International Myeloma Society
21ST ANNUAL Meeting & Exposition

September 25-28, 2024 • Riocentro • Rio de Janeiro, Brazil

Newly Diagnosed

TE

NOA LAVI

NDMM-TE

Induction (other then Dara-based Quadruplet):

- **GEM-Bela-VRd trail** - phase 2 Bela-VRd for NDMM TE

Upfront ASCT (vs No ASCT in 1st line):

- Efficacy and safety of Isa-KRd induction before response-adapted consolidation in transplant eligible NDMM: an interim analysis of the **IFM2020-02 MIDAS study**

Maintenance:

- **[CASSIOPEIA- MRD Update]**
- Dara-Len vs Len Alone as Maintenance Therapy in NDMM After Transplant: Primary Results from the **Phase 3 AURIGA Study**
- Phase II study – Iberdomide maintenance therapy
- Maintenance cessation

Belantamab Mafodotin in Combination with VRd for the Treatment of Newly Diagnosed Transplant Eligible Multiple Myeloma Patients: Results from the Phase II, Open Label, Multicenter, GEM-BELA-VRd Trial

González-Calle V; Rey-Bua B; Puertas B; Rodríguez Otero P; de la Rubia J; de Arriba F; Cabañas Perianes V; González E; Ocio EM; Encinas C; Suárez Cabrera A; Bargay J; Martínez-López J; González MS; Hernández-Rivas JA; Rosiñol L; Hernández MT; Paiva B; Cedena T; Puig N; Lahuerta JJ; Bladé J; San-Miguel JF; Mateos MV

On behalf of GEM-PETHEMA

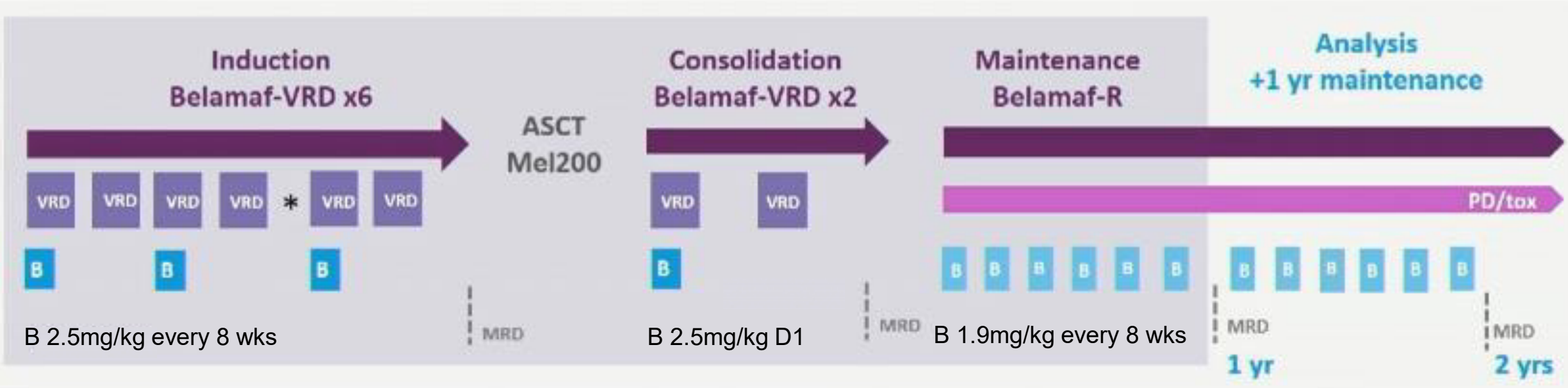
Background

- Treatment of transplant-eligible newly diagnosed myeloma patients (TE NDMM) involves induction, autologous stem cell transplantation (ASCT), +/- consolidation and maintenance [1]
- Quadruplet combinations are currently stardard of care (SOC) in TE NDMM pts. The addition of anti-CD38 moAbs to VRd deepen responses without impairing safety [2]
- In the Spanish trial GEM 2012, it was demonstrated that VRD is effective and well-tolerated for TE NDMM [3]
- BCMA is an optimal immune target. Antibody-drug conjugated belantamab mafodotin (belamaf) in combination has shown to be superior to other SOC in the relapse setting in two ph3 trials, [4,5] in one of them, compared to antiCD38 MoAbs combinations [4]
- The role of belamaf in the frontline setting with transplant eligible patients is not well established, with this aim, the Spanish myeloma group conducted GEM-BELA-VRd trial

1-Dimopoulos MA et al. Ann Oncol, 2021; 2-Sonneveld P et al NEJM, 2024; 3-Rosiñol L et al. Blood, 2019; 4- V. Hungria, P. NEJM 2024; 5-Dimopoulos MA et al. NEJM 2024.

Study design GEM-Bela-VRD:

phase II, open label, multicenter, non-randomized single arm clinical trial



VRD (bortezomib 1.3 mg/m² (subcutaneous) on days 1, 4, 8, and 11 of each cycle; lenalidomide 25 mg/d on days 1 to 21; and dexamethasone 40 mg on days 1 to 4 and 9 to 12) at 4-week intervals for 6 cy.

R (Lenalidomide 10 mg/day on days 1-28 continuously (may increase up to 15 mg/day) until PD or patient withdrawal.

Belantamab **2.5 mg/kg iv every 8 wks** (on day 1 of cycles 1, 3 and 5 of induction and on day 1 of cycle 1 of consolidation)

Belantamab **1.9 mg/kg iv every 8 wks** until PD, patients withdrawal, death or up to **two years as maintenance**

* *Stem cell mobilization and collection*

Primary endpoint: Safety (ocular events, KVA scale, AEs CTCAE v 4.0)

Key secondary endpoints: ORR, CR rate, MRD rate after induction, consolidation, maintenance, efficiency of CD34+ cells collection, PFS and OS

NCT04802356

Induction: ocular safety analysis
Changes in best corrected visual acuity (BCVA)

Ocular AEs were the most frequent: blurred vision (any grade 89.6%; G3-4 41.7%); foreign body sensation (any 62.5%, G3-4 18.8%); dry eye (any 58.3%, G3-4 14.6%); eye irritation (37.5%, G3-4 8.3%); photophobia (31.3%, G3-4 8.3%) or eye pain (12.5%, G3-4 2.1%)

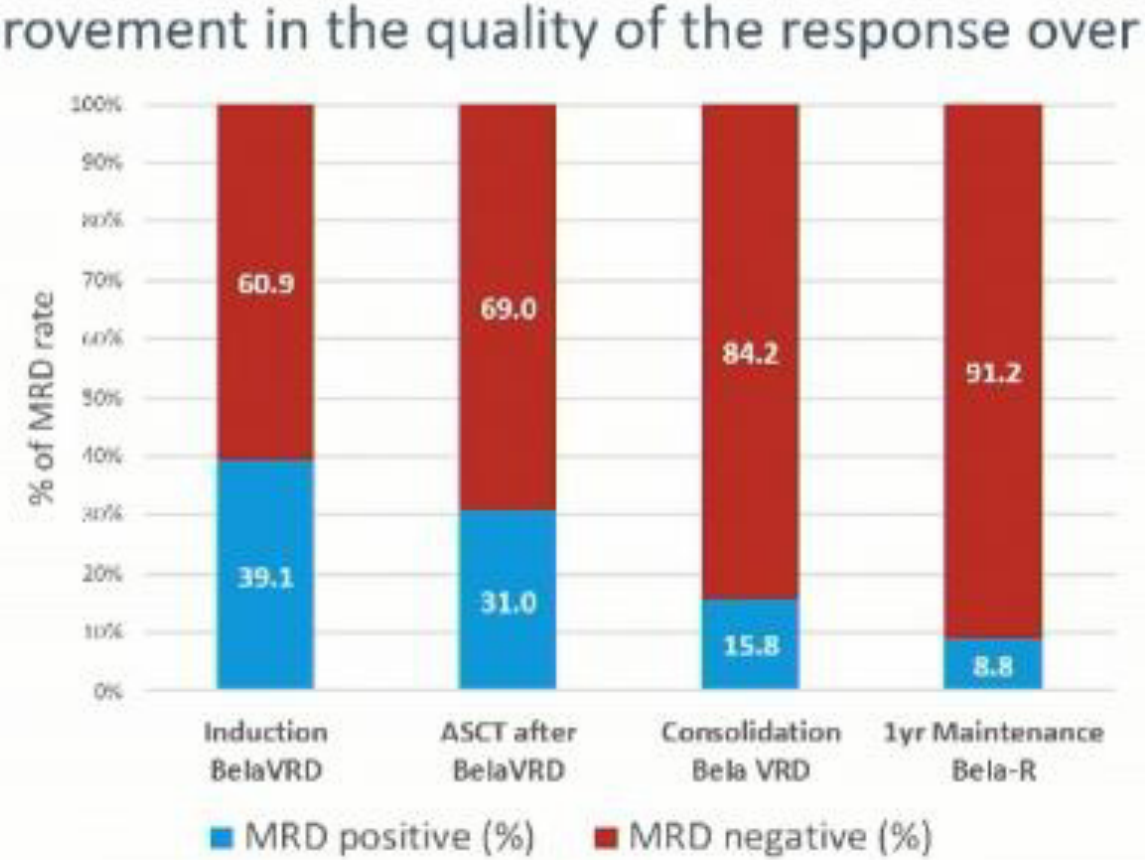
30% of patients had dose reductions, 48% had dose delays/interruptions, and 2% discontinued due to any ocular event during induction

