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Newly Diagnosed Multiple Myeloma: Evolving Strategies for Frontline Treatment to Achieve Deeper and More Durable Responses

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Disclosures

- **Amrita Krishnan, MD, PhD:** Advisory Board—AbbVie Inc.; consultant—Adaptive Biotechnologies, , AstraZeneca, BMS, Celgene, GlaxoSmithKline, Johnson & Johnson (Janssen), Pfizer, Regeneron, Roche, Sanofi, Stock BMS, ArcellX
- **Suzanne Lentzsch, MD, PhD:** Consultancy—Regeneron, Pfizer, Janssen, Takeda, GSK, BMS, Sanofi; research funding—Sanofi; royalties—anselamimab

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No product promotion or recommendation should be inferred.

Learning Objectives

- Describe the significance of risk stratification, transplant eligibility, and MRD status when considering optimal frontline therapy and subsequent treatment sequencing for the patient with MM
- Evaluate the most recent clinical trial data, evidence-based guidelines, and treatment implications associated with novel and emerging MM frontline therapies
- Assess and implement effective strategies to mitigate and/or manage AEs and address therapeutic resistance in MM treatment regimens to improve QoL and survival outcomes

MRD = minimal/measurable residual disease; MM = multiple myeloma; AE = adverse event; QoL = quality of life.

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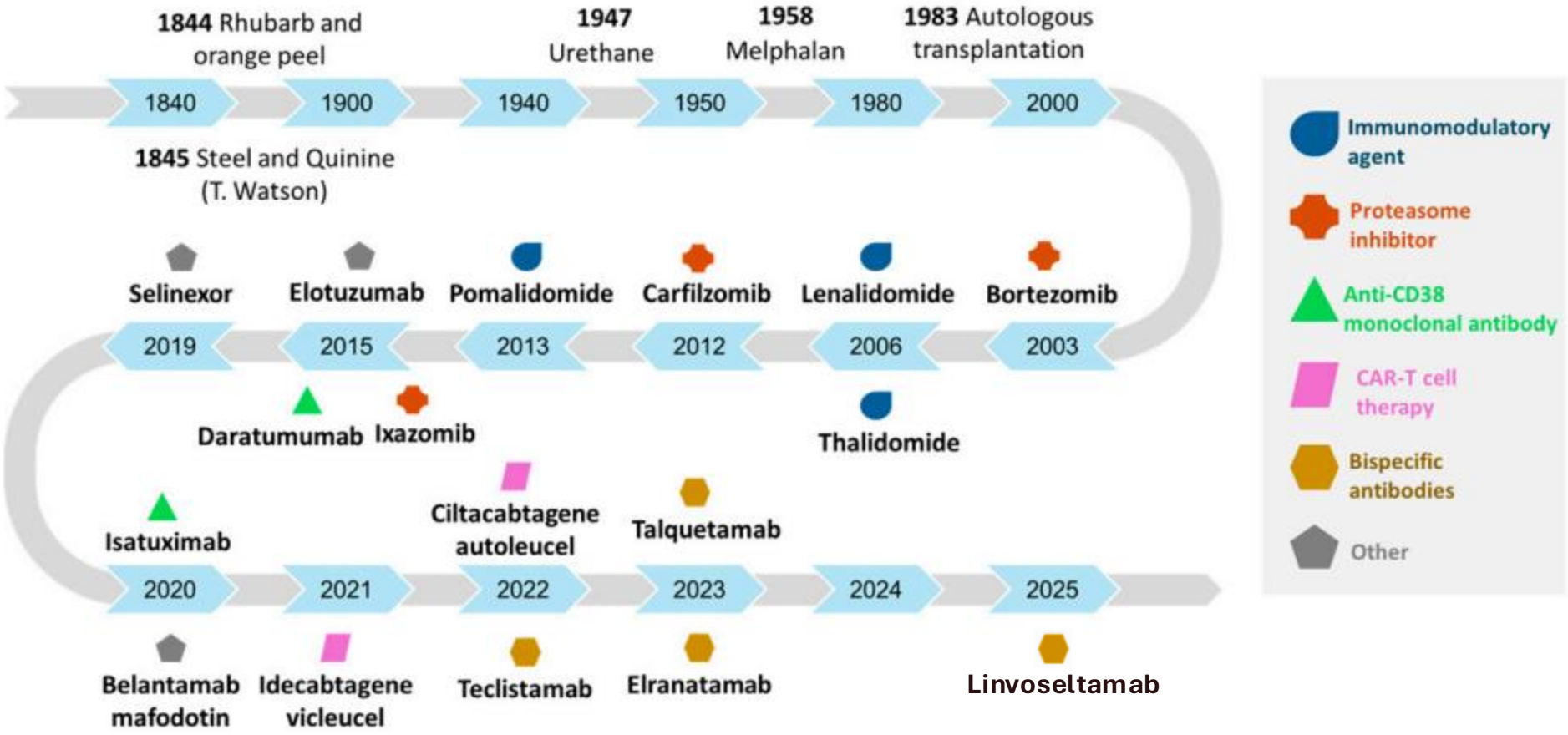
Multiple Myeloma Overview

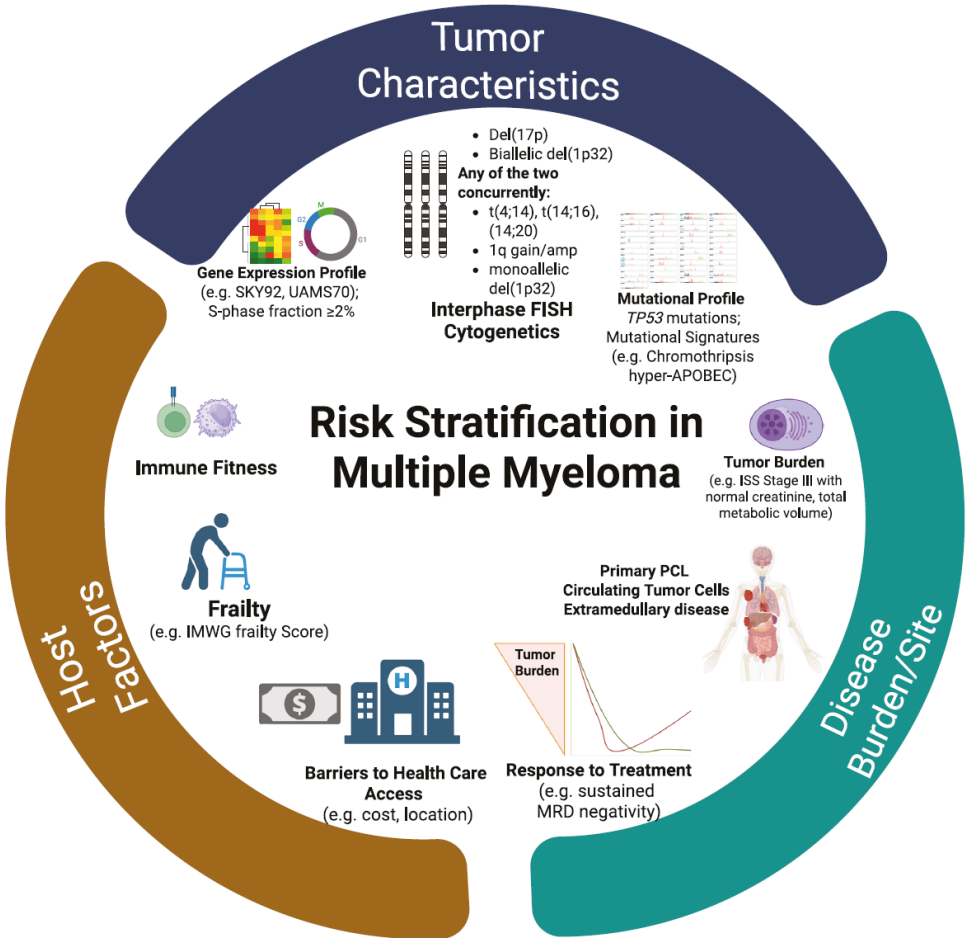
MM Care Evolution: Drugs by Year of FDA Approval



FDA = US Food and Drug Administration.
Adapted from Besliu C, et al. *Cancers*. 2025;17(3):525.

Approach to NDMM

- IMWG high-risk 2025
  - Deletion 17p and/or a TP53 mutation. Clonal cell fraction is 20%
  - IGH translocation—t(4;14), t(14;16), t(14;20)—with 1q gain and/or deletion of 1p
  - A monoallelic deletion of 1p with 1q additional copies or a biallelic deletion of 1p
  - Beta-2 microglobulin of at least 5.5 only when the creatinine is normal



NDMM = newly diagnosed multiple myeloma; IGH = immunoglobulin heavy chain; FISH = fluorescence in situ hybridization; ISS = International Staging System; IMWG = International Myeloma Working Group; PCL = plasma cell leukemia.

Zanwar S, Rajkumar SV. Leukemia. 2025 [Epub ahead of print]. Avet-Loiseau H, et al. *J Clin Oncol*. 2025;43(24):2739-2751.

Evolving Strategies in Transplant-Eligible NDMM

- Optimize 1st-line treatment
  - Induction, ASCT, consolidation, maintenance(doublet/triplet)
- Use effective drugs early
  - Daratumumab, isatuximab, VRd, KRd
- Introduce new complementary modalities
  - Bispecifics and CAR-T
- Intensify treatment for high-risk NDMM
- MRD monitoring and MRD-guided treatment
  - Escalate or stop treatment

ASCT = autologous stem cell transplantation; VRd = bortezomib, lenalidomide, dexamethasone ; KRd = carfilzomib, lenalidomide, dexamethasone.

NDMM: Many Options

- Quadruplet or triplet induction?
- CD38 ab: which one?
- Bortezomib or carfilzomib backbone?
- Transplant or no transplant?
- Len or doublet/triplet maintenance?
- Risk—new IMWG classification?
- Frailty/performance status
- Tumor burden/EM disease
- Comorbidities
- Non-clinical factors, eg, social/caregiver support

EM = extramedullary.

Risk Stratification and Staging

mSMART Classification
R-ISS Staging

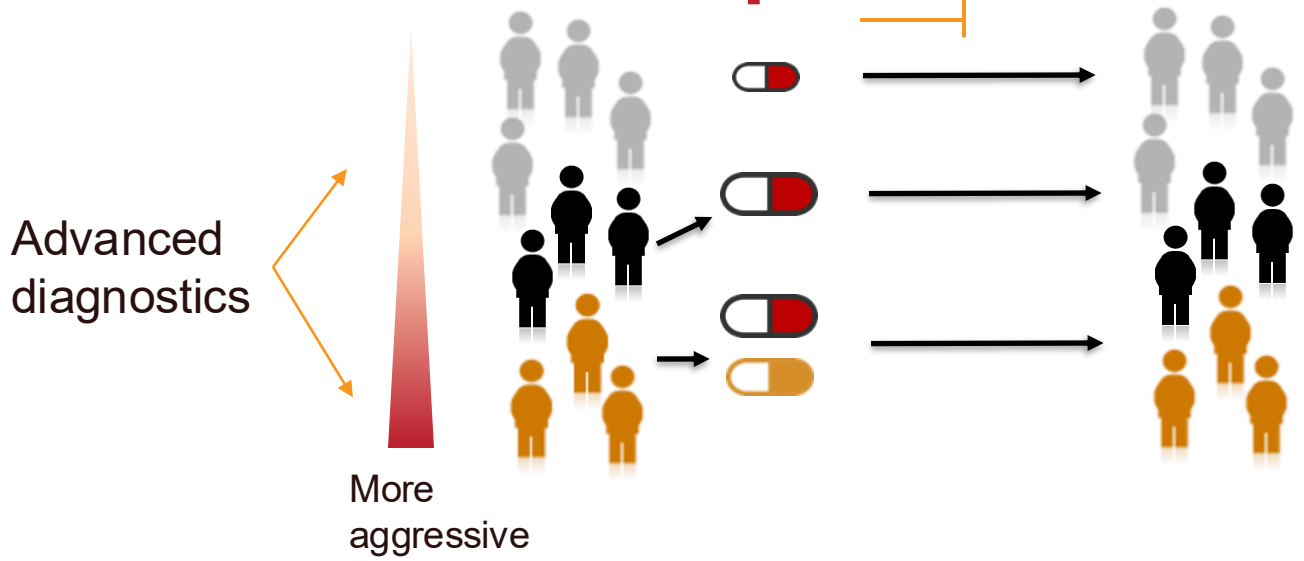
Risk Stratification and Staging

- Quadruplet regimens that include monoclonal anti-CD38 antibodies show unprecedented response rates, MRD negativity rates, and PFS in patients with NDMM[6-8]
- Even with quads → HRMM has significantly poorer survival outcomes than patients with SR disease[1-4]
- There are several definition of high-risk MM
  - ISS disease stage, LDH level, and del(17p), t(4;14), and/or 1q21+ have the greatest impact on PFS and OS2[2,3]
  - Co-occurrence of several HR aberrations/features leads to further deterioration of prognosis[1-4]
  - Functional HR characterized by relapse within 18 mos post-ASCT
  - MRD negativity correlates with improved PFS and OS in both SR and HRMM[5]

SOC = standard of care; HRMM = high-risk multiple myeloma; PFS = progression-free survival; LDH = lactate dehydrogenase; OS = overall survival; SR = standard-risk; OS2 = overall survival in second-line therapy; R-ISS = revised ISS.

1. Chalopin T, et al. *Br J Haematol*. 2021;194(3):635-638. 2. Schmidt T, et al. *Blood Cancer J*. 2021;11(4):83. 3. D'Agostino M, et al. *J Clin Oncol*. 2022;40(29):3406-3418. 4. Sonneveld P, et al. *Blood*. 2016;127(24):2955-2962. 5. Cavo M, et al. *Blood*. 2022;139(6):835-844. 6. Moreau P, et al. *Lancet Oncol*. 2021;22(3):e105-e118. 7. Costa LJ, et al. *J Clin Oncol*. 2022;40(25):2901-2912. 8. Voorhees PM, et al. *Blood*. 2020;136(8):936-945.

Ideal Risk-Adapted Treatment



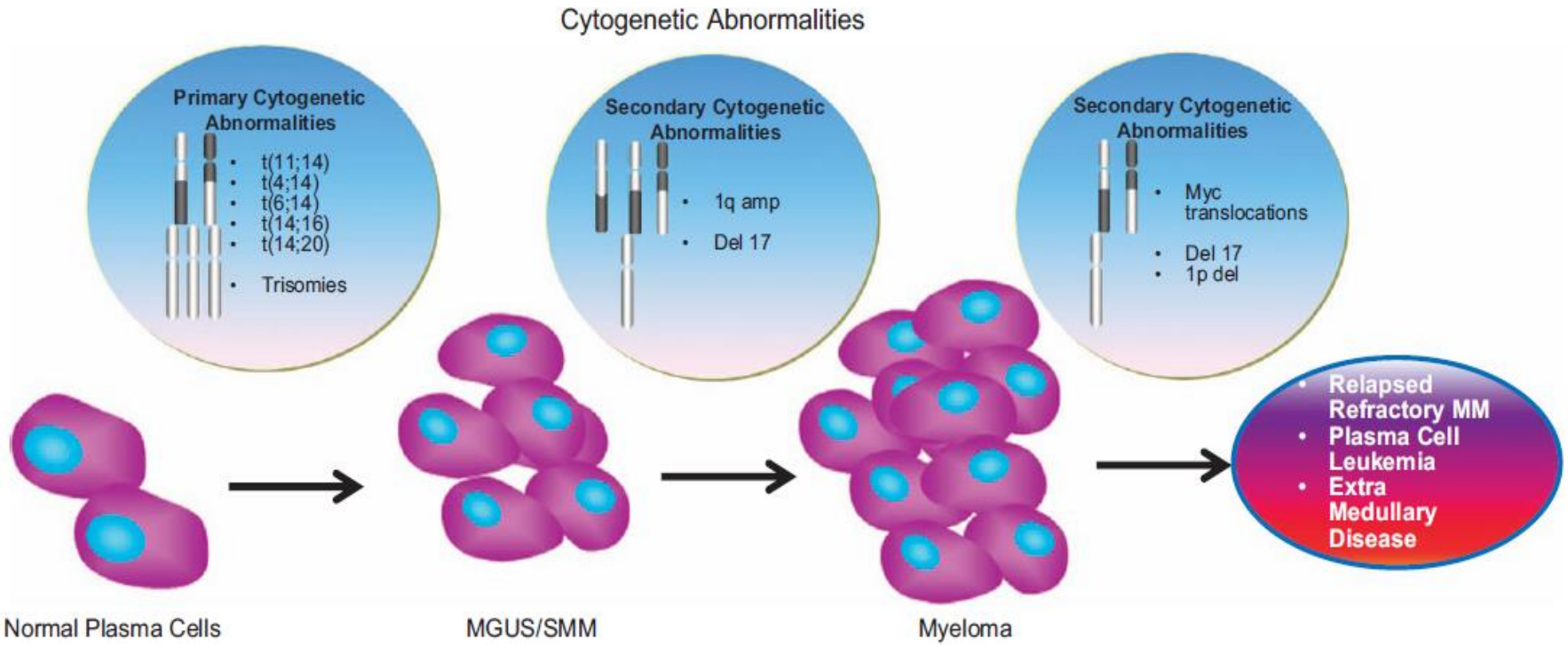
Better outcomes
Better patient experience
Better value for healthcare systems
Patient-centric allocation of resources

Risk Stratification and Staging

- Explosion of frontline treatments + advances in disease detection = need for consolidated definition of HRMM
- **Multiple ways to consider "risk"**
  - Frailty: IMWG frailty score
  - Tumor burden
  - CTCs at diagnosis and after treatment ("PRD")
  - MRD
  - Genetic lesions
  - Cytogenetics—no-hit, single-hit, double-hit
  - NGS
  - GEP
- **Combination approaches: the way of the future?**
  - PRD + MRD
  - IRMMa
  - SKY92

CTC = circulating tumor cell; PRD = peripheral residual disease; NGS = next-generation sequencing; GEP = gene expression profiling; IRMMa = Individual Risk Model for Myeloma.

High-Risk Cytogenetics in Myeloma



High-risk cytogenetic abnormalities on FISH

- t(4;14), t(14;16), del(17p), ??t(14;20)
- +1q (especially if ≥4 copies)
- del(1p)

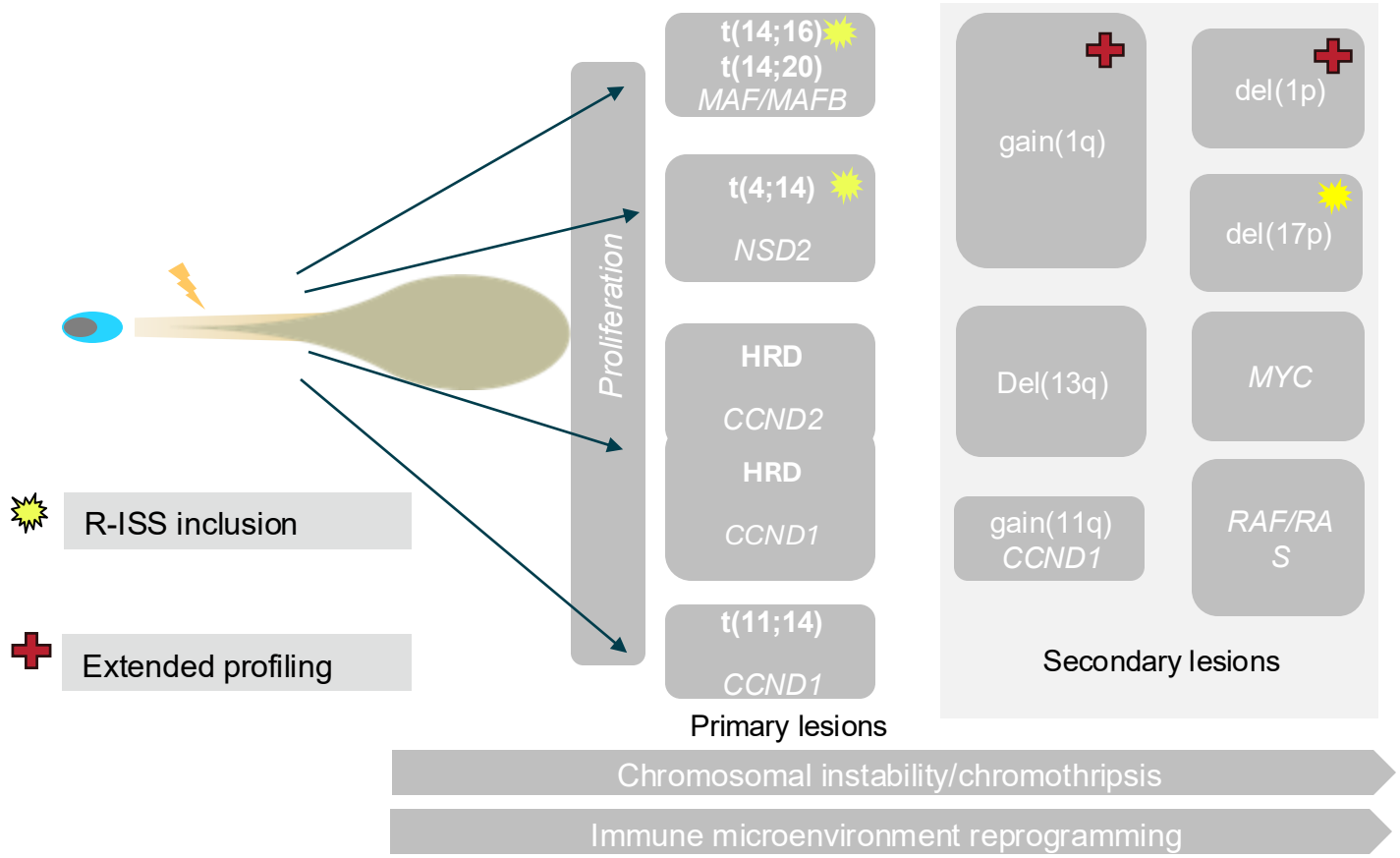
Rajan AM, Rajkumar SV. *Blood Cancer J*. 2015;5(10):e365.

R-ISS: First Attempts to Identify HRMM

Table 1. Standard Risk Factors for MM and the R-ISS

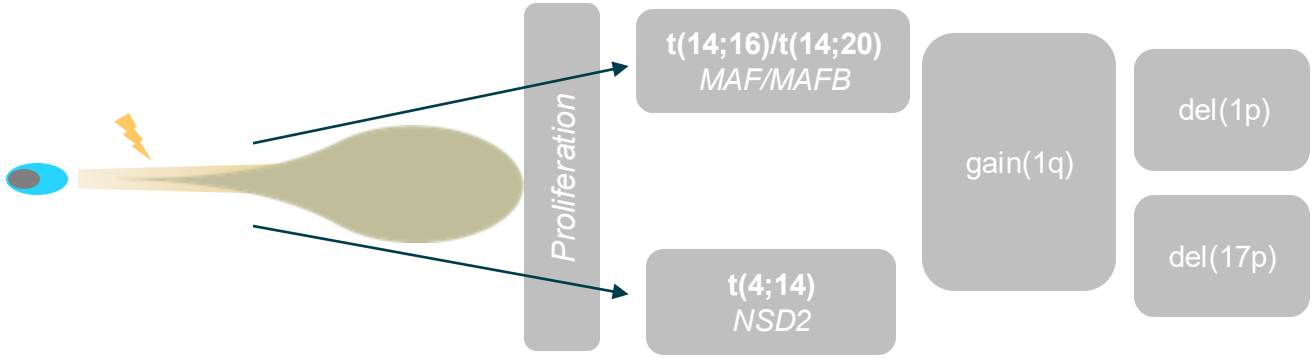
Prognostic Factor	Criteria
ISS stage	
I	Serum β_2-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
II	Not ISS stage I or III
III	Serum β_2-microglobulin ≥ 5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < the upper limit of normal
High	Serum LDH > the upper limit of normal
A new model for risk stratification for MM	
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

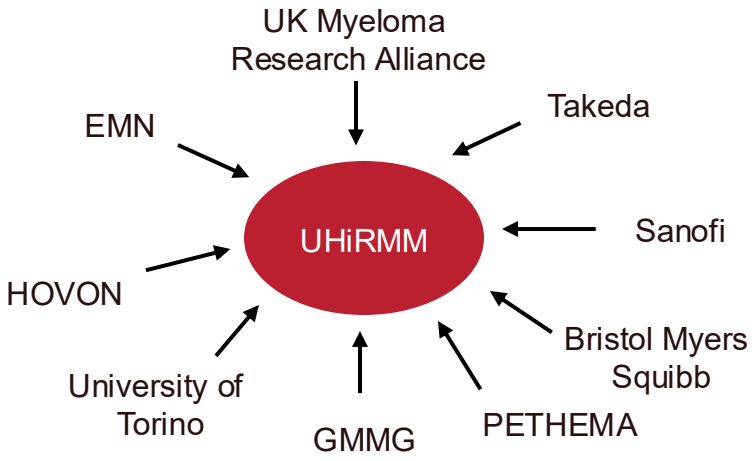
Abbreviations: CA, chromosomal abnormalities; iFISH, interphase fluorescent in situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, revised International Staging System.



