MAT-GLB-2405526-1.0 - 09/2024

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IMS 2024

Beyond a one-size-fits-all approach: Personalizing therapy in NDMM

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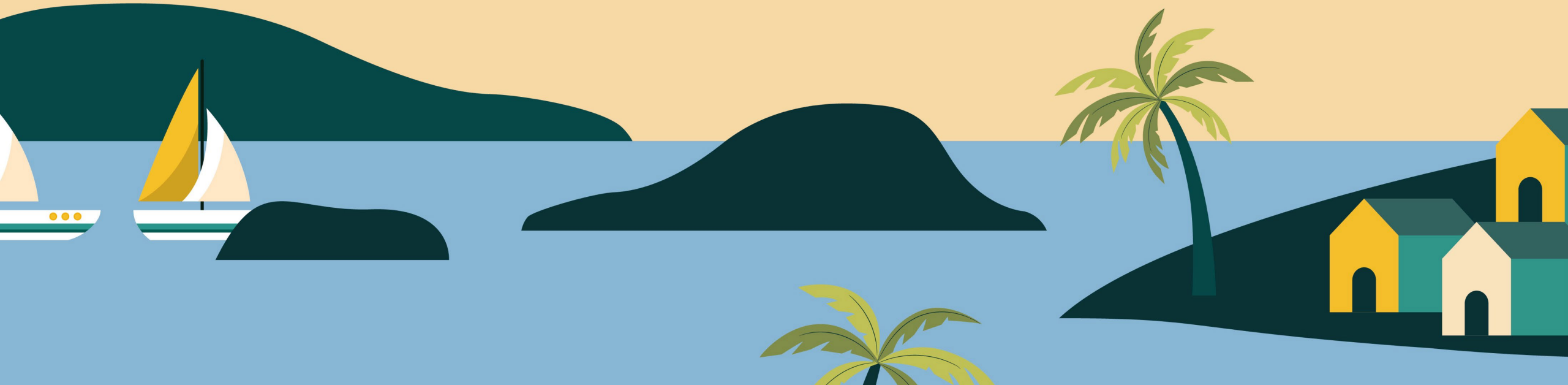
Tailored to fit: New approaches in Ti NDMM

Xavier Leleu



Disclosures

- **Honoraria**: from Amgen, BMS, Gilead, GSK, Janssen, Novartis, Oncopeptide, Pfizer, Sanofi, and Takeda

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Polling question

If access was not an issue, would you consider a quadruplet over a triplet as an upfront regimen in Ti NDMM patients?

- Yes, I would consider a quadruplet regimen
- No, I would choose a triplet regimen
- Other/more information required

NDMM, newly diagnosed multiple myeloma; Ti, transplant ineligible

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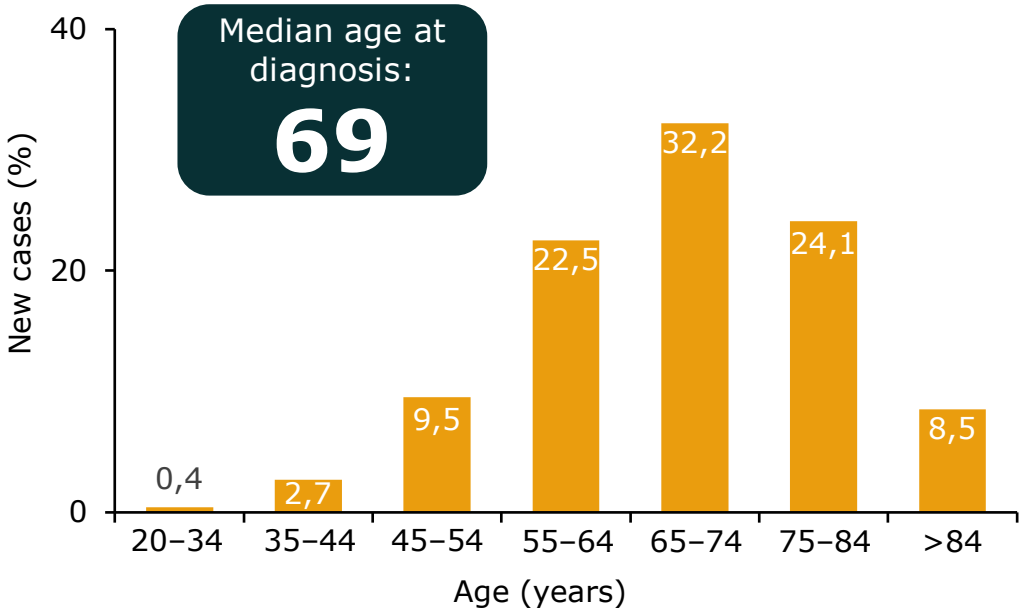
Multiple myeloma is more prevalent in the elderly

Incidence of NDMM cases by age group[1]



Most NDMM patients do not receive transplant[2,3]

US-based electronic health records from 2011 to 2019 (N=6271) showed that a **higher percentage** of **patients were considered Ti** compared with Te and even fewer patients receive transplant[2]:

- **Ti 51%** — n=3168
- **Te 49%** — n=3103
- **Received ASCT 25%** — n=1563

Additionally, of **1279** NDMM patients identified across five countries* from 430 doctors surveyed, more patients were considered Ti vs Te[3]:

- **Ti 66%** — n=838
- **Te 34%** — n=441

MM is most frequently diagnosed in patients ages 65–74 years, and in real-world practice, the majority of patients are considered transplant-ineligible and do not receive transplant[1–3]

*France, Germany, Spain, Italy, and UK. ASCT, autologous stem cell transplant; NDMM, newly diagnosed multiple myeloma; Te, transplant eligible; Ti, transplant ineligible

1. https://seer.cancer.gov/statfacts/html/mulmy.html [accessed Sept 2024];
2. Kumar S, et al. Cancer Med 2021;10:5866–77; 3. Blin N, et al. EHA 2023; Poster 927

