DGHO Kongress 2023

Multiples Myelom: Therapie des nicht für eine Transplantation geeigneten Patienten

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Ein Kompetenznetzwerk des UKE

Disclosures

1. Employment or Leadership Position: none

2. Advisory Role or Expert Testimony: Abbvie, Adaptive, Amgen, Bristol Myers Squibb, Celgene, Janssen, GSK, Karyopharm, Novartis, Oncopeptides, Pfizer, Roche Pharma, Takeda, Sanofi, Stemline

3. Stock Ownership: none

4. Patent, Copyright, Licensing: none

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8. Other Conflicts of Interest: none

Distribution of Age in Newly Diagnosed Multiple Myeloma[1–3]

35.5% of patients diagnosed with MM are aged <65[4]

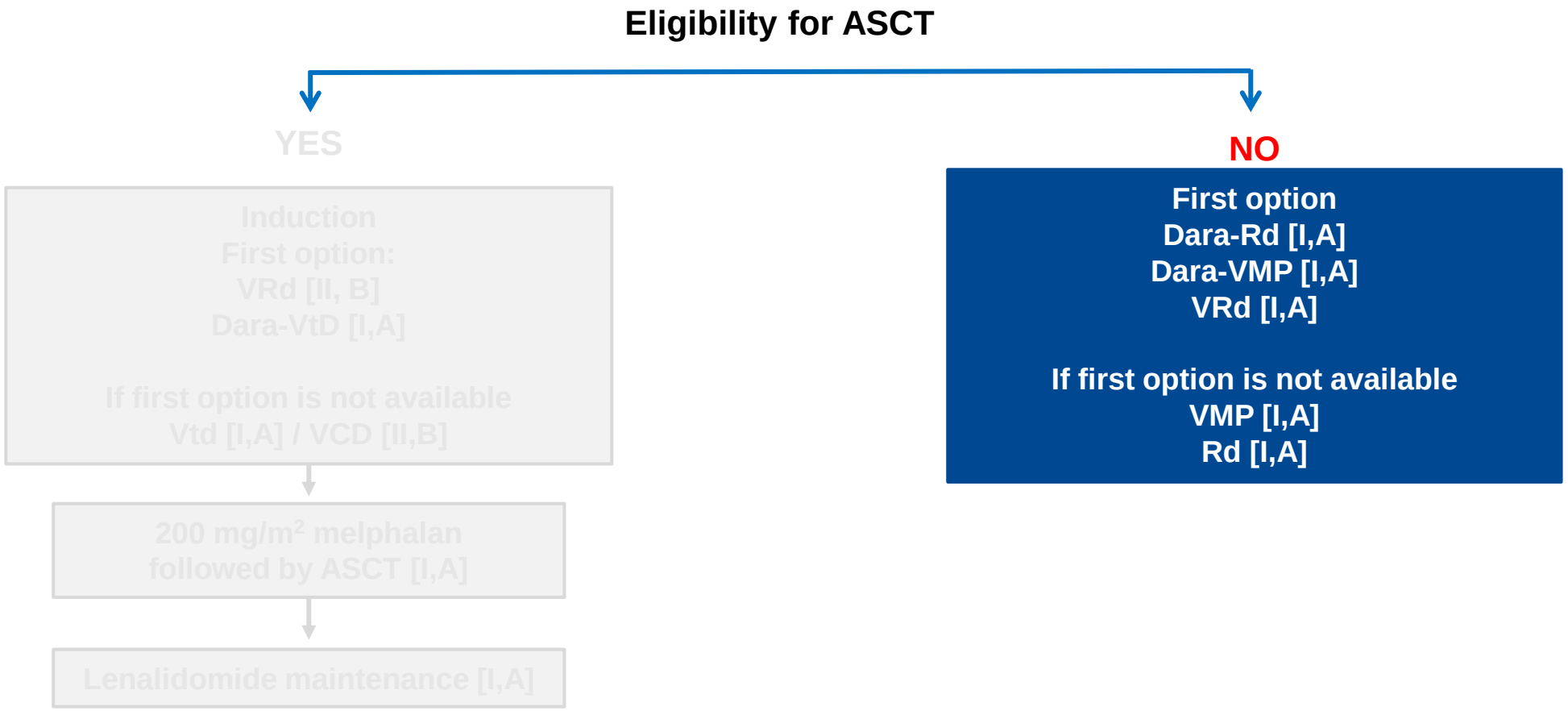
32.6% of patients are aged ≥75 at diagnosis[4]

31.9% of patients are aged 65–74 at diagnosis, with the median age being **69**[4]

Approximately 30% of patients with MM are frail at diagnosis[2]

1. Möller MD, et al. Curr Opin Oncol 2021;33:648–657; 2. Dimopoulos MA, et al. Ann Oncol 2021;32:309–322; 3. Larocca A, et al. Leukemia 2018;32:1697–1712; 4. Cancer Stat Facts: Myeloma. Available at: https://seer.cancer.gov/statfacts/html/mulmy.html (last accessed June 2023).

ESMO guidelines 2021: Primärtherapie des Multiplen Myeloms

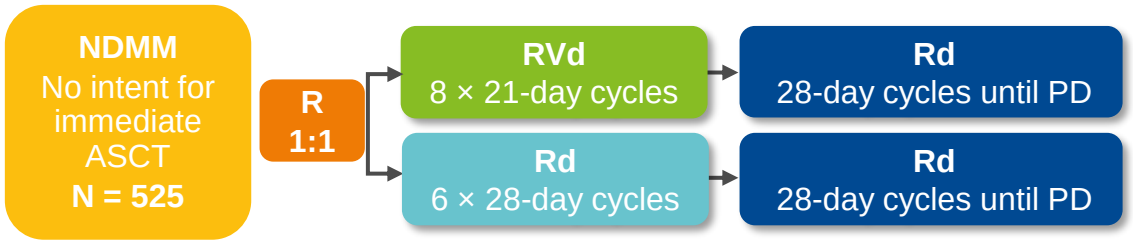


ASCT, autologous stem cell transplantation; Dara-Rd, daratumumab, lenalidomide, dexamethasone; Dara-VMP, daratumumab, bortezomib, melphalan, prednisone; Dara-Vtd, daratumumab, bortezomib, thalidomide, dexamethasone; Rd, lenalidomide, dexamethasone; VCD, bortezomib/cyclophosphamide/dexamethasone; VMP, bortezomib, melphalan, prednisone; VRd, bortezomib, lenalidomide, dexamethasone; VTD, bortezomib/thalidomide/dexamethasone.

1. Dimopoulos MA et al. Ann Oncol 2021; 32:309-322.

RVd in non stem-cell transplantation NDMM

SWOG S0777



Primary endpoint:
PFS

Characteristic	RVd (n = 264)	Rd (n = 261)
Median age (range), years	63 (-)	63 (-)
Age ≥ 65 years, %	38	48
ECOG PS > 1, %	12	16
High-risk cytogenetics, %	-	-

Durie BGM et al. Lancet 2017;389:519–27.