Palumbo A, et al. *J Clin Oncol*. 2015;33(26):2863-2869.

Federated Multi-Trial Analysis: Number of Lesions Matters!





>12,000 patients
Randomized phase 2/3 trials
NDMM and RRMM

2022 onwards

- RADAR
- 1q meta
- FORTE
- MASTER
- R2-ISS
- GRIFFIN
- >12,000 pt meta-analysis
- And more

EMN = European Myeloma Network; GMMG = German-Speaking Myeloma Multicenter Group; PETHEMA = Programa Español de Tratamientos en Hematología; HOVON = Hemato-Oncologie voor Volwassenen Nederland; UHiRMM = ultra-high-risk multiple myeloma; RRMM = relapsed/refractory multiple myeloma.

Boyd KD, et al. *Leukemia*. 2012;26(2):349-355. Shah V, et al. *Leukemia*. 2018;32(1):102-110. Weingold N, et al. *Haematologica*. 2021;106(10):2754-2758. Mina R, et al. *Lancet Oncol*. 2023;24(1):64-76. Panopoulou A, et al. *Blood*. 2023;141(14):1666-1674. Kaiser MF, et al. *J Clin Oncol*. 2025;43(24):2679-2691.

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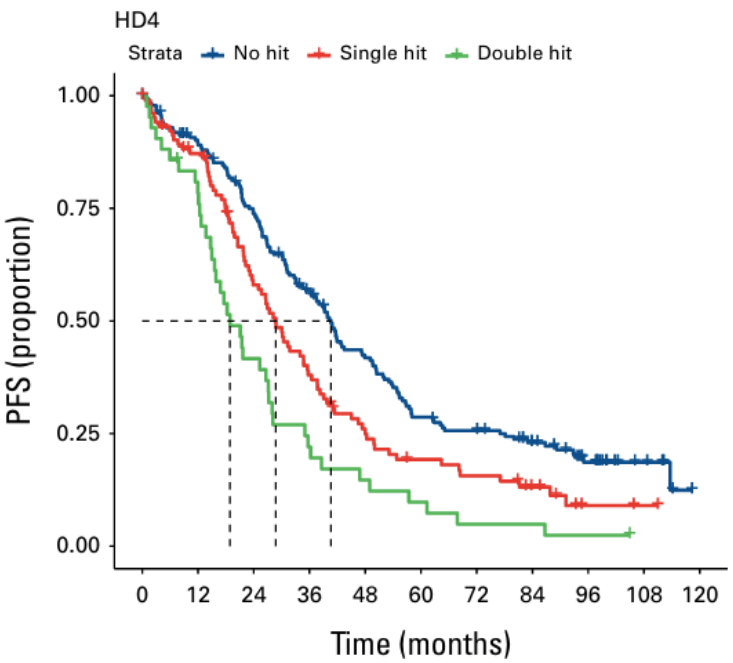
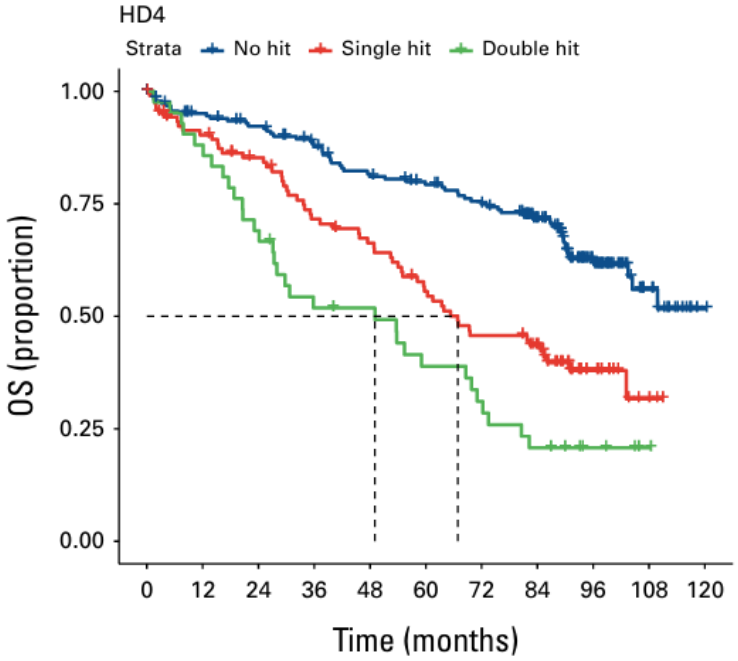
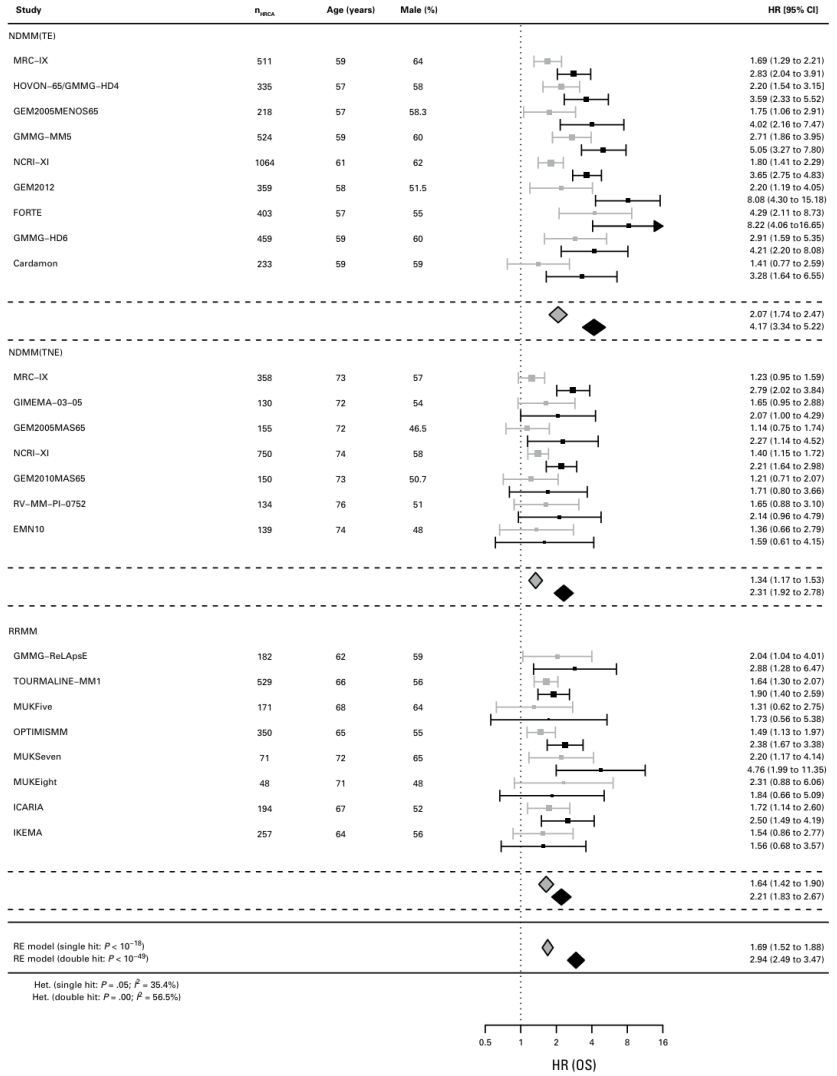
Single- vs Double-Hit MM

Consistent association with survival outcomes across TE NDMM, TNE NDMM, RRMM







2+ HRCA = double hit = "ultra high-risk MM"
Consistent across (1) TE NDMM (2) TNE NDMM (3) RRMM

TE = transplant-eligible; TNE = transplant-non-eligible; HRCA = high-risk cytogenetic abnormalities.
Kaiser MF, et al. *J Clin Oncol*. 2025;43(24):2679-2691.

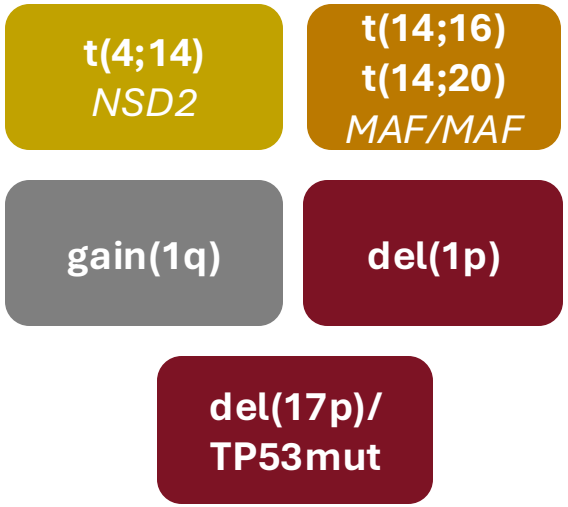
Toward a Novel Risk Stratification System

IMS 2024—What Is High-Risk MM ?

- Myeloma with at least 20% of cells showing the genetic characteristic of deletion 17p
- Myeloma with a TP53 mutation
- Myeloma with a biallelic deletion of 1p32, ie, only when both arms of the chromosome are missing
- Myeloma that has any two of the following intermediate-risk genetic characteristics found together
  - Translocation t(4;14) or t(4;16)
  - Gain of 1q
  - Monoallelic deletion of 1p32 (where only one chromosome is missing)

Corre J, et al. Presented at: 21st International Myeloma Society (IMS) Annual Meeting; 2024.

Updated IMS-IMWG Risk Definition—Just Published!



1. IgH translocation t(4;14), t(14;16), t(14;20) with 1q+ and/or del (1p32)

or

2. Monoallelic del(1p32) with 1q+ or biallelic deletion del1p32

or

3. Del(17p) with cutoff 20% and/or tp53 mutation

or

4. β2M >5.5, *but only when creatinine normal*

Avet-Loiseau H, et al. *J Clin Oncol*. 2025;43(24):2739-2751.

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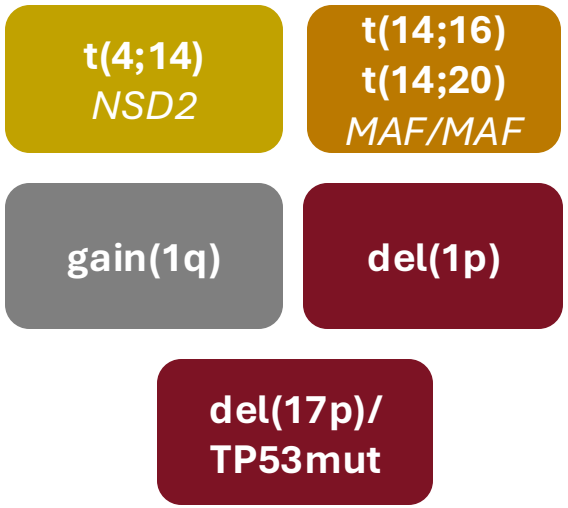
Updated IMS-IMWG Risk Definition—Just Published!



★ **Requires NGS!**

1. IgH translocation t(4;14), t(14;16), t(14;20) with 1q+ and/or del (1p32)

or

2. Monoallelic del(1p32) with 1q+ or biallelic deletion del1p32

or

★ **3. Del(17p) with cutoff 20% and/or tp53 mutation**

or

4. β2M >5.5, *but only when creatinine normal*

Avet-Loiseau H, et al. *J Clin Oncol*. 2025;43(24):2739-2751.

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mSMART 4.0: Classification of Active MM

High-Risk Myeloma

- **High-risk cytogenetic abnormalities**
  - Del 17p[a] and/or *TP53* mutation
  - Bi-allelic del 1p
  - t(4;14), (14;16), or t(14;20) *plus* either Gain/amp 1q or Del 1p
  - Gain/amp 1q *plus* Del 1p
- **B2M >5.5 with normal renal function**
- **High plasma cell S-phase**
- **Primary plasma cell leukemia**
- **Newly diagnosed myeloma with extramedullary disease**

Double-hit myeloma = Patients meeting criteria for high-risk myeloma with presence of two or more of the four high-risk qualifying cytogenetic abnormalities as listed above[b]

Standard-Risk Myeloma

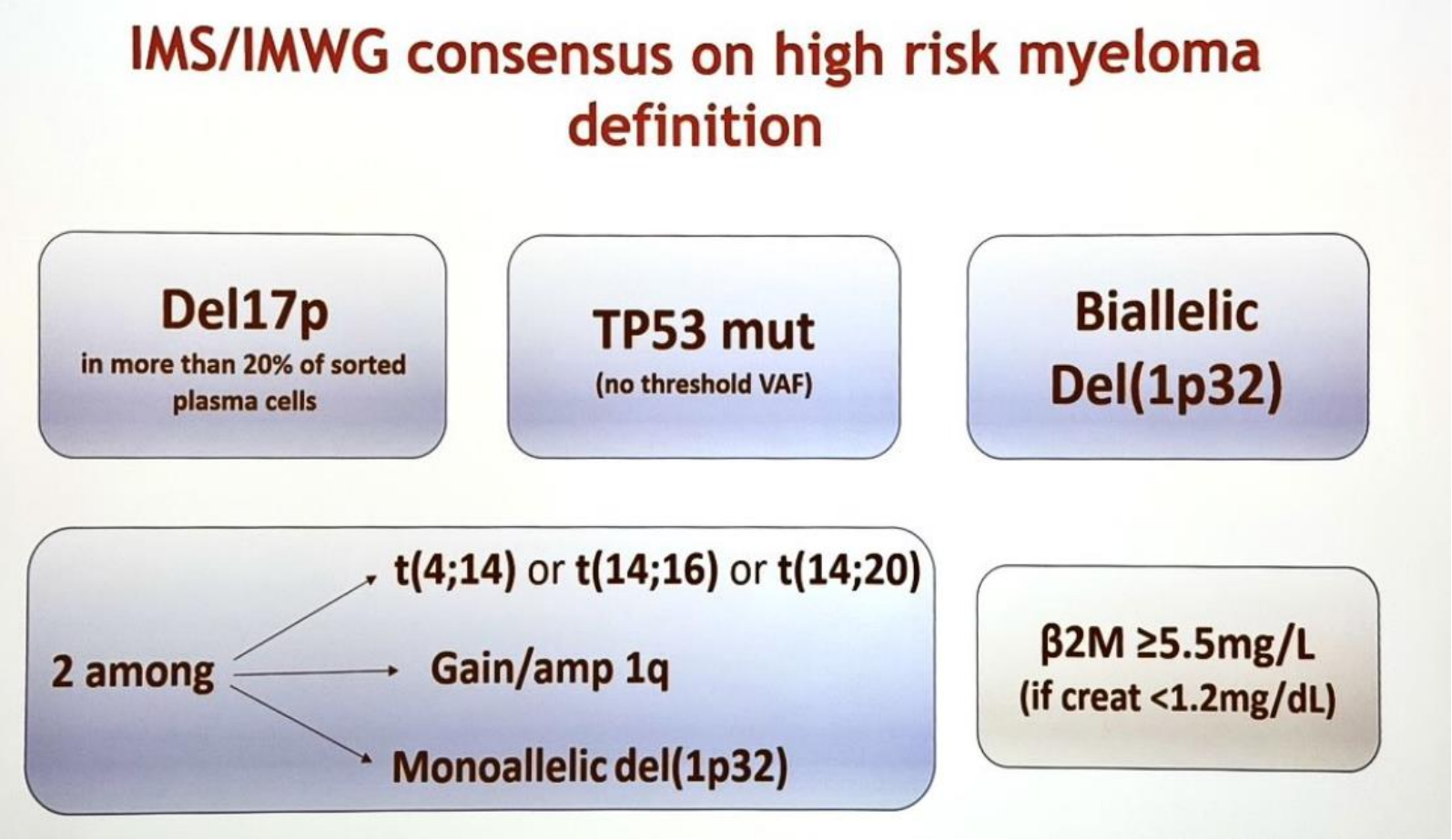
MM with no high-risk abnormalities including isolated

- Trisomies
- t(11;14)
- t(6;14)

@VincentRK
Mayo mSmart→ "goal is to be completely aligned with IMS-IMWG"

Rajkumar V [www.msmart.org]. Last updated October 2024. https://www.msmart.org/mm-treatment-guidelines.
[a]del(17p) threshold to consider high risk is if the abnormality is detected in ≥ 20% of clonal plasma cells. [b]For example, presence of del 17p (high-risk qualifying cytogenetic abnormality) plus both t(4;14) and del 1p (second additional high-risk qualifying abnormality).

Summary and Future Considerations



- **IMS-IMWG risk definition is the new SOC and should be used for all clinical trials**
- Future expansion into multiple risk levels?
- Will imaging, "tumor burden," and/or GEP be incorporated in the future?
- Most urgently: how to make NGS accessible in the clinic?

Avet-Loiseau H, et al. *J Clin Oncol*. 2025;43(24):2739-2751.

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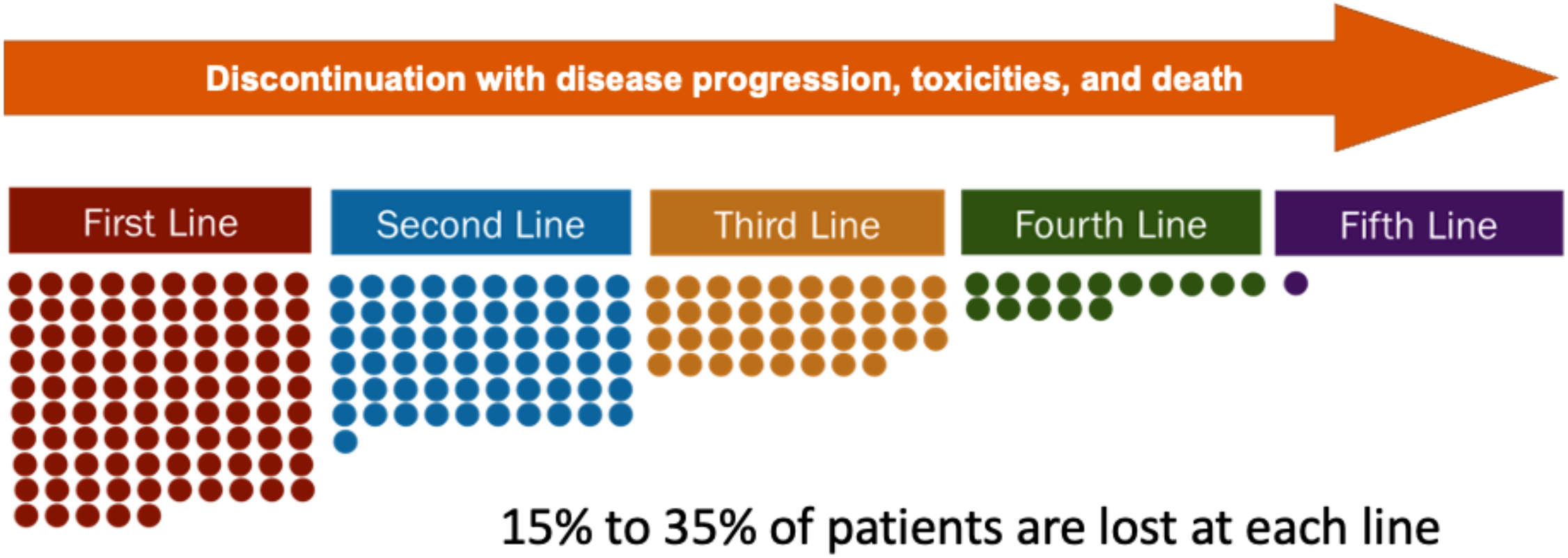
Multidrug Regimens in the Frontline Setting

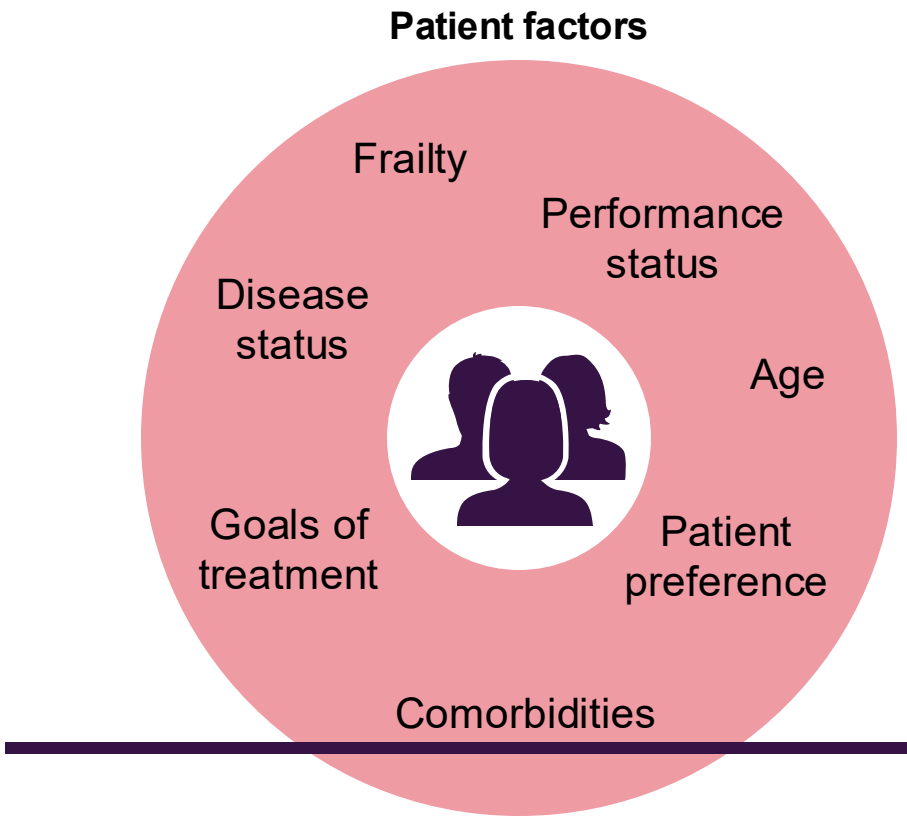
Transplant-Ineligible NDMM (TI)

Use Best Available Therapy in Every Line



Yong K, et al. *Br J Haematol*. 2016;175(2):252-264.

The TI Population Represents a Spectrum of Patients with Different Needs



What is the best treatment strategy at diagnosis based on my patient's condition and disease characteristics?

How can I tailor my treatment strategy to best fit my patient's needs?

Terpos E, et al. *Blood Cancer J*. 2021;11(2):40. Dimopoulos MA, et al. *Ann Oncol*. 2021;32(3):309-322. Grant SJ, et al. *Hematology Am Soc Hematol Educ Program*. 2021;2021(1):46-54.