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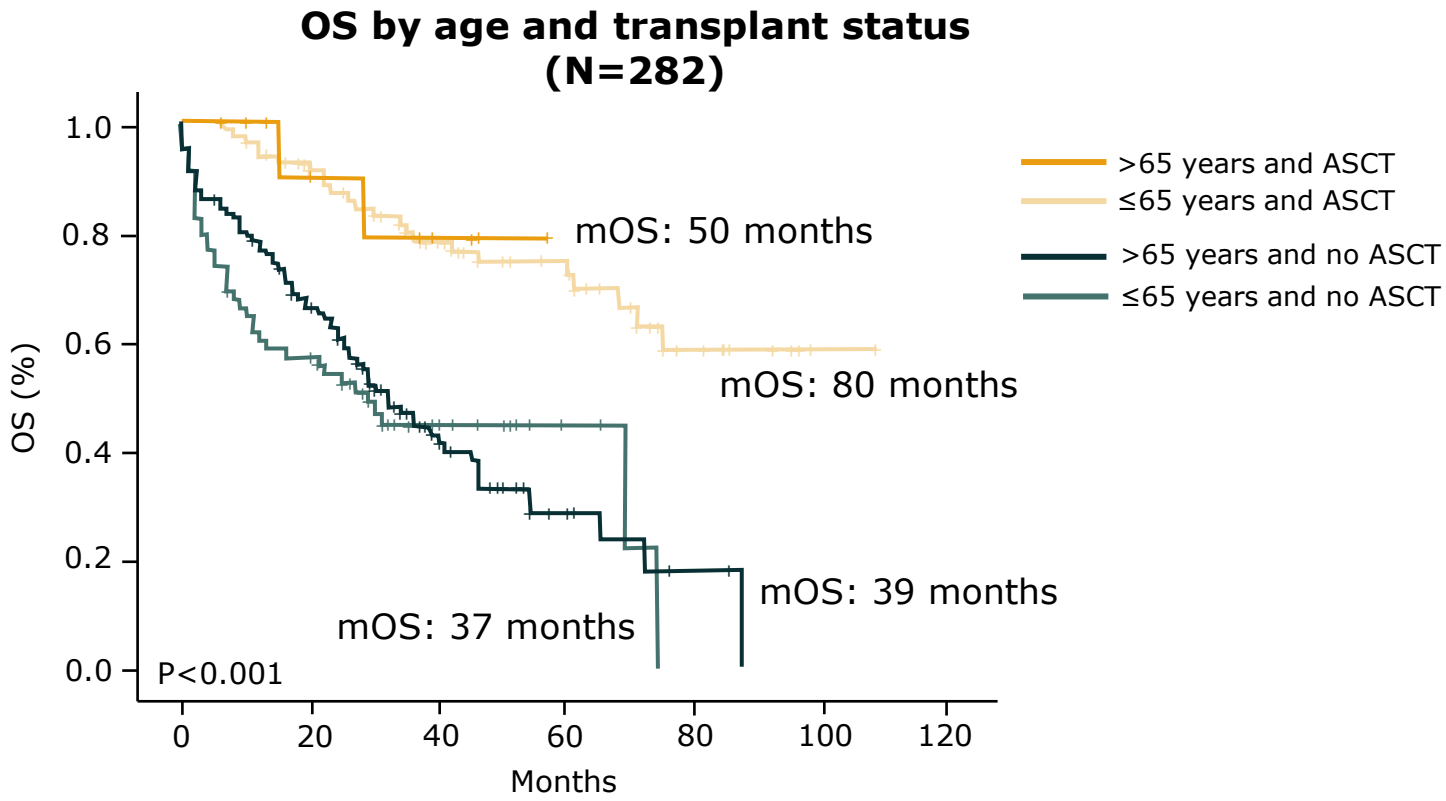
Ti NDMM patients are associated with worse survival outcomes than Te NDMM patients



Ti patients have poorer survival outcomes than Te patients, regardless of patient age;
Ti patients remain an unmet medical need, requiring new treatment strategies that balance efficacy and safety

ASCT, autologous stem cell transplant; m, median; NDMM, newly diagnosed multiple myeloma; OS, overall survival; Te, transplant eligible; Ti, transplant ineligible

Bove V, et al. Hematol Transfus Cell Ther 2021;43:295–302

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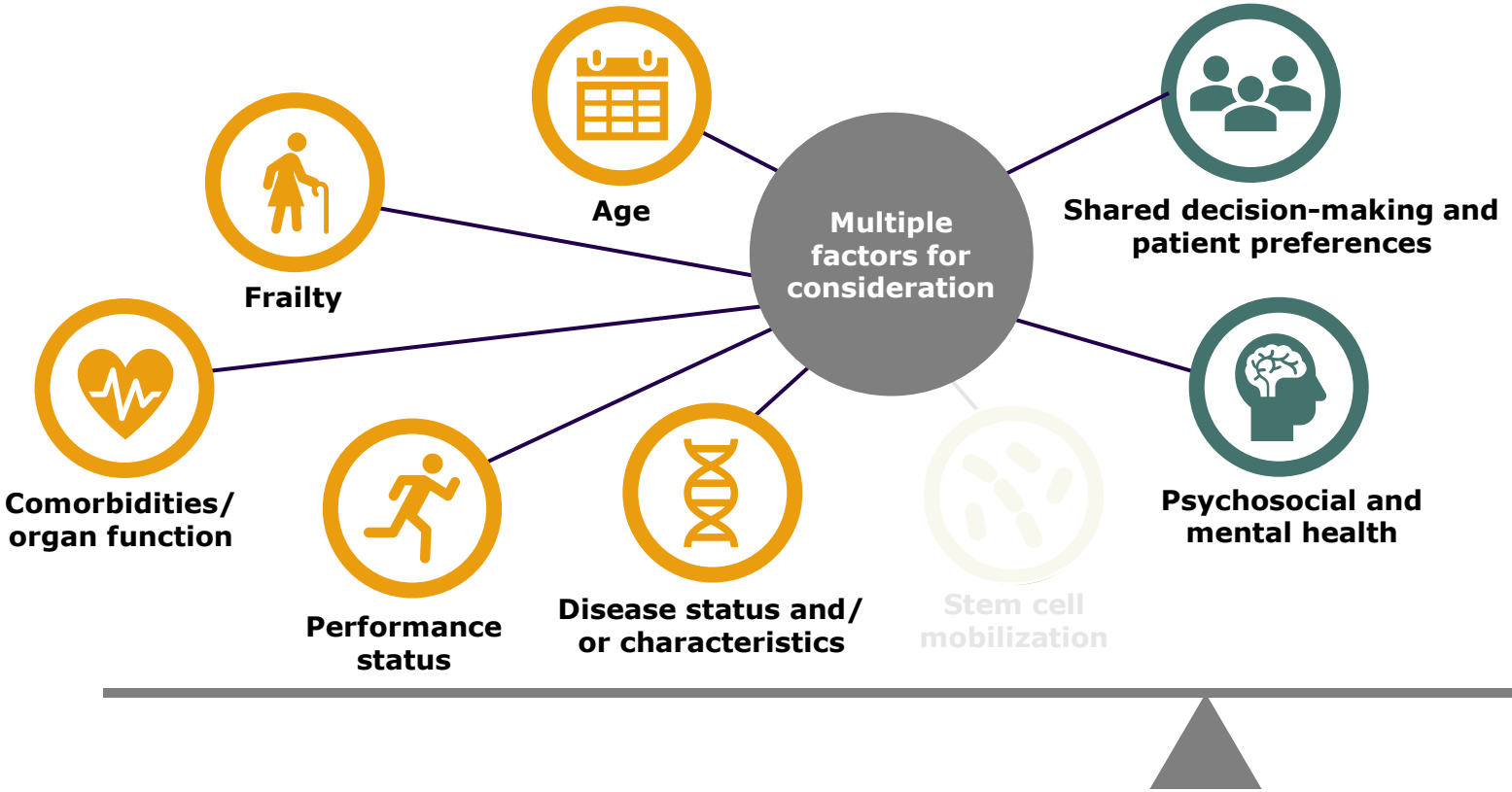
The diversity of patient populations in Ti NDMM means flexibility is required to tailor treatment to patient needs