1yr-maintenance: ocular safety analysis
Changes in best corrected visual acuity (BCVA)

Ocular AEs were the most frequent: blurred vision (any grade 72.9%; G3-4 33.3%); dry eye (any 56.3%, G3-4 27.1%); foreign body sensation (any 47.9%, G3-4 16.7%); photophobia (43.8%, G3-4 16.7%); eye irritation (29.2%, G3-4 10.4%) or eye pain (20.8%, G3-4 4.2%)

54% of patients had dose reductions, 70% had dose delays/interruptions, and 4% discontinued due to eye-related events and non-selective proteinuria during first year of maintenance

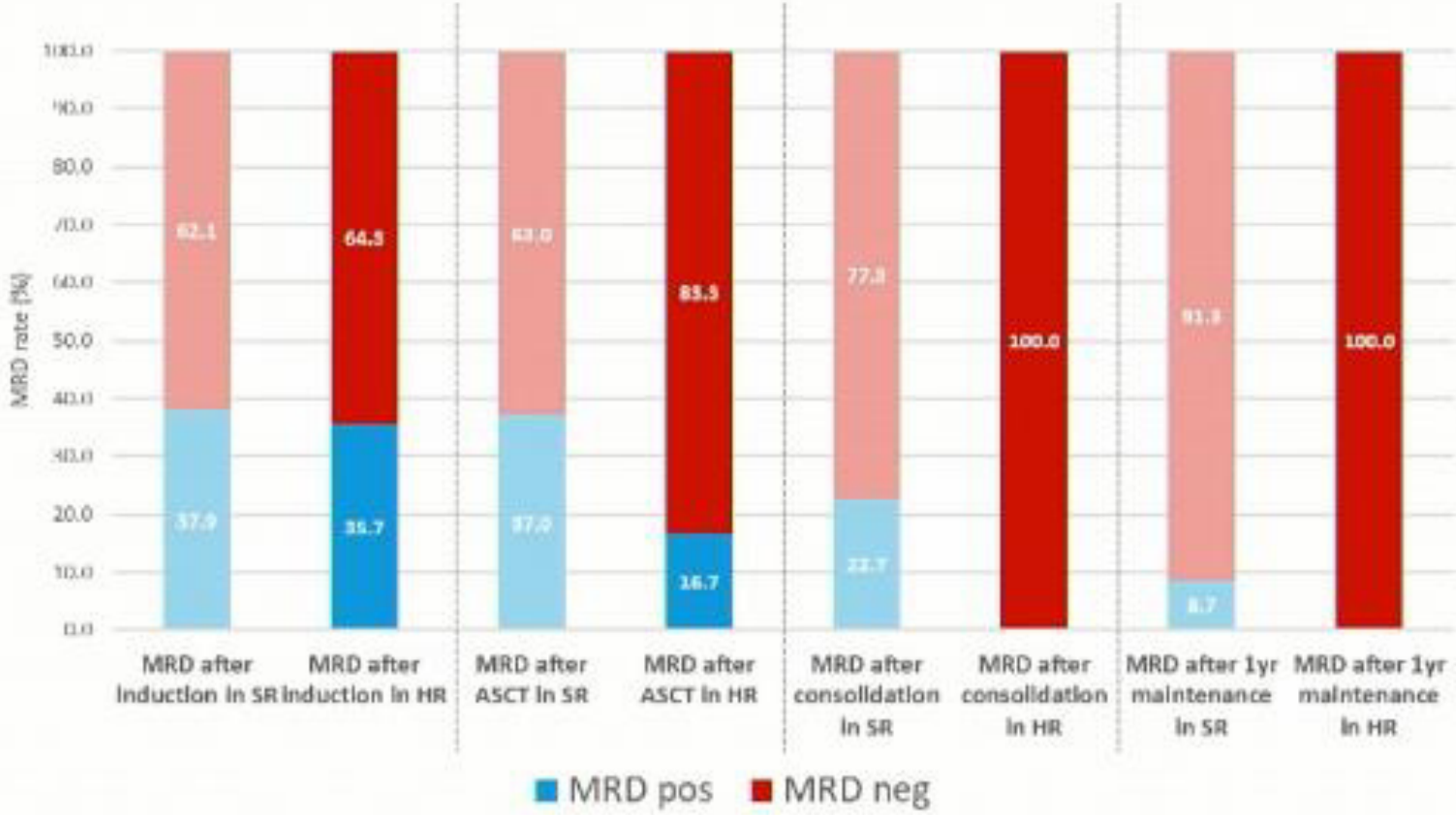
GEM-Bela-VRD: MRD analysis by flow cytometry in the evaluable patients across the different phases of treatment



[a]MRD: minimal residual disease. Negative MRD was defined as the proportion of patients who reached MRD negativity among those with available samples for MRD analysis by flow cytometry at different timepoints (sensitivity at least 10^{-5})

GEM-Bela-VRD: MRD analysis in the evaluable patients across the different phases of treatment by cytogenetic status

HR: high risk
(dark color)
SR: standard risk
(light color)