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Phase III Studies Investigating CD38 mAb-VRd Quad in TI NDMM

IMROZ

N=446
- ✓ TI NDMM
- ✓ 18-80 years
- × ECOG PS >2
- × Grade >1 PN or ≥1 PN with pain

3:2

Induction (6-week cycles) → Continuous phase (4-week cycles)

- **Isa-VRd** x4 cycles → **Isa-Rd**
- **VRd** x4 cycles → **Rd**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: PFS

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-17), **monthly** (Cycle 18+)
V (1.3 mg/m²): Administered **twice-weekly** (Week 1-3 of cycles 2-4) during induction only

BENEFIT

N=270
- ✓ TI NDMM
- ✓ 65-79 years
- × ECOG PS >2

1:1

4-week cycles

- **Isa-VRd** x12 cycles → **Isa-VR** x6 cycles → **Isa-R**
- **Isa-Rd** x12 cycles → **Isa-R** x6 cycles → **Isa-R**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: MRD- (10^{-5})

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-12), **monthly** (Cycle 13+)
V (1.3 mg/m²): Administered **weekly** (Cycle 1-12) and then **every 2 weeks** (Cycle 3-18)

CEPHEUS

N=395
- ✓ NDMM and transplant not planned as initial therapy
- ✓ ≥18 years
- × ECOG PS >2

1:1

Induction (3-week cycles) → Continuous phase (4-week cycles)

- **D-VRd** x8 cycles → **DRd**
- **VRd** x8 cycles → **Rd**

Until PD or unacceptable toxicity

Primary Endpoint: MRD- (10^{-5})

Dara SC (1800 mg): Administered **weekly** (Cycle 1-2), **every 3 weeks** (Cycle 3-8), **monthly** (Cycle 9+)
V (1.3 mg/m²): Administered **twice-weekly** (Cycle 1-8)

As no head-to-head comparisons are available, direct comparison between trials is not intended and should not be inferred.
ECOG PS = Eastern Cooperative Oncology Group performance status; mAB = monoclonal antibody; PN = peripheral neuropathy; PD = progressive disease.

Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated November 27, 2024. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03319667. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 7, 2022. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT04751877. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 15, 2025. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03652064. Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501.

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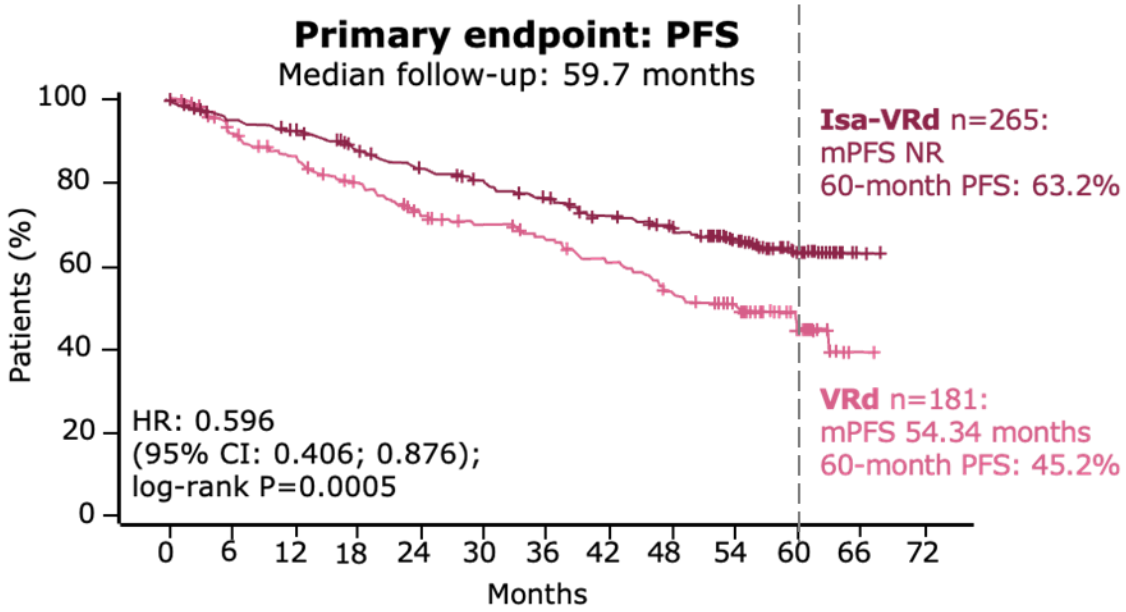
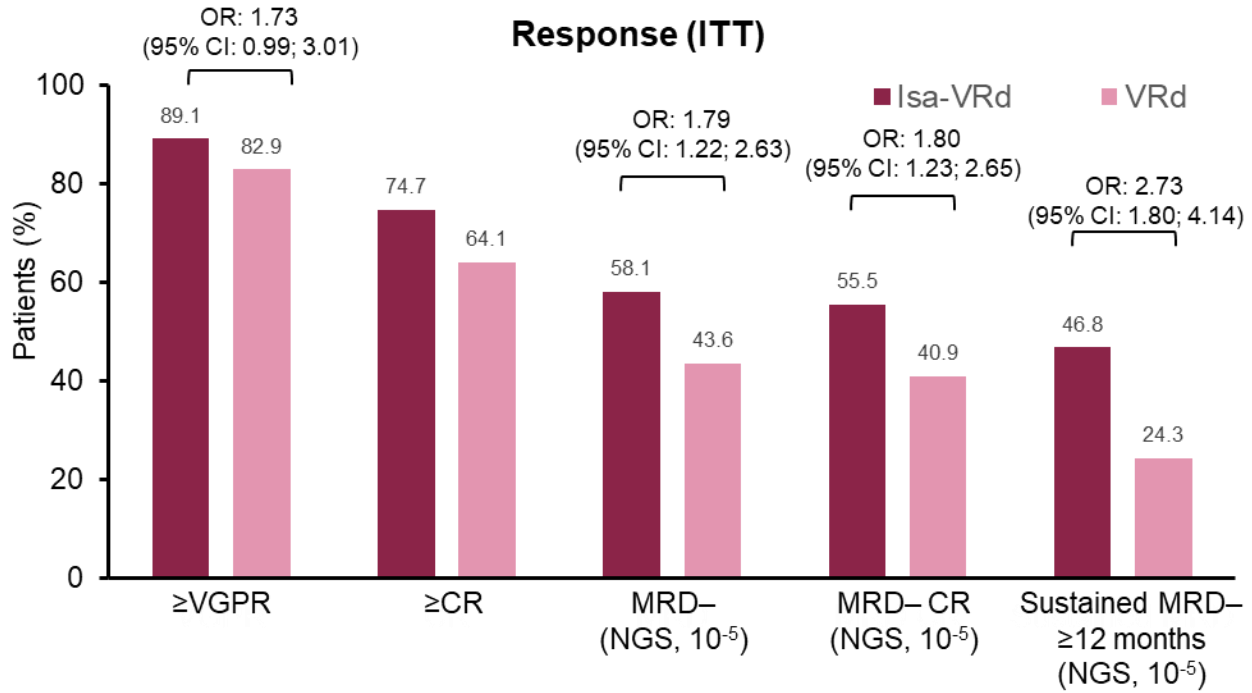
IMROZ: First Global Phase III Study of Isa-VRd vs VRd in TI NDMM

IMROZ: Isa-VRd vs VRd (N=446) in NDMM not intended for transplant

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-17), **monthly** (Cycle 18+)
V SC (1.3 mg/m²): Administered **twice-weekly** (Week 1-3 of cycles 2-4) during induction only





- At a median follow-up of 5 years, Isa-VRd followed by Isa-Rd resulted in a statistically significant reduction in the risk of progression or death by 40.4%, and consistent deep responses vs VRd followed by Rd
- A 60-month PFS rate of 63.2% vs 45.2% with Isa-VRd and VRd, respectively, highlights a PFS benefit in patients with NDMM not intended for transplant

ITT = intent-to-treat; mPFS = median PFS; NR = not reached; CR = complete response; VGPR = very good partial response.

Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609. ClinicalTrials.gov [www.clinicaltrials.gov.] Last updated November 27, 2024. Accessed November 27, 2024. https://clinicaltrials.gov/study/NCT03319667.

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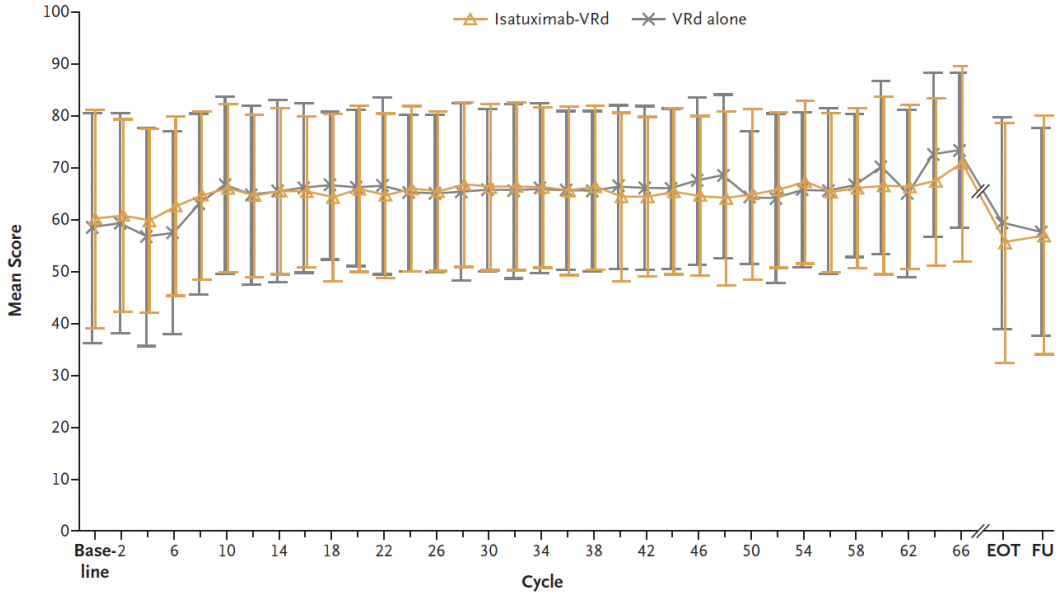
IMROZ: First Global Phase III Study of Isa-VRd vs VRd in Ti NDMM

IMROZ: Isa-VRd vs VRd (N=446) in NDMM not intended for transplant

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2–17), **monthly** (Cycle 18+)
V SC (1.3 mg/m²): Administered **twice-weekly** (Week 1-3 of cycles 2-4) during induction only

Safety, %	Isa-VRd (n=263)	VRd (n=181)
Grade ≥3 TEAE	91.6	84.0
Serious TEAE	70.7	67.4
Discont. due to AE	22.8	26.0
Grade 5 TEAE*	11.0	5.5
Grade ≥3 AE (≥20% patients in any arm)		
Lymphopenia	60.1	53.0
Neutropenia	54.4	37.0
Leukopenia	31.6	16.0
Thrombocytopenia	30.0	27.6
Infections	44.9	38.1

Mean EORTC QLQ-C30 GHS/QOL score over time



Isa-VRd followed by Isa-Rd was well-tolerated, and the safety profile remains consistent with the known safety profiles of individual agents; patient QOL remained stable over time in both treatment arms and was not negatively affected by the addition of isatuximab.

*Exposure-adjusted grade 5 TEAE rate was 0.03 and 0.02 (events/patient-year) in the Isa-VRd vs VRd arms, respectively.
TEAE = treatment-emergent adverse event; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer 30-item cancer QOL questionnaire; EOT = end of treatment; GHS = global health status.
Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609.

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Phase III Studies Investigating CD38 mAb-VRd Quad in TI NDMM

IMROZ

N=446
- ✓ TI NDMM
- ✓ 18-80 years
- × ECOG PS >2
- × Grade >1 PN or ≥1 PN with pain

3:2

Induction (6-week cycles) → Continuous phase (4-week cycles)

- **Isa-VRd** x4 cycles → **Isa-Rd**
- **VRd** x4 cycles → **Rd**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: PFS

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-17), **monthly** (Cycle 18+)
V (1.3 mg/m²): Administered **twice-weekly** (Week 1-3 of cycles 2-4) during induction only

BENEFIT

N=270
- ✓ TI NDMM
- ✓ 65-79 years
- × ECOG PS >2

1:1

4-week cycles

- **Isa-VRd** x12 cycles → **Isa-VR** x6 cycles → **Isa-R**
- **Isa-Rd** x12 cycles → **Isa-R** x6 cycles → **Isa-R**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: MRD- (10^{-5})

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-12), **monthly** (Cycle 13+)
V (1.3 mg/m²): Administered **weekly** (Cycle 1-12) and then **every 2 weeks** (Cycle 3-18)

CEPHEUS

N=395
- ✓ NDMM and transplant not planned as initial therapy
- ✓ ≥18 years
- × ECOG PS >2

1:1

Induction (3-week cycles) → Continuous phase (4-week cycles)

- **D-VRd** x8 cycles → **DRd**
- **VRd** x8 cycles → **Rd**

Until PD or unacceptable toxicity

Primary Endpoint: MRD- (10^{-5})

Dara SC (1800 mg): Administered **weekly** (Cycle 1-2), **every 3 weeks** (Cycle 3-8), **monthly** (Cycle 9+)
V (1.3 mg/m²): Administered **twice-weekly** (Cycle 1-8)

As no head-to-head comparisons are available, direct comparison between trials is not intended and should not be inferred

Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated November 27, 2024. Accessed August 15, 2024.
https://clinicaltrials.gov/study/NCT03319667. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 7, 2022. Accessed August 15, 2024.
https://clinicaltrials.gov/study/NCT04751877. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 15, 2025. Accessed August 15, 2024.
https://clinicaltrials.gov/study/NCT03652064. Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501.

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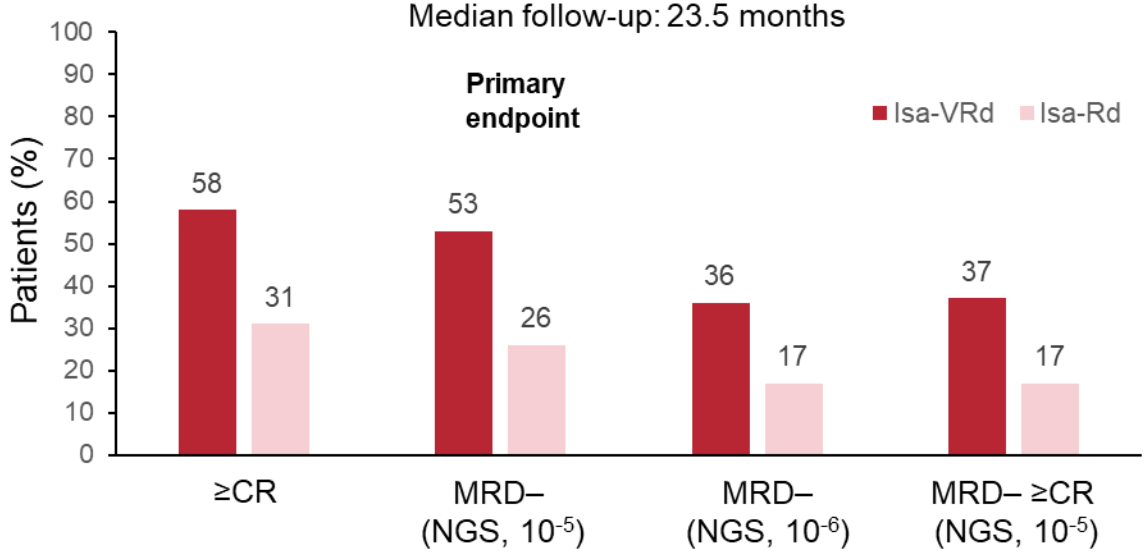
BENEFIT: VRd Using Weekly Bortezomib in Combination with Isatuximab

BENEFIT/IFM2020-05: Isa-VRd vs Isa-Rd (N=270) in TI NDMM

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-12), **monthly** (Cycle 13+)
V SC (1.3 mg/m²): Administered **once weekly** (Cycle 1-12) and then **every 2 weeks** (Cycle 13-18)
d (20 mg): Administered **weekly** (Cycle 1-12); then **discontinued**

Response at 18 months
Median follow-up: 23.5 months



Longer follow-up examining PFS and OS is ongoing

Safety (≥25% patients in any arm), %	Isa-VRd (n=135)	Isa-Rd (n=135)
Grade ≥3 neutropenia	40	45
Grade ≥3 lymphopenia	33	24
Grade ≥2 respiratory infections	35	40
Grade ≥2 infection of other types*	36	28
Grade ≥2 diarrhoea	29	22
Grade ≥2 peripheral neuropathy	27	10

Isa-VRd using once-weekly bortezomib dosing demonstrated deep responses and a manageable safety profile vs Isa-Rd in TI NDMM patients; these findings provide further supplemental evidence to the PFS results seen in IMROZ and demonstrate the flexibility of Isa-VRd to provide benefit across the diverse TI NDMM populations.

*Infections not including the respiratory system.

Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 7, 2022. Accessed November 27, 2024. https://clinicaltrials.gov/study/NCT04751877.

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Phase III Studies Investigating CD38 mAb-VRd Quad in TI NDMM

IMROZ

N=446
- ✓ Ti NDMM
- ✓ 18-80 years
- × ECOG PS >2
- × Grade >1 PN or ≥1 PN with pain

3:2

Induction (6-week cycles)
- **Isa-VRd** x4 cycles
- **VRd** x4 cycles

Continuous phase (4-week cycles)
- **Isa-Rd**
- **Rd**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: PFS

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-17), **monthly** (Cycle 18+)
V (1.3 mg/m²): Administered **twice-weekly** (Week 1-3 of cycles 2-4) during induction only

BENEFIT

N=270
- ✓ Ti NDMM
- ✓ 65-79 years
- × ECOG PS >2

1:1

4-week cycles
- **Isa-VRd** x12 cycles → **Isa-VR** x6 cycles → **Isa-R**
- **Isa-Rd** x12 cycles → **Isa-R** x6 cycles → **Isa-R**

Until PD, unacceptable toxicity, or patient withdrawal

Primary Endpoint: MRD- (10^{-5})

Isa IV (10 mg/kg): Administered **weekly** (Cycle 1), **every 2 weeks** (Cycle 2-12), **monthly** (Cycle 13+)
V (1.3 mg/m²): Administered **weekly** (Cycle 1-12) and then **every 2 weeks** (Cycle 9-12)

CEPHEUS

N=395
- ✓ NDMM and transplant not planned as initial therapy
- ✓ ≥18 years
- × ECOG PS >2

1:1

Induction (3-week cycles)
- **D-VRd** x8 cycles
- **VRd** x8 cycles

Continuous phase (4-week cycles)
- **DRd**
- **Rd**

Until PD or unacceptable toxicity

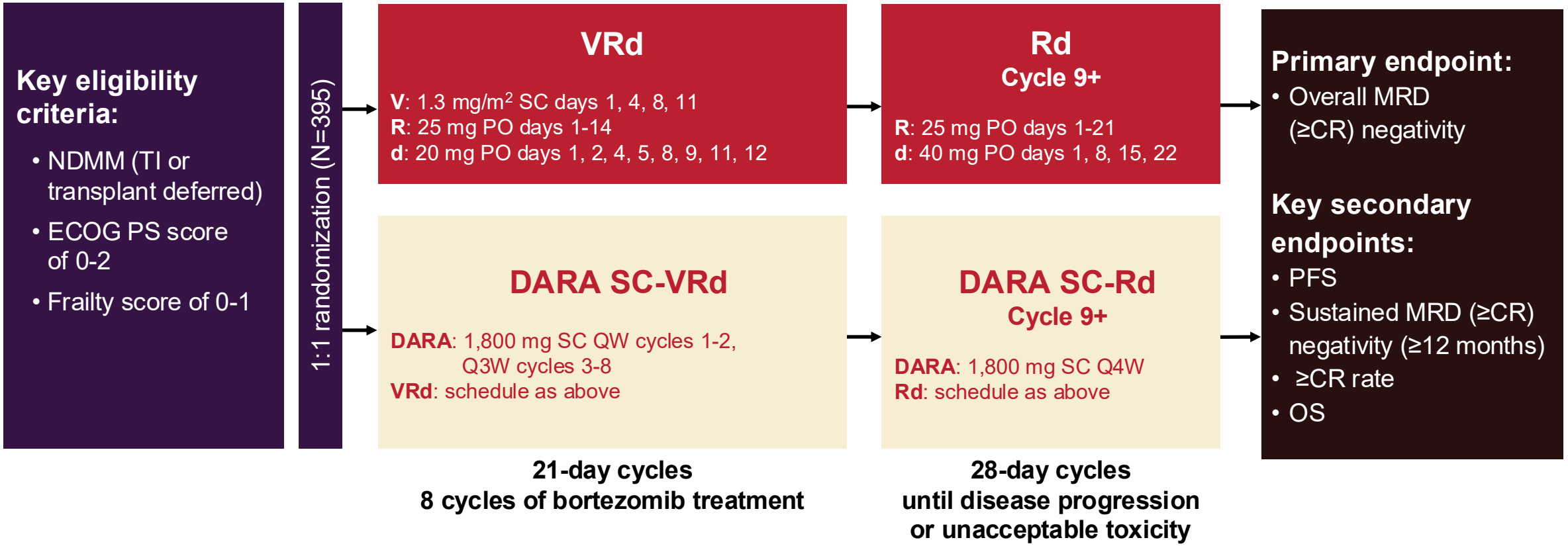
Primary Endpoint: MRD- (10^{-5})

Dara SC (1800 mg): Administered **weekly** (Cycle 1-2), **every 3 weeks** (Cycle 3-8), **monthly** (Cycle 9+)
V (1.3 mg/m²): Administered **twice-weekly** (Cycle 1-8)

As no head-to-head comparisons are available, direct comparison between trials is not intended and should not be inferred

Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated November 27, 2024. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03319667. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 7, 2022. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT04751877. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 15, 2025. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03652064. Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501.

CEPHEUS: Phase 3 Study of DARA-VRd vs VRd in TI or Transplant-Deferred Patients with NDMM



Usmani SZ, et al. Presented at: 21st IMS Annual Meeting; 2024. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 15, 2025. Accessed August 26, 2024. https://clinicaltrials.gov/study/NCT03652064.