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?

The Ti NDMM population represents a spectrum of patients with individual needs. Multiple factors need to be considered to determine the best treatment strategy at diagnosis

1. Grant SJ, et al. Hematology Am Soc Hematol Educ Program 2021;2021:46–54;
2. https://www.myeloma.org/autologous-stem-cell-transplant [accessed Sept 2024];
3. Kaweme NM, et al. Front Med 2021;8:612696; 4. Antoine-Pepeljugoski C, Braunstein MJ. Curr Oncol Rep 2019;21:64;
5. Gay F, et al. Haematologica 2018;103:197–211;
6. Dimopoulos MA, et al. Ann Oncol 2021;32:309–22; 7. Goel U, et al. Am J Hematol 2022;97:S3–25

NDMM, newly diagnosed multiple myeloma; Ti, transplant ineligible

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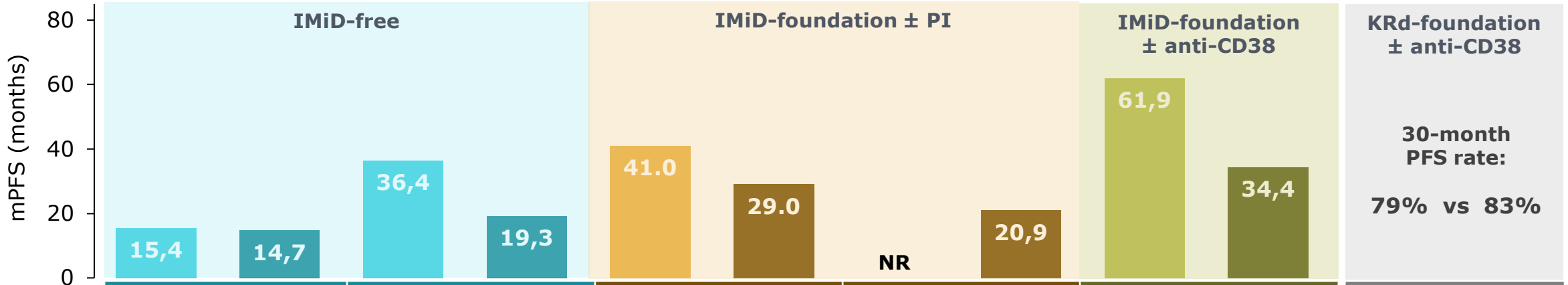
Previously reported RCT data have shown benefit in Ti NDMM populations

PFS: Ti NDMM



	UPFRONT[1]		ALCYONE[2]		SWOG S0777[3]		EMN20[4]		MAIA[5]		GEM2017FIT[6]	
	VTd (n=167)	Vd (n=168)	DVMP* (n=350)	VMP* (n=356)	VRd (n=235)	Rd (n=225)	KRd (n=42)	Rd (n=40)	DRd* (n=368)	Rd (n=369)	DKRd (n=153)	KRd (n=154)
mFU, months	42.7		40.1		84.0		31.4		64.5		33.0	
ORR, %	80	73	91	74	90	79	95	78	93	82	88	82
≥CR	4	3	46	25	24	12	52	5	51	30	61	58
MRD– (10^{-5}), %	–	–	28	7	–	–	60	0	32	11	84	75

Triplet combinations have demonstrated improved patient outcomes vs doublets in Ti NDMM, and further improvement has been observed with novel quadruplet regimens

*Approved regimen in Ti NDMM. CR, complete response; d, dexamethasone; D, daratumumab; FU, follow-up; IMiD, immunomodulatory drug; Isa, isatuximab; K, carfilzomib; m, median; M, melphalan; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NR, not reached; ORR, overall response rate; P, prednisone; PFS, progression-free survival; PI, proteasome inhibitor; R, lenalidomide; RCT, randomized clinical trial; T, thalidomide; Ti, transplant ineligible; V, bortezomib

1. Niesvizky R, et al. J Clin Oncol 2015;33:3921–9;
2. Mateos MV, et al. Lancet 2020;395:132–41;
3. Durie B, et al Blood Cancer J 2020;10:53;
4. Bringhen S, et al. ASH 2023; Presentation 205;
5. Kumar S, et al. ASH 2022; Poster 4559; 6. Mateos MV, et al. ASH 2023; Presentation 209

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

Phase III studies are investigating CD38 mAb-based quadruplet therapy using various dosing schedules in Ti NDMM

IMROZ[1,2]

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

3:2

Initiation (6-week cycles) → Maintenance 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 weekly (C1), every 2 weeks (C2–17), monthly (C18+)
V SC: 1.3 mg/m^2 **twice-weekly** (W1–2 and 4–5 of C1–4) during initiation only
d IV/PO: 20 mg during C1–17* then **weekly** (C18+)

BENEFIT[3–5]

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

1:1

Induction (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 weekly (C1), every 2 weeks (C2–12), monthly (C13+)
V SC: 1.3 mg/m^2 **weekly** (W1–3 of C1–12) and then **every 2 weeks** (C13–18)
d PO: 20 mg **weekly** (C1–12) then discontinued

*Administered on Days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, and 33, or on Days 1, 4, 8, 11, 15, 22, 25, 29, and 32 in patients aged ≥75 years. C, cycle; d, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; Isa, isatuximab; IV, intravenous; mAb, monoclonal antibody; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; PD, progressive disease; PFS, progression-free survival; PO, orally; R, lenalidomide; SC, subcutaneous; Ti, transplant ineligible; V, bortezomib; W, week