SWOG S0777: VRd→Rd vs continuous Rd: updated analysis[1]

ORR (CR, %): 82 (16) vs 72 (8)[2]

FIGURE: (A) PFS and (B) OS in patients stratified by age

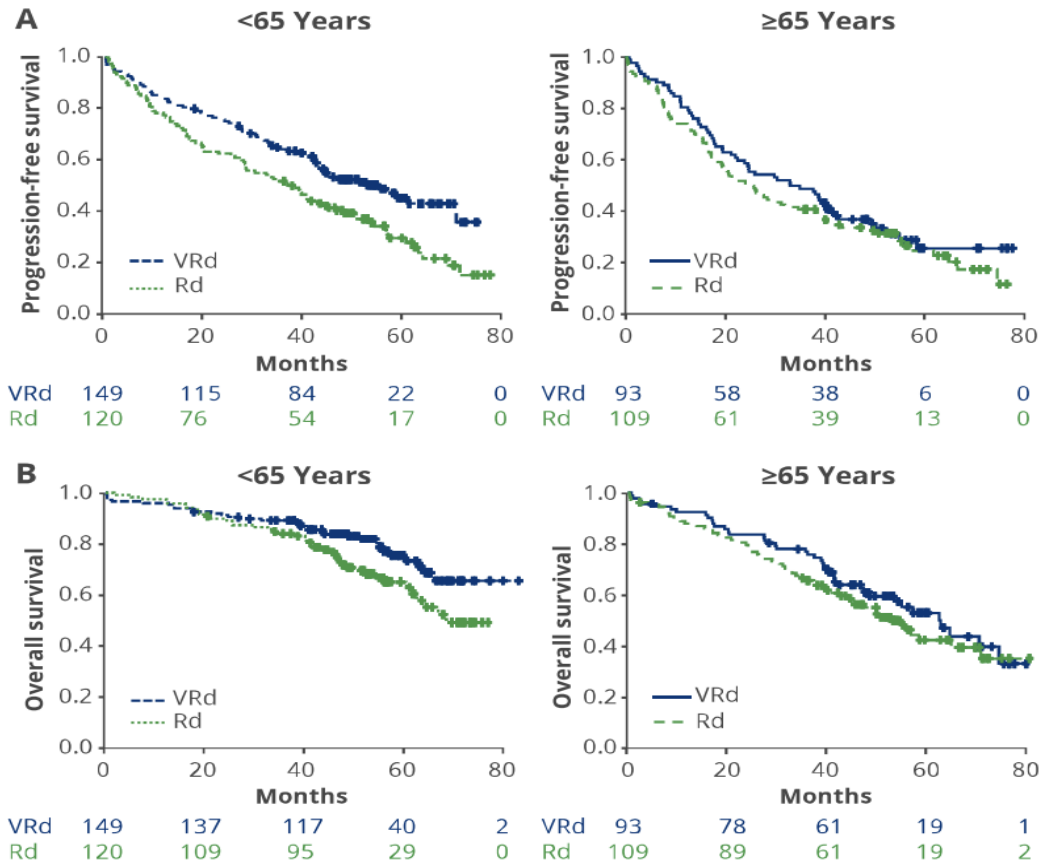


TABLE 2: Age-stratified analyses of PFS, OS, and safety

	Outcome	Age <65 years (n=269)		Age ≥65 years (n=202)	
		VRd (n=149)	Rd (n=120)	VRd (n=93)	Rd (n=109)
PFS	Median PFS, months	55.4	36.6	33.1	25.8
	HR (95% CI)	0.63 (0.46–0.87)		0.83 (0.60–1.16)	
	Adjusted HR[a] (95% CI)	0.61 (0.45–0.84)		0.90 (0.65–1.26)	
OS	Median OS, months	Not reached	68.9	62.9	53.0
	HR (95% CI)	0.61 (0.39–0.97)		0.83 (0.55–1.23)	
	Adjusted HR[a] (95% CI)	0.62 (0.39–0.99)		0.88 (0.59–1.31)	
Safety[b]	Grade ≥3 TEAE	87%	79%	93%	89%
	Treatment discontinuation due to toxicity	29%	18%	47%	26%

HRs are from Cox proportional hazard regressions with treatment arm as the explanatory variable. A HR <1 indicates advantage of VRd over Rd.
[a]Adjusted hazard ratio estimates reflect results from weighted Cox regression models where IPTW was used to balance the VRd and Rd trial arms on the following baseline characteristics within each age subgroup (≥65, <65 years): age, sex, ISS stage, ECOG PS score, hemoglobin (<10 g/dL, ≥10 g/dL), serum creatinine (<2 mg/dL, ≥2 mg/dL), cytogenetic risk by FISH test (high, intermediate, low, normal/missing/insufficient), and lactate dehydrogenase (<190 IU/L, ≥190 IU/L). Absolute standardized mean differences for all covariates were <0.1 with IPTW. [b]Eligible safety assessment population was n=467.
CI, confidence interval; FISH, fluorescence in situ hybridization; HR, hazard ratio; IPTW, inverse probability treatment weighting; OS, overall survival; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

Bortezomib twice a week IV x 8 cycles

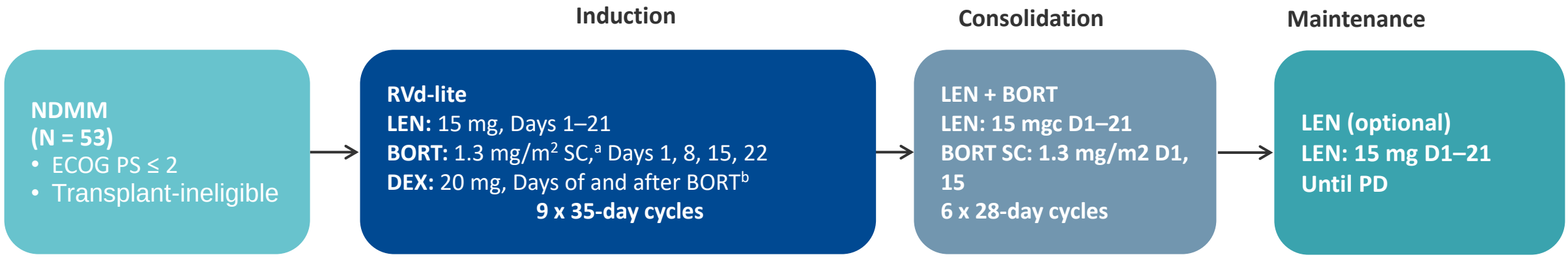
CR, complete response; IV, intravenous; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; VRd, bortezomib, lenalidomide, dexamethasone.

1. Durie B, et al. ASH 2022 (Abstract No. 4497 – Poster); 2. Durie BGM, et al. Lancet 2017;389:519–27.

RVd in non stem-cell transplantation NDMM: RVd Lite

Updated analysis (61-month follow-up) of a Phase 2 study of RVd-lite in transplant-ineligible NDMM patients

Primary endpoint: ORR; **Secondary endpoints:** safety, PFS, OS, PK profile of IV and SC BORT



Patient characteristics	(n = 50)
Median age (range), years	72 (65–91)
ISS stage I / II / III, %	38 / 34 / 28

66% of patients received LEN Maintenance

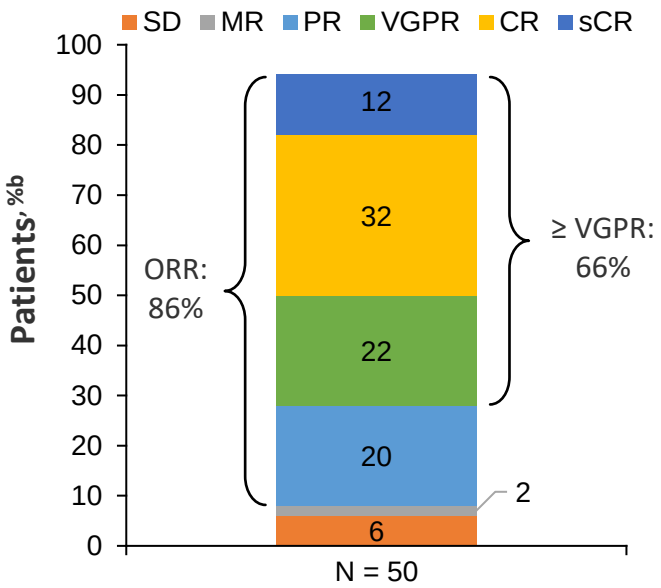
[a] 50 patients received ≥ 1 dose of treatment.