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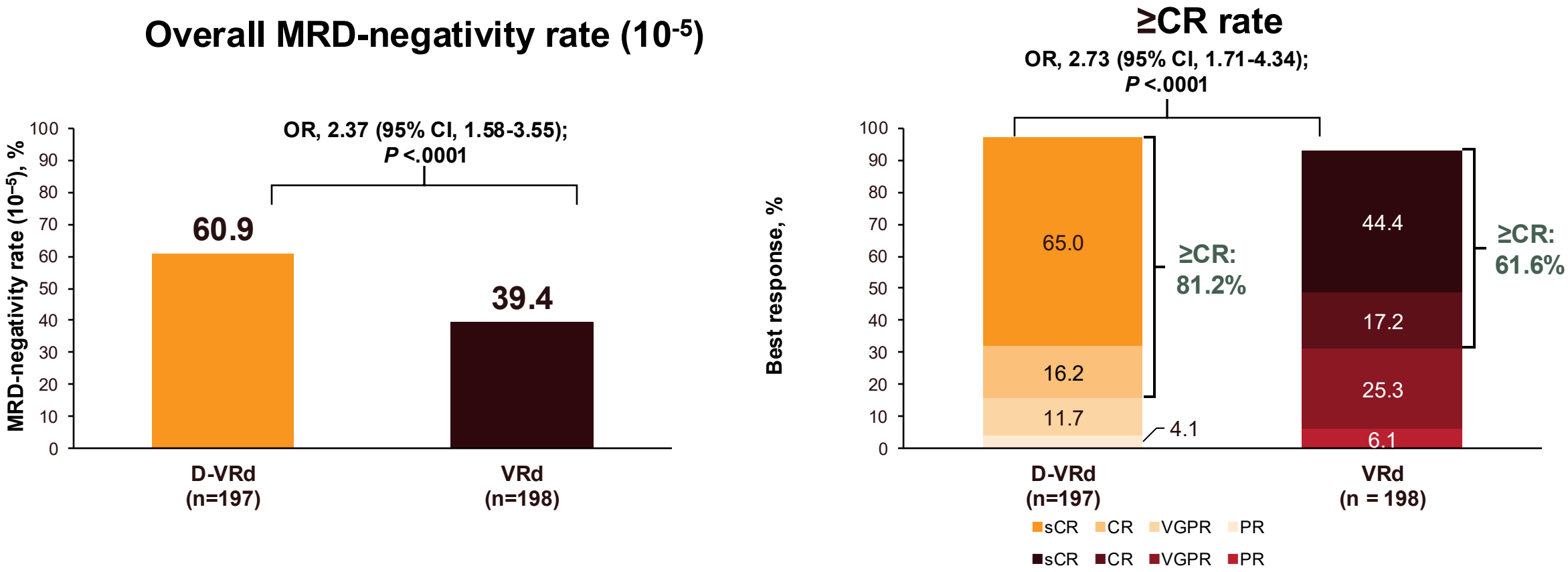
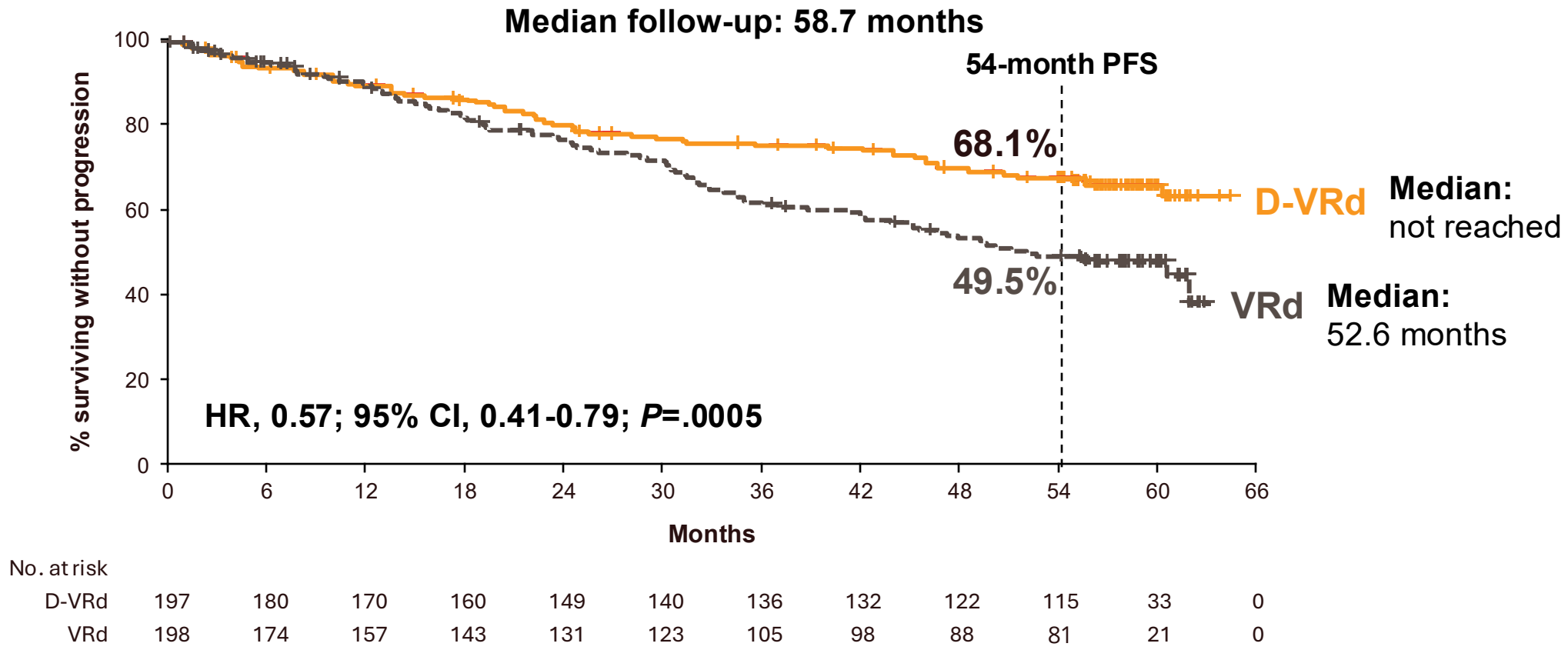
CEPHEUS: Primary Endpoint of Overall MRD-Negativity Rate[a] (10–5; ITT Population)



Daratumumab significantly increased overall MRD-negativity rate and overall ≥CR rate by approximately 20%.

[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity (10^{-5}) and ≥CR.
sCR = stringent complete response; PR = partial response.
Usmani SZ, et al. Presented at: 21st IMS Annual Meeting; 2024.

CEPHEUS: PFS (ITT Population)



Daratumumab significantly improved PFS, with a 43% reduction in the risk of disease progression or death.

Usmani SZ, et al. Presented at: 21st IMS Annual Meeting; 2024.

Continued Treatment/ Maintenance in TI MM Patients

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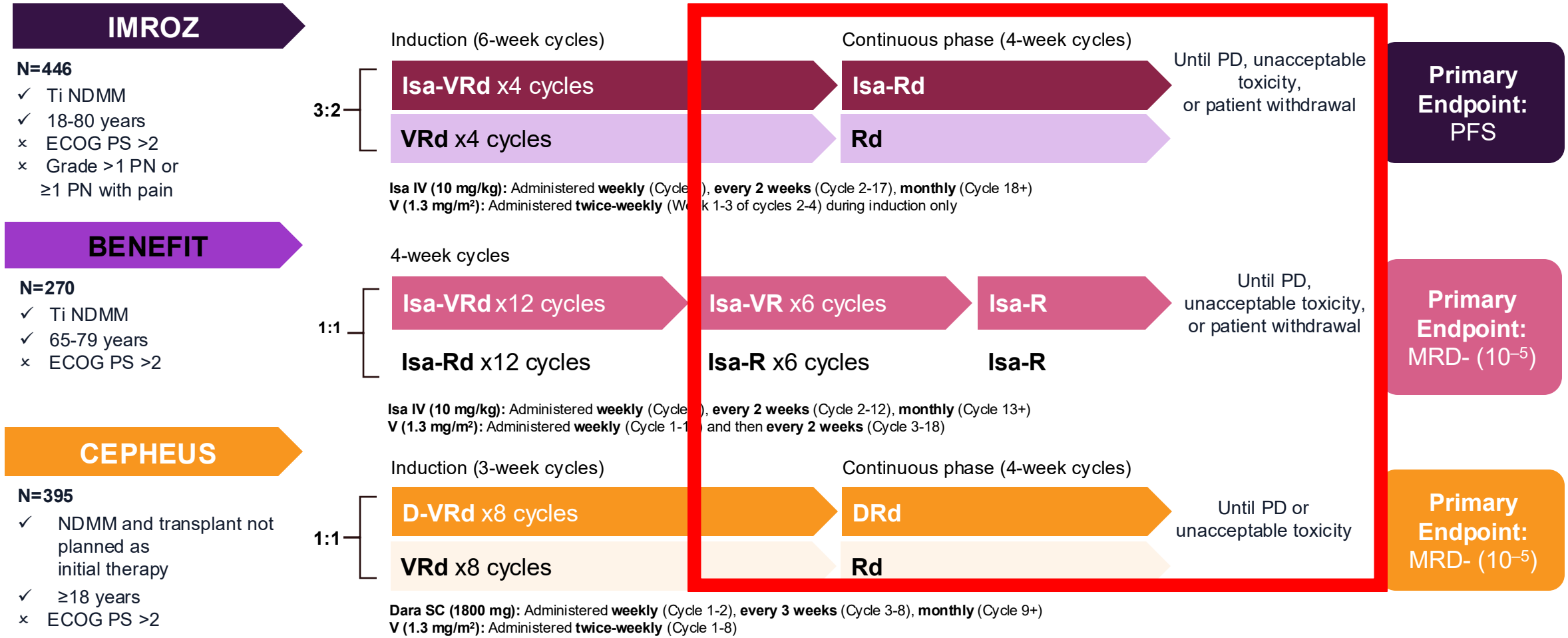
Continued Treatment after CD38 mAb-VRd Quad in Ti NDMM



As no head-to-head comparisons are available, direct comparison between trials is not intended and should not be inferred

Facon T, et al. *N Engl J Med*. 2024;391(17):1597-1609. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated November 27, 2024. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03319667. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 7, 2022. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT04751877. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 15, 2025. Accessed August 15, 2024. https://clinicaltrials.gov/study/NCT03652064. Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501.

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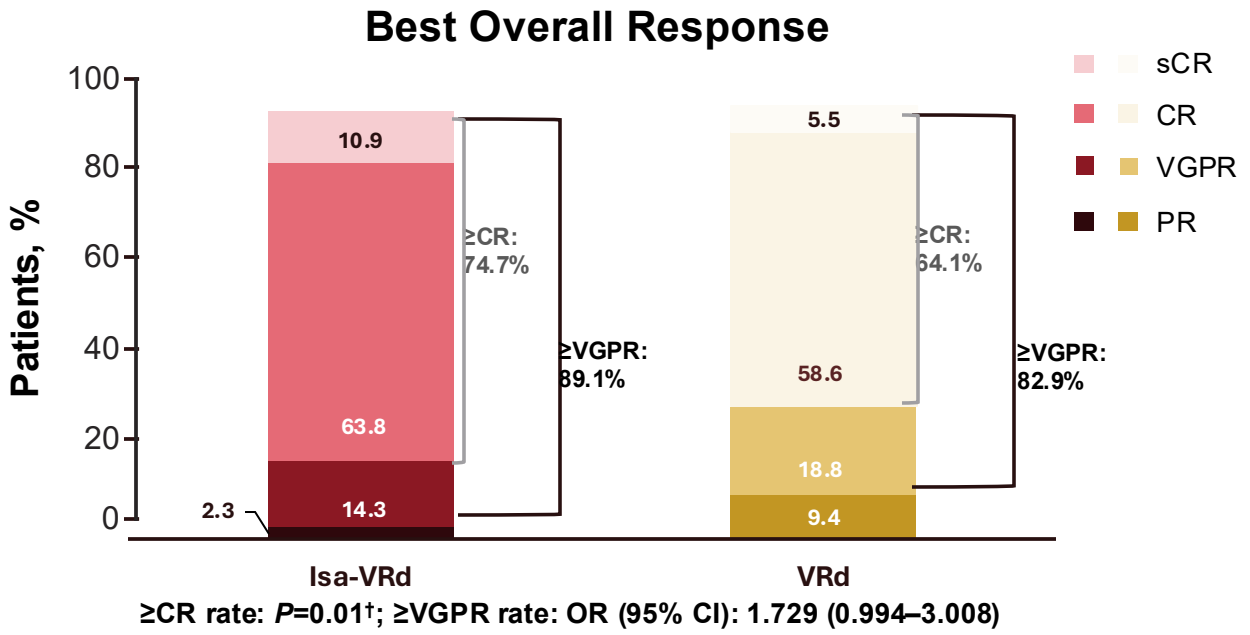
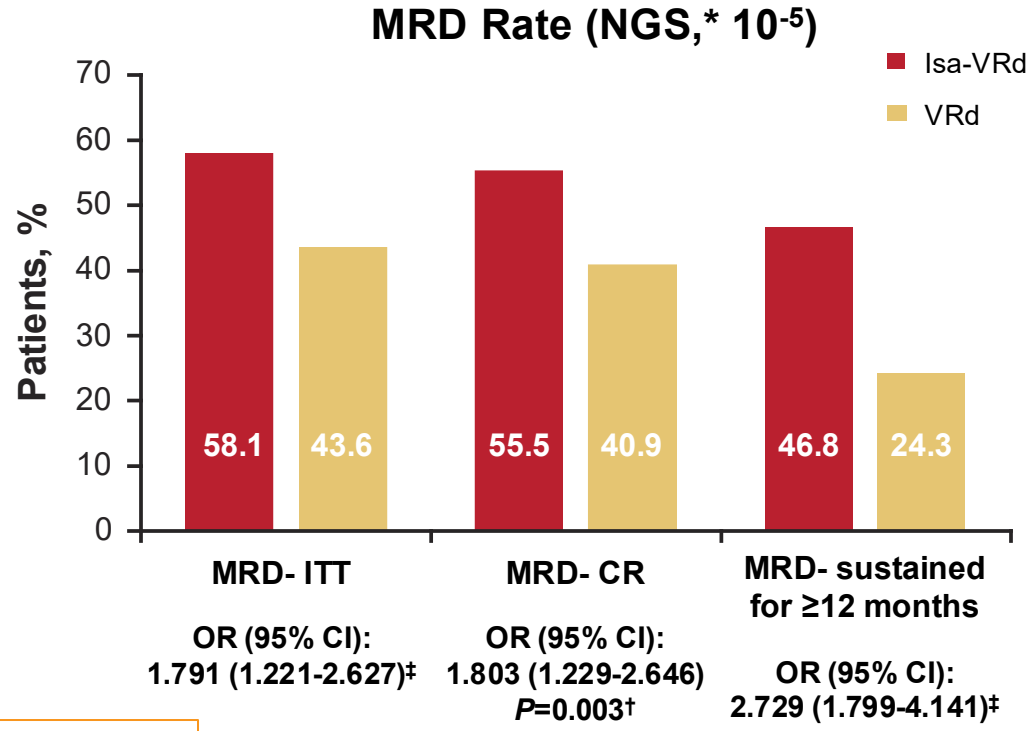
IMROZ Trial for TI: MRD Improvement with Isa-VRd versus VRd





Time to MRD-, median (95% CI)
Isa-VRd: 14.72 (11.53-24.08) months
VRd: 32.79 (17.51-45.11) months

Isa-VRd followed by Isa-Rd resulted in deep response rates, with a significant improvement in the MRD- CR rate, as well as higher rates of MRD- and sustained MRD- for ≥12 months at any point in the ITT population.

*clonoSEQ® assay. †Stratified Cochran-Mantel-Haenszel test. Two-sided significance level is 0.025. ‡*P* value not reported; not a key secondary endpoint.
Facon T, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 2024.

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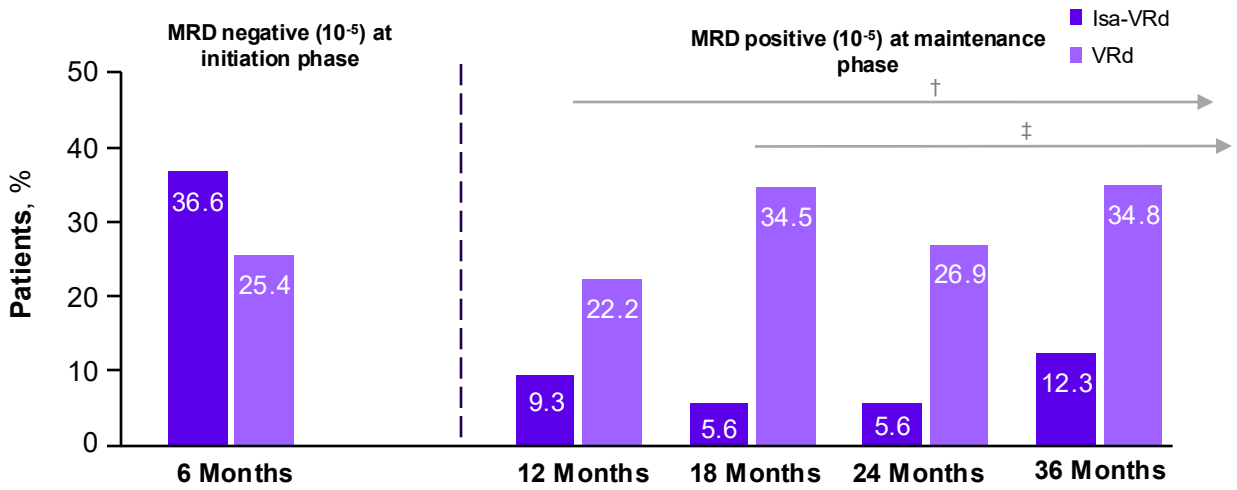
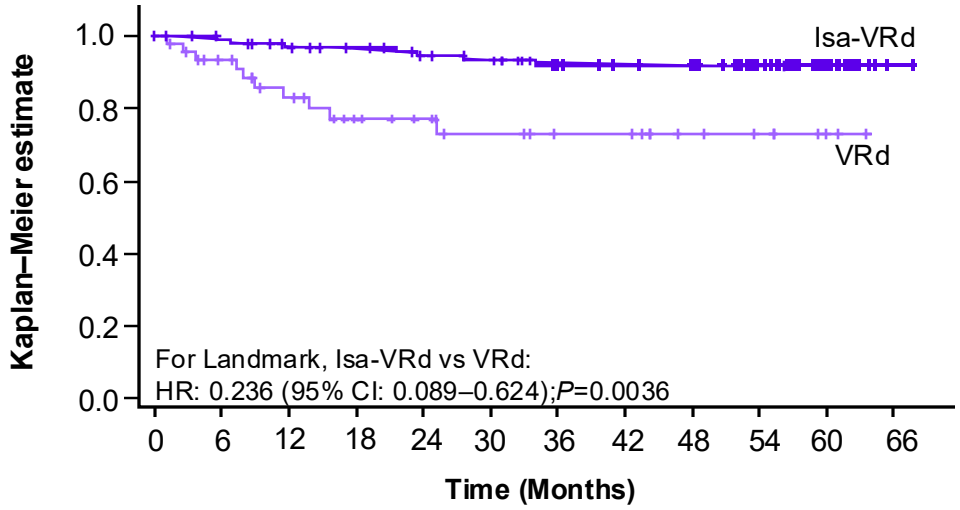
IMROZ: Is There Value in Continuing on Quadruplet Therapy upon Loss of MRD-?

Conversion from MRD- during initiation phase to MRD+ at various timepoints during maintenance phase



Time to progression after conversion from MRD- at initiation phase to MRD+ during maintenance phase



Loss of MRD- status during maintenance was at least 2- to 5-fold lower with Isa-VRd vs VRd.
Those that lost MRD still had a clinically significant longer time to progression with Isa-VRd.

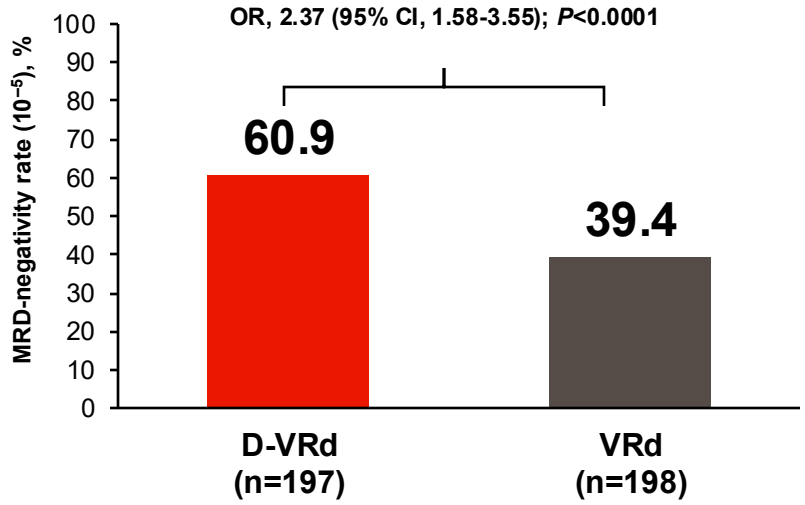
Ph. = phase.

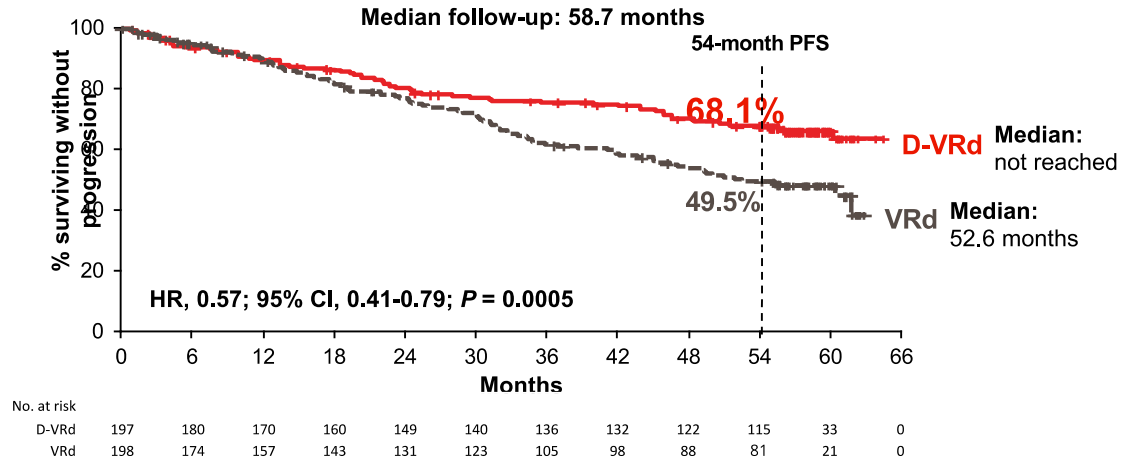
Orlowski RZ, et al. Presented at: 66th American Society of Hematology (ASH) Annual Meeting; 2024. Lentzsch S. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; 2025.

CEPHEUS for TI or Deferred: D-VRd Led to Higher MRD Negativity, Improved PFS versus Triplets

Primary endpoint: Higher overall MRD-negativity rate (10^{-5}) with D-VRd

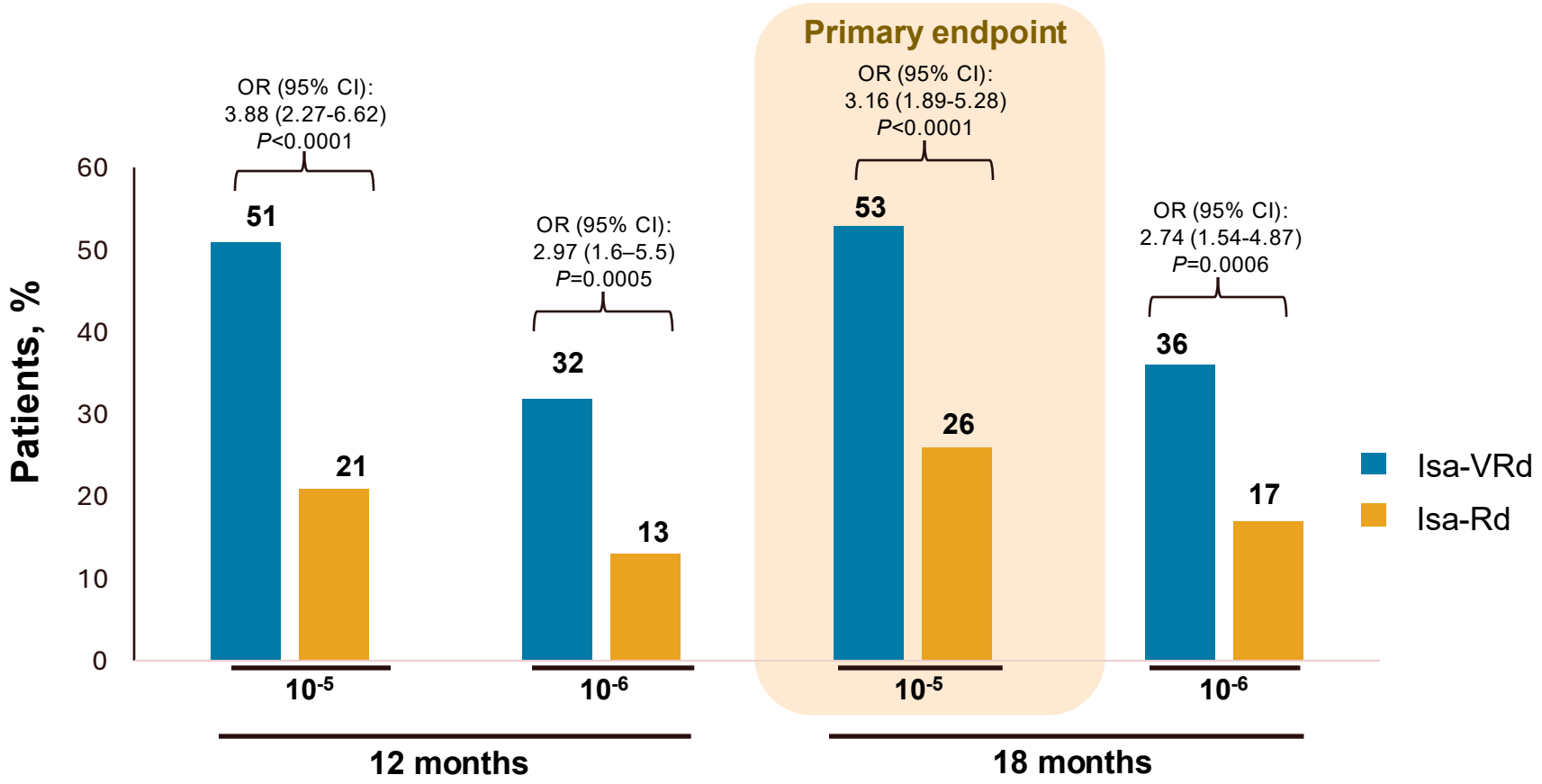
Secondary endpoint: Daratumumab significantly improved PFS, with a 43% reduction in the risk of disease progression or death





Usmani S, et al. Presented at: 21st IMS Annual Meeting; 2024. Lentzsch S. Presented at: ASCO Annual Meeting; 2025.

