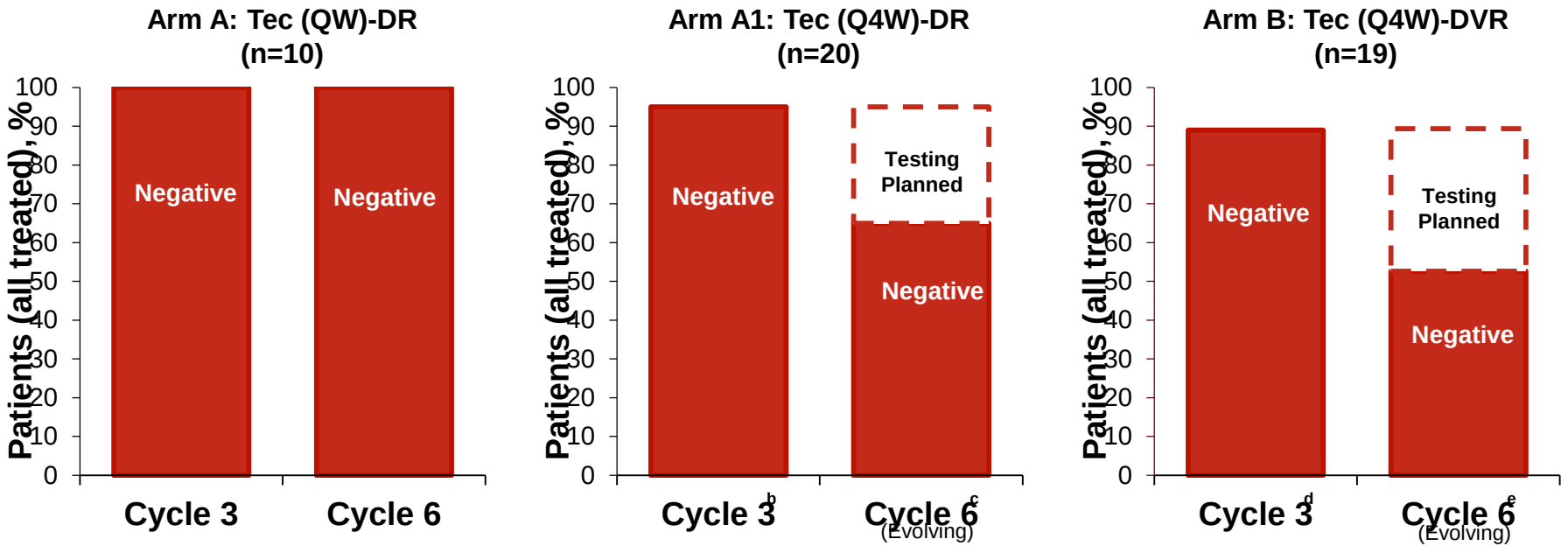
TEAE, n (%)[a]	Arm A: Tec (QW)-DR (n=10)		Arm A1: Tec (Q4W)-DR (n=20)		Arm B: Tec (Q4W)-DVR (n=19)		Total (N=49)	
	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4	All grade	Grade 3/4
Any infection	10 (100)	4 (40)	18 (90)	9 (45)	11 (57.9)	4 (21.1)	39 (79.6)	17 (34.7)
Infections[b]								
URTI	6 (60)	0	8 (40)	1 (5)	6 (31.6)	0	20 (40.8)	1 (2)
COVID-19	2 (20)	0	4 (20)	1 (5)	3 (15.8)	3 (15.8)	9 (18.4)	4 (8.2)
Nasopharyngitis	3 (30)	0	2 (10)	0	2 (10.5)	0	7 (14.3)	0
Bronchitis	2 (20)	0	0	0	0	0	2 (4.1)	0
Infection (NOS)	0	0	1 (5)	1 (5)	2 (10.5)	1 (5.3)	3 (6.1)	2 (4.1)
Pneumonia	1 (10)	1 (10)	1 (5)	0	2 (10.5)	2 (10.5)	4 (8.2)	3 (6.1)