O'Donnell EK, et al. ASH 2019: Abstract 3178. Poster presentation.

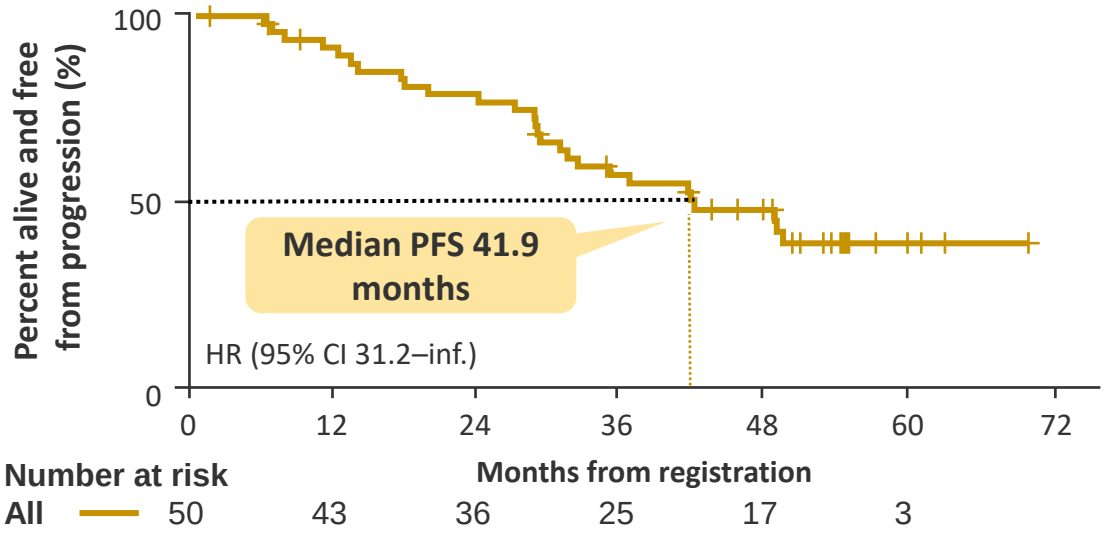
Modified RVd (RVd-lite) in transplant-ineligible NDMM

Baseline characteristics	N = 50
Median age, years (range)	73 (65–91)
ISS stage at diagnosis, %	
I	38
II	34
III	28
ECOG PS score, %	
0	50
1	36
2	14

Response rate



PFS



≥ CR was 44% (ITT population; N = 50)
ORR was 86%; ≥ VGPR was 66% for patients evaluable for response[a] after 4 cycles (n = 46)
Median TTR was 1.1 months

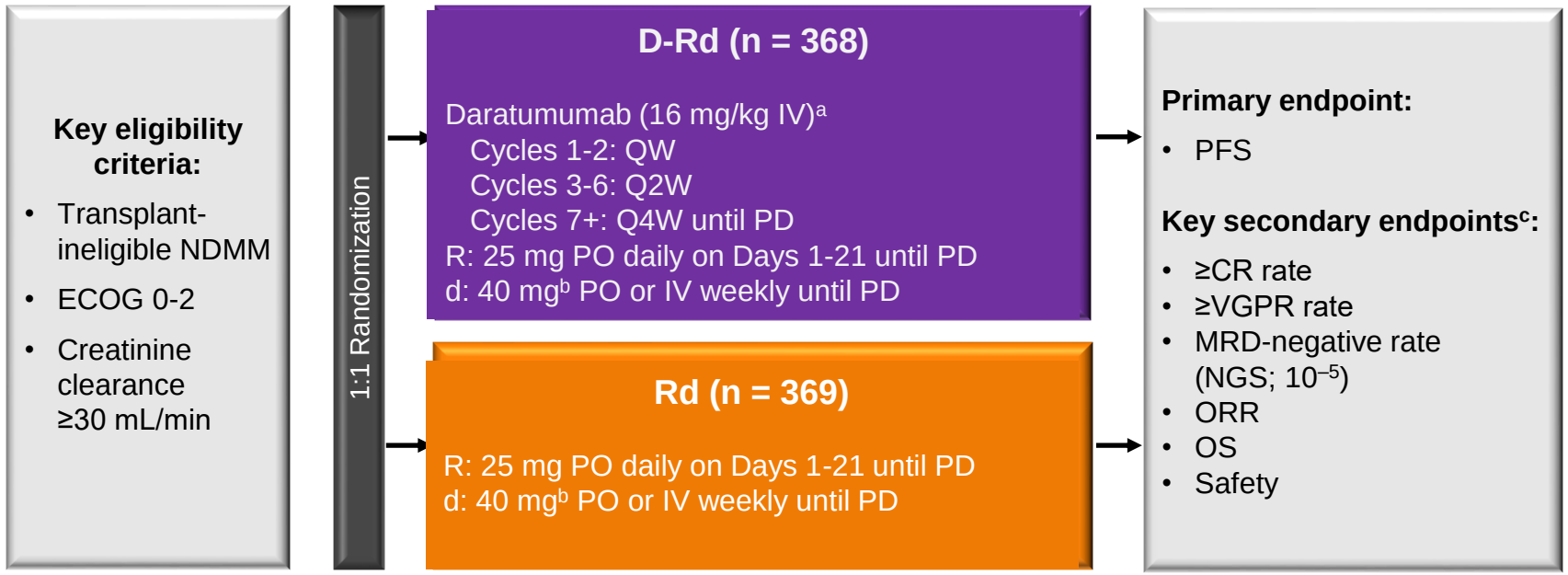
Grade 3 or 4 AEs of interest:
- Peripheral neuropathy (2%), neutropenia (14%)

RVd-lite is Investigational only, not approved.
[a] The first 10 patients received bortezomib i.v. for cycle 1 only followed by s.c. administration; subsequent patients received bortezomib s.c.; [b] 6% of patients received < 4 cycles of therapy and were therefore not evaluable.
AE, adverse event; CR, complete response; d, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance status; ISS, International Staging System; MR, minimal response; ORR, overall response rate; PFS, progression-free survival; R, lenalidomide; sCR, stringent complete response; TTR, time to response; V, bortezomib; VGPR, very good partial response

O'Donnell EK et al. Br J Haematol 2018;182:222-30.
O'Donnell EK et al. ASH 2019; abstract 3178.