BENEFIT Trial for TI: Primary Endpoint—MRD- Rate at 18 Months



Isa-VRd resulted in deep response rates, with a significant improvement in the MRD at 12 and 18 months, and at 10^{-5} and 10^{-6} in the ITT population.

*MRD was assessed on the basis of IMWG recommendations.

Kumar S, et al. *Lancet Oncol*. 2016;17(8):e328-e346. Leleu XP, et al. *J Clin Oncol*. 2024;42(Suppl 16):7501.

Key Learning Points

- Quads including CD38 mAb, such as isatuximab or daratumumab (CEPHEUS, IMROZ, and BENEFIT trials), in TI result in higher MRD- associated with improved survival
- Sustained MRD negativity (10^{-5}) ≥CR rates for ≥24 months were more than twice as high with D-VRd vs VRd
- Improvement on outcome is not associated with significant toxicity or impact on QoL
- Quadruplets including CD38 mAb should be a new standard for patients with TI NDMM

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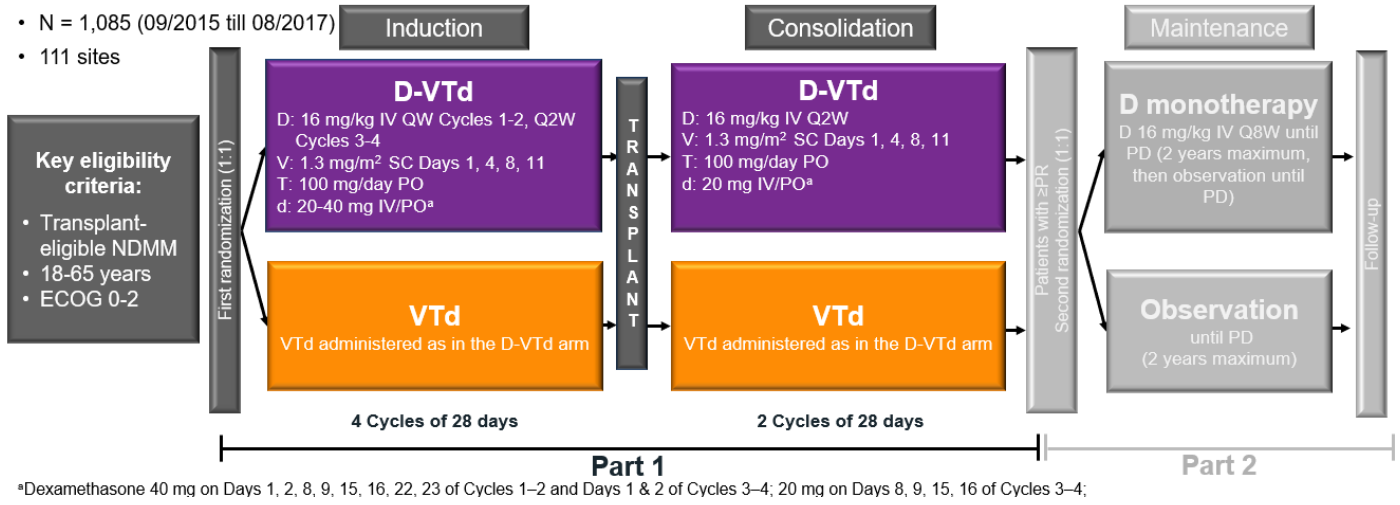
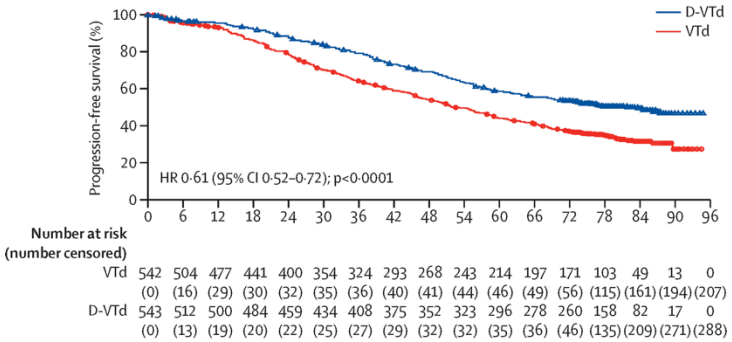
Transplant-Eligible and Investigational Frontline Treatments

Where We Started: Dara-VTd vs VTd—CASSIOPEIA trial

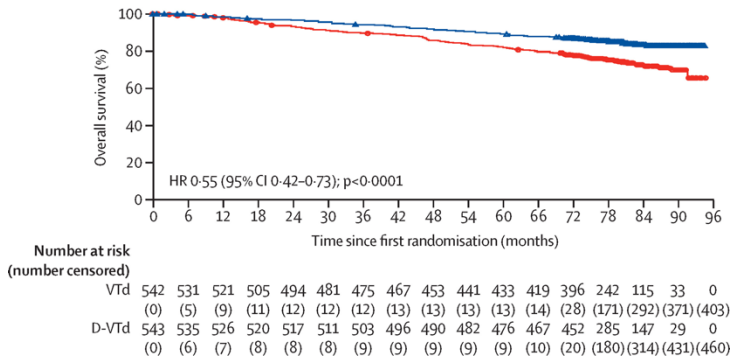


[a]Dexamethasone 40 mg on Days 1, 2, 8, 9, 15, 16, 22, 23 of Cycles 1–2 and Days 1 & 2 of Cycles 3–4; 20 mg on Days 8, 9, 15, 16 of Cycles 3–4;

PFS

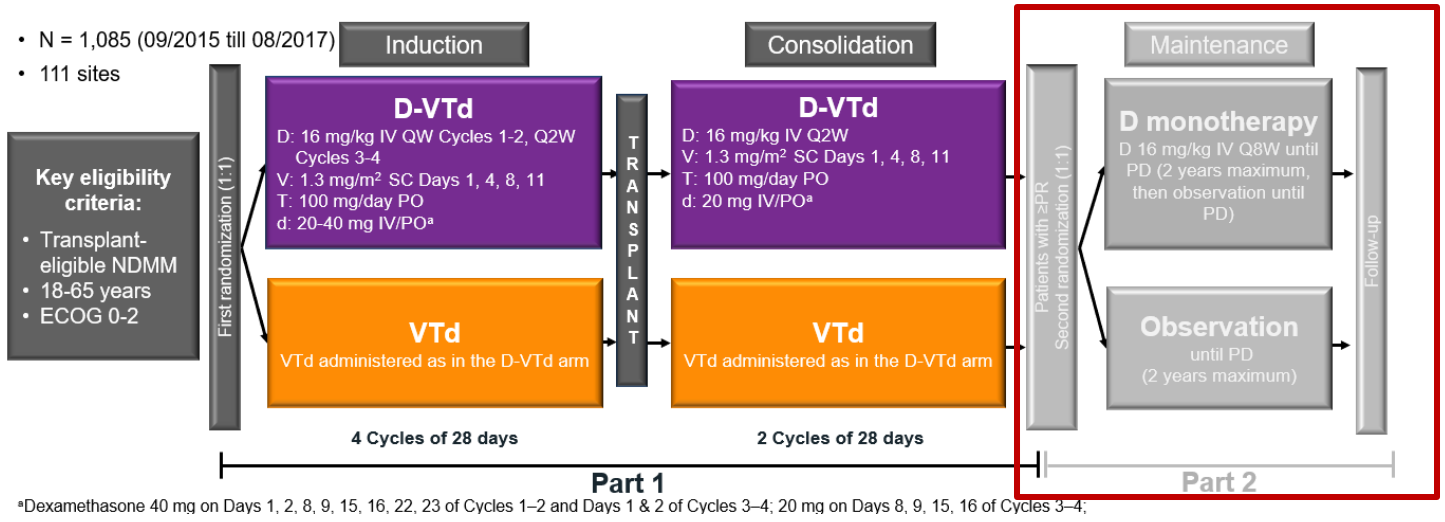


OS

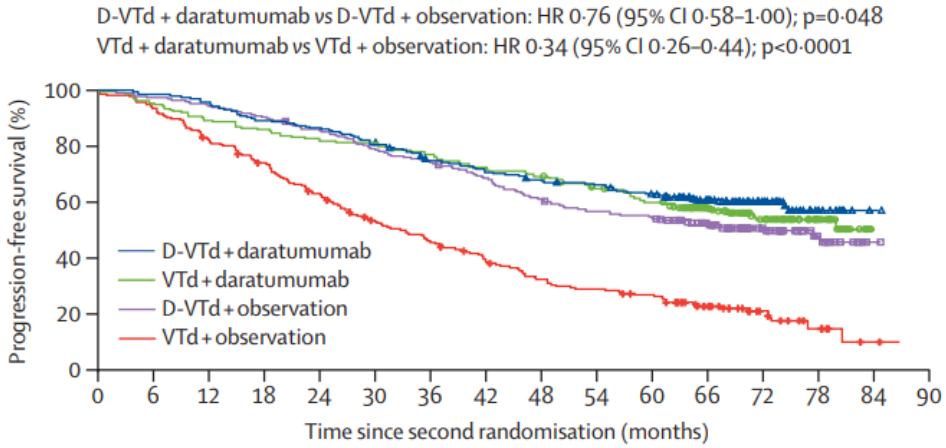


VTd = bortezomib, thalidomide, dexamethasone.
Moreau P et al. *Lancet Oncol*. 2024;25(8):1003-1014.

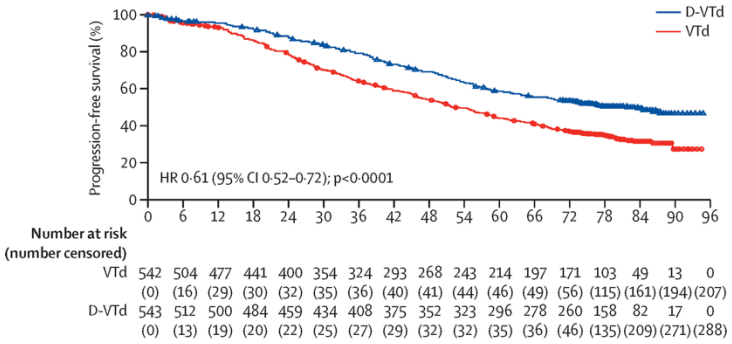
Where We Started: Dara-VTd vs VTd—CASSIOPEIA trial



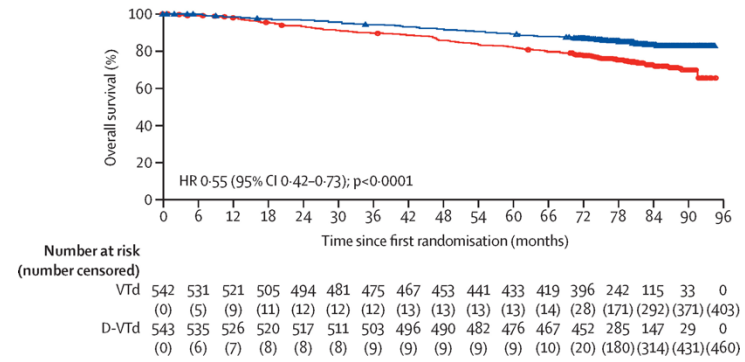
PFS from 2nd randomization



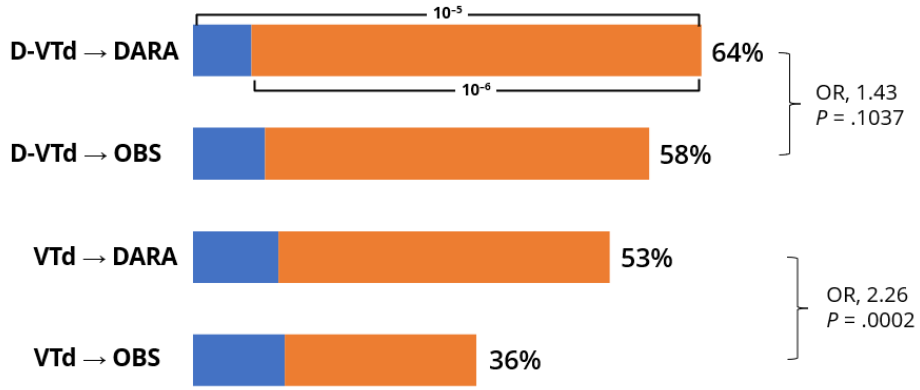
PFS



OS



Rates of ≥CR + MRD-negativity at any time point during maintenance



OBS = observation.

Moreau P, et al. *Lancet Oncol*. 2024;25(8):1003-1014. Avet-Loiseau H, et al. Presented at: ASH Annual Meeting; 2021.

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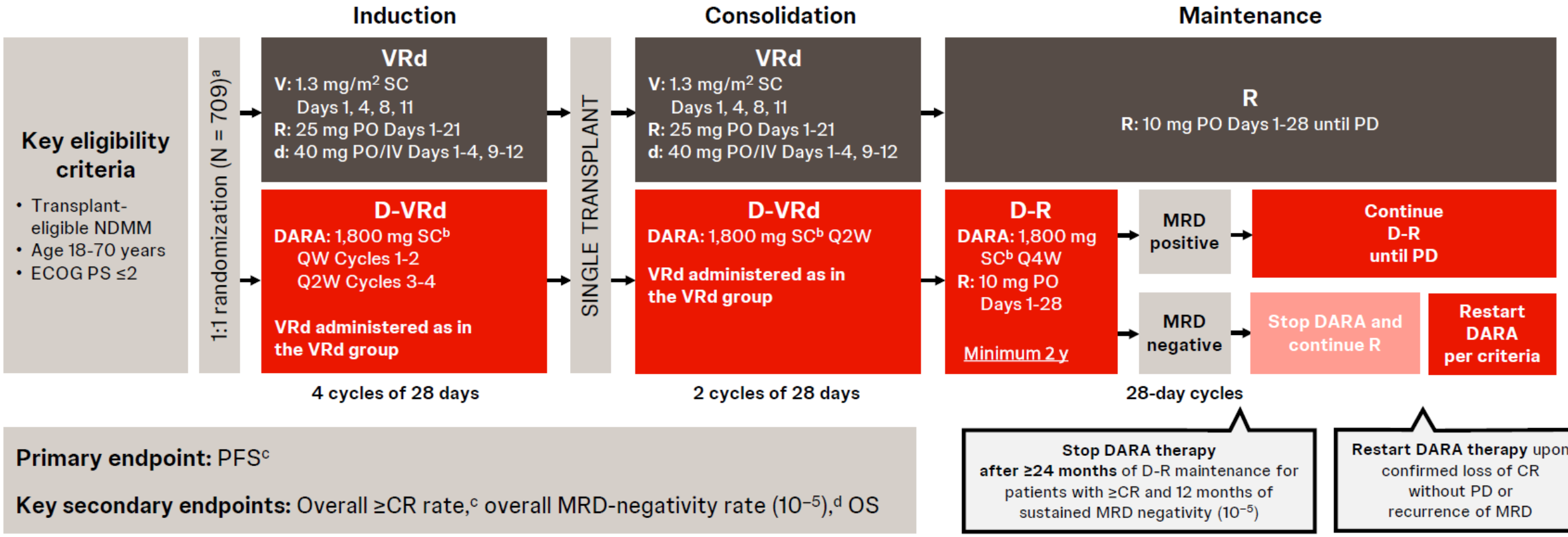
PERSEUS: Dara-VRd



Primary endpoint: PFS[c]

Key secondary endpoints: Overall ≥CR rate,[c] overall MRD-negativity rate (10^{-5}),[d] OS

Stop DARA therapy after ≥24 months of D-R maintenance for patients with ≥CR and 12 months of sustained MRD negativity (10^{-5})

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

Sonneveld P, et al. Presented at: 29th European Hematology Association (EHA) Congress; 2024.

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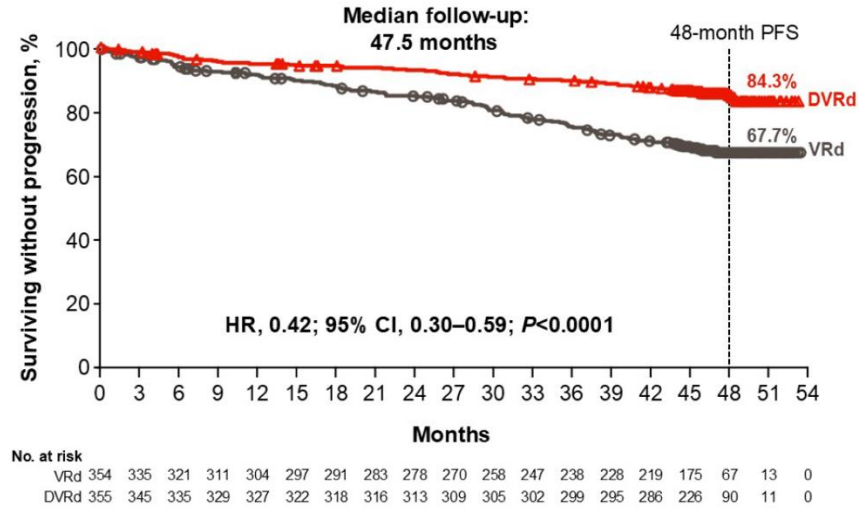
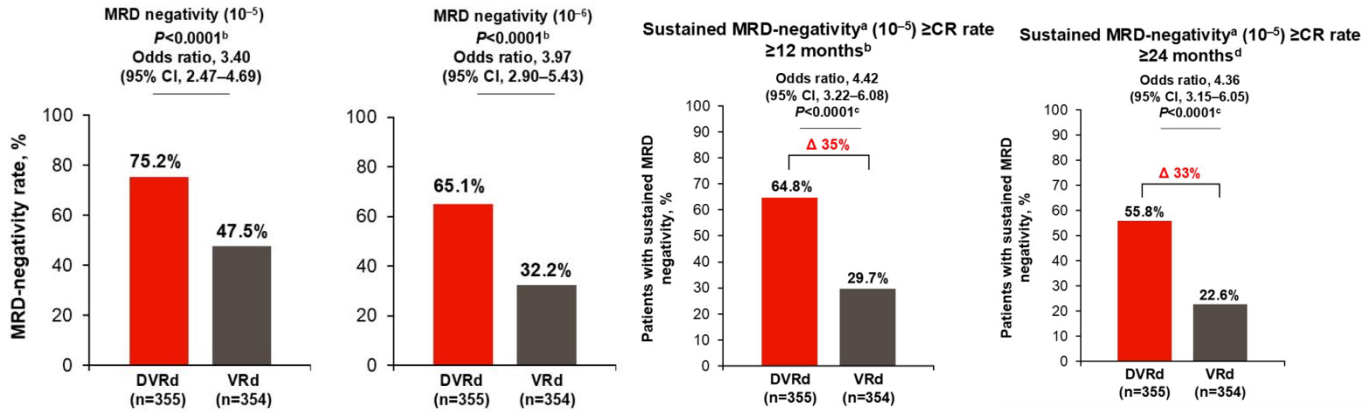
PERSEUS: Dara-VRd

PFS by Treatment Arm



Overall and Sustained MRD Negativity



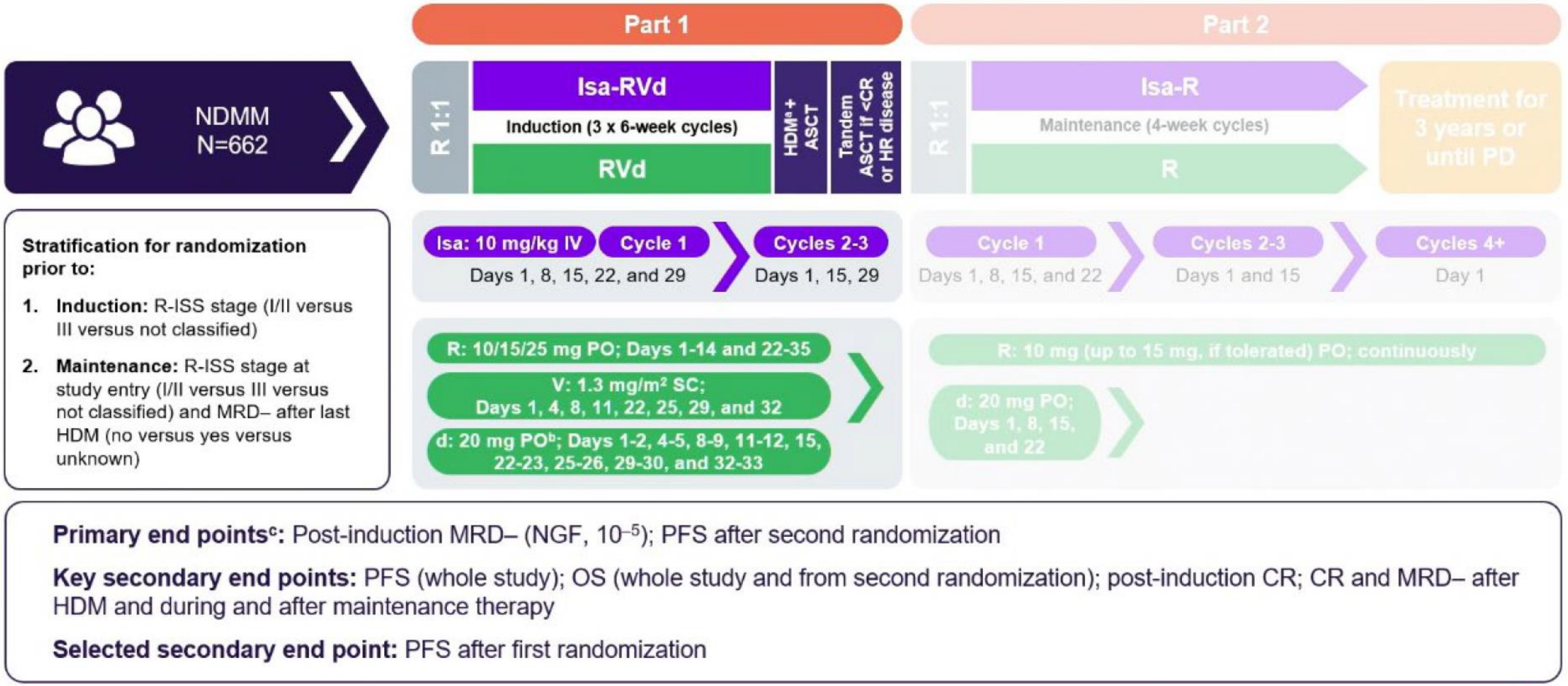
- Median follow-up: 48 months
- Safety
  - Grade ≥3 infection: 35.4% vs 27.4%
  - Grade ≥3 neuropathy: 4.3% vs 4%
  - Grade 5 AEs: 3.7% vs 4.6%
  - Most common grade 3 or 4 event (at the 48-month follow-up) was neutropenia (62.1%); dose reductions or temporary hold of lenalidomide and/or use of G-CSF recommended for management

TEAE, n (%)		Dara-RVd (n=351)		RVd (n=347)	
		Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Hematologic AEs	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)
Specific nonhematologic AEs	Peripheral neuropathy	188 (53.6)	15 (4.3)	179 (51.6)	14 (4.0)
	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)
	URTI	111 (31.6)	2 (0.6)	87 (25.1)	6 (1.7)

URTI = upper respiratory tract infection.