- 17 (34.7%) patients had grade 3/4 infections
  - URTI and COVID-19 were the most common all grade
  - No discontinuations due to infection
  - No grade 5 infections
- Hypogammaglobulinemia[c] was reported in 45 (91.8%) patients
  - 44 (89.8%) received ≥1 dose of IVIg[d]
- Infection prophylaxis, including Ig replacement, was strongly recommended[e]

Data cutoff: September 30, 2024. [a]AEs are graded according to the NCI-CTCAE Version 5.0. [b]Infections reported in >10% of patients in any arm. [c]Includes patients with ≥1 TEAE of hypogammaglobulinemia or post-baseline IgG value <400 mg/dL. [d]Includes patients who started IVIg prior to Tec. [e]Prophylaxis for *Pneumocystis jirovecii* pneumonia and herpes zoster reactivation was also recommended, as well as routine antibiotic prophylaxis.
D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; Ig, immunoglobulin; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NOS, not otherwise specified; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; TEAE, treatment-emergent adverse event; Tec, teclistamab; URTI, upper respiratory tract infection; V, bortezomib.

Presented by MS Raab at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA

GMMG-HD10/DSMM-XX/MajesTEC-5: MRD Negativity (10^{-5})[a]



100% of evaluable patients achieved MRD negativity by C3; no patients were MRD positive

Data cutoff: September 30, 2024. [a]MRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. MRD was determined by NGF testing. [b]In Arm A1, 1 patient did not have bone marrow collected after C3. [c]In Arm A1, 1 patient did not have MRD testing (10^{-5}) after C6. [d]In Arm B, 1 patient was not tested at C3, but was MRD-negative at C6; 1 patient discontinued before C3 and had no on-study MRD testing. [e]In Arm B, 1 patient was MRD negative at 10^{-4} after C6 and was considered indeterminate and without available MRD testing (10^{-5}); 1 patient discontinued before C3 and had no on-study MRD testing.
C, Cycle; D, daratumumab; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; MRD, minimal residual disease; NGF, next-generation flow cytometry; QW, weekly; Q4W, every 4 weeks; R, lenalidomide; Tec, teclistamab; V, bortezomib.

GMMG-HD10/DSMM-XX/MajesTEC-5: Conclusions

- Tec-DR[a] and Tec-DVR[a] induction was feasible, with very high and early clinical efficacy in patients with TE NDMM
- MRD negativity (10^{-5}) was achieved in 100% of MRD-evaluable patients after C3 and maintained in evaluable patients through C6
- No TEAE-related discontinuations and no new safety signals compared with individual regimen components
- Infections were common, 34.7% of patients had grade 3/4 infections, and no grade 5 events were reported
  - Infection prophylaxis, including Ig replacement, was adopted
- Stem cell mobilization was feasible with Tec-D(V)R[a]

Teclistamab in combination with daratumumab-based standard of care in patients with transplant-eligible NDMM demonstrates promising efficacy with unprecedented early MRD-negativity rates

[a]Dexamethasone was also administered in C1 and C2.
C, Cycle; D, daratumumab; d, dexamethasone; GMMG/DSMM, German-speaking Myeloma Multicenter Group/Deutsche Studiengruppe Multiples Myelom; Ig, immunoglobulin; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; R, lenalidomide; TE, transplant-eligible; Tec, teclistamab; TEAE, treatment-emergent adverse event; V, bortezomib.