Dara-Rd in der Erstbehandlung der nicht-transplantierbaren Patienten

- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



Stratification factors
- ISS (I vs II vs III)
- Region (NA vs other)
- Age (<75 vs ≥75 years)

Patient Characteristics	Total (N = 737)
Age	
Median (range), years	73 (45-90)
Distribution, n (%)	
<65 years	8 (1)
65-<70 years	147 (20)
70-<75 years	261 (35)
≥75 years	321 (44)
ECOG status,[a] n (%)	
0	250 (34)
1	365 (50)
≥2	122 (17)
Cytogenetic profile[d]	
N	642
Standard risk, n (%)	550 (86)
High risk, n (%)	92 (14)

Facon et al. N Engl J Med 2019

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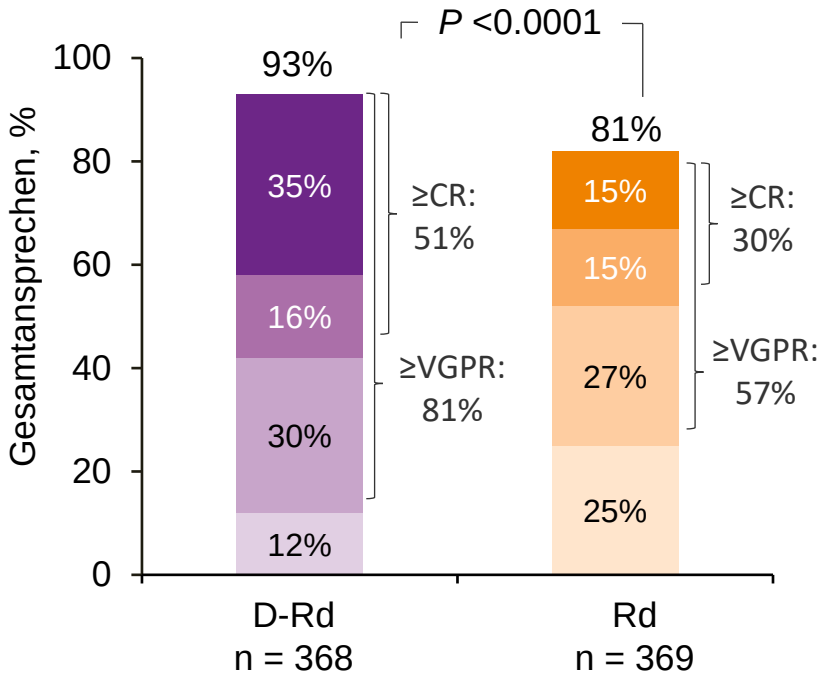
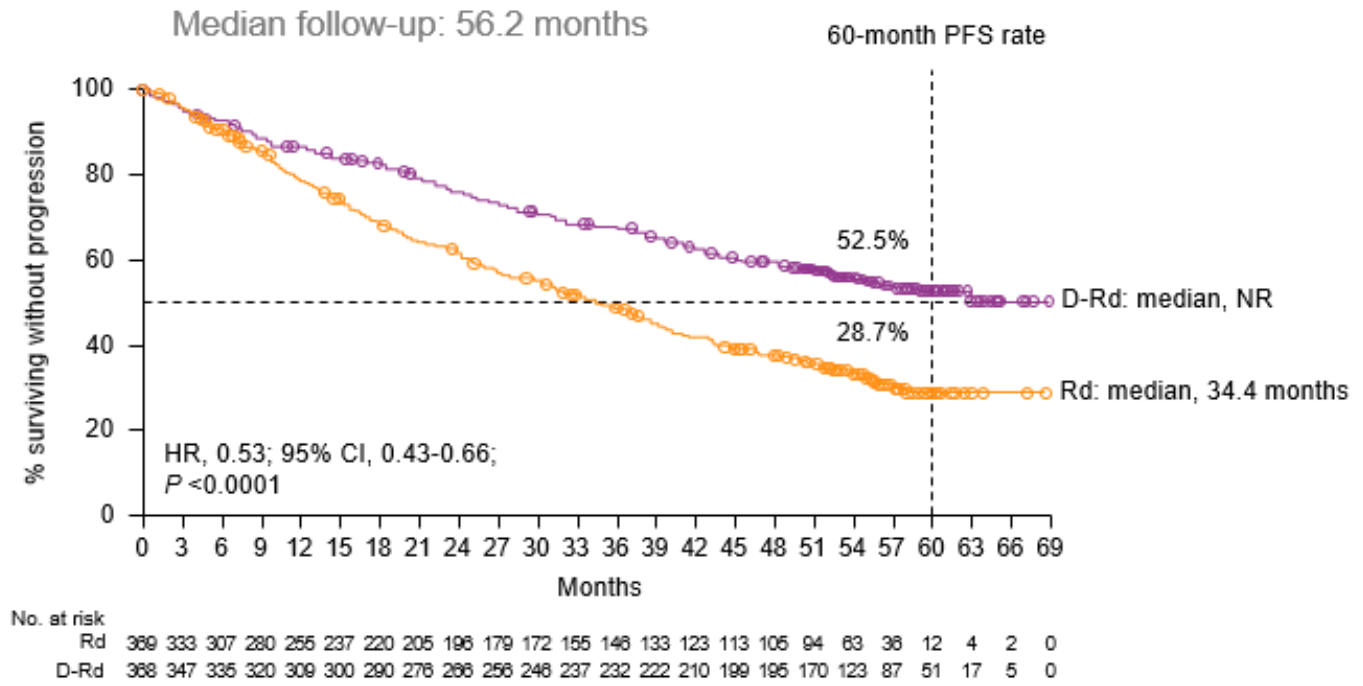
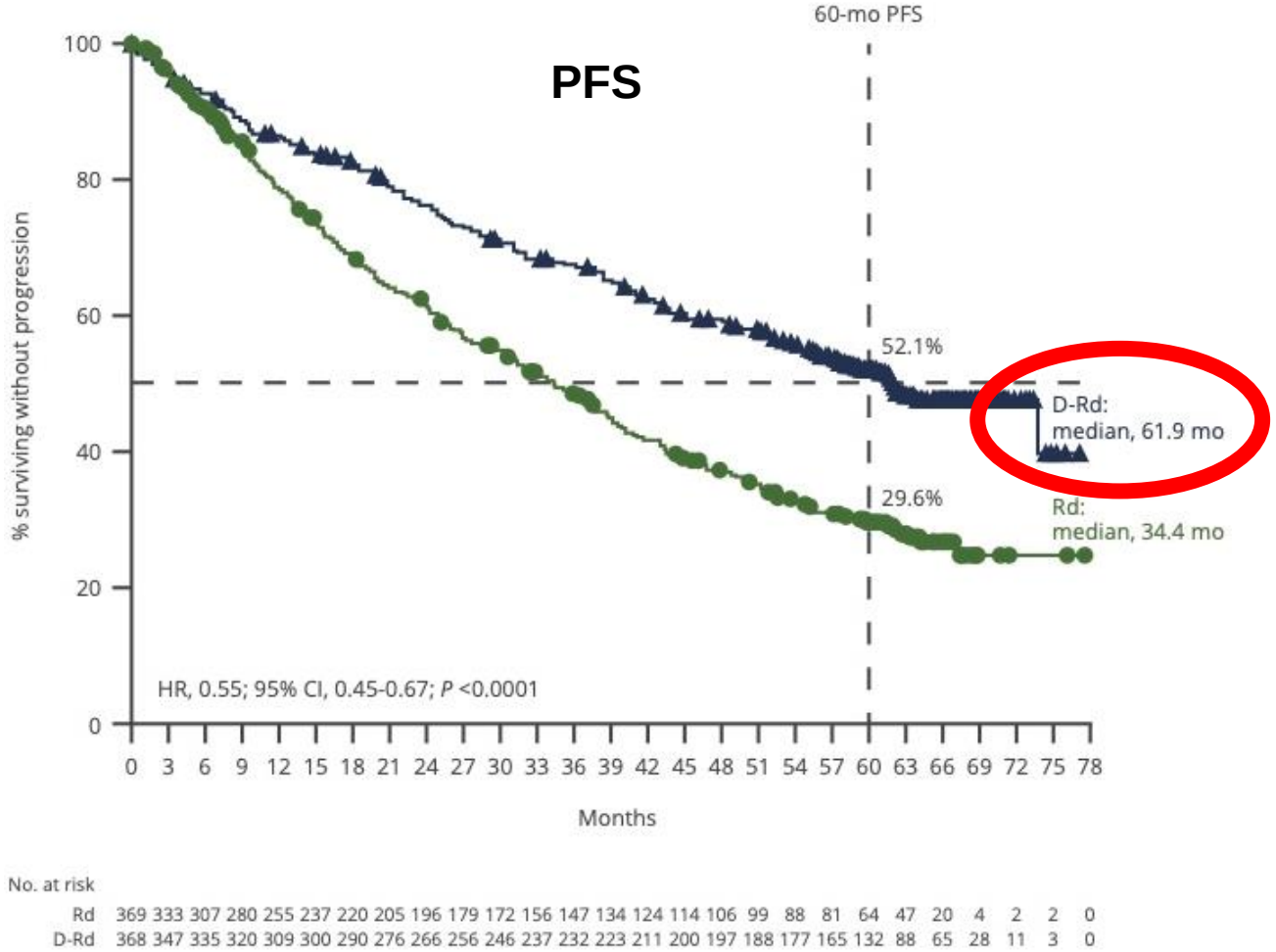
Dara-Rd – Gesamtansprechen und PFS