Sonneveld P, et al. Presented at: 29th EHA Congress; 2024.

GMMG-HD7: Isa-VRd



HDM = high-dose melphalaln; NGF = next-generation flow cytometry.
Goldschmidt H, et al. Presented at: 66th ASH Annual Meeting; 2024.

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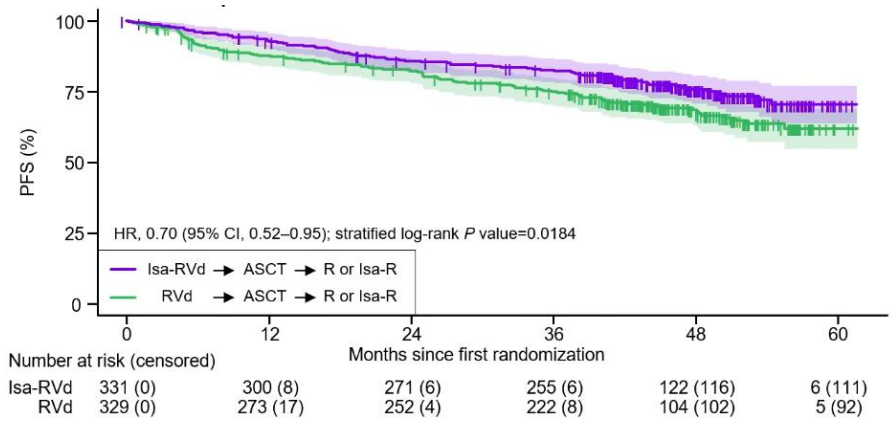
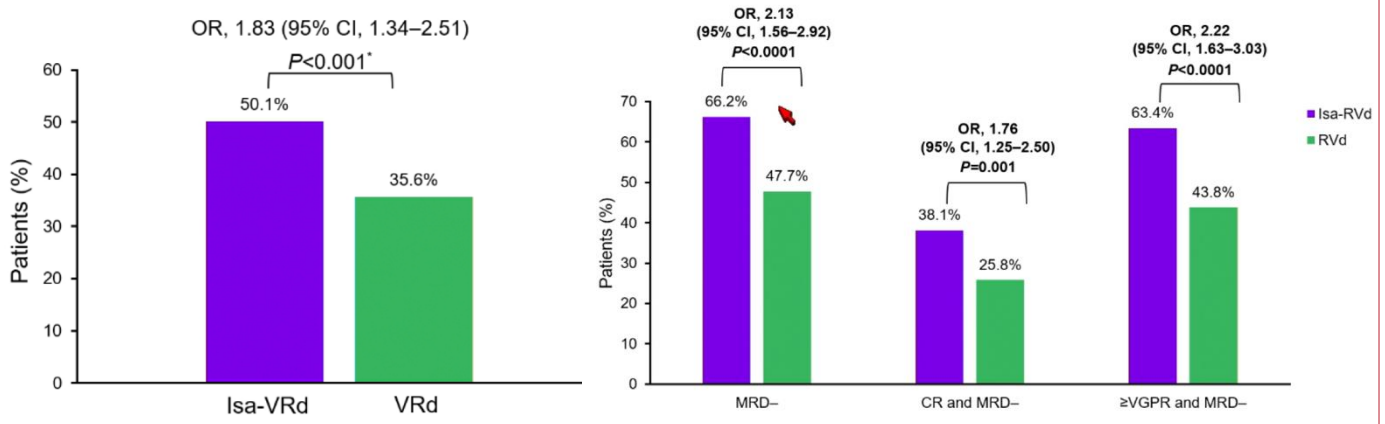
GMMG-HD7: Isa-VRd

PFS by Treatment Arm



MRD Negativity (10^{-5})



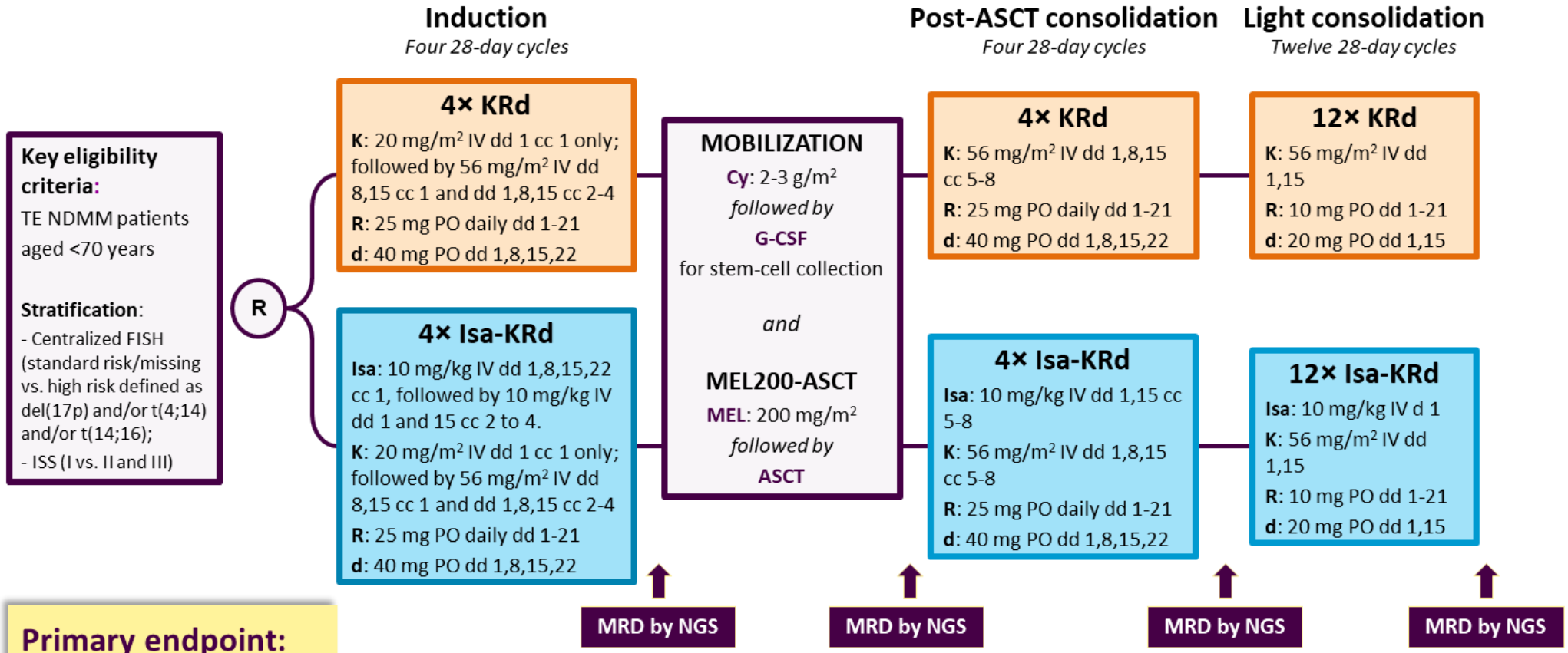
- Median follow-up: 48 months
- Safety
  - Grade ≥3 infection: 12% v 10% (1 grade 5 in Isa arm)
  - Grade ≥3 neuropathy: 7% v 8%; reduce or hold bortezomib and/or switch to once-weekly, subcutaneous administration to mitigate
  - Grade 5 AEs: 1% v 2%

TEAEs, n (%)[3]		Isa-RVd (n=330)	RVd (n=328)
Serious AE		115 (34.8)	119 (36.3)
Deaths		4 (1.2)	8 (2.4)
Hematologic AEs	Neutropenia	87 (26.4)	30 (9.1)
	Lymphopenia	48 (14.5)	65 (19.8)
	Anemia	13 (3.9)	20 (6.1)
	Thrombocytopenia	21 (6.4)	15 (4.6)
Specific nonhematologic AEs	PN	25 (7.6)	22 (6.7)
	Thromboembolic events	5 (1.5)	9 (2.7)
	Infusion-related reactions	4 (1.2)	NA

Goldschmidt H, et al. Presented at: 66th ASH Annual Meeting; 2024.

Isa-KRd: Phase 3 ISKIA EMN24/HOVON Trial

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



Primary endpoint:
MRD negativity by NGS after post-ASCT consolidation

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.

Gay F, et al. Presented at: 65th ASH Annual Meeting; 2023.

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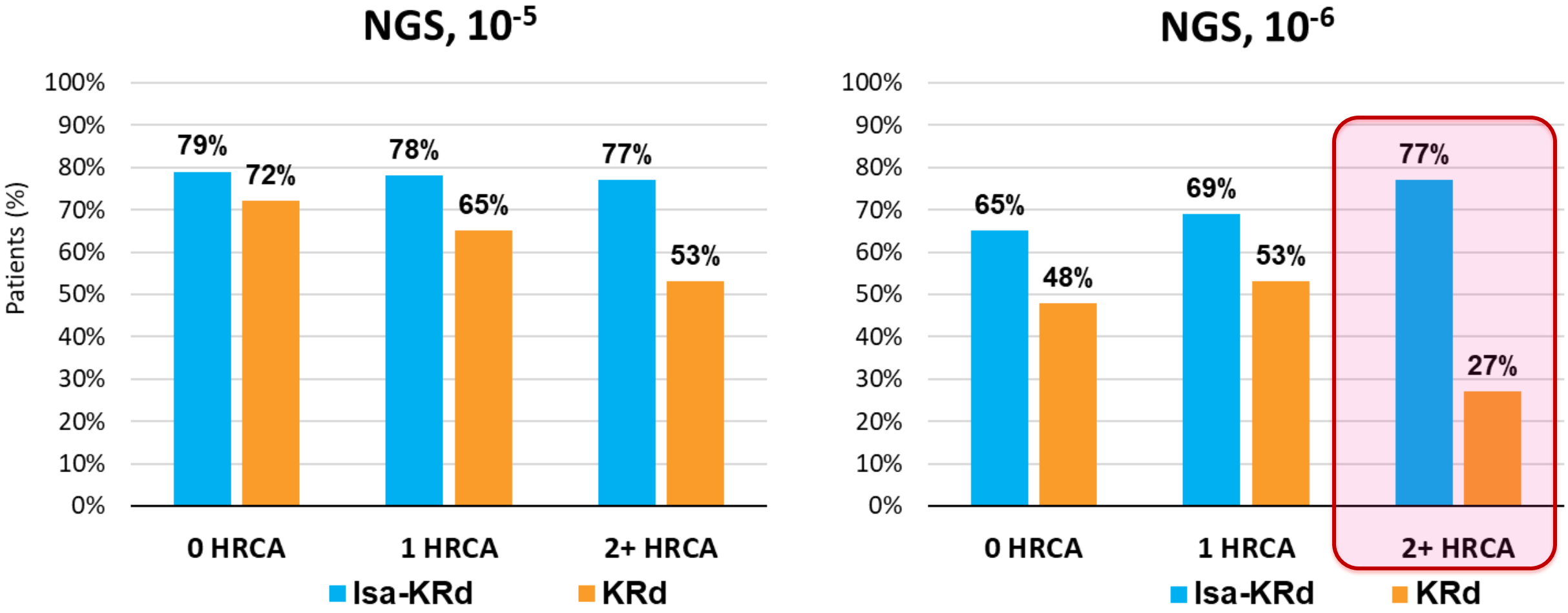
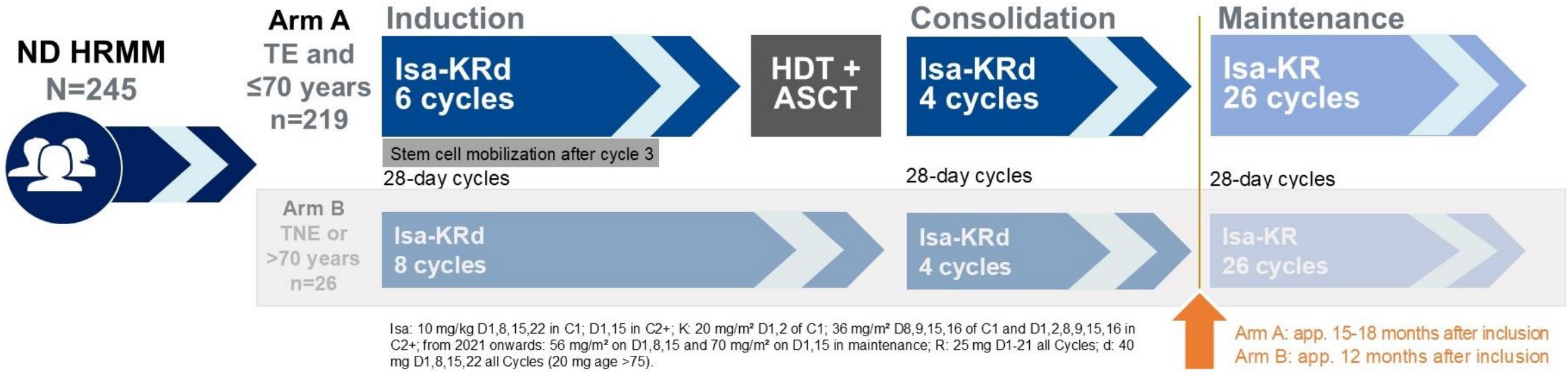
Post-Consolidation MRD Negativity by NGS: Subgroup Analysis by Cytogenetic Risk



1 HRCA was defined as the presence of one of the following high-risk cytogenetic abnormalities: del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21); 2+ HRCA was defined as the presence of at least two high-risk cytogenetic abnormalities.
Gay F, et al. Presented at: 65th ASH Annual Meeting; 2023.

GMMG-Concept: Phase 2 Study of Isa-KRd in High-Risk NDMM

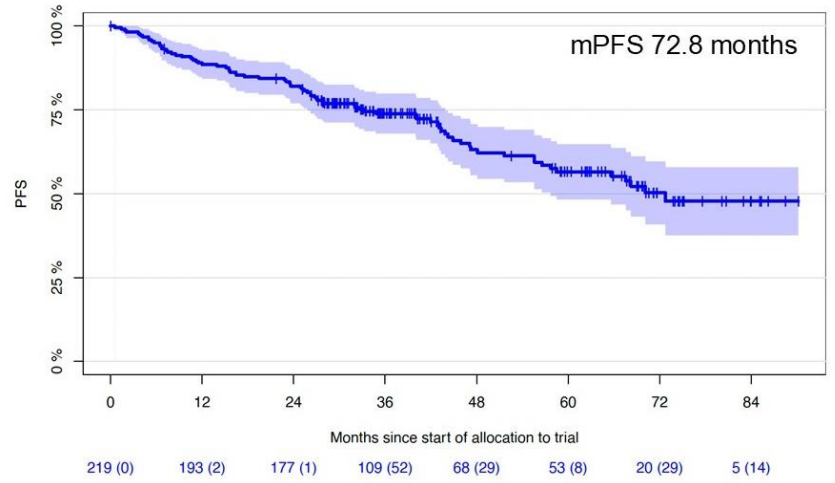


HRMM criteria: ISS stage II or III **PLUS** ≥1 of: del(17p), t(4;14), t(14;16) and/or ≥3 copies 1q21 (amp1q21)
Primary objective: MRD negativity after consolidation (NGF, 10^{-5})
Secondary objective: PFS; Selected tertiary objectives: ORR, OS

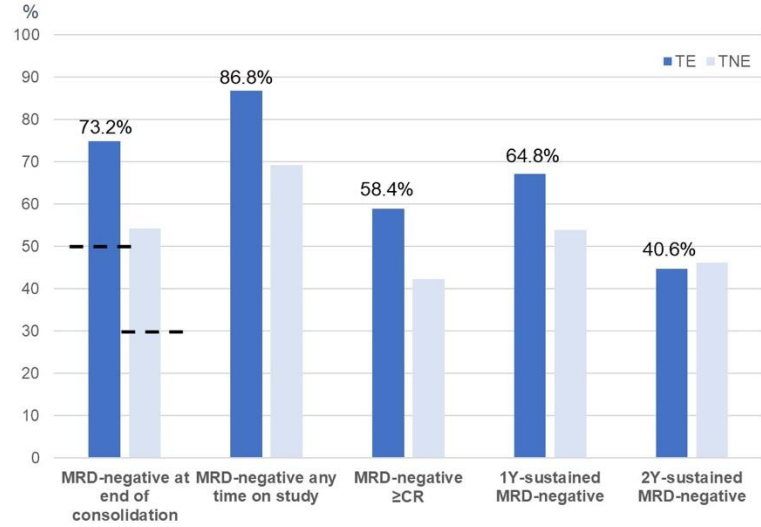
ORR = objective response rate.
Leypoldt L, et al. Presented at: ASCO Annual Meeting; 2025.

GMMG-Concept: Phase 2 Study of Isa-KRd in High-Risk NDMM

PFS: TE NDMM



MRD Negativity (10^{-5})



- Median follow-up: 43 months
- Safety
  - Grade ≥3 infection: 28%
  - Grade ≥3 cardiac AEs: 2% (TE arm); 20% (TI arm)
- Carfilzomib dosing: once weekly (56 mg/m^2) vs twice weekly (36 mg/m^2) had more dose reductions but fewer carfilzomib discontinuations

Leypoldt L, et al. Presented at: ASCO Annual Meeting; 2025.

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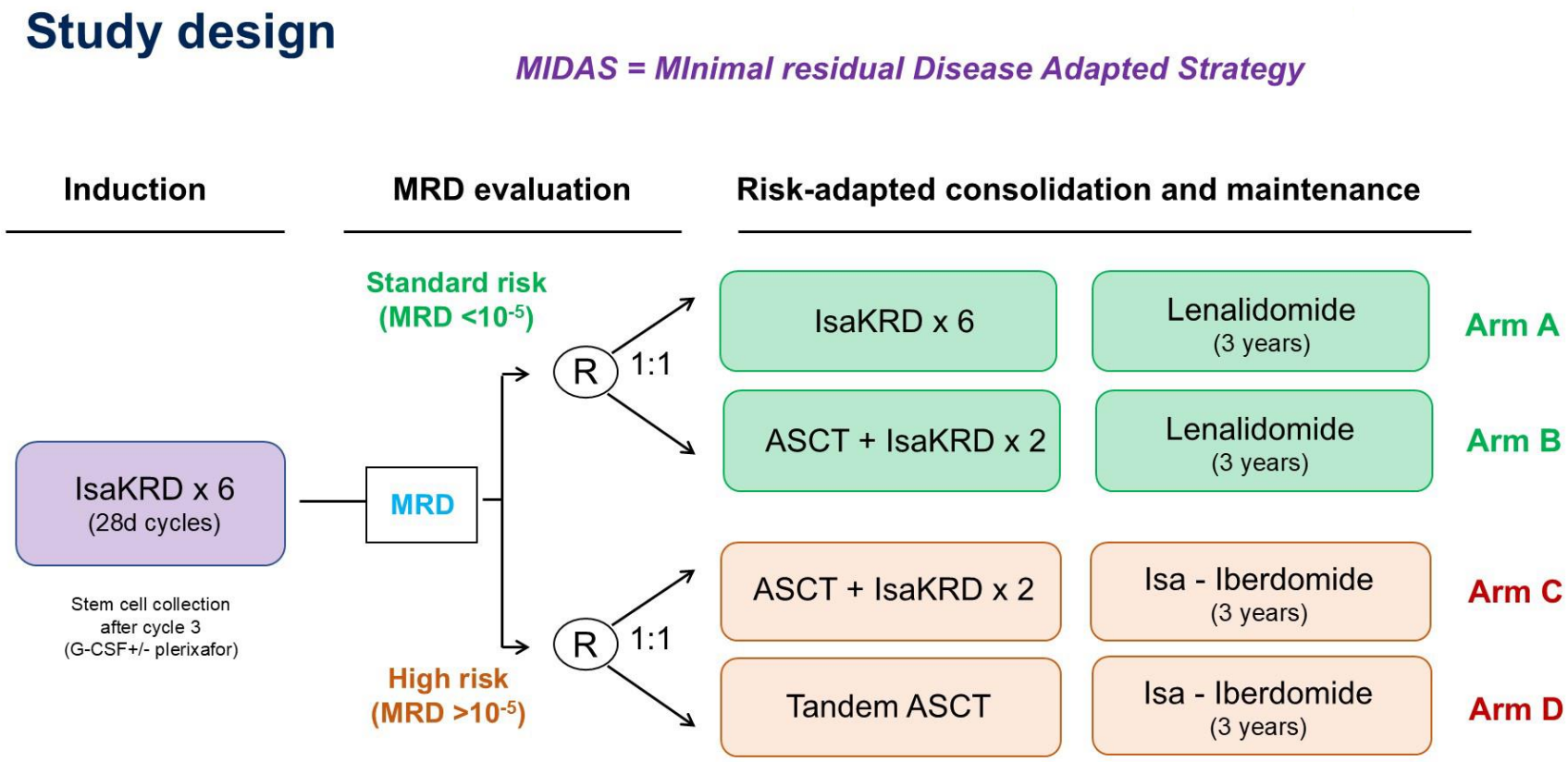
Summary of Quad Induction in Transplant-Eligible NDMM

ASCO 2025 updates to **ADVANCE** (Dara-KRd vs KRd) and **IsKia** are expected to further clarify the role of CD38 antibodies with carfilzomib-based induction, of high interest for patients with high-risk disease or intolerance to bortezomib.

	PERSEUS[1]	GMMG-HD7[2]	GRIFFIN[3,4]	MASTER[5]	GMMG-CONCEPT[6]	IsKia[7]
Induction Maintenance	**Dara-RVd vs RVd Dara-R vs R**	**Isa-RVd vs RVd Isa-R vs R**	**Dara-RVd vs RVd Dara-R vs R**	**Dara-KRd R/MRD surveillance**	**Isa-KRd Isa-KR**	**Isa-KRd vs KRd R**
Total N	355 vs 354	331 vs 329	104 vs 103	123 (standard- and high-risk, transplant-eligible patients)	99 (transplant eligible, high-risk disease)	151 vs 151 (standard- and high-risk, transplant-eligible patients)
Median follow-up	47.5 mo	NA	49.6 mo	42.2 mo	44 mo	21 mo
≥VGPR[a] ≥CR[a]	NA 88% vs 70%	83% vs 69% 44% vs 34%	90% vs 73% 52% vs 42%	NA 72%	91% 73%	94% vs 94% 74% vs 72%
MRD-neg 10^{-5} [a]	75% vs 48%	66% vs 48%	50% vs 20%	81%	68%	77% vs 67%
PFS[a]	4 year: 84% vs 68%	NA	4 year: 87% vs 70%	NA	3 year: 69%	1 year: 95% vs 95%

Table courtesy Vij R. Presented at: DAVA Oncology 12th Summit on Hematologic Malignancies; 2025. 1. Sonneveld P, et al. Presented at: ASH Annual Meeting; 2023. 2. Raab MS, et al. Presented at: EHA Congress; 2024. 3. Voorhees PM, et al. *Lancet Haematol*. 2023;10(10):e825-e837. 4. Sborov DW, et al. Presented at: IMS Annual Meeting; 2022. 5. Costa LJ, et al. *Lancet Haematol*. 2023;10(11):e890-e901. 6. Leypoldt LB, et al. *J Clin Oncol*. 2024;42(1):26-37. 7. Gay F, et al. Presented at: ASH Annual Meeting; 2023.

MIDAS = MInimal Residual Disease Adapted Strategy



Perrot A, et al. Presented at: ASCO Annual Meeting; 2025.