1. Facon T, et al. N Engl J Med 2024; doi: 10.1056/NEJMoa2400712. Online ahead of print;
2. Clinicaltrials.gov. NCT03319667; 3. Leleu X, et al. Nature 2024;
4. Clinicaltrials.gov. NCT04751877;
5. Leleu X, et al. ASCO 2024; Presentation 7501;

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

Phase III studies are investigating CD38 mAb-based quadruplet therapy using various dosing schedules in Ti NDMM

CEPHEUS[1,2]

N=395

- ✓ **Ti or transplant-deferred NDMM**
- ✓ ≥18 years
- × ECOG PS >2
- × Frailty score ≥2*

1:1

Induction (3-week cycles)

- **DVRd** 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 weekly (C1–2), every 3 weeks (C3–8), monthly (C9+)
V SC: 1.3 mg/m² **twice-weekly** (W1–2 of C1–8); then discontinued
d PO: **20 mg** during C1–8† then **40 mg weekly** for C9+

GEM2017FIT[3,4]

N=462

- ✓ **Ti NDMM**
- ✓ 65–80 years
- ✓ Fit patient (GAH ≤42)
- × ECOG PS >2

1:1:1

Induction

- **DKRd** x18 cycles
- **KRd** x18 cycles
- **VMP** x9 cycles → **Rd** x9 cycles

Consolidation

- **DRd** x4 cycles
- **DRd** x4 cycles

Maintenance

- **MRD–** → **DR** / **Obs**
- **MRD+** → **DR** / **Obs**

Until PD

Primary endpoint: MRD– (NGF, 10^{-5}) after 18 cycles

Dara SC: DKRd arm – 1800 mg weekly (C1–2), every 3 weeks (C3–6), monthly (C7–18), then monthly for additional 24 cycles
VMP/KRd arm – weekly (C19–20), every 2 weeks (C21–22), then monthly for additional 24 cycles
V SC: 1.3 mg/m² **twice-weekly** (C1), **weekly** (C2–9), then discontinued
K IV: **36 mg/m² twice-weekly** (C1–2), **56 mg/m² weekly** (C3–18)
d PO: DKRd arm – 40 mg **weekly** (C1–9); **KRd arm –** 40 mg **weekly** (C1–22); **VMP arm** – 40 mg **weekly** (C10–22)

*According to Myeloma Geriatric Assessment score. †Administered on Days 1, 2, 4, 5, 8, 9, 11, 12. C, cycle; d, dexamethasone; Dara, daratumumab; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IMS, International Myeloma Society; Isa, isatuximab; IV, intravenous; M, melphalan; mAb, monoclonal antibody; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; P, prednisone; PD, progressive disease; PO, orally; R, lenalidomide; SC, subcutaneous; Ti, transplant ineligible; V, bortezomib; W, week

1. Clinicaltrials.gov. NCT03652064;
2. Usmani SZ, et al. IMS 2024; OA-63;
3. Mateos MV, et al. ASH 2023; Presentation 209;
4. Clinicaltrials.gov. NCT03742297

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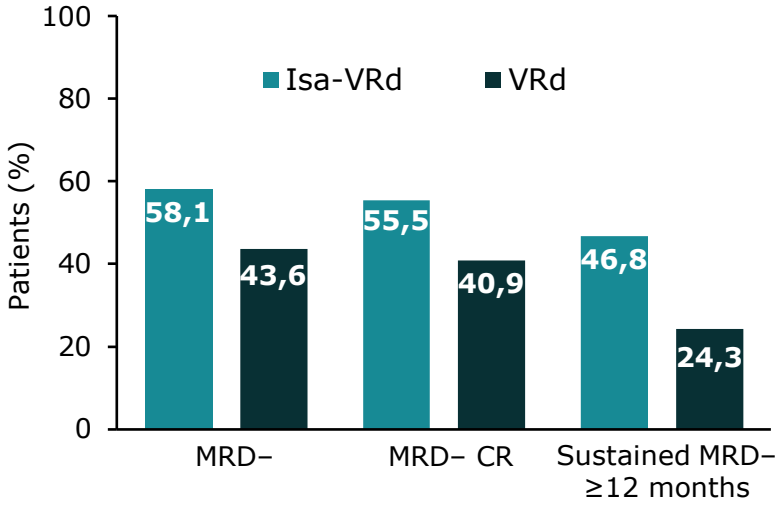
As no head-to-head comparisons are available, direct comparison between trials is not intended and should not be inferred

IMROZ: First global Phase III study of Isa-VRd vs VRd in Ti NDMM

IMROZ: Isa-VRd vs VRd (N=446) in Ti NDMM

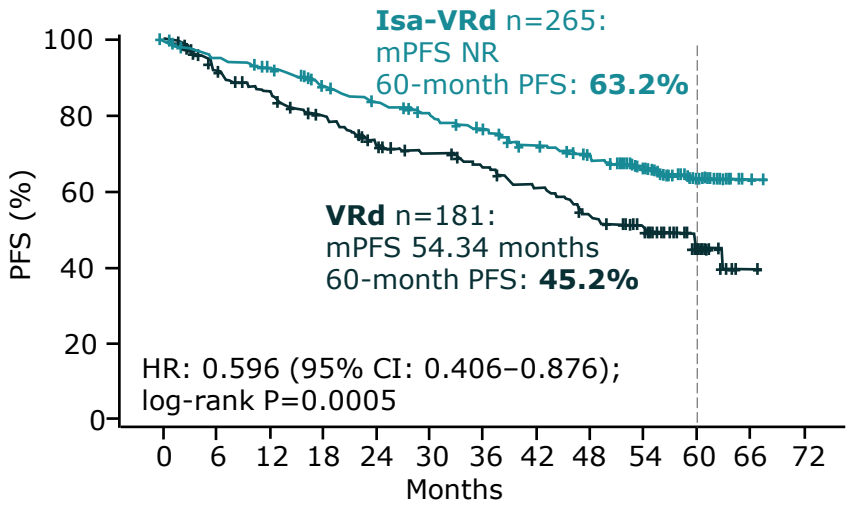
Isa IV: 10 mg/kg weekly (C1), every 2 weeks (C2–17), monthly (C18+)
V SC: 1.3 mg/m^2 **twice-weekly** (W1–2 and 4–5 of C1–4) during initiation only
d IV/PO: **20 mg** during C1–17* then **weekly** (C18+)

MRD– rates (NGS, 10^{-5}; ITT)



Median follow-up: 5 years

Primary endpoint: PFS



OS rates (ITT)