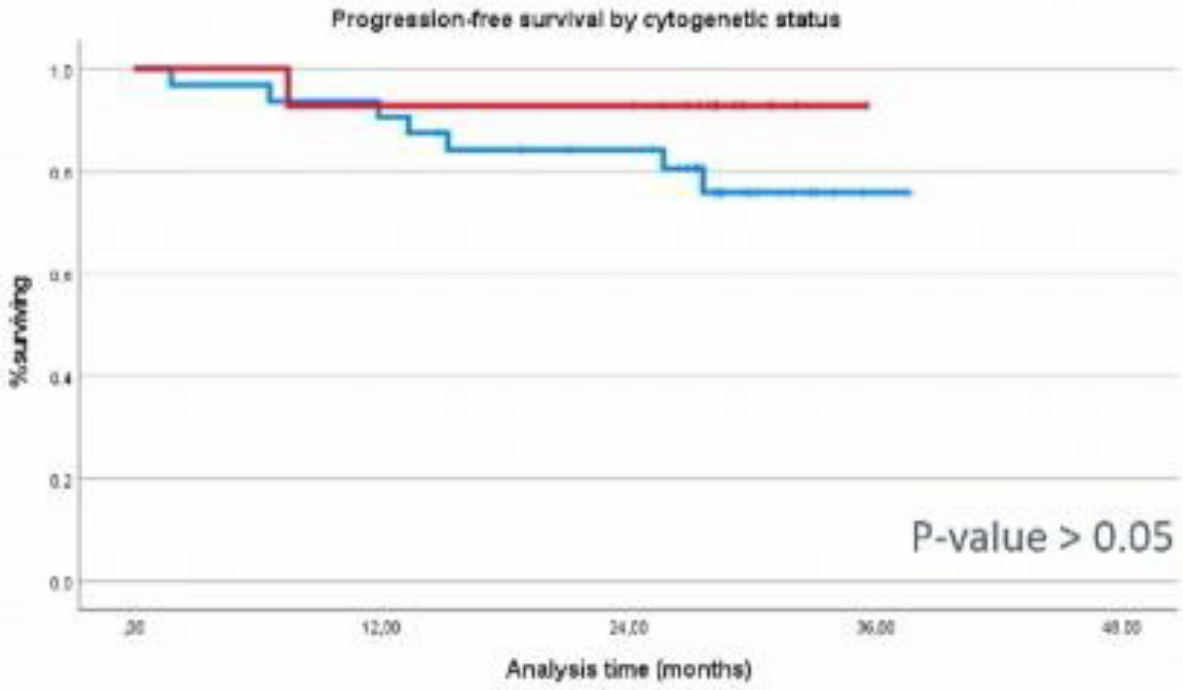


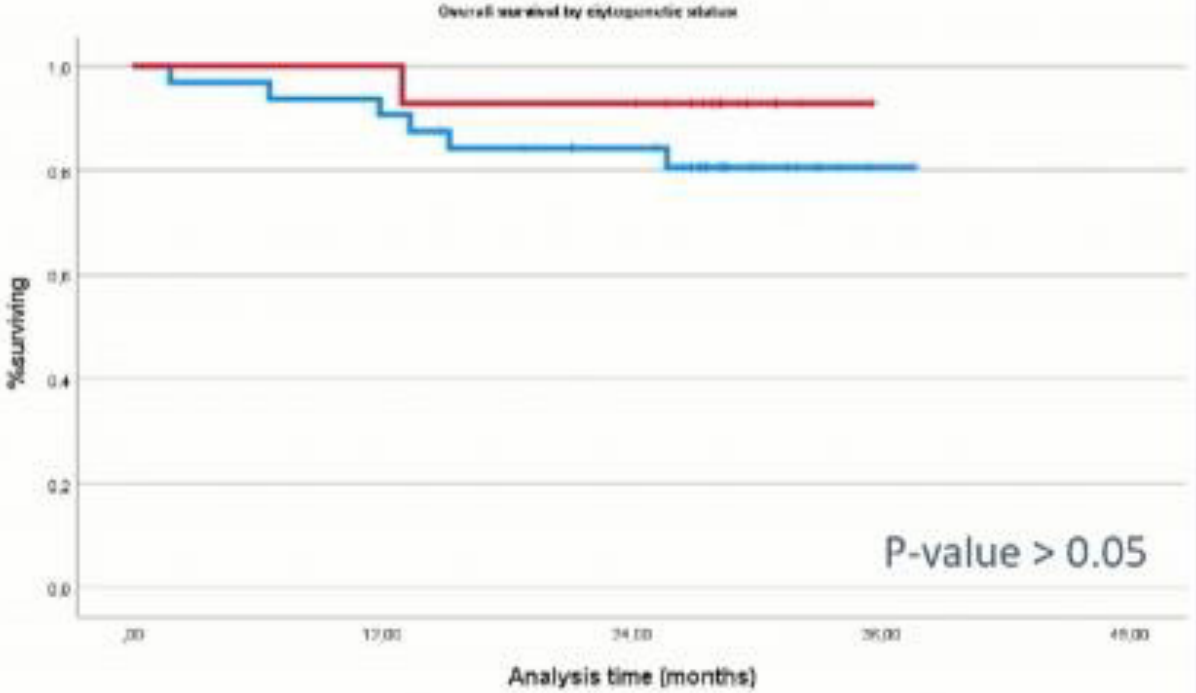
All patients with HR cytogenetics evaluable for MRD had negative MRD after consolidation and maintenance with belamaf-VRD

Cytogenetics (detected/no. studied, %)	
High risk*	14/46 (30.4)
del(17p) &	5/46 (10.9)
t(4;14) ¶	8/47 (17.0)
t(14;16) ¶	2/47 (4.3)

Gem-Bela-VRD
Efficacy analysis - PFS and OS by cytogenetic status

Median Follow-up 28.5 m (18.8-37.6)





High risk: (t(4;14), t14;16) or del(17p)
1/14 (7%) progressed (triple hit)
12m-PFS: 91% and 24m-PFS: 91%

Standard risk
7/32 (22%) progressed
12m-PFS: 91% and 24m-PFS: 82%

High risk: (t(4;14), t14;16) or del(17p)
1/14 (7%) died (triple hit)
12m-OS: 93% and 24m-OS: 93%

Standard risk
6/32 (19%) died
12m-OS: 91% and 24m-OS: 82%

International Myeloma Society

Conclusions

- The addition of belamaf to VRD in TE NDMM patients resulted in a safety profile consistent to that reported in other studies with VRD (GEM2012) or belamaf in combination
  - Consisted mainly of eye-related AEs manageable with dose modifications of belamaf
  - Expected hematological toxicity and respiratory infections, also due to the impact of the COVID -19 pandemic during trial recruitment and mainly during induction
- The efficacy of the combination seems to be encouraging
  - Depth of response improved over the treatment, with 82% of CR after 1yr of maintenance in the ITT population, and 91% of evaluable patients with MRD negative rate
  - Similar CR, MRD rate, PFS and OS were observed in MM patients with high-risk cytogenetics
- Maintenance is ongoing and further analysis after completing 2 years of maintenance are planned

Efficacy and safety of Isa-KRD induction before response-adapted consolidation in transplant eligible newly diagnosed multiple myeloma: an interim analysis of the IFM2020-02 MIDAS study

A Perrot, C Touzeau, J Lambert, C Hulin, D Caillot, L Karlin, B Arnulf, P Rey, L Garderet, M Macro, M Escoffre-Barbe, J Gay, T Chalopin, K Belhadj, JM Schiano, M Tiab, M Mohty, F Kuhnowski, J Fontan, S Manier, F Orsini-Piocelle, L Vincent, X Leleu, J Corre, P Moreau