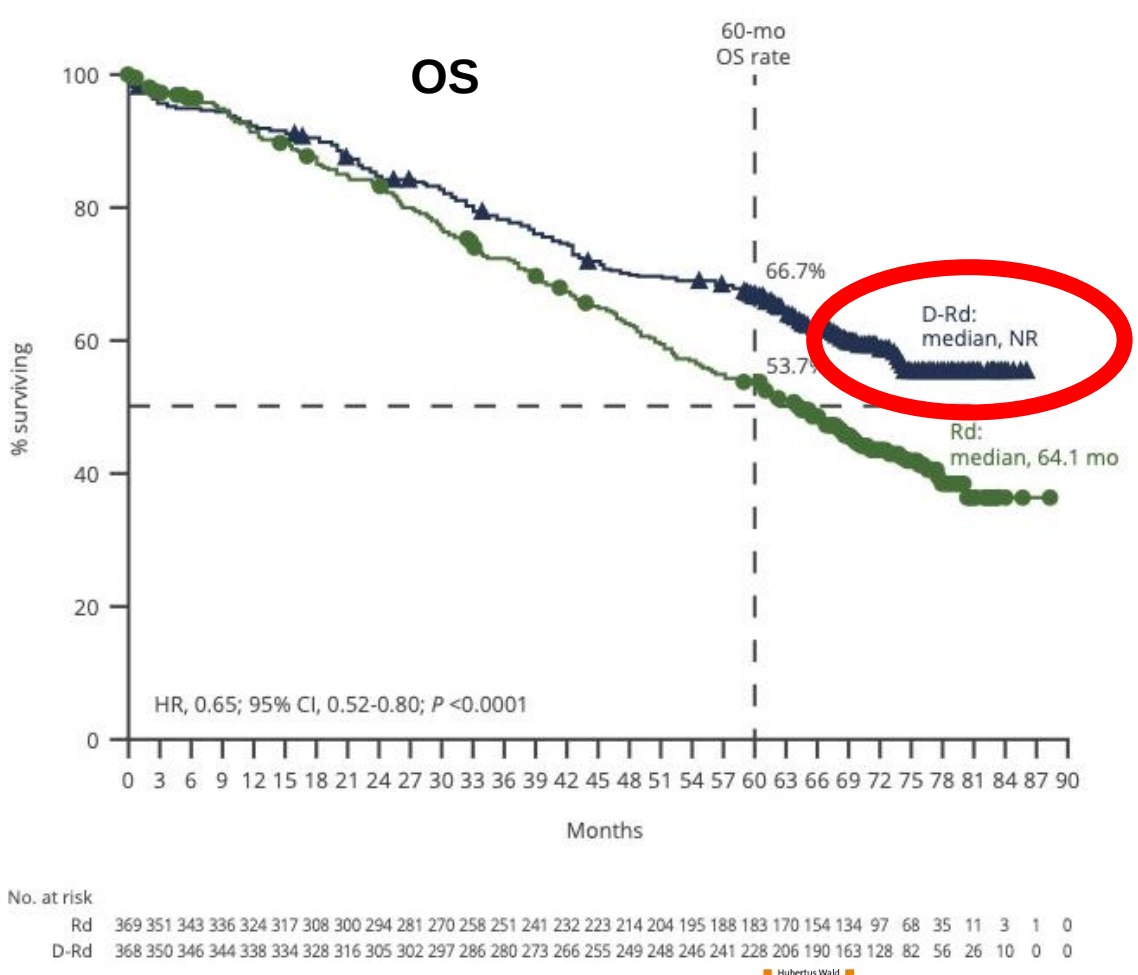




24% of patients with D-Rd were MRD negative (7% with Rd)

MAIA updated analysis: PFS[1]