	Isa-VRd	VRd
60-month OS rate, %	72.3	66.3
HR (95% CI)	0.776 (0.407–1.48)	

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 in consistent deep responses vs VRd followed by Rd. The 60-month PFS and OS rates highlight the PFS and OS benefit of Isa-VRd vs VRd in Ti NDMM patients

*Administered on Days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, and 33, or on Days 1, 4, 8, 11, 15, 22, 25, 29, and 32 in patients aged ≥75 years. C, cycle; CI, confidence interval; CR, complete response; d, dexamethasone; HR, hazard ratio; Isa, isatuximab; ITT, intention-to-treat; IV, intravenous; m, median; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; NR, not reached; OS, overall survival; PFS, progression-free survival; PO, orally; R, lenalidomide; SC, subcutaneous; Ti, transplant ineligible; V, bortezomib; W, week

1. Facon T, et al. N Engl J Med 2024; doi: 10.1056/NEJMoa2400712. Online ahead of print;
2. Facon T, et al. ASCO 2024; Presentation 7500

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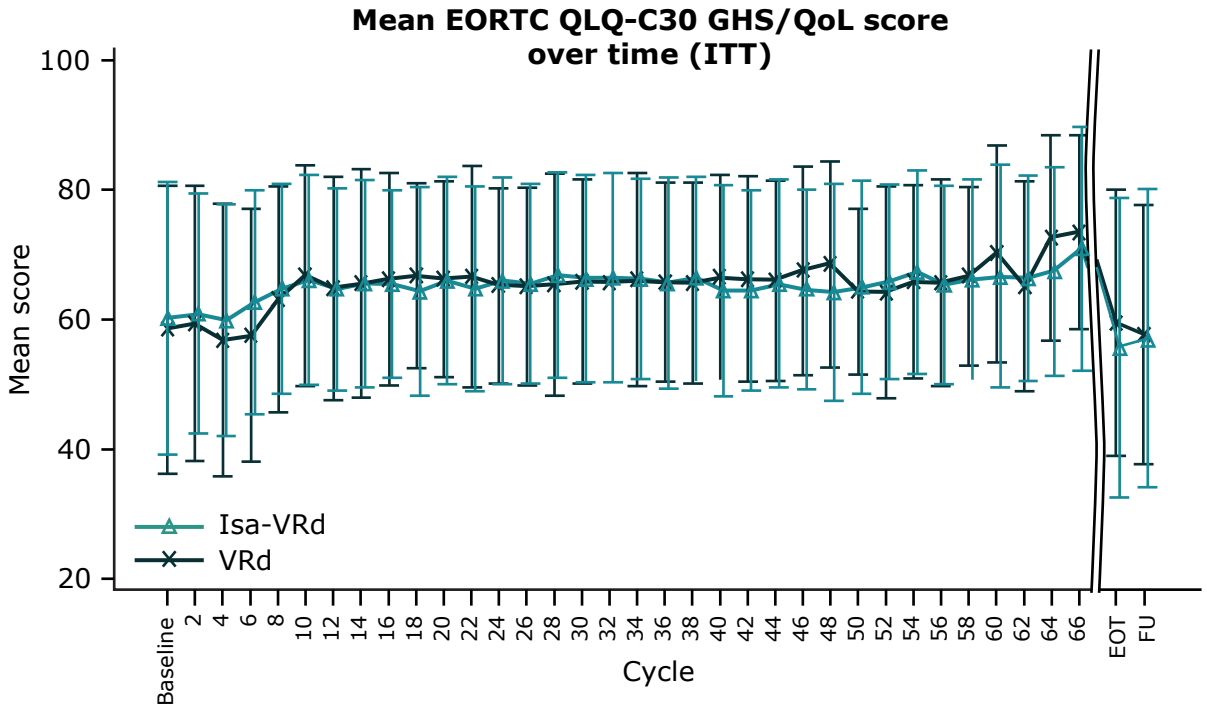
IMROZ: First global Phase III study of Isa-VRd vs VRd in Ti NDMM

IMROZ: Isa-VRd vs VRd (N=446) in Ti NDMM

Safety, %	Isa-VRd (n=263)	VRd (n=181)
Grade ≥3 TEAE	91.6	84.0
Serious AEs	70.7	67.4
Discontinuations due to AEs	22.8	26.0
Grade 5 AE*	11.0	5.5
Grade ≥3 AEs (≥20% patients in any arm)		
Lymphopenia	60.1	53.0
Neutropenia	54.4	37.0
Leukopenia	31.6	16.6
Thrombocytopenia	30.0	27.6
Infections	44.9	38.1
Grade ≥3 peripheral neuropathy	7.2	6.1



Isa-VRd is 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. AE, adverse event; d, dexamethasone; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Cancer specific module with 30 items; EOT, end of treatment; FU, follow-up; GHS, global health status; Isa, isatuximab; ITT, intention-to-treat; NDMM, newly diagnosed multiple myeloma; QoL, quality of life; R, lenalidomide; SC, subcutaneous; TEAE, treatment-emergent adverse event; Ti, transplant ineligible; V, bortezomib

1. Facon T, et al. N Engl J Med 2024; doi: 10.1056/NEJMoa2400712. Online ahead of print;
2. Facon T, et al. ASCO 2024; Presentation 7500

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IMROZ: First global Phase III study of Isa-VRd vs VRd in Ti NDMM

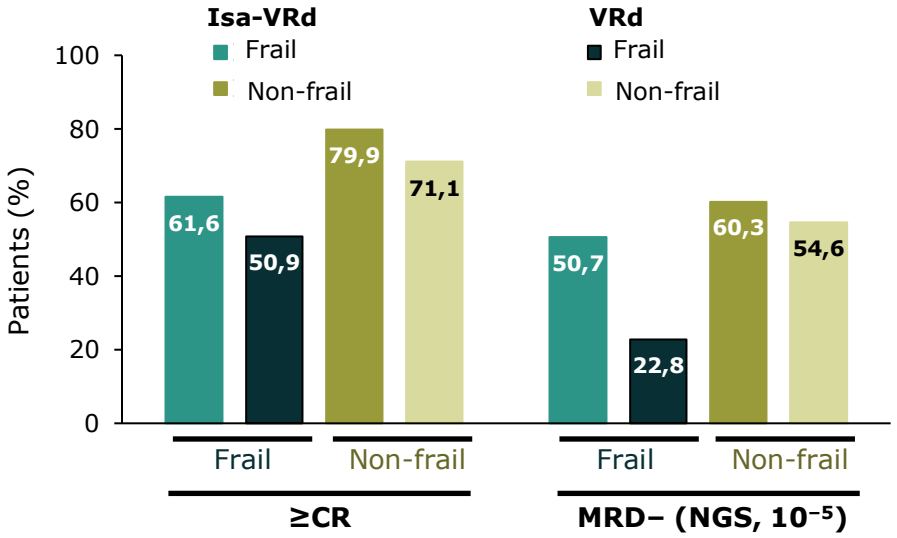
IMROZ: Isa-VRd vs VRd (N=446) in Ti NDMM