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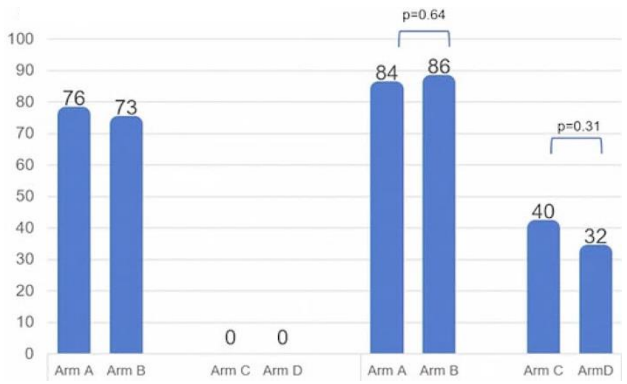
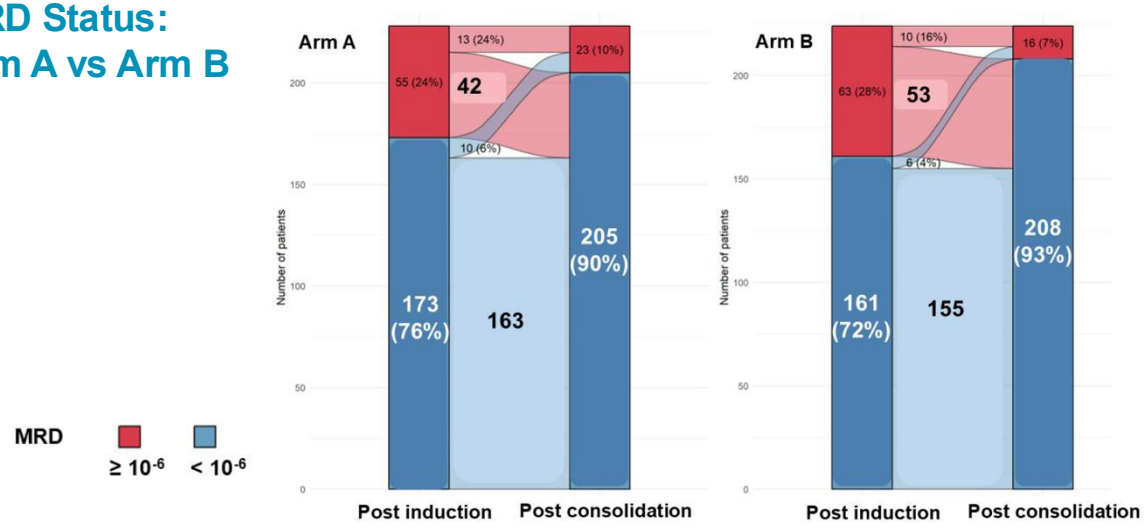
MIDAS = MInimal Residual Disease Adapted Strategy

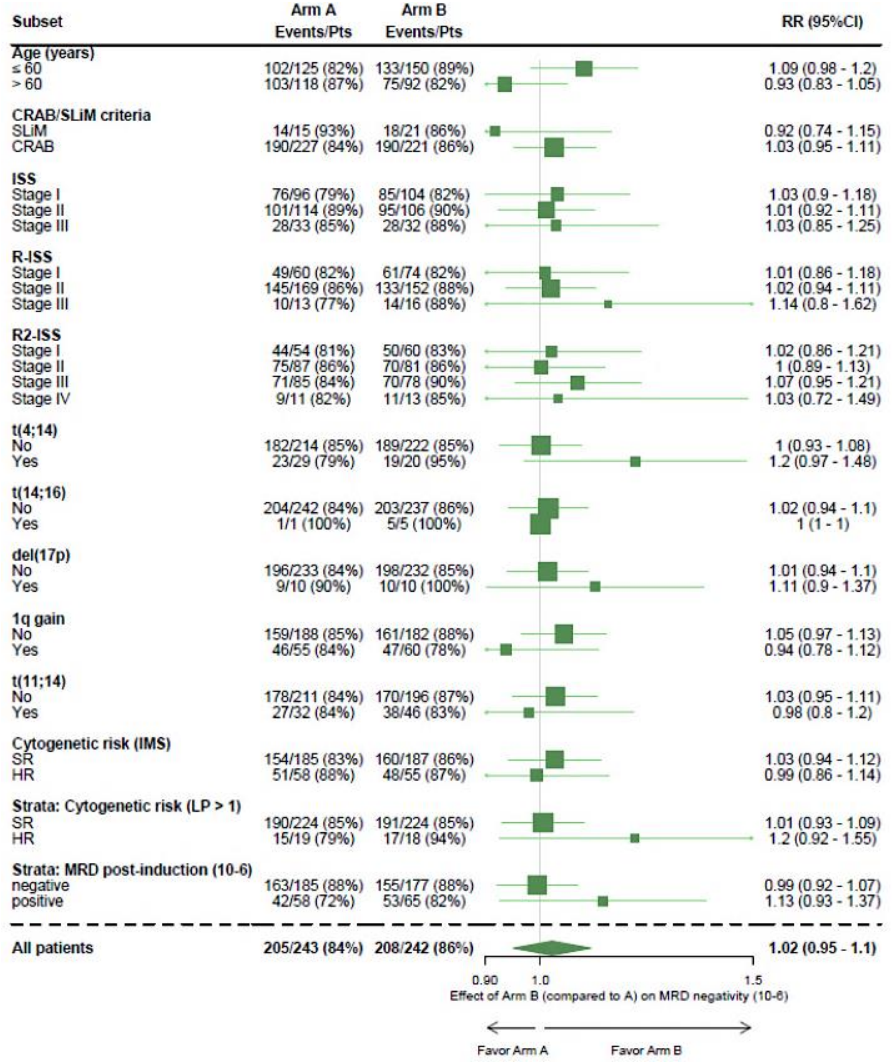
MRD Negative (10^{-6})



MRD Status: Arm A vs Arm B



MRD by Subgroups: Arm A vs B



SLiM = greater than or equal to sixty percent clonal plasma cells in the bone marrow, involved/uninvolved free light chain (FLC) ratio of 100 or more with the involved FLC being greater than or equal 100 mg/L, magnetic resonance imaging (MRI) more than one focal marrow lesion; CRAB = increased calcium levels, renal insufficiency, anemia, presence of bone lesions.

Perrot A, et al. Presented at: ASCO Annual Meeting; 2025.

MIDAS: Should We Stop HCT in MRD Neg?

- MIDAS—only one MRD timepoint
- PERSEUS—sustained MRD important
- MIDAS—what about high-risk cytogenetics?

HCT = hematopoietic cell transplantation.

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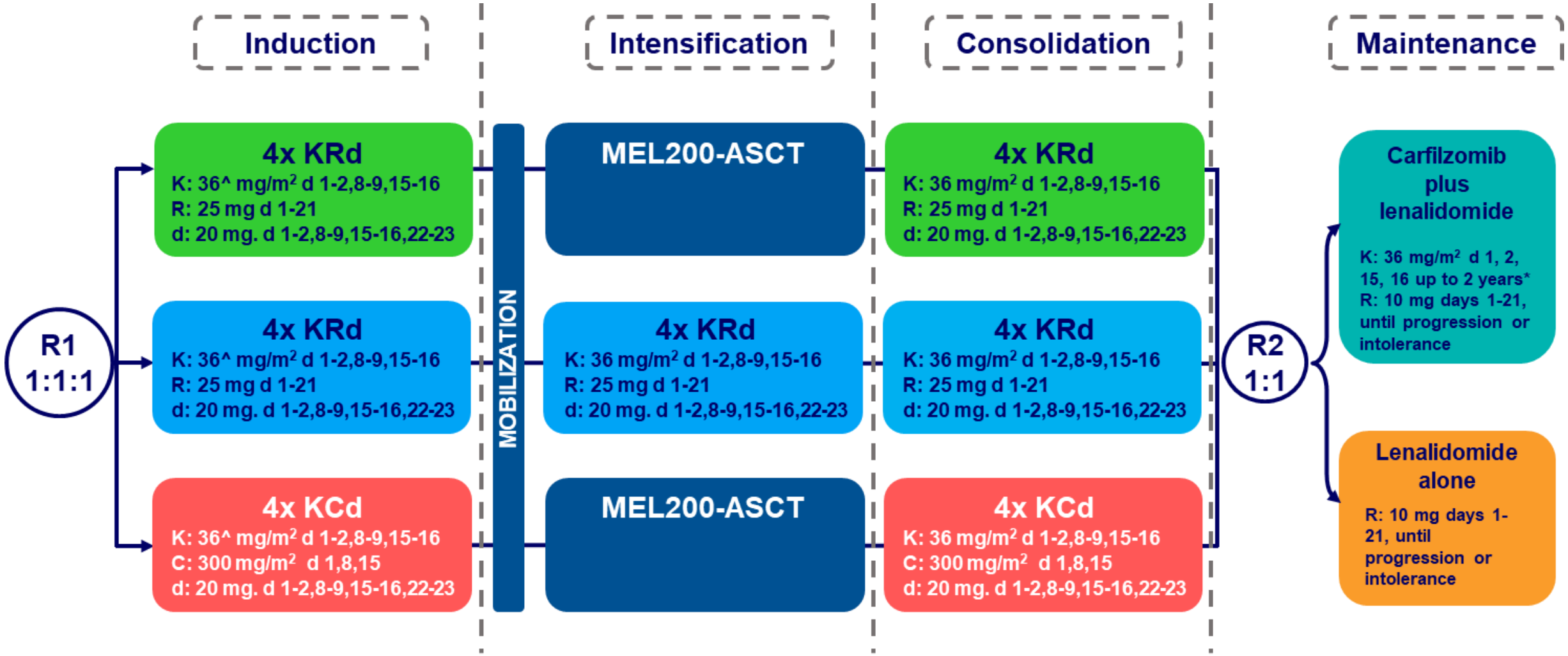
Maintenance: The Road Ahead

- Current state: deepens response, prolongs response, prolongs survival
- Lenalidomide until disease progression
- Future state
  - Single-agent antibody (Cd38, BisAb)
  - Doublet (CD38 + Len)
  - Triplet (CD38 + Len + PI)
  - Fixed duration; MRD guided

BisAb = bispecific antibody; PI = protease inhibitor.
Berg T [www.irvinestandard.com]. Last updated February 5, 2024. https://www.irvinestandard.com/2024/more-freeway-improvements-are-on-the-way.

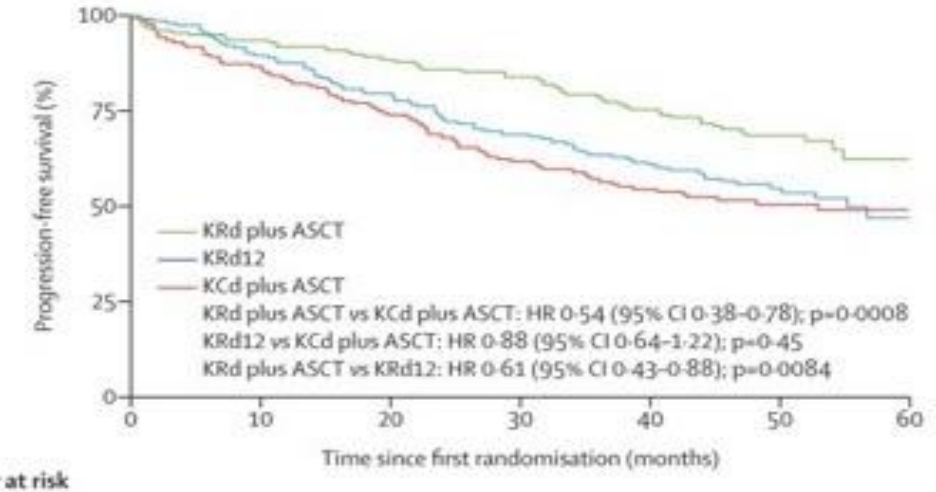
KRd: FORTE Trial—Doublet Maintenance



^20 mg/m2 on days 1-2, cycle 1 only. *Carfilzomib 70 mg/m2 days 1, 15 every 28 days up to 2 years for patients that have started the maintenance treatment from 6 months before the approval of Amendment 5·0 onwards.
R1 = first randomization (induction/consolidation treatment); R2 = second randomization (maintenance treatment); KCd = carfilzomib, cyclophosphamide, lenalidomide; d = days; MEL200 = melphalan at 200 mg/m2.
Gay F, et al. *Lancet*. 2021;22(12):1705-1720.

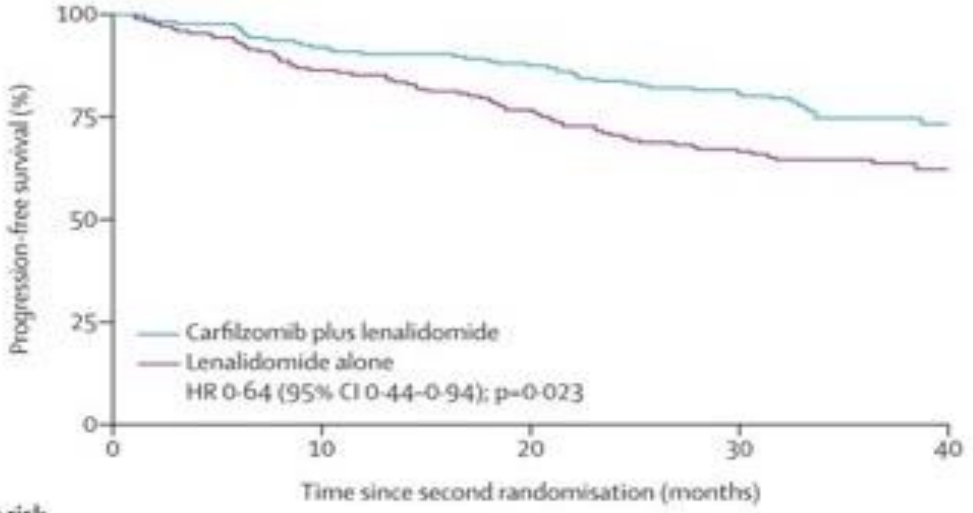
FORTE Trial: PFS Doublet Maintenance

PFS from 1st randomization



Number at risk (number censored)							
KRd plus ASCT	158 (0)	147 (1)	137 (3)	129 (4)	111 (9)	61 (51)	5 (103)
KRd12	157 (0)	135 (6)	120 (6)	103 (7)	90 (9)	51 (39)	5 (81)
KCd plus ASCT	159 (0)	137 (1)	115 (3)	94 (5)	80 (8)	46 (37)	6 (76)

PFS from 2nd randomization

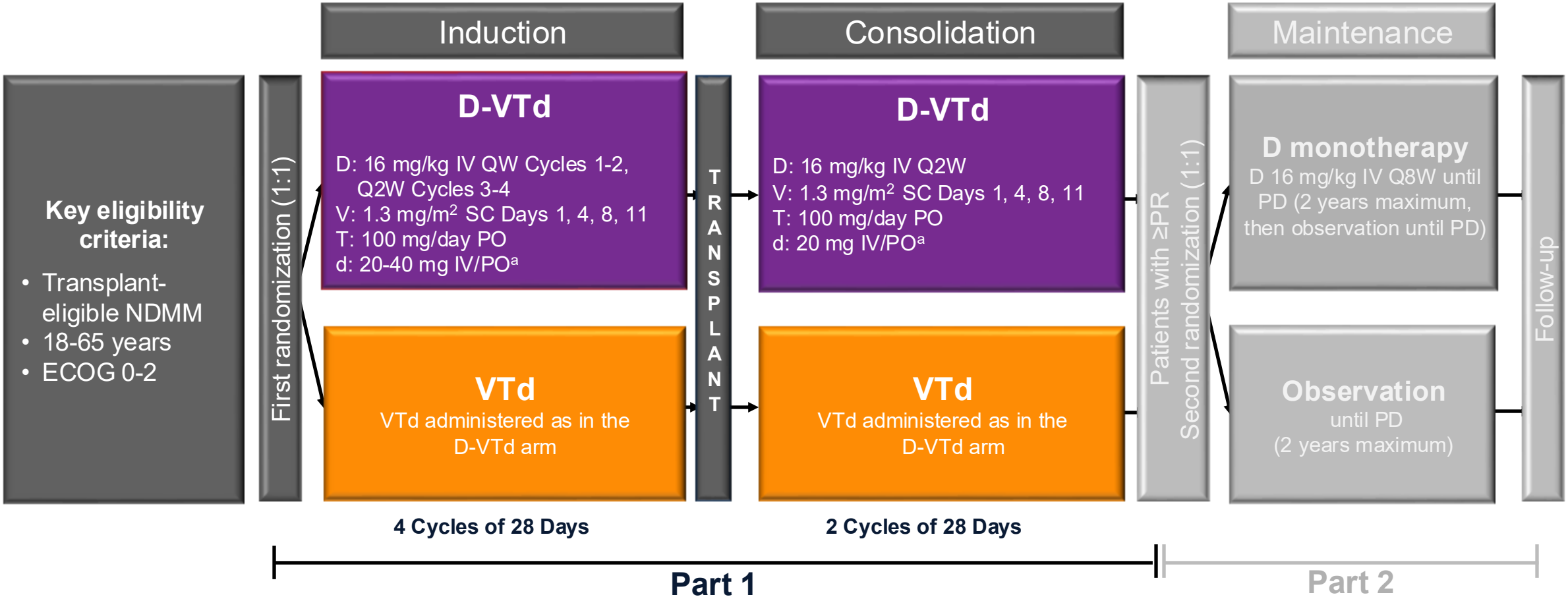


Number at risk (number censored)					
Carfilzomib plus lenalidomide	178 (1)	162 (2)	151 (5)	123 (22)	41 (95)
Lenalidomide alone	178 (0)	154 (0)	135 (2)	108 (11)	39 (75)

Gay F et al. *Lancet*. 2021;22(12):1705-1720.

CD38 Maintenance: CASSIOPEIA

Phase 3 study of D-VTd versus VTd in transplant-eligible NDMM (N=1,085), 111 sites from 9/2015 to 8/2017



ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated April 13, 2025. Accessed September 1, 2024. https://clinicaltrials.gov/study/NCT02541383.

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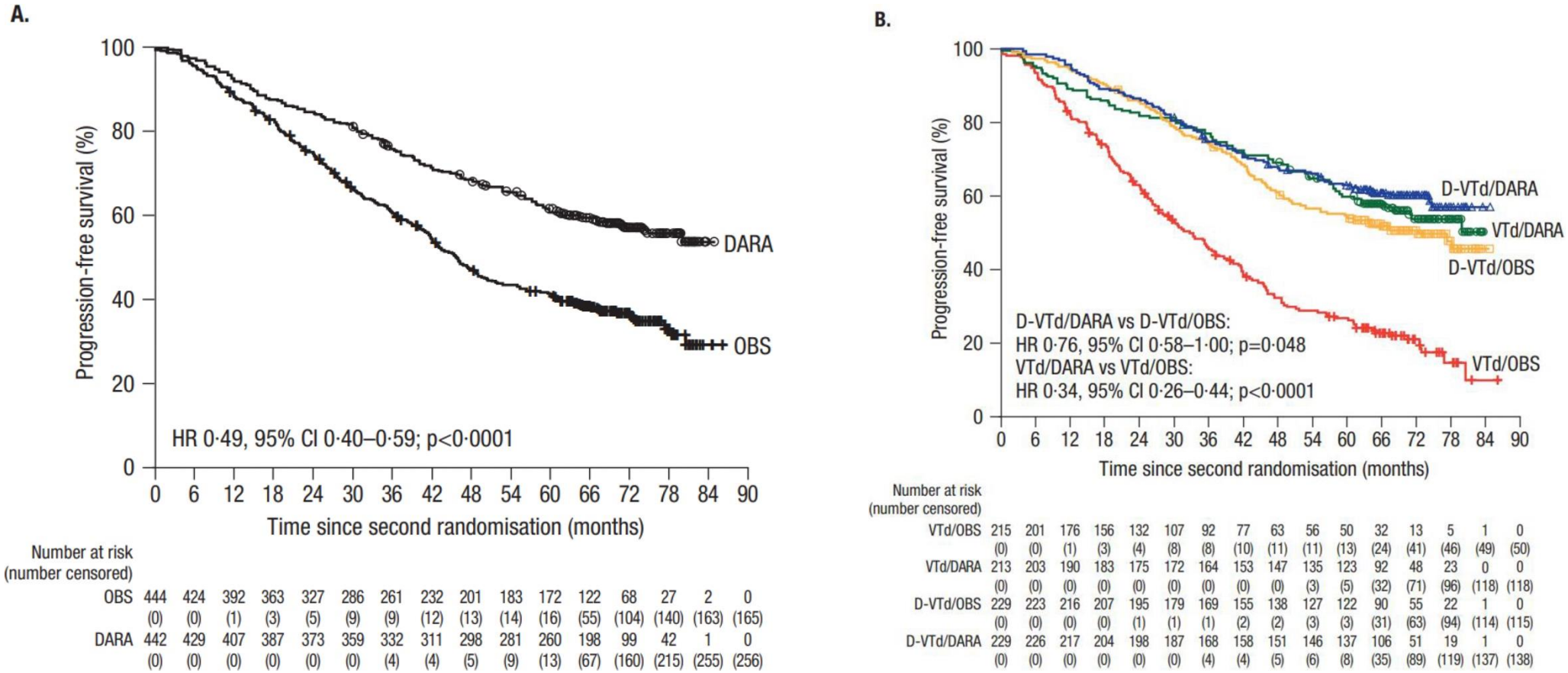
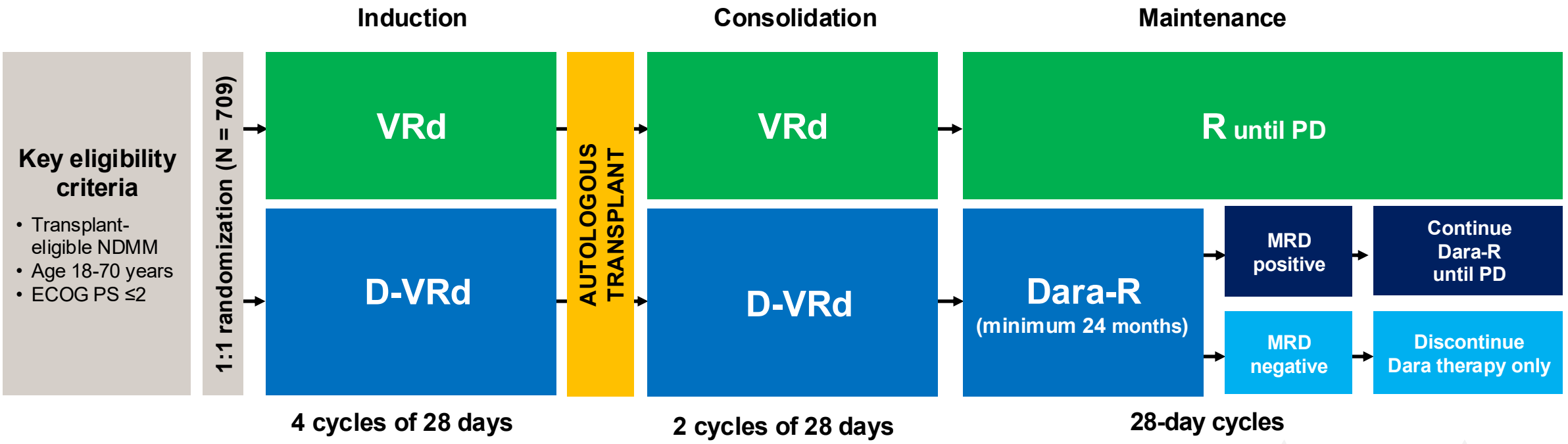
CD38 Maintenance



- **DARA maintenance reduced the risk of progression or death by 51% versus OBS**
- **The longest PFS was observed in patients who received D-VTd + DARA maintenance**

D-VTd = daratumumab, bortezomib, thalidomide, dexamethasone.
Moreau P, et al. *Lancet Oncol*. 2024;25(8):1003-1014.