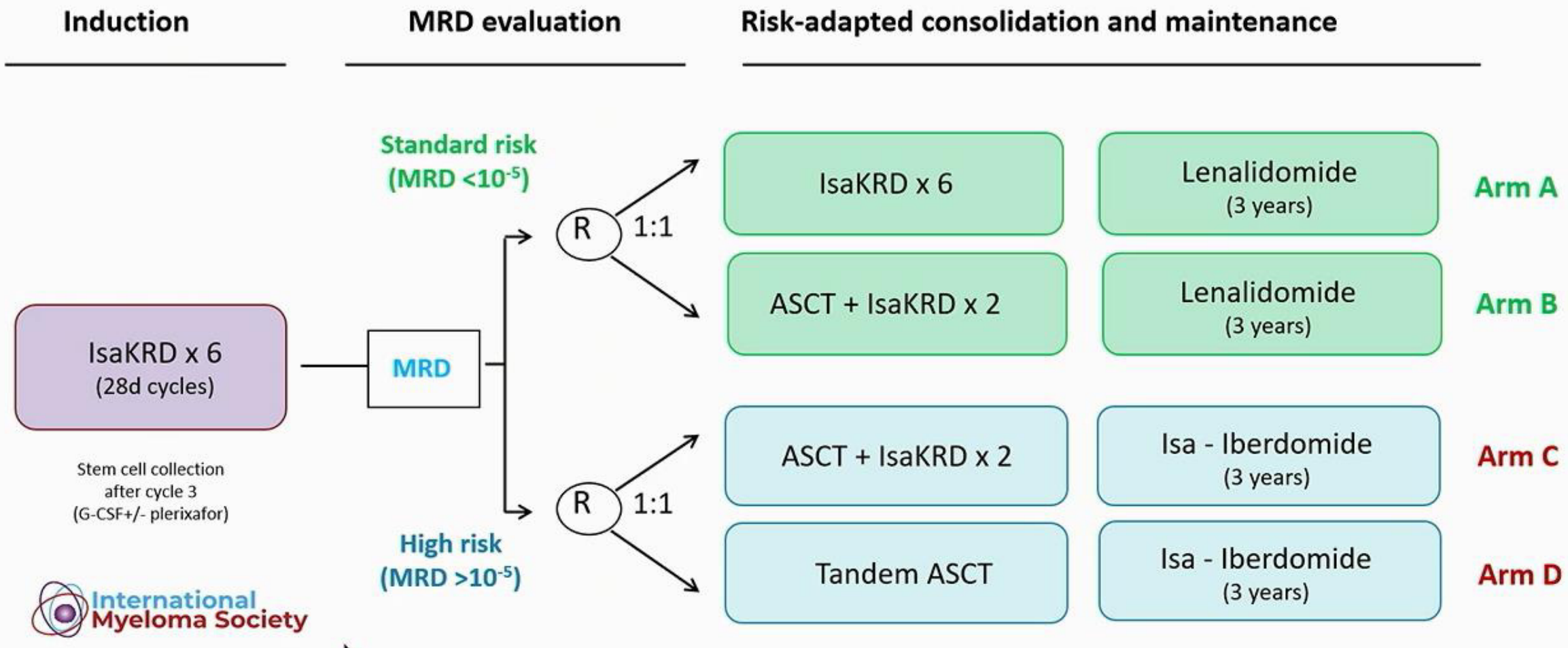
On behalf the IFM group

Background

- In patients with TE NDMM, induction therapy with a quadruple regimen before ASCT is standard.
- **Quadruplet regimens have revolutionized frontline therapy, significantly improving prognosis**.
  - CASSIOPEIA (*Moreau P et al., Lancet 2019*; *Moreau P et al., Lancet Oncol 2024*)
  - GRIFFIN & PERSEUS (*Voorhees PM et al., Lancet Haematol 2023*; *Sonneveld P et al. N Engl J Med 2024*)
  - IsKia (*Gay F et al. ASH 2023*)
- **To date, no prospective trials have compared upfront ASCT versus no ASCT following quadruplet induction. The role of upfront ASCT remains a topic of debate**, and risk-adapted strategies are needed to determine its utility after quadruplet induction.
  - Tools for stratifying risk: (R-)ISS, cytogenetics at diagnosis, depth of response/MRD
  - First trial on MRD-driven consolidation: MASTER phase 2 trial (*Costa LJ et al., Lancet Haematol 2023*)
- **The phase 3 IFM2020-02-MIDAS trial is an ongoing study assessing a MRD-adapted consolidation and maintenance strategy following IsaKRD induction.**
- **Here, we present the efficacy and safety data of this induction regimen.**

Study design

MIDAS = MInimal residual Disease Adapted Strategy

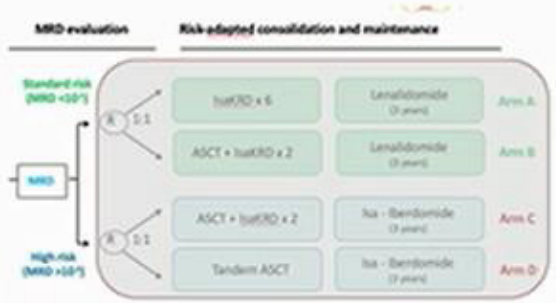


Study design

MIDAS = MInimal residual Disease Adapted Strategy

Induction

791 patients were included in 72 centers between 8 Dec 2021 and 10 Jul 2023



IsaKRD x 6
(28d cycles)

Stem cell collection
after cycle 3
(G-CSF+/- plerixafor)

Isatuximab 10 mg/kg C1: D1, D8, D15, D22
C2+: D1, D15

Carfilzomib C1: 20 mg/m² D1, then 56 mg/m² D8, D15
C2+: 56 mg/m² D1, D8, D15

Lenalidomide 25 mg/d, D1-D21

Dexamethasone 40 mg weekly

MRD-negativity rates after induction

MRD was evaluated at C6D28 in 751 patients, regardless of response

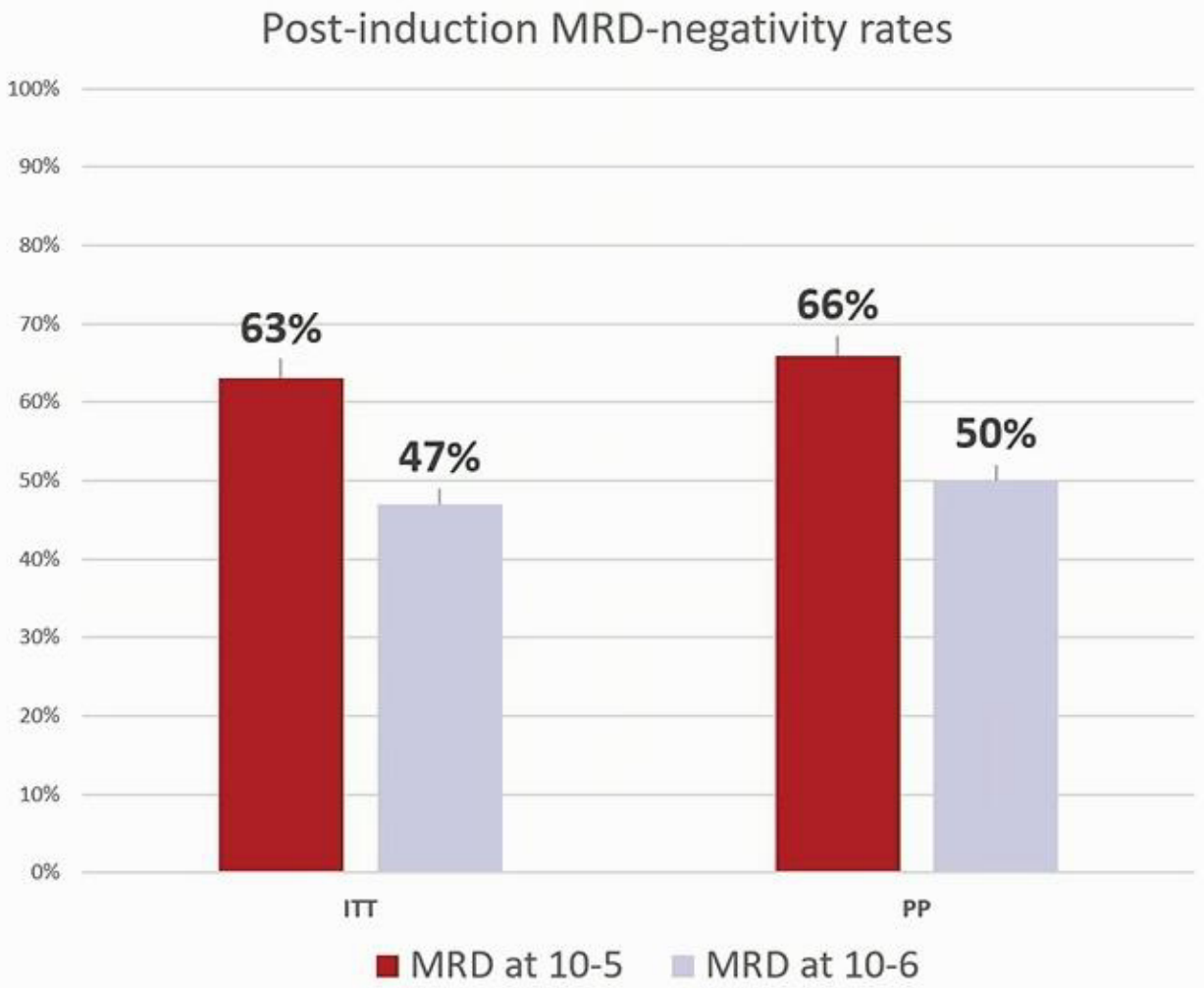
- primarily using NGS
- flow cytometry for 16 patients

MRD-negativity rate: 63% at 10^{-5}

Subgroup analyses of MRD-negativity

No significant differences according to:

- Age
- ISS stage
- R-ISS stage
- R2-ISS stage
- IFM LP score
- IMS/IMWG consensus definition