Frailty subgroup analysis*

In total, **29%** of patients were **frail**† (28% Isa-VRd; 32% VRd) and **70%** were **non-frail**† (72% Isa-VRd; 67% VRd)‡

Median follow-up: 5 years

Depth of response



PFS

	Frail	Non-frail
HR	0.584¶	0.593§
95% CI	0.340–1.004	0.403–0.873

Safety

	Frail		Non-frail	
	Isa-VRd	VRd	Isa-VRd	VRd
TEAEs leading to discontinuation,%	29.2	35.1	20.7	22.3
Grade ≥3 URTI‖, %	2.78	5.26	NR	NR
Pneumonia#, %	36.1	28.1	NR	NR

Median relative dose intensity of Isa was similar across subgroups (≥92%)

Post-hoc subgroup analysis of frailty in the IMROZ trial demonstrated that Isa-VRd can be an effective option with a manageable safety profile for frail patients with Ti NDMM, accounting for approximately one third of patients in the IMROZ trial

*Data reported here are the only data currently available per the IMS 2024 abstract. †Frailty scores based on age, modified CCI, patient medical history, and ECOG PS at baseline: score 0/1, non-frail; score ≥2, frail. ‡Data on frailty was missing in 1% of patients. ¶P=0.0516. §P=0.008. ‖P=0.654. #P=0.351. CCI, Charlson Comorbidity Index; CI, confidence interval; CR, complete response; d, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HR, hazard ratio; Isa, isatuximab; ITT, intention-to-treat; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NR, not reported; PFS, progression-free survival; R, lenalidomide; TEAE, treatment-emergent adverse event; Ti, transplant ineligible; URTI, upper respiratory tract infection; V, bortezomib

1. Facon T, et al. N Engl J Med 2024; doi: 10.1056/NEJMoa2400712. Online ahead of print;
2. Manier S, et al. IMS 2024; P-426

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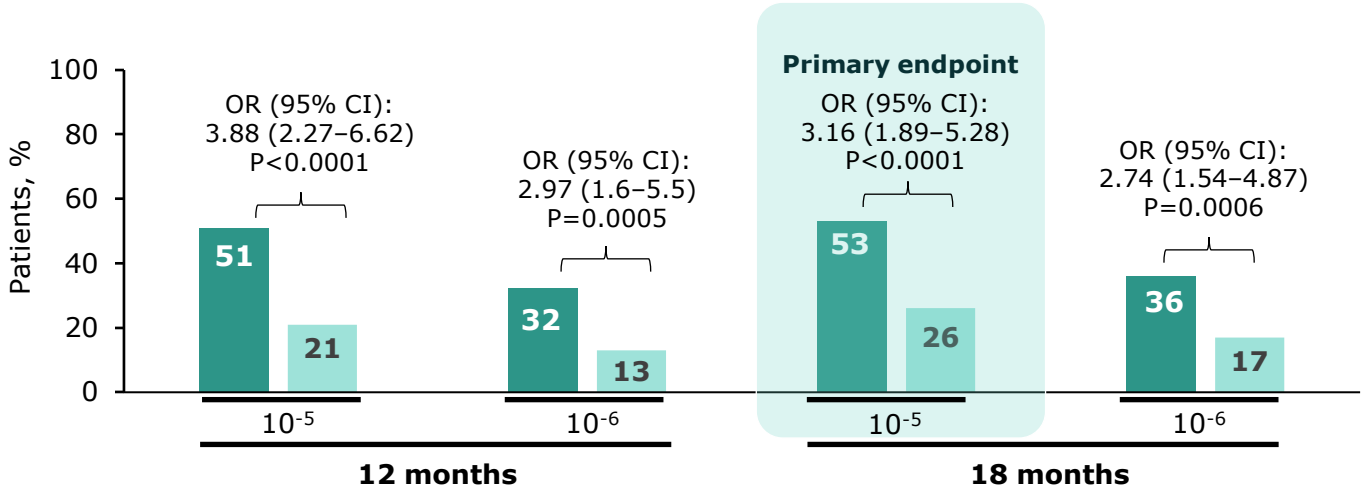
BENEFIT/IFM2020-05: Phase III study of VRd using weekly bortezomib dosing in combination with isatuximab

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

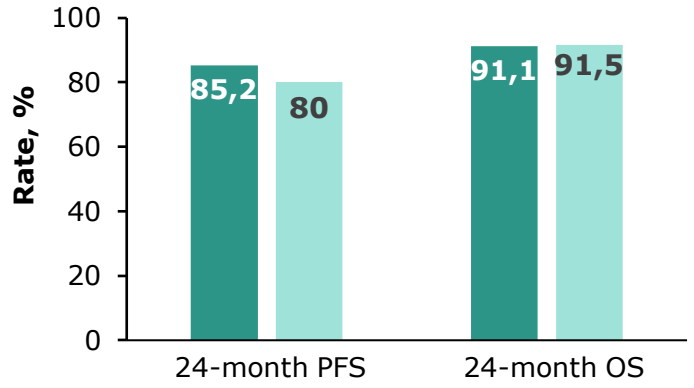
Isa IV: 10 mg/kg weekly (C1), every 2 weeks (C2–12), monthly (C13+)
V SC: 1.3 mg/m^2 **once weekly** (C1–12) and then **every 2 weeks** (C13–18) then **discontinued**
d PO: 20 mg weekly (C1–12) then **discontinued**

Median follow-up: 23.5 months

MRD– rates (NGS)



24-month PFS and OS rates



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 supplemental evidence for the PFS results seen in IMROZ and demonstrate the flexibility of Isa-VRd to provide benefit across the diverse Ti NDMM populations

C, cycle; CI, confidence interval; CR, complete response; d, dexamethasone; Isa, isatuximab; IV, intravenous; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; OR, odds ratio; OS, overall survival; PFS, progression-free survival; PO, orally; R, lenalidomide; SC, subcutaneous; Ti, transplant ineligible; V, bortezomib