Rezidiviertes Myelom

Belantamab Mafodotin, Bortezomib, and Dexamethasone vs Daratumumab, Bortezomib, and Dexamethasone in Relapsed/Refractory Multiple Myeloma: Overall Survival Analysis and Updated Efficacy Outcomes of the Phase 3 DREAMM-7 Trial

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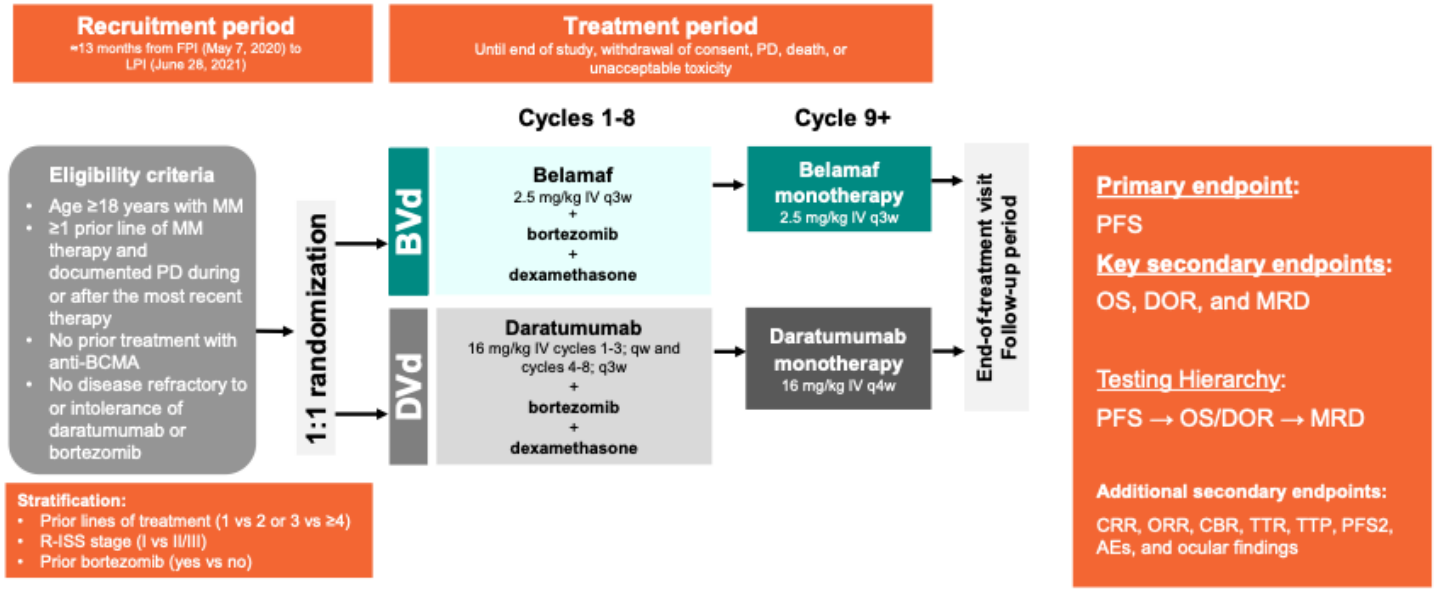
Presented at: 66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA, and virtual

NX-DE-BLM-PPT-240039, Dec 24

DREAMM-7: Study Design and Endpoints[1]

Combinations Were Followed by Belamaf vs Daratumumab Monotherapy at Cycle 9 and Beyond