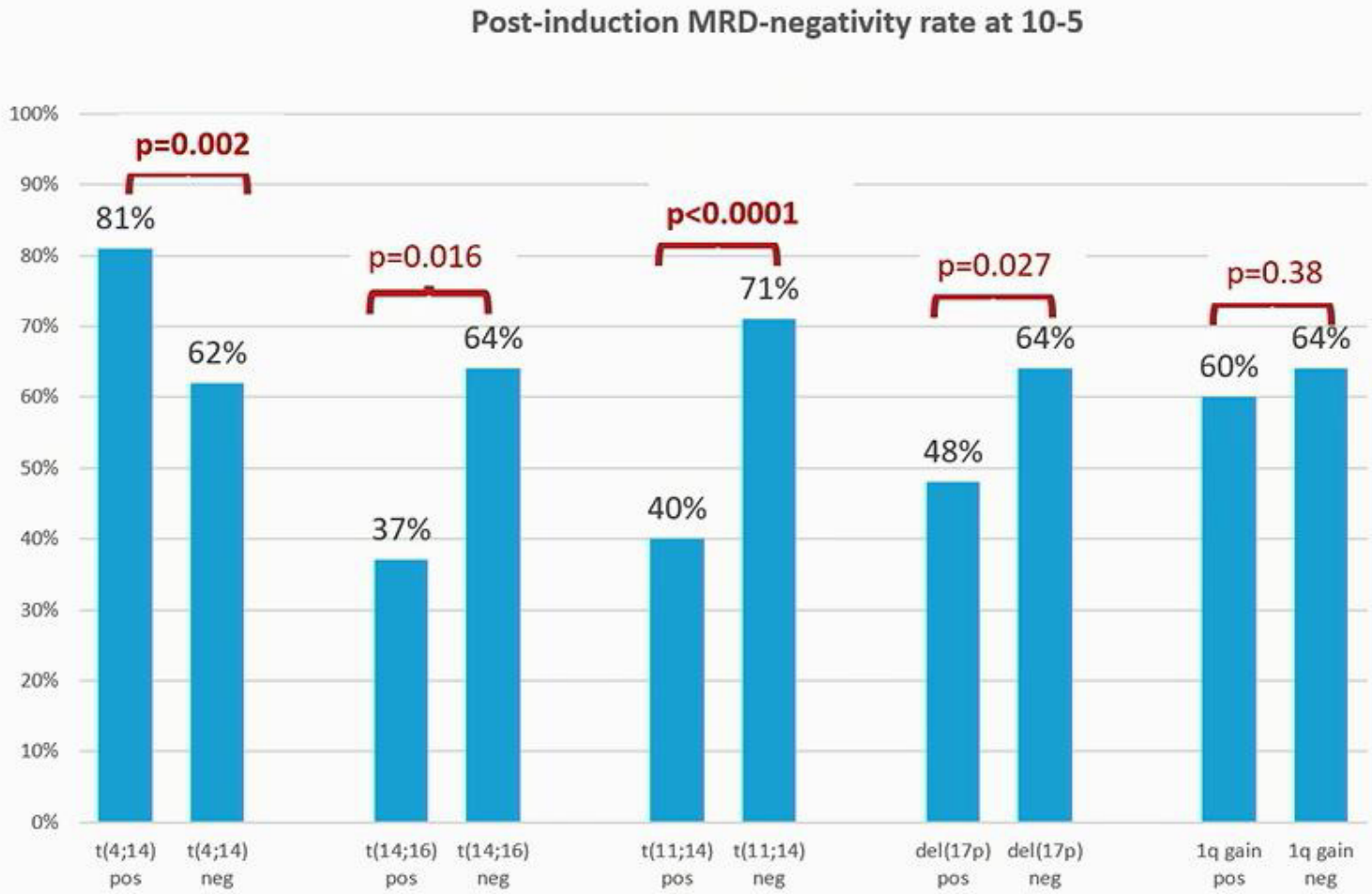
Subgroup analyses of MRD-negativity

Interesting variability across some cytogenetic groups

MRD-negativity rate after induction (sensitivity level 10^{-5}):

- **t(4;14): 81%**
- **t(11;14): 40%**
- **t(14;16): only 7 patients**
- **del(17p): 48%**

Post-consolidation results and kinetics are pending



Conclusion - Perspectives

- **The MIDAS trial was designed to tailor therapy based on MRD status after 6 cycles of IsaKRD**
- **Our findings confirm that six cycles of IsaKRD induce exceptionally high response and MRD-negativity rates, not only at a sensitivity of 10^{-5} but also at 10^{-6}**
- **These rates are the highest reported to date:**
  - **MRD-negativity rate at 10^{-5} = 63%** (35%, 22%, 45% in CASSIOPEIA, GRIFFIN, IsKia trials, respectively)
  - **nCR/CR rate = 64-66%** (41% after GMMG HD7 induction; *Goldschmidt H et al., Lancet Haematol 2022*)
- **MRD status after induction does not appear to align consistently with initial cytogenetic risk**: a longer follow-up is needed to better interpret the significance of achieving MRD-negativity in patients with different cytogenetic abnormalities
- **IsaKRD induction ensures successful stem cell collection, with no new safety signals**
- **Further follow-up of the MIDAS cohort is required to confirm these benefits in the final analysis**

HOSPITAL UNIVERSITARIO DE SALAMANCA

IBSAL Instituto de Investigación Biomédica de Salamanca

CIC Centro de Investigación del Cáncer

University of Salamanca

Maintenance approaches post-trasplant

- If our final goal is to reach MRD-ve with high sensitivity level and sustained over time, what would be the best approach after induction with PI, IMiD and antiCD38 to upgrade the response?
  - —Daratumumab-lenalidomide assuming most patients will be exposed or
  - —New CELMoD's like Iberdomide
  - —T cell redirecting therapy: CAR-T or Bispecific monoclonal antibody

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IBSAL

Subcutaneous Daratumumab Plus Lenalidomide Versus Lenalidomide Alone as Maintenance Therapy in Newly Diagnosed Multiple Myeloma After Transplant: Primary Results From the Phase 3 AURIGA Study

Ashraf Badros[1], Laahn Foster[2], Larry D Anderson Jr[3], Chakra P Chaulagain[4], Erin Pettijohn[5], Andrew J Cowan[6], Caitlin Costello[7], Sarah Larson[8], Douglas W Sborov[9], Kenneth H Shain[10], Rebecca Silbermann[11], Nina Shah[12,*], Alfred Chung[12], Maria Krevvata[13], Huiling Pei[14], Sharmila Patel[15], Vipin Khare[15], Annelore Cortoos[15], Robin Carson[13], Thomas S Lin[15], Peter Voorhees[16]

- To date, no randomized trial has directly compared DARA-based maintenance therapy versus SoC R maintenance therapy in TE patients with NDMM
- **Here, we report the primary results of the phase 3 AURIGA study that evaluated the addition of DARA to R maintenance in TE patients with NDMM who were anti-CD38 naïve and MRD positive[a] following ASCT after SoC induction/consolidation**

Presented by A Badros at the 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil

AURIGA: Study Design

- Objective: To determine the impact of adding DARA to R maintenance on MRD-negative conversion

Key eligibility criteria

- 18-79 years of age
- NDMM with ≥4 cycles of induction therapy and underwent ASCT within 12 months of the start of induction
- ≥VGPR at screening[a]
- MRD[b] positive (10^{-5}) post-ASCT
- No prior anti-CD38
- Randomization within 6 months of ASCT date

Stratification factor

- Cytogenetic risk[c] (standard risk/unknown vs high risk)

1:1 RANDOMIZATION (N = 200)

Maintenance: up to 36 cycles[d] (28-day cycles)

D-R

D: 1,800 mg SC[e] QW Cycles 1-2, Q2W Cycles 3-6, Q4W Cycles 7+

R: 10 mg PO daily Days 1-28 (after Cycle 3, 15 mg PO daily if tolerated)

R

R: 10 mg PO daily Days 1-28 (after Cycle 3, 15 mg PO daily if tolerated)

Primary endpoint

- MRD-negative (10^{-5}) conversion rate from baseline to 12 months after maintenance treatment
  - N = 214 planned to achieve ≥85% power to detect 20% improvement