Phase III PERSEUS: Doublet Maintenance



Primary endpoint: PFS

Key secondary endpoints: Overall ≥CR rate, overall MRD-negativity rate, OS

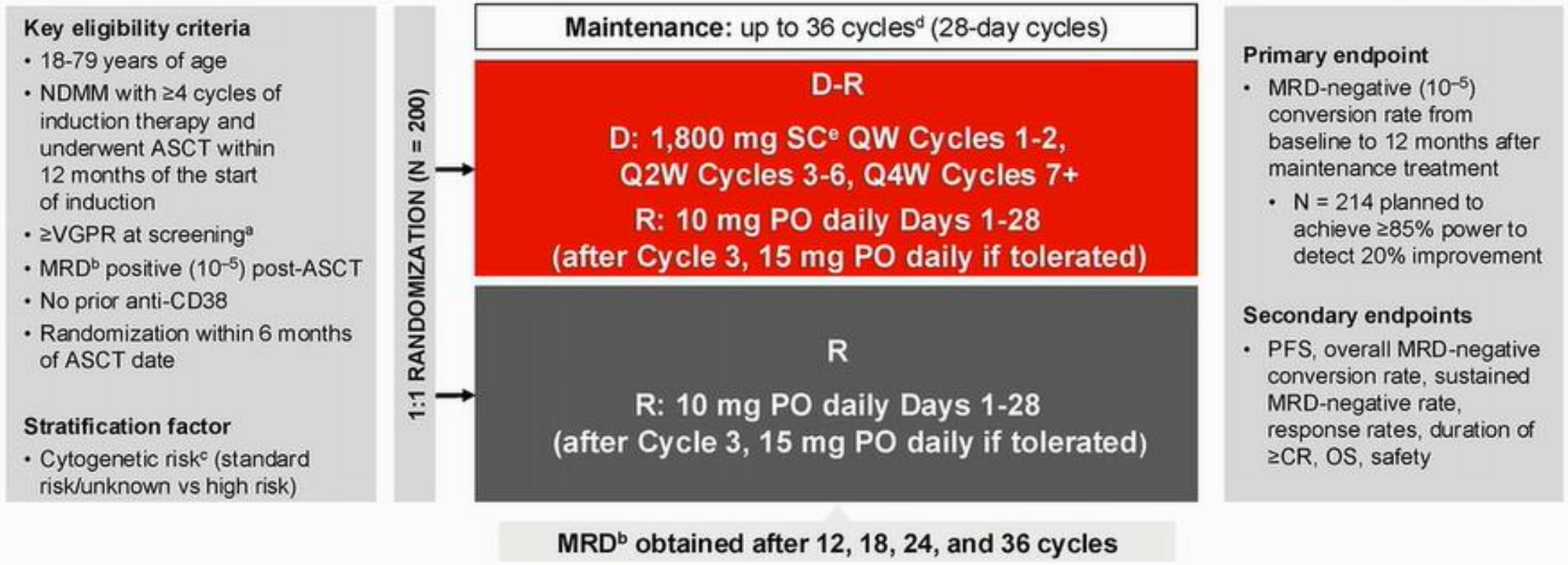
Discontinue Dara therapy only after ≥24 months of D-R maintenance for patients with ≥CR and 12 months of (sustained) MRD negativity

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

MRD was assessed using the clonoSEQ assay 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.
Courtesy of Sonneveld P. Presented at: ASH Annual Meeting; 2023.

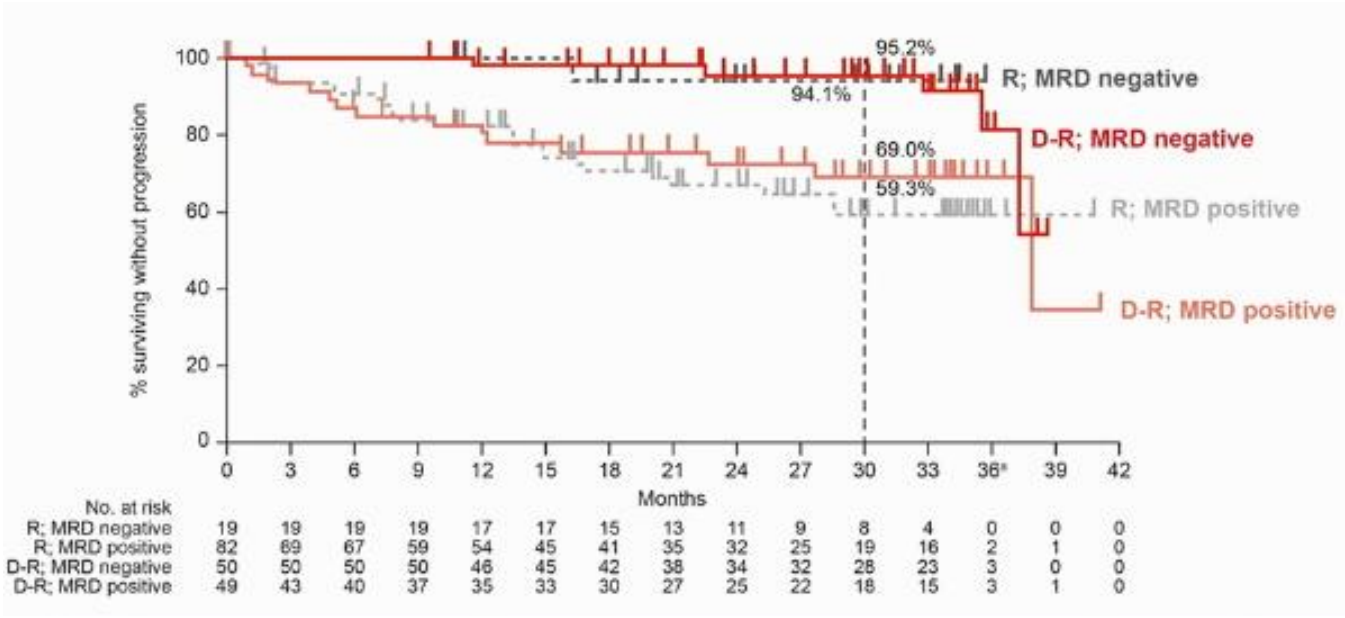
Phase III AURIGA: Design

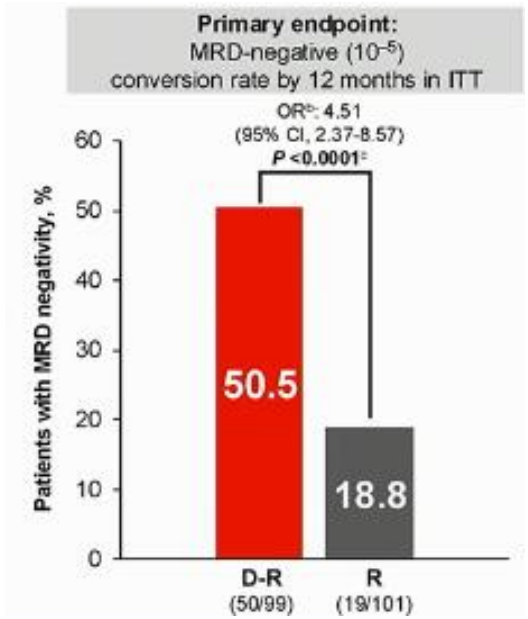
- Objective: To determine the impact of adding DARA to R maintenance on MRD-negative conversion

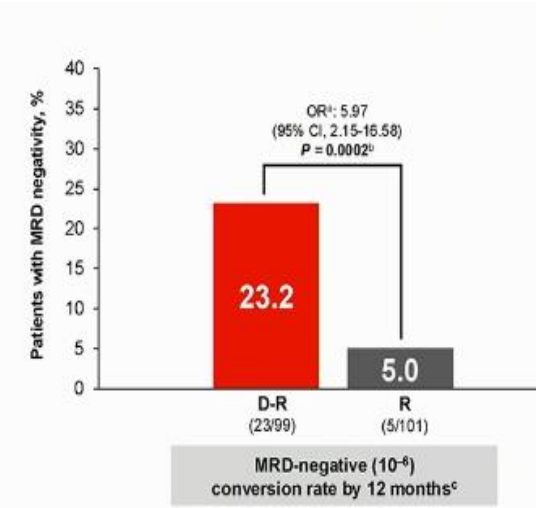


Badros A, et al. *Blood*. 2025;145(3):300-310.

AURIGA: MRD-Neg Conversion (10^{-5} and 10^{-6}) and PFS by MRD-Neg Conversion Status at 12 Months





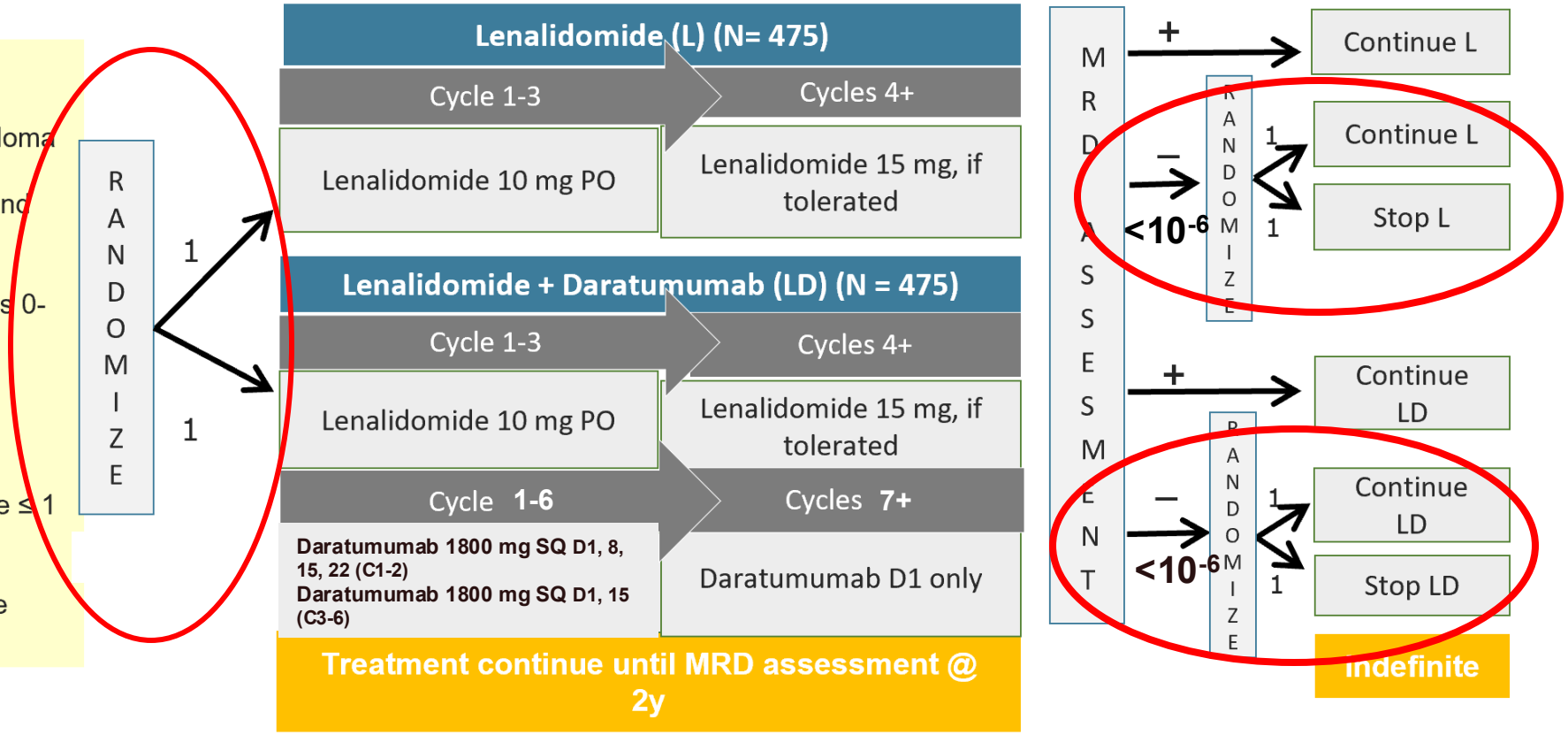


Badros A, et al. *Blood*. 2025;145(3):300-310.

DRAMMATIC Trial Schema

Key eligibility

- First Registration: Study-Entry
  - Symptomatic multiple myeloma requiring systemic therapy prior to induction therapy and ASCT
  - Age 18-75
  - Zubrod Performance Status 0-2
- Second Registration: Eligibility
  - Lenalidomide REMS requirements
  - Lab normalization
  - ASCT related toxicity grade ≤ 1
- Third Registration: Second Randomization
  - Received 2 yr maintenance
  - MRD results



- Registration Step 1: *baseline specimen for ID (B-cell clonality) mandatory
- Registration Step 2: within 180 days after ASCT (***1st randomization***)
- Registration Step 3: completed 24 months of maintenance and MRD-neg + ≥VGPR (*<10^{-6}) (***2nd randomization***)

REMS = risk evaluation and mitigation strategy.

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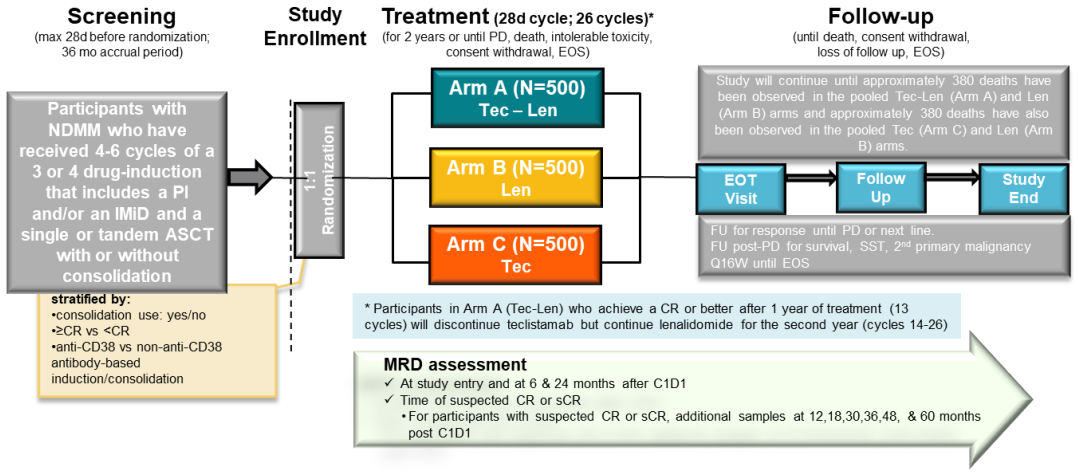
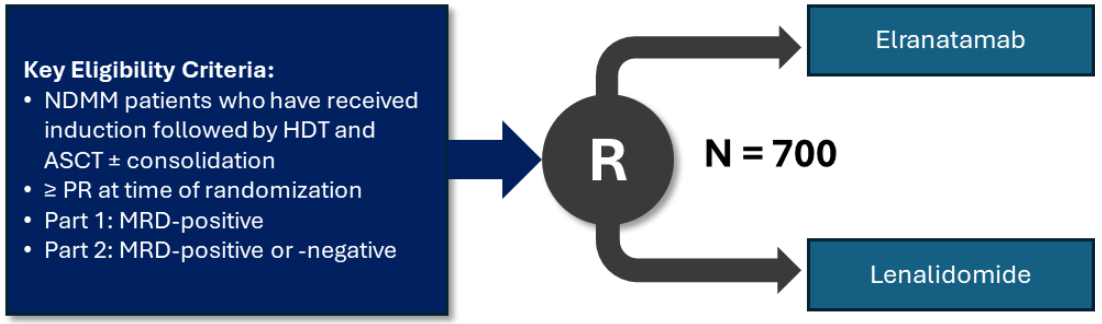
Frontline Immunotherapies for TE NDMM Patients

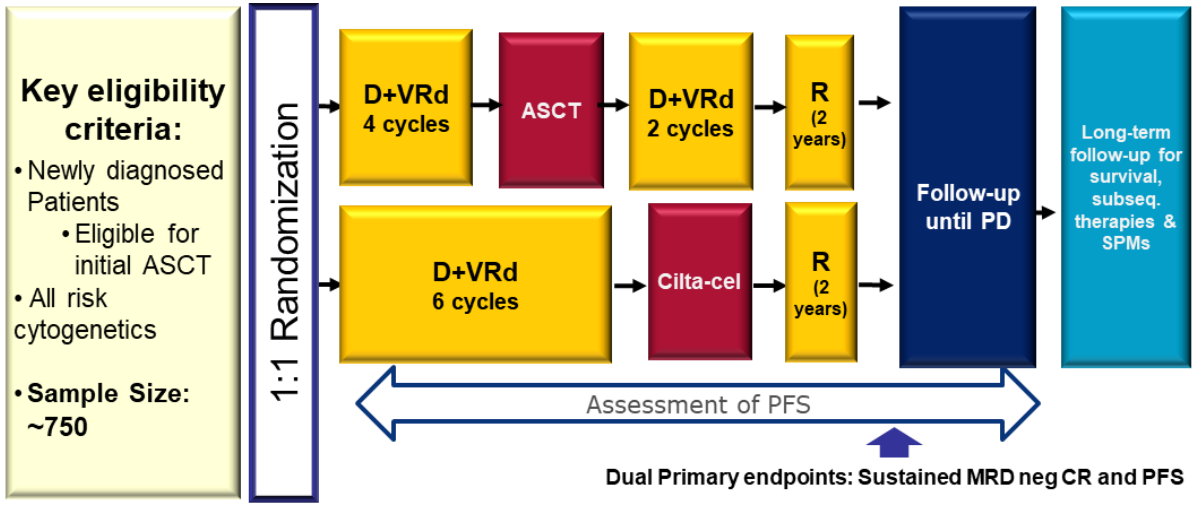
MajesTEC-4



MagnetisMM-7



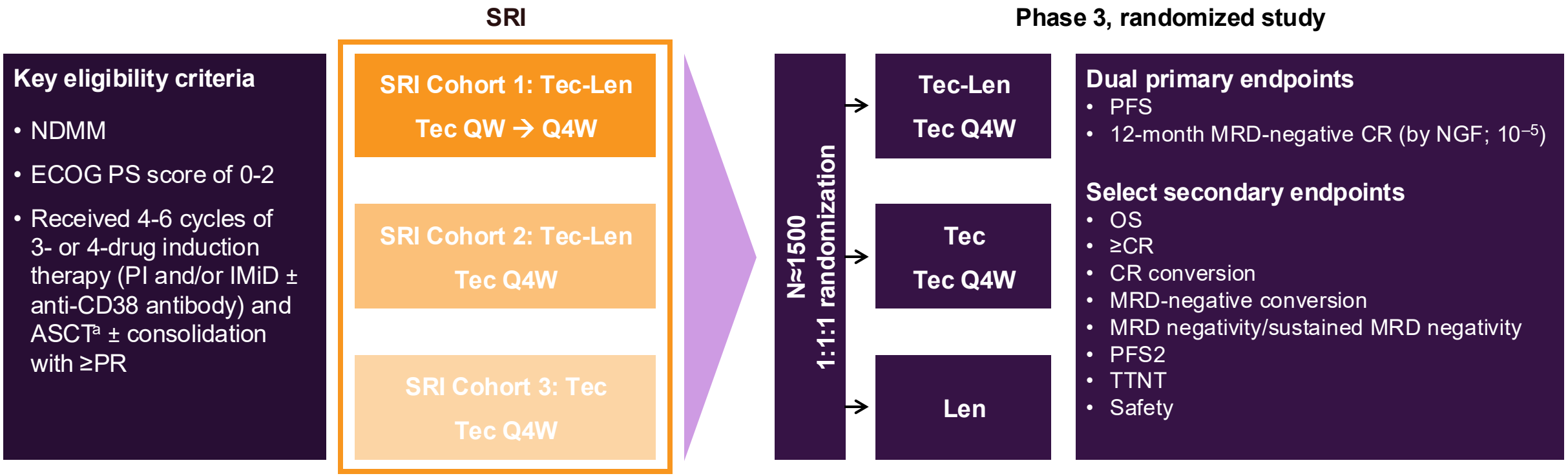
CARTITUDE-6



IMiD = immunomodulatory drug; SPM = subsequent primary malignancy; EOS = end of study; FU = follow-up; SST = secondary solid tumor.

ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated August 17, 2025. Accessed August 6, 2024. https://clinicaltrials.gov/study/NCT05243797. ClinicalTrials.gov [www.clinicaltrials.gov]. Last updated September 10, 2025. Accessed August 6, 2024. https://clinicaltrials.gov/study/NCT05317416. ClinicalTrials.gov [www.clinicaltrials.gov]. Updated September 12, 2025. Accessed August 6, 2024. https://clinicaltrials.gov/study/NCT05257083.

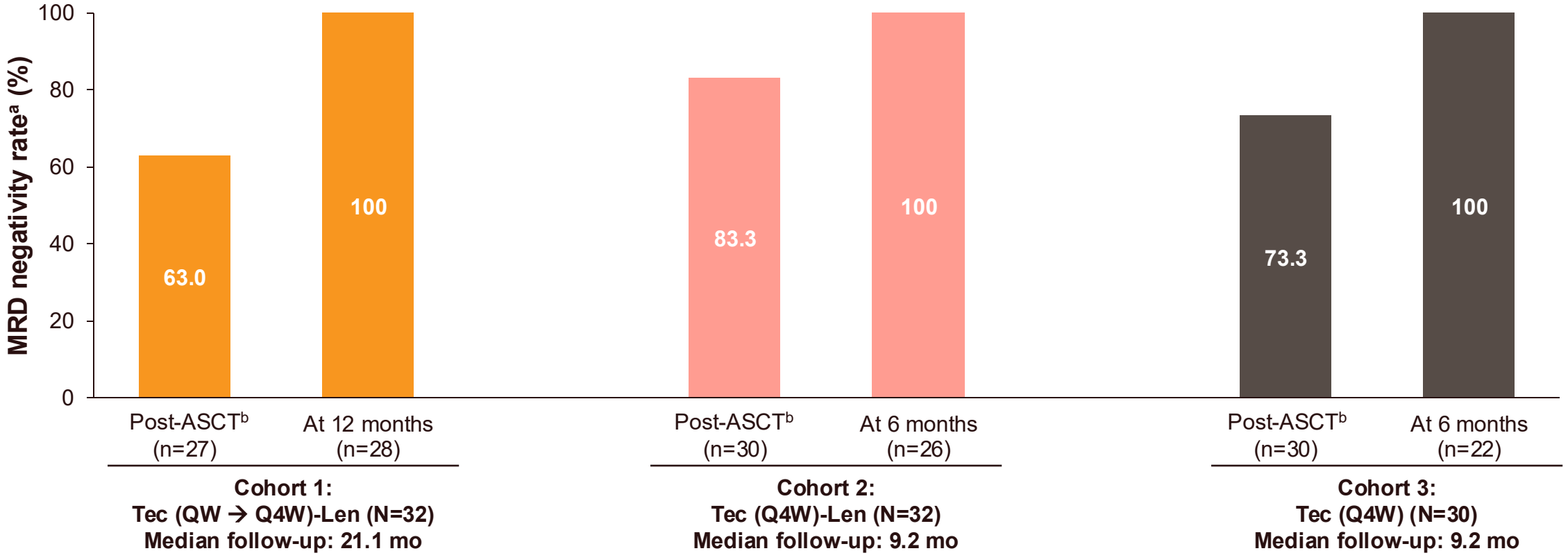
EMN30/MajesTEC-4: Study Design



PFS2 = progression-free survival on second-line therapy; TTNT = time to next treatment.

Zamagni E, et al. *Blood*. 2024;144(Suppl 1):494.

EMN30/MajesTEC-4 SRI: MRD Negativity (10^{-5}) in Evaluable Patients Post-ASCT and during Maintenance



100% of evaluable patients were MRD-negative during maintenance.

Data cutoff date: September 9, 2024.
[a]MRD-negativity rate was defined as the proportion of patients who achieved MRD negativity (10^{-5}), regardless of response. Percentages are out of evaluable patients. Among 87 evaluable patients, 23 patients were MRD-positive at screening (Cohort 1, n=10; Cohort 2, n=5; Cohort 3, n=8). All patients who were MRD-positive at study entry and had an assessment during treatment were MRD-negative during treatment. One patient in Cohort 1 was MRD-positive at 18 months. [b]Post-ASCT ± consolidation.
SRI = safety run-in.

Key Learning Points

- Quadruplet induction is current SOC
- Transplant remains a backbone for most patients (?curative)
- Intensified maintenance
- Fixed-duration maintenance
- Future SOC—? T cell-directed therapy