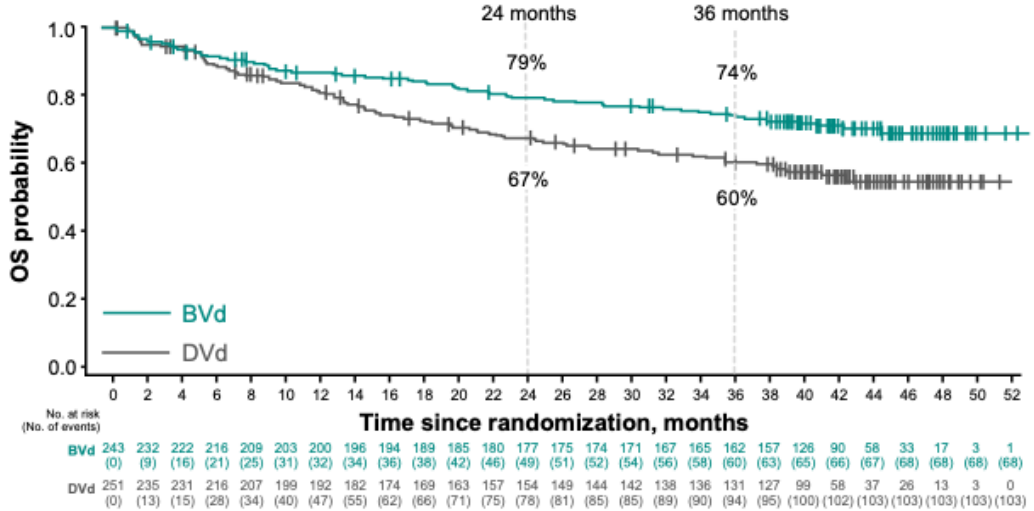


AE, adverse event; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; BVd, belantamab mafodotin, bortezomib, and dexamethasone; CBR, clinical benefit rate; CRR, complete response rate; DOR, duration of response; DVd, daratumumab, bortezomib, and dexamethasone; FPI, first patient in; IV, intravenous; LPI, last patient in; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on second line of therapy; q3w, every 3 weeks; q4w, every 4 weeks; qw, once weekly; R-ISS, Revised International Staging System; TTP, time to progression; TTR, time to response.

1. Hungria V, et al. *N Engl J Med*. 2024;391(5):393-407.

DREAMM-7: Overall Survival

BVd Had an Early, Sustained, and Statistically Significant OS Benefit vs DVd



OS[a]	BVd (N=243)	DVd (N=251)
Events, n (%)	68 (28)	103 (41)
OS, median (95% CI), months[b]	NR (NR, NR)	NR (41.0, NR)
HR (95% CI)[c]	0.58 (0.43-0.79)	
P value[d]	.00023	
24-month survival, % (95% CI)	79 (73-84)	67 (61-73)
36-month survival, % (95% CI)	74 (68-79)	60 (54-66)

Median OS was not reached.
Predicted median OS based on modeling is 84 months with BVd and 51 months with DVd.[e]

BVd, belantamab mafodotin, bortezomib, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; HR, hazard ratio; ITT, intention to treat; NR, not reached; OS, overall survival; R-ISS, Revised International Staging System.
[a] Two patients in the ITT population were randomized, not treated, rescreened, and rerandomized. They are counted as 4 unique patients in this output. [b] CIs were estimated using the Brookmeyer-Crowley method. [c] HRs were estimated using a Cox proportional hazards model stratified by the number of lines of prior therapy (1 vs 2 or 3 vs ≥4), prior bortezomib (no vs yes), and R-ISS stage at screening (I vs II or III), with a covariate of treatment. [d] *P* value is from a 1-sided stratified log-rank test. At 171 actual events (48.2% OS information fraction), OS was declared significant if the *P* value was <.00112. [e] Post hoc analysis was performed with simulation using an exponential distribution to predict median OS values in each arm using the observed data at this interim analysis 2, with a 39.4-month median follow-up, to extrapolate time to death in ongoing censored patients. Predicted median OS values are subject to change as data mature.

NX-DE-BLM-PPT-240039, Dec 24

Zusammenfassung

- **Neue IMWG Responsekriterien** mit pragmatischen Änderungen erwartet
- **Erstlinientherapie mit etablierten Quadruplettherapien etabliert**
- **Dexamethason sollte zurückhaltend eingesetzt werden**
- **Neue Immuntherapien hoch-effektiv in der Erstlinientherapie**
- **Rezidivtherapien mit zahlreichen neuen Optionen am Horizont** (ADC-Revival, neue CARs und Bispecifcs)

Danke!

Heidelberg, Germany

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