Secondary endpoints

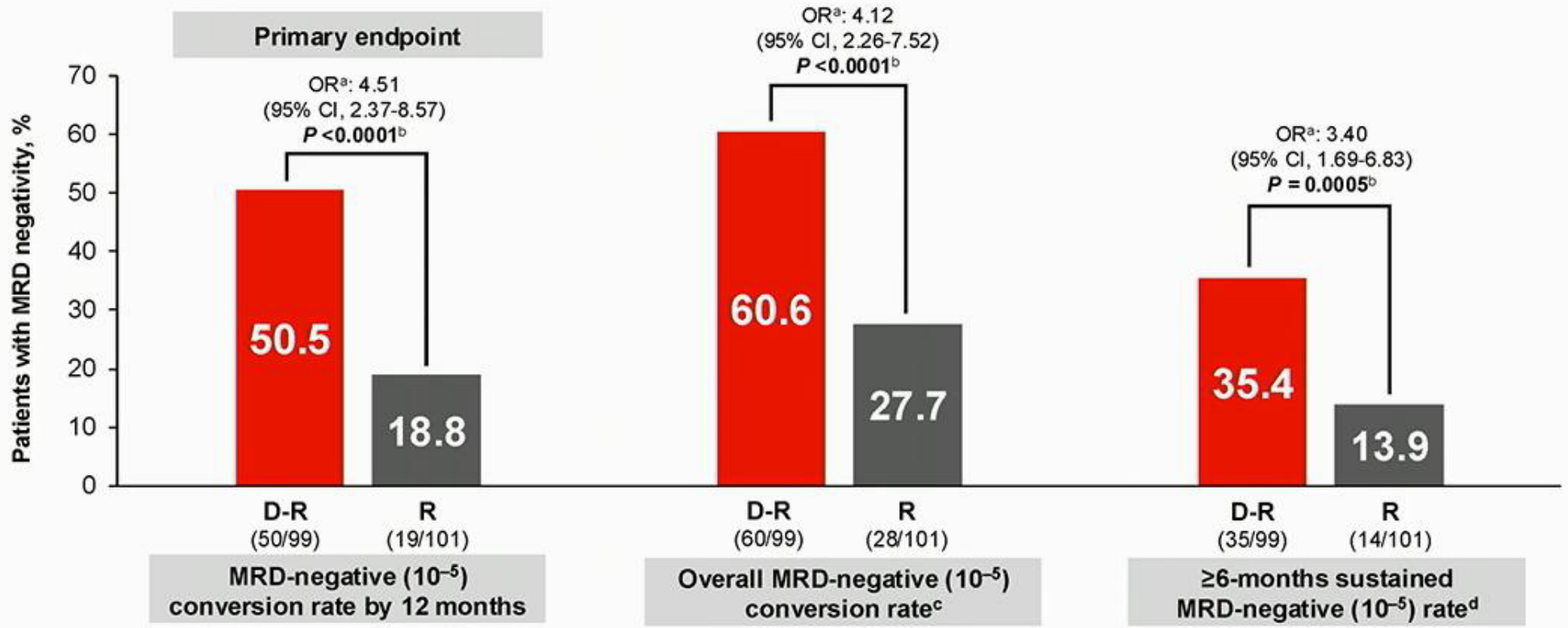
- PFS, overall MRD-negative conversion rate, sustained MRD-negative rate, response rates, duration of ≥CR, OS, safety

MRD[b] obtained after 12, 18, 24, and 36 cycles

Auriga phase 3 clinical trial is useful to give information about Response-adapted therapy
Patients included in the trial were AntiCD38 mAb-naïve

Presented by A Badros at the 21st International Society of Myeloma (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil

AURIGA: Increased MRD-negative Conversion Over Time and Sustained MRD Negativity at the 10^{-5} Threshold



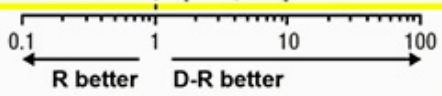
The addition of DARA to R more than doubled the MRD-negative conversion rate by 12 months

DARA more than doubled overall MRD-negative conversion rate and sustained MRD-negative rate

AURIGA: MRD-negative (10^{-5}) Conversion Rate From Baseline to 12 Months of Maintenance Treatment in Subgroups

- MRD-negative (10^{-5}) conversion rates by 12 months were consistently higher with D-R versus R across all clinically relevant subgroups

	D-R MRD-negative rate, n/N (%)	R MRD-negative rate, n/N (%)	OR (95% CI)
ITT (overall)	50/99 (50.5)	19/101 (18.8)	4.51 (2.37-8.57)
Sex			
Male	32/61 (52.5)	11/58 (19.0)	4.71 (2.06-10.78)
Female	18/38 (47.4)	8/43 (18.6)	3.94 (1.45-10.68)
Age			
<65 years	30/61 (49.2)	12/61 (19.7)	3.95 (1.76-8.85)
≥65 years	20/38 (52.6)	7/40 (17.5)	5.24 (1.86-14.74)
Race			
White	31/67 (46.3)	14/68 (20.6)	3.32 (1.55-7.10)
Black	12/20 (60.0)	4/24 (16.7)	7.50 (1.85-30.34)
Other	7/12 (58.3)	1/9 (11.1)	11.20 (1.04-120.36)
Weight			
≤70 kg	12/23 (52.2)	4/18 (22.2)	3.82 (0.96-15.18)
>70 kg	38/76 (50.0)	15/81 (18.5)	4.40 (2.14-9.03)
Baseline ECOG PS score			
0	20/45 (44.4)	9/55 (16.4)	4.09 (1.62-10.31)
≥1	30/54 (55.6)	10/46 (21.7)	4.50 (1.86-10.88)
ISS at diagnosis			
I	19/40 (47.5)	8/38 (21.1)	3.39 (1.25-9.19)
II	13/28 (46.4)	7/37 (18.9)	3.71 (1.23-11.25)
III	15/23 (65.2)	3/23 (13.0)	12.50 (2.83-55.25)
Cytogenetlc risk at diagnosis			
High risk[a]	7/22 (31.8)	1/15 (6.7)	6.53 (0.71-60.05)
Standard risk	35/63 (55.6)	14/66 (21.2)	4.64 (2.15-10.04)
Revised cytogenetic risk at diagnosis			
High risk[b]	14/32 (43.8)	4/30 (13.3)	5.06 (1.43-17.88)
Standard risk	28/52 (53.8)	12/53 (22.6)	3.99 (1.72-9.26)



Benefit favoring D-R in MRD-negative conversion rate was observed in patients with high-risk and standard-risk disease

[a]High-risk cytogenetics are defined as ≥1 abnormality including del[17p], t[4;14], or t[14;16]. [b]Revised high-risk cytogenetics are defined as ≥1 abnormality including del[17p], t[4;14], t[14;16], t[14;20], or gain/amp[1q21].

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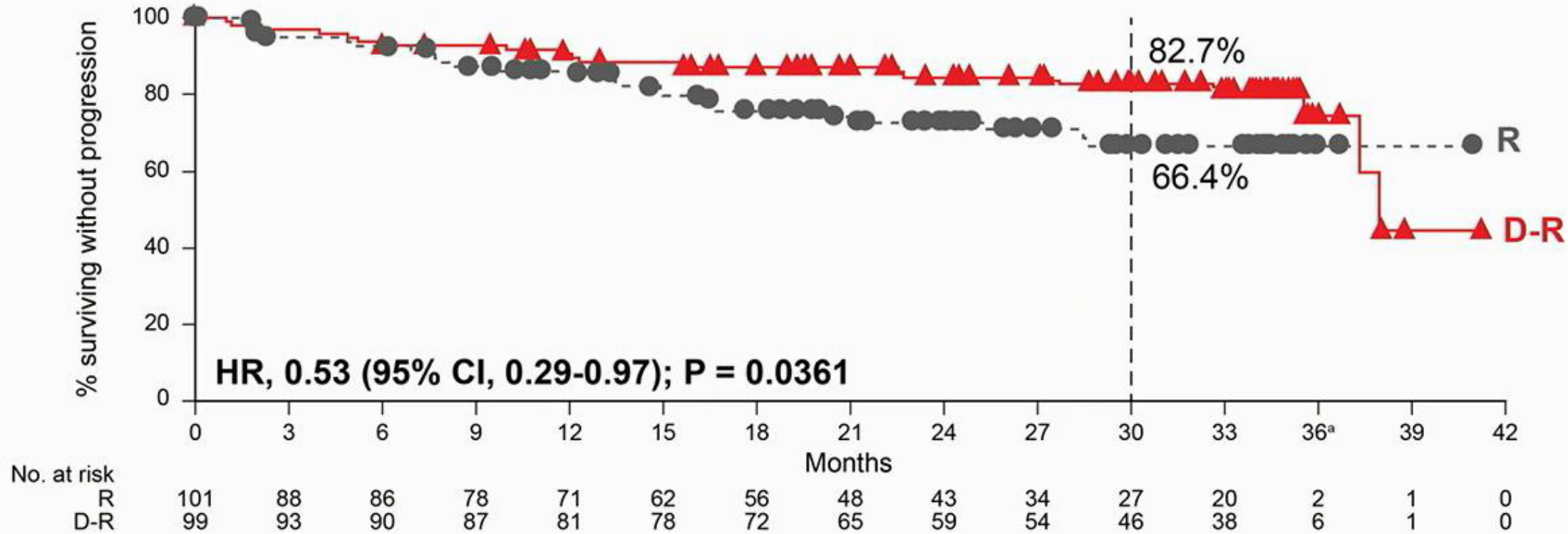
AURIGA: PFS in the ITT Population

- Median follow-up: **32.3** months



PFS favored D-R versus R, with a 47% reduction in the risk of disease progression or death

HR, hazard ratio. [a]Per study protocol, disease assessments stopped at the end of study treatment (Cycle 36), after which patients were only followed for survival. At the time of this analysis, the number of patients who reached end of study treatment was low, thus resulting in a low number of patients at risk.