Leleu X, et al. Nat Med 2024;30:2235–41

The safety profile of Isa-VRd was consistent across both IMROZ and BENEFIT/IFM2020-05 Phase III trials in Ti NDMM patients

BENEFIT/IFM2020-05:
Isa-VRd vs Isa-Rd (N=270) in Ti NDMM[1,2]

Safety, %	Isa-VRd (n=135)	Isa-Rd (n=135)
Death due to AE	2	2
Serious AE[2]	34	35
Grade ≥2 AE (≥20% patients in any arm)		
Respiratory infections	35	40
Infection of other types*	36	28
Diarrhea	29	22
Peripheral neuropathy	27	10
Grade ≥3 AE		
Neutropenia	40	45
Lymphopenia	33	24
Anemia	10	5
Thrombocytopenia	12	5

*Infections not including the respiratory system

IMROZ:
Isa-VRd vs VRd (N=446) in Ti NDMM[3,4]

Safety, %	Isa-VRd (n=263)	VRd (n=181)
Grade 5 AE†	11.0	5.5
Serious AE	70.7	67.4
Grade ≥3 TEAE	91.6	84.0
Grade ≥3 AE (≥20% patients in any arm)		
Lymphopenia	60.1	53.0
Neutropenia	54.4	37.0
Leukopenia	31.6	16.6
Thrombocytopenia	30.0	27.6
Infections	44.9	38.1
Grade ≥3 peripheral neuropathy	7.2	6.1

†Exposure-adjusted Grade 5 TEAE rate was 0.03 and 0.02 (events/patient-year) in the Isa-VRd vs VRd arms, respectively

Isa-VRd with weekly and twice-weekly V dosing is well-tolerated and the safety profile remains consistent with the known safety profiles of individual agents, allowing for flexibility in dosing to meet patient needs

AE, adverse event; d, dexamethasone; Isa, isatuximab; NDMM, newly diagnosed multiple myeloma; QoL, quality of life; R, lenalidomide; SC, subcutaneous; TEAE, treatment-emergent adverse event; Ti, transplant ineligible; V, bortezomib

1. Leleu X, et al. Nat Med 2024;30:2235–41;
2. Leleu X, et al. ASCO 2024; Presentation 7501;
3. Facon T, et al. N Engl J Med 2024; doi: 10.1056/NEJMoa2400712. Online ahead of print;
4. Facon T, et al. ASCO 2024; Presentation 7500

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

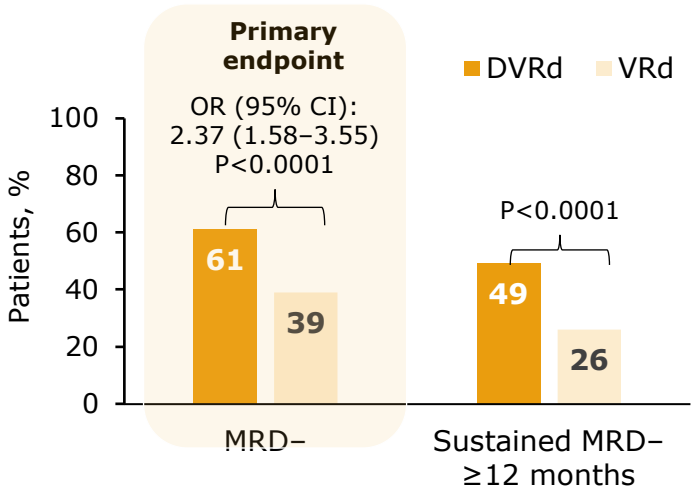
CEPHEUS: Phase III study of DVRd vs VRd in patients with Ti or transplant-deferred NDMM

CEPHEUS: DVRd vs VRd (N=395) in Ti or transplant-deferred NDMM*

Dara SC: 1800 mg weekly (C1–2), every 3 weeks (C3–8), monthly (C9+)
V SC: 1.3 mg/m² **twice weekly** (W1–2 of C1–8) then **discontinued**
d PO: 20 mg during C1–8† then **40 mg weekly** for C9+

Median follow-up: 58.7 months

MRD– rates (NGS, 10^{-5})



PFS

	DVRd (n=197)	VRd (n=198)
mPFS, months	NR	52.6
HR (95% CI)	0.57 (0.41– 0.79)	
P-value	0.0005	
54-month PFS rate, %	68.1	49.5

Safety

	DVRd	VRd
Median treatment duration, months	56.3	34.3
Grade 5 TEAE rates,‡ per patient-months	0.39	0.31

DVRd significantly increased overall MRD negativity (primary endpoint) and sustained MRD negativity vs VRd, and also significantly improved PFS, reducing the risk of progression or death by 43%

*Data reported here are the only data currently available per the IMS 2024 abstract. †Administered on Days 1, 2, 4, 5, 8, 9, 11, 12. ‡Adjusted for treatment exposure. ASCT, autologous stem-cell transplant; C, cycle; CI, confidence interval; d, dexamethasone; Dara/D, daratumumab; HR, hazard ratio; m, median; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; NR, not reached, OR, odds ratio; PFS, progression-free survival; PO, orally; R, lenalidomide; SC, subcutaneous; TEAE, treatment-emergent adverse event; Ti, transplant ineligible; V, bortezomib; W, week

Usmani SZ, et al. IMS 2024; OA-63

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CEPHEUS: Phase III study of DVRd vs VRd in patients with Ti or transplant-deferred NDMM

CEPHEUS: DVRd vs VRd (N=395) in Ti or transplant-deferred NDMM*

Dara SC: 1800 mg weekly (C1–2), every 3 weeks (C3–8), monthly (C9+)
V SC: 1.3 mg/m² **twice weekly** (W1–2 of C1–8) then **discontinued**
d PO: 20 mg during C1–8† then **40 mg weekly** for C9+

Median follow-up: 58.7 months

MRD– rates (NGS, 10^{-5})

PFS

	DVRd (n=197)	VRd (n=198)
mPFS, months	NR	52.6
HR (95% CI)	0.57 (0.41– 0.79)	
P-value	0.0005	
54-month PFS rate, %	68.1	49.5

Safety

	DVRd	VRd
Median treatment duration, months	56.3	34.3
Grade 5 TEAE rates,‡ per patient-months	0.39	0.31

Treatment-emergent adverse events were consistent with the known safety profiles for Dara and VRd