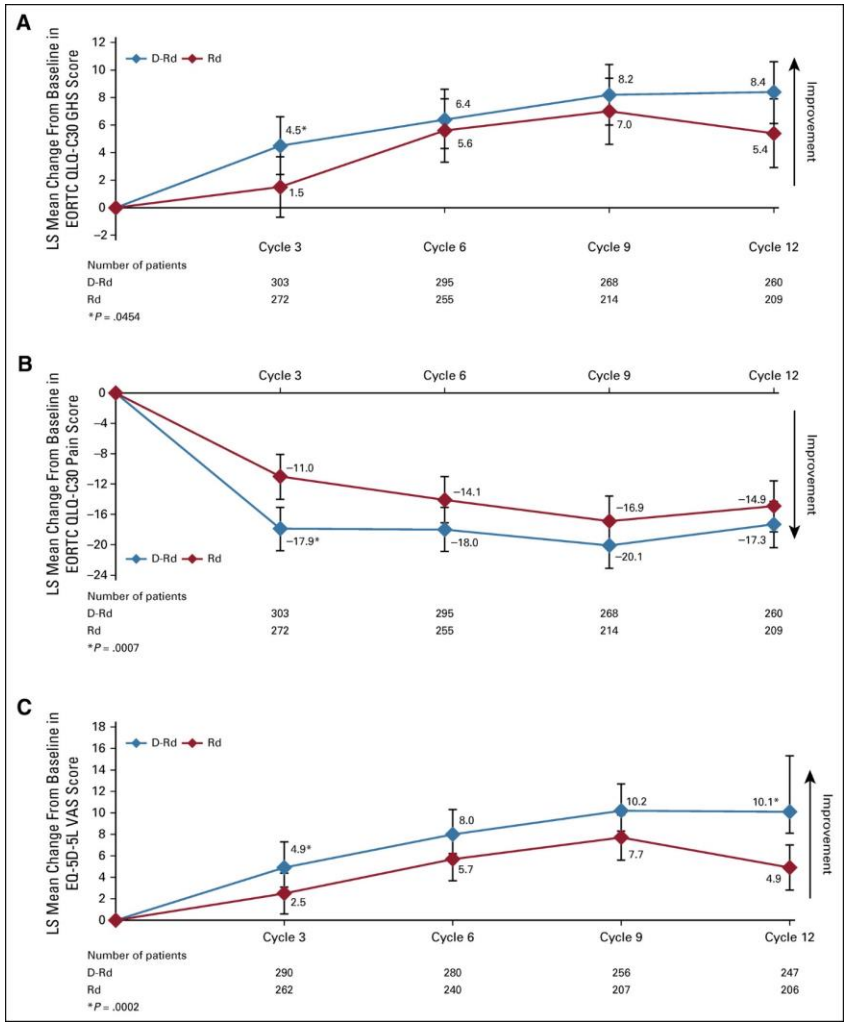


Median follow-up of 64.5 months for PFS

CI, confidence interval; D-Rd, daratumumab, lenalidomide, dexamethasone; HR, hazard ratio; mo, months; NR, not reached; OS, overall survival; PFS, progression-free survival; Rd, lenalidomide, dexamethasone.

1. Kumar S, et al. ASH 2022 (Abstract No. 4559 – Poster).

Quality of Life is Improved with DRd



- A global health status benefit was achieved with D-Rd, regardless of age (< 75 and ≥ 75 years), baseline ECOG) performance status score, or depth of response.
- D-Rd treatment resulted in significantly greater reduction in pain scores as early as cycle 3, the magnitude of change was sustained through cycle 12.

Perrot,…,Weisel, J Clin Oncol 2021

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Ergebnisse: Lebensqualität ist abhängig vom Therapieansprechen

	Clinical Response			
	(s)CR *v* VGPR/PR		SD *v* VGPR/PR	
EORTC QLQ-C30 Scale	HR (95% CI)	*P*	HR (95% CI)	*P*
GHS[a]	0.72 (0.60 to 0.86)	.0004	1.57 (1.17 to 2.12)	.0031
Physical functioning	0.87 (0.73 to 1.04)[b]	.135[b]	1.51 (1.10 to 2.05)[a]	.0097[a]
Role functioning[a]	0.84 (0.71 to 0.99)	.0335	1.32 (1.00 to 1.75)	.0484
Emotional functioning[a]	0.79 (0.65 to 0.96)	.0159	1.49 (1.08 to 2.07)	.016
Cognitive functioning	0.87 (0.75 to 1.01)[b]	.0695[b]	1.16[b] (0.87 to 1.55)	.3141[b]
Social functioning	0.85 (0.72 to 0.99)[a]	.045[a]	1.23 (0.92 to 1.64)[b]	.1661[b]
Pain[a]	0.70 (0.59 to 0.84)	.0001	1.58 (1.17 to 2.13)	.0027
Fatigue	0.93 (0.80 to 1.08)[c]	.3511[c]	1.26 (0.97 to 1.64)[b]	.0896[b]
Nausea or vomiting	0.91 (0.76 to 1.09)[c]	.3016[c]	1.13 (0.80 to 1.59)[b]	.4819[b]
Dyspnea[a]	0.64 (0.54 to 0.77)	< .0001	1.30 (0.96 to 1.76)	.094
Insomnia	0.88 (0.74 to 1.04)[b]	.1293[b]	1.23 (0.91 to 1.67)[b]	.1721[b]
Appetite loss	0.88 (0.74 to 1.06)[b]	.1751[b]	1.45 (1.06 to 1.97)[a]	.02[a]
Constipation	0.93 (0.78 to 1.11)[c]	.4087[c]	1.37 (1.01 to 1.85)[a]	.04[a]
Diarrhea	0.97 (0.82 to 1.14)[c]	.6809[c]	1.15 (0.83 to 1.59)[b]	.4114[b]

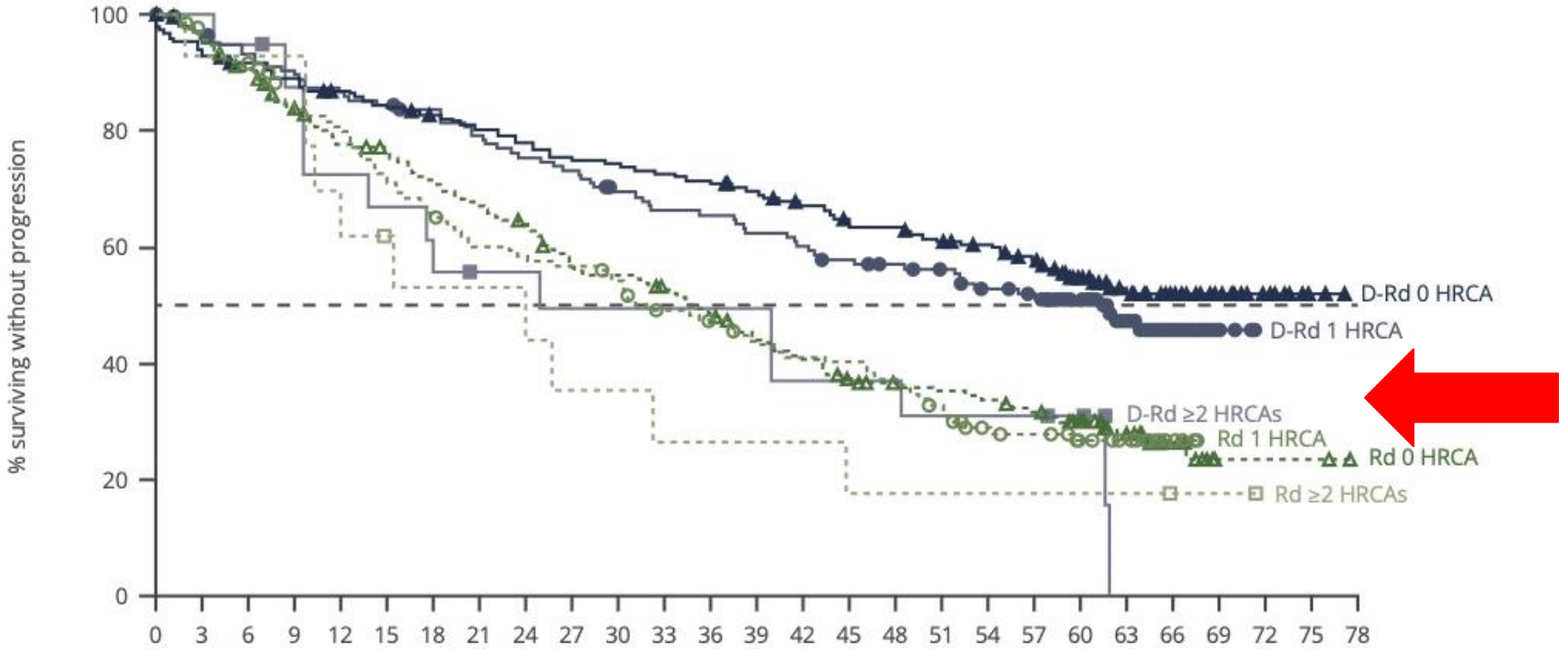
Verbesserungen der Symptome, aber auch der Psyche und der Rolle im eigenen Alltag korrelieren signifikant mit der Ansprechtiefe

Auch ältere und alte Patienten profitieren von einer maximalen Remissionstiefe!