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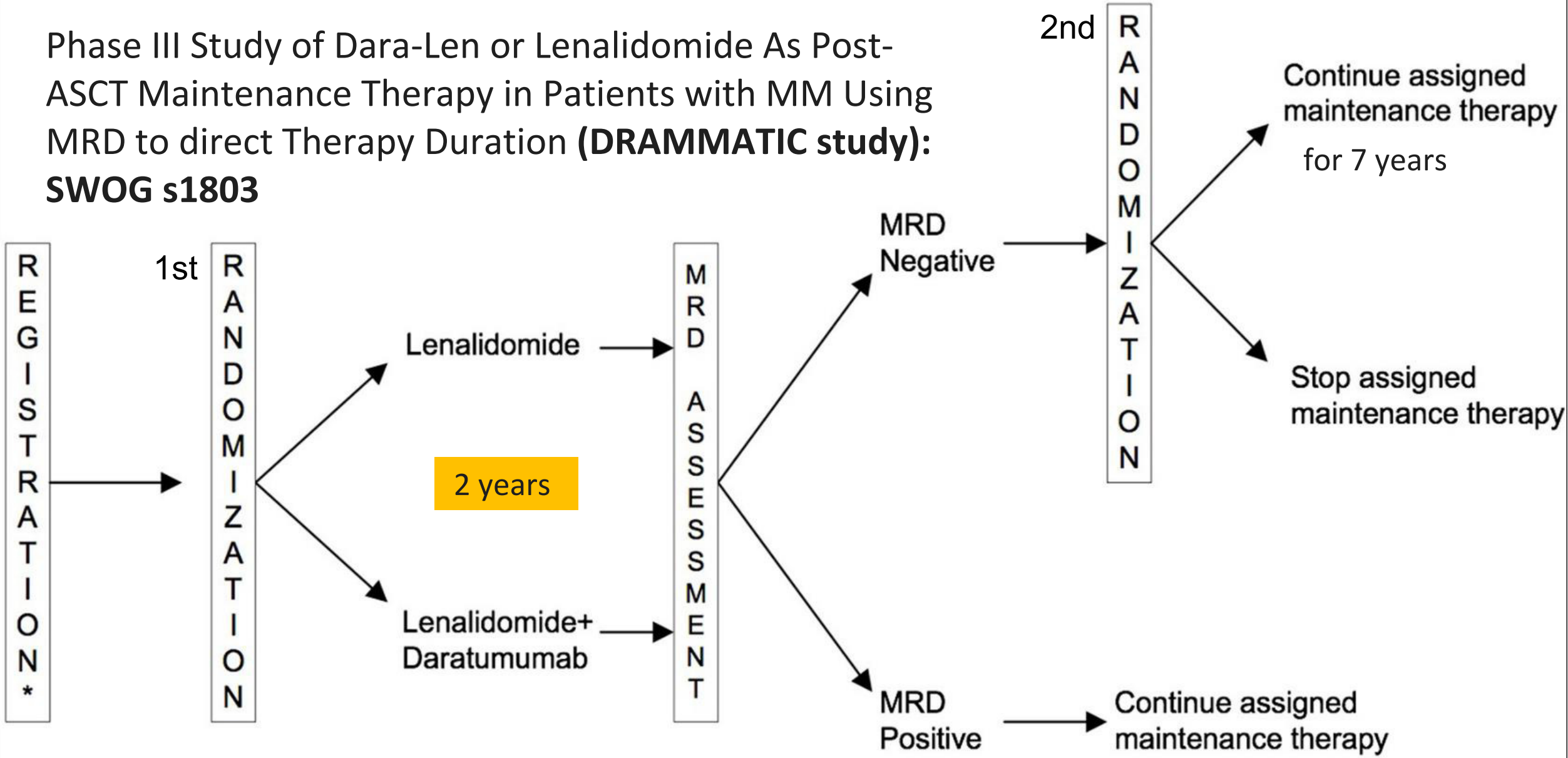
AURIGA: Conclusions

- In TE patients with NDMM who were anti-CD38 naïve and MRD positive post-ASCT, D-R maintenance versus R alone resulted in:
  - More than doubling of the MRD-negative conversion rate by 12 months and overall at 10^{-5}
  - Improved MRD-negative conversion rates by 12 months across subgroups and disease risk status at 10^{-5}
  - More than doubling of ≥6-month sustained MRD-negative rate at 10^{-5}
  - Quadrupling of MRD-negative conversion rate by 12 months at 10^{-6}
  - Further deepening of response rates
  - 47% reduction in the risk of disease progression or death, with a 30-month PFS rate of 83%
  - No new safety concerns

AURIGA data demonstrate the benefit of D-R maintenance therapy versus R alone in patients who were MRD positive after ASCT

Phase III Study of Dara-Len or Lenalidomide As Post-ASCT Maintenance Therapy in Patients with MM Using MRD to direct Therapy Duration **(DRAMMATIC study): SWOG s1803**



Prior daratumumab therapy is allowed

Phase II study of iberdomide maintenance therapy following autologous stem cell transplant in patients with multiple myeloma: results of a planned interim analysis

Tanya M. Wildes,[1] Vera J. Suman,[2] Marnee Strege,[1] Joseph Tario, Jr.,[3] Sarah A. Holstein[1]

[1]University of Nebraska Medical Center, Omaha, NE, USA; [2]Mayo Clinic, Rochester, MN, USA; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