*Data reported here are the only data currently available per the IMS 2024 abstract. †Administered on Days 1, 2, 4, 5, 8, 9, 11, 12. ‡Adjusted for treatment exposure. ASCT, autologous stem-cell transplant; C, cycle; CI, confidence interval; d, dexamethasone; Dara/D, daratumumab; HR, hazard ratio; m, median; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next-generation sequencing; NR, not reached, OR, odds ratio; PFS, progression-free survival; PO, orally; R, lenalidomide; SC, subcutaneous; TEAE, treatment-emergent adverse event; Ti, transplant ineligible; V, bortezomib; W, week

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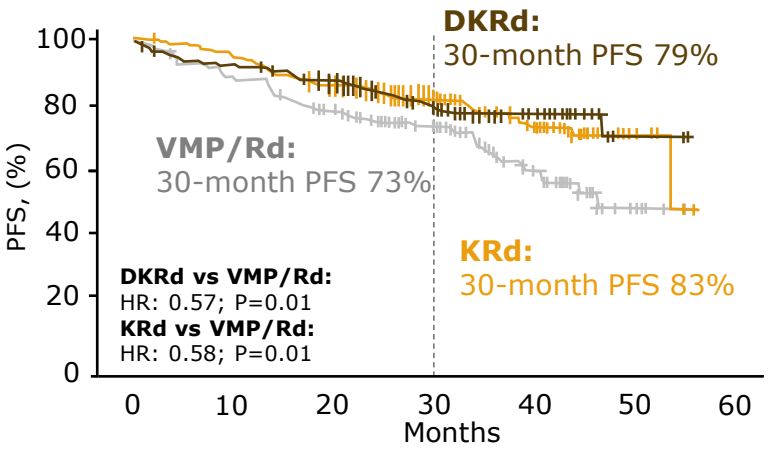
GEM2017FIT: Spanish Phase III study of DKRd vs KRd vs VMP/Rd in Ti NDMM

GEM2017FIT: Phase III; DKRd vs KRd vs VMP/Rd in elderly fit Ti NDMM (N=461)

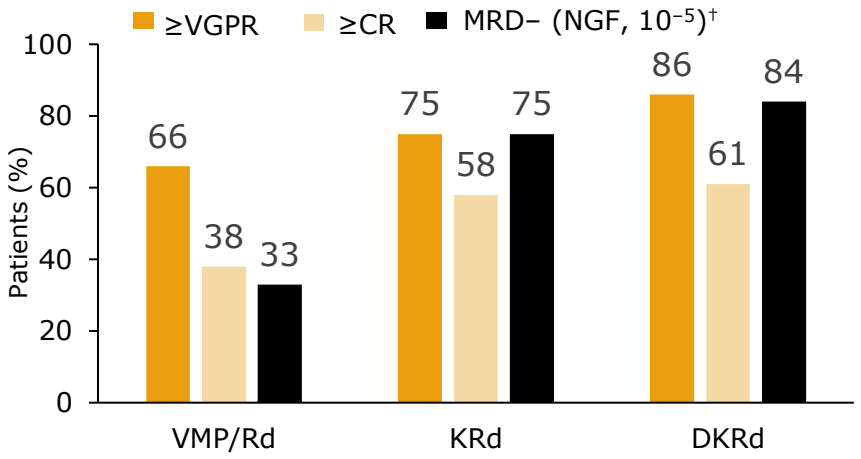
Dara SC: 1800 mg*
V SC: 1.3 mg/m² **twice-weekly** (C1), **weekly** (C2–9), then discontinued
K IV: **36 mg/m² twice-weekly** (C1–2), **56 mg/m² weekly** (C3–18)
d PO: DKRd arm – 40 mg **weekly** (C1–9); **KRd arm** – 40 mg **weekly** (C1–22); **VMP arm** – 40 mg **weekly** (C10–22)

Median follow-up: 33 months

PFS



Response after 18 induction cycles



Grade 3–4 AEs (≥10% patients in any arm), %	VMP/Rd (n=154)	KRd (n=154)	DKRd (n=153)
Neutropenia	50	24	47
Thrombo-cytopenia	34	16	17
Anemia	11	5	10
Infection	12	15	16
Cardiovascular toxicity‡	5	11	14
GI symptoms	9	7	12
Rash	2	12	6

Improved response rates and PFS were seen with DKRd and KRd vs VMP/Rd

*DKRd arm – 1800 mg weekly (C1–2), every 3 weeks (C3–6), monthly (C7–18), then monthly for additional 24 cycles; VMP/KRd arm – weekly (C19–20), every 2 weeks (C21–22), then monthly for additional 24 cycles. †Primary endpoint. ‡Cardiac failure: 2%, 2% and 5% in VMP/Rd, KRd, and DKRd arms, respectively; hypertension: 5% and 2% in KRd and DKRd arms, respectively. AE, adverse event; CR, complete response; d, dexamethasone; D, daratumumab; GI, gastrointestinal; HR, hazard ratio; K, carfilzomib; M, melphalan; MRD, minimal residual disease; NGF, next-generation flow; P, prednisone; PFS, progression-free survival; R, lenalidomide; Ti, transplant ineligible; V, bortezomib; VGPR, very good partial response

Mateos MV, et al. ASH 2023; Presentation 209

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Conclusions

Most cases of NDMM are diagnosed in patients aged 65–74 years, and the majority of patients with NDMM do not receive transplant

Despite the introduction of novel therapies, patients with Ti NDMM have poorer survival outcomes compared with those with Te NDMM and remain a population with unmet medical needs

Triplet therapy is the current standard of care in Ti NDMM; however, Phase III trials using CD38 mAb-based quadruplet therapy have demonstrated improved outcomes in this patient population

Regimens tailored to patient and disease characteristics are being investigated to meet the diverse needs of this patient population

mAb, monoclonal antibody; NDMM, newly diagnosed multiple myeloma; Te, transplant eligible; Ti, transplant ineligible

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Polling question

If access was not an issue, would you consider a quadruplet over a triplet as an upfront regimen in Ti NDMM patients?

- **Yes, I would consider a quadruplet regimen**
- **No, I would choose a triplet regimen**
- **Other/more information required**

NDMM, newly diagnosed multiple myeloma; Ti, transplant ineligible

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Polling question

If access was not an issue, which quadruplet treatment option would you most likely choose for Ti NDMM patients?

- **Anti-CD38 mAb + IMiD + PI + dex**
- **Anti-CD38 mAb + IMiD + PI + dex with modified dosing to meet individual patient needs**
- **More information required**
- **I would not consider a quadruplet regimen in Ti NDMM patients**

dex, dexamethasone; IMiD, immunomodulatory drug; mAb, monoclonal antibody; NDMM, newly diagnosed multiple myeloma; PI, proteasome inhibitor; Ti, transplant ineligible

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