Perrot…Weisel, J Clin Oncol 2021

Herausforderungen: Patient:innen mit Hochrisikoerkrankung

- **Subgroup analysis of PFS among patients with revised standard cytogenetic risk (0 HRCA), 1 HRCA, or ≥2 HRCAs[1]**



No. at risk																										
Rd 0 HRCA	187	169	153	139	127	123	115	108	102	89	87	81	75	67	61	54	50	48	46	42	34	25	13	2	2	2	0
Rd 1 HRCA	137	124	117	106	98	87	79	72	70	68	64	56	53	48	45	44	40	35	26	25	19	15	4	0	0	0	0
Rd ≥2 HRCAs	15	13	12	12	8	7	6	6	6	4	4	3	3	3	3	2	2	2	2	2	2	2	1	1	0	0	0
D-Rd 0 HRCA	176	164	158	151	148	144	139	135	131	127	125	122	120	115	109	102	102	97	93	87	68	48	36	18	9	2	0
D-Rd 1 HRCA	137	131	126	122	117	114	111	105	100	97	90	86	85	81	78	74	71	68	62	59	49	32	22	6	0	0	0
D-Rd ≥2 HRCAs	19	19	18	16	13	12	10	9	9	8	8	8	8	8	6	6	6	5	5	5	4	0	0	0	0	0	0

D-Rd, daratumumab, lenalidomide, dexamethasone; HRCA, high risk cytogenetic abnormalities; PFS, progression-free survival; Rd, lenalidomide, dexamethasone.

1. Moreau P et al. ASH 2022 (Abstract 3245 – poster).

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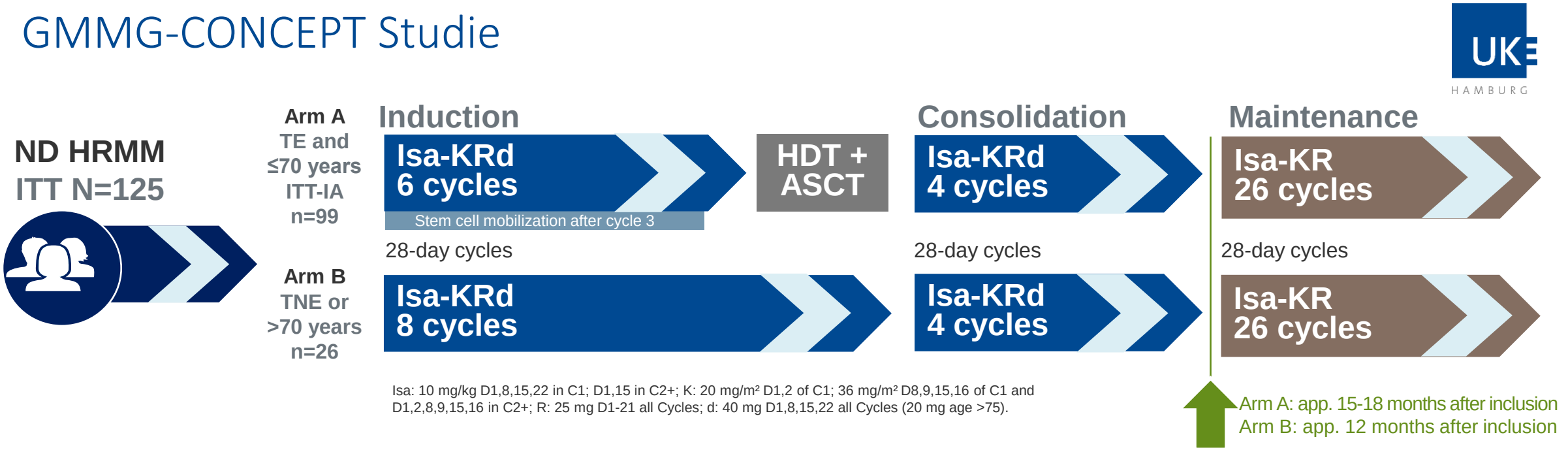
GMMG-CONCEPT Studie



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; Key tertiary objectives: ORR, OS, safety