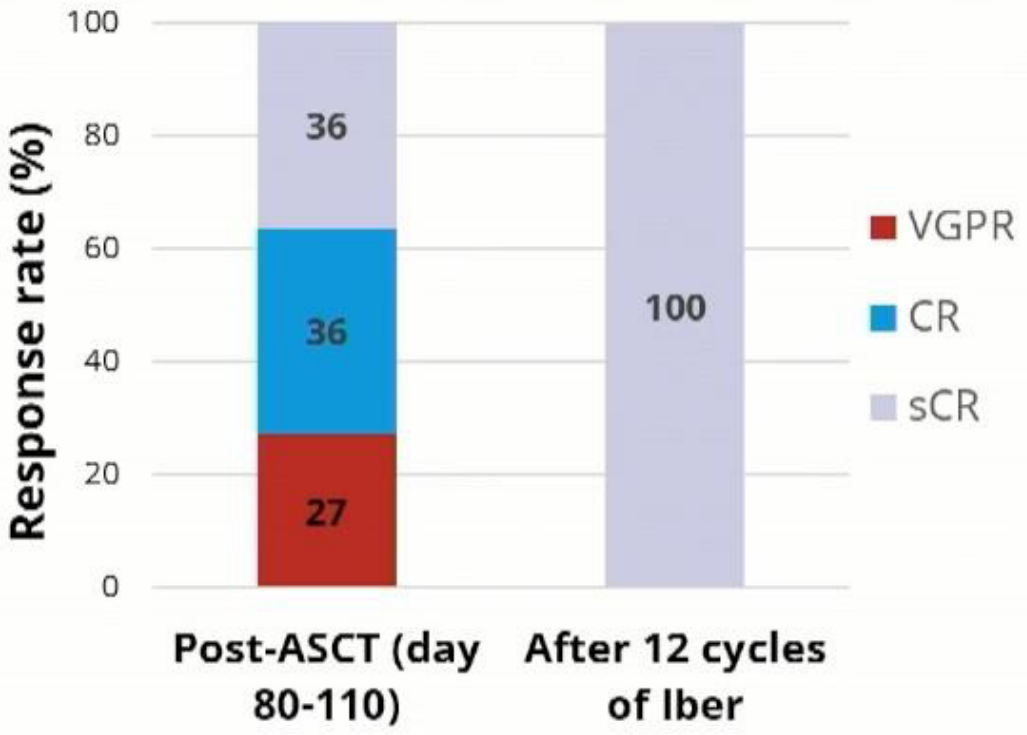
Background

- Lenalidomide (Len) maintenance post-ASCT is established as a standard of care based on CALGB 100104 and other randomized trials[1-4]
  - Meta-analysis demonstrated superior PFS (HR 0.48, 95% CI 0.41-0.55) and OS (HR 0.75, 95% CI 0.63-0.90) compared to placebo/observation[5]
  - Most common AEs include cytopenias, diarrhea, and infections and early treatment discontinuation remains a problem
  - Meta-analysis revealed only 70% remained on Len maintenance at one-yr and 54% at two-yrs[5]
- Iberdomide (Iber) is a novel, oral, potent cereblon E3 ligase modulator (CELMoD) under development in MM
  - Iber binds cereblon with higher affinity than Len, leading to more rapid degradation of target proteins and enhanced potency *in vitro*[6-7]
  - CC-220-MM-001 phase I/II trial established the MTD/RP2D of Iber alone and in combination with chemotherapy in patients with RRMM[8]
  - Ongoing trials are evaluating Iber in the NDMM setting, including as post-ASCT maintenance (EMN26)[9]

Here, we report the results of a planned interim analysis of a Phase II trial assessing Iber maintenance therapy after upfront ASCT in MM.

1. McCarthy et al., *NEJM*, 2012; 366:1770-1781; 2. Attal et al., *NEJM*, 2012; 366:1782-1791; 3. Palumbo et al., *NEJM*, 2014; 371: 895-905; 4. Jackson et al., *Lancet Oncol*, 2019;20:57-73; 5. McCarthy et al., *JCO*, 2017;35:3279-3289; 6. Matyskiela et al.,. *J Med Chem*, 2018;61:535-542; 7. Bjorklund et al., *Leukemia*, 2020, 34:1197-2001; 8. Lonial et al., *Lancet Haematol*, 2022, 9:e822-e832; 9. van de Donk et al., ASH 2023.

Response after one year of iberdomide maintenance



	N (%)
MRD-neg post-ASCT (day 80-110)	9/11 (82%)
MRD-neg after 1 yr of maintenance	10/11 (91%)
Sustained MRD-neg x 1 yr	8/9 (89%)
Conversion from MRD-pos to MRD-neg	2/2 (100%)

All Grade 2 or higher Treatment-related* AEs

Hematologic treatment-related AEs:

	Grade 2 n (%)	Grade 3 n (%)
Neutrophil count decrease	1 (9%)	5 (45%)
Febrile neutropenia	0	1 (9%)
Anemia	1 (9%)	0
White blood cell count decrease	4 (36%)	2 (18%)

Non-hematologic treatment-related AEs*:

	Grade 2 n (%)	Grade 3 n (%)
Infection	5 (45%)**	0
COVID-19	1 (9%)	0
Gastrointestinal	1 (9%)	0
Pneumonia	1 (9%)	0
Upper respiratory	5 (45%)	0
Diarrhea	1 (9%)	0
Rash	0	1 (9%)
Thromboembolic event	1 (9%)	0

*possibly, probably or definitely related to treatment;
No grade 4 toxicities were reported

**some pts had more than 1 infection

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Conclusions

- The planned interim analysis confirmed the initial feasibility of Iber maintenance post-ASCT, with all 11 patients completing the first year of maintenance, permitting continuation of the trial as planned
  - No new safety signals have been identified
- Promising efficacy with 100% sCR and 91% MRD-negativity after 1-yr of maintenance
- Study enrollment is nearing completion
- Longer follow-up will enable assessment of Iber maintenance duration, PFS, and rate of sustained MRD-negativity
- The results of this trial, the EMN26 trial, and ultimately the phase 3 EXCALIBER-Maintenance trial (Len vs Iber) will inform the potential role for Iber in the post-ASCT maintenance setting

Ongoing maintenance therapy may impact patient HRQoL outcomes – fatigue, diarrhea, and financial.

Current guidelines lack data on optimal duration of maintenance based on MRD status

Maintenance Therapy Cessation for Three-year Sustained MRD Negative Multiple Myeloma Patients

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Clinical Trial Design

Eligible Patients:

3 years of sustained MRD negativity* on maintenance, n=50

77%- stage 1
15% HR
43%- prior ASCT

*MRD tested by multiparametric flow cytometry (10^{-5})

Intervention:
Stop Maintenance + Surveillance
3 years

Surveillance:
Serum testing every 3 months
MRD testing on bone marrow every 6 months
PET-CT scan every 12 months

Correlatives:
Health-related QoL – (PROMIS-29 + GI) baseline, every 3 mo x 1 year, and then every 6 months
Microbiota + Immune Studies at baseline, 3 mo, 12 mo, 24, mo, 36 mo

Primary Endpoint:
Sustained MRD negative rate at 1 year

Secondary Endpoints:
-HRQoL
-Sustained MRD negative rate at 3 years
-Time to Event -PFS, EFS, and Duration of MRD response
-Re-treatment responses
-Microbiome and Immunosurveillance

Two-Stage Study Design:
-Stage 1: 15 patients*
-Stage 2: 35 patients
*Proceed to stage 2 if ≥8 remain MRD neg at 1 year

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Roshal M, et al. MRD detection in multiple myeloma: comparison between MSKCC 10-color single-tube and EuroFlow 8-color 2-tube methods. *Blood Adv*. 2017;1(12):728-732.

Duration of MRD Negative Response after Cessation

Primary Endpoint+	n\N(%)
MRD negative status at 12 months, n/N(%)*	33/39 (85%)**

MRD Negative Disease State at 24 months = 78% (95% CI 66-93%)

Treatment Free Survival after Cessation

TFS rate at 24 months - 81% (95% CI 69-96%)

Progression Free Survival after Cessation

PFS rate at 24 months - 89% (95% CI 85-100%)

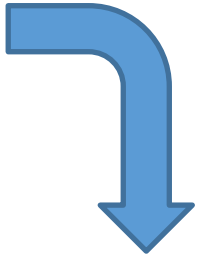
Duration of MRD Negative Response by Risk – SR vs. HR/NR after Cessation

MRD Negative Disease State at 24 months SR vs. HR/NR:

81% (95% CI 68-98%) vs. 67% (95% CI 42-100%), p=0.21

MRD Conversion after Cessation

	n\N(%)
MRD Negative Status among Evaluable**	31/43 (72)
MRD Conversion from Negative to Positive**	12/43 (28)
Stable MRD Positive without Clinical POD	7/12
Clinical POD	5/12
Median time for MRD conversion (months)	16 mo (6-49)



Asymptomatic Stable MRD Positive without Clinical POD	n=7
Patients who remained off therapy	3/7
• 2 pts re-tested MRD status, both remain positive • Median f/up since MRD positivity 6 months	
Patients who restarted maintenance (lenalidomide)	4/7
• 2 pts re-tested MRD status since restarting maintenance: -1 pt remains MRD positive -1 patient re-converted MRD negative • Median f/up since MRD positivity 14 months	

Conclusion

- Cessation of therapy is feasible in 3-year sustained MRD negative patients
  - **MRD negative rate at 1 year of stopping therapy is 33/39 (85%) – Primary Endpoint**
  - MRD Negative Disease State at 24 months = 78% (95% CI 66-93%)
  - PFS rate at 24 months - 89% (95% CI 85-100%)
- Asymptomatic MRD positive conversion, n=7
  - After restart of maintenance: 1 re-conversion to MRD neg; 1 remain MRD pos
  - No clinical PODs thus far
- Future
  - Ongoing efforts for QOL assessments and immune profiling, including microbiome analysis are underway
  - The SWOG 1803 randomizes maintenance continuation vs. discontinuation in two-year MRD negative sustained patients.