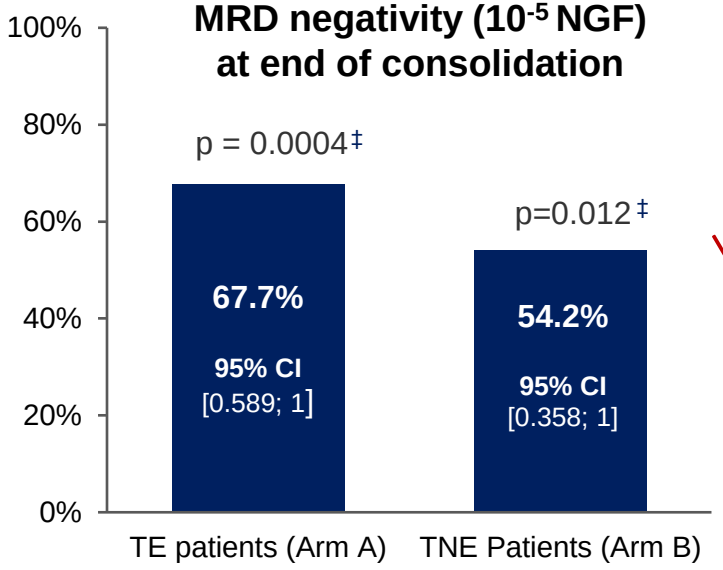
Leypoldt et al., J Clin Oncol 2023

Patientencharakteristika

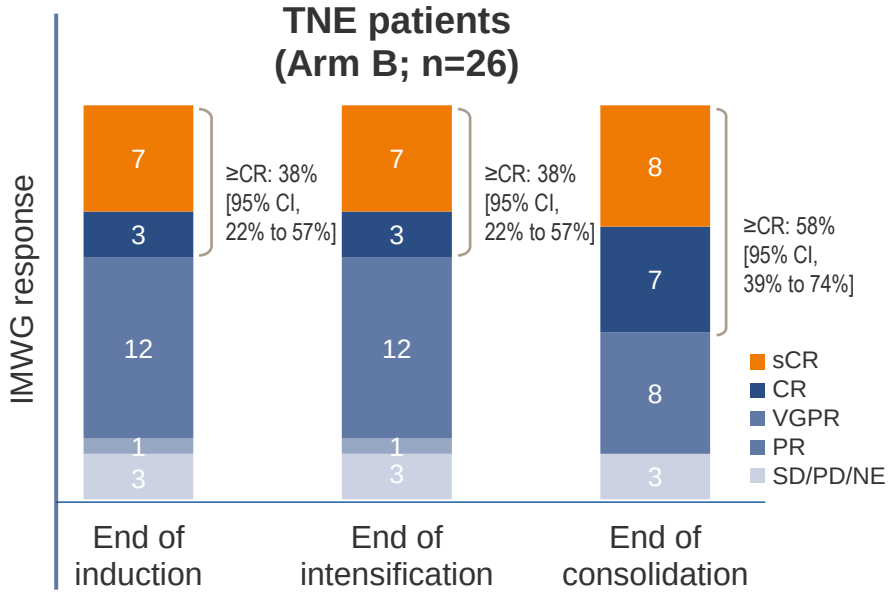
Characteristic		TE patients (n=99)	TNE patients (n=26)	Total (N=125)
Age	Years, median (range)	58 (35–73)	74 (64–87)	62 (35–87)
Sex	Female sex, No. (%)	52 (52.5)	14 (53.8)	66 (52.8)
ECOG	ECOG 0–1, No. (%)	85 (85.9)	18 (69.2)	103 (82.4)
	ECOG 2–3, No. (%)	14 (14.1)	7 (26.9)	21 (16.8)
ISS	II, No. (%)	53 (53.5)	13 (50.0)	66 (52.8)
	III, No. (%)	45 (45.5)	13 (50.0)	58 (46.4)
R2-ISS	I + II, No. (%)	48 (48.5)	10 (38.5)	58 (46.4)
	III + IV, No. (%)	51 (51.5)	15 (57.7)	66 (52.8)
	Not classifiable, No. (%)	0 (0)	1 (3.8)	1 (0.8)
FISH	del(17p), No. (%)	44 (44.4)	11 (42.3)	55 (44.0)
	t(4;14), No. (%)	42 (42.4)	6 (23.1)	48 (38.4)
	t(14;16), No. (%)	17 (17.2)	2 (7.7)	19 (15.2)
	amp1q21 (≥4 copies), No. (%)	31 (31.3)	14 (53.8)	45 (36.0)
HRCA	1 HRCA, No. (%)	60 (60.6)	17 (65.4)	77 (61.6)
	≥2 HRCAs, No. (%)	31 (31.3)	7 (26.9)	38 (30.4)
	Not classifiable*, No. (%)	8 (8.1)	2 (7.7)	10 (8.0)
LDH	Elevated LDH (>ULN), No. (%)	24 (24.2)	8 (30.8)	32 (25.6)
1 prior cycle	Therapy before enrollment, No. (%)	31 (31.3)	11 (42.3)	41 (33.6)
BM infiltration	Plasma cell infiltration %, median (range)	60 (0–100)	50 (5.5–100)	60 (1–100)

Leypoldt et al., J Clin Oncol 2023

CONCEPT- Studie: Ergebnisse TNE-Patient:innen



Lisa Leypoldt et al., Abstract 163
Präsentation V299 (14.10. 15.45 Uhr)
Multiples Myelom - Klinisch I
Young Investigator Award



MRD status, n (%)	TE patients (Arm A) (n=93*)	TNE patients (Arm B) (n=24†)
Negative	**63 (67.7)**	**13 (54.2)**
Positive	3 (3.2)	0 (0)
Not done/missing	2 (2.2)	0 (0)
Time point not reached	25 (27.0)	11 (45.8)

6 TE and 2 TNE patients were not assessable

Leypoldt et al., J Clin Oncol 2023

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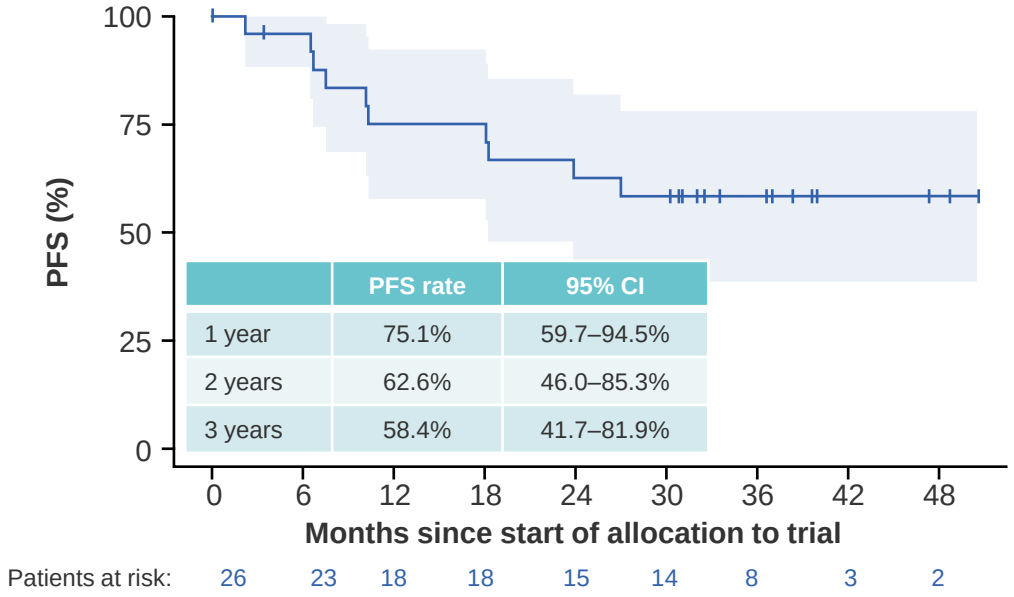
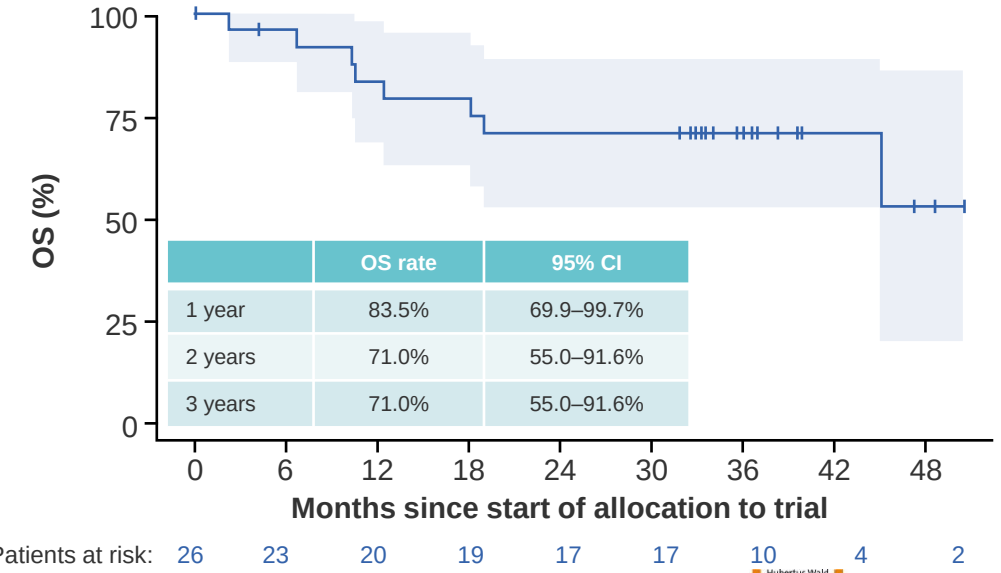
CONCEPT-Studie: Ergebnisse TNE Patient:innen

Median PFS and median OS were not reached with a median follow-up of 33 (PFS) and 35 (OS) months

Secondary endpoint of PFS was met for study arm B



	PFS rate	95% CI
1 year	75.1%	59.7–94.5%
2 years	62.6%	46.0–85.3%
3 years	58.4%	41.7–81.9%



	OS rate	95% CI
1 year	83.5%	69.9–99.7%
2 years	71.0%	55.0–91.6%
3 years	71.0%	55.0–91.6%

Leypoldt et al., J Clin Oncol 2023

CI, confidence interval; OS, overall survival; PFS, progression-free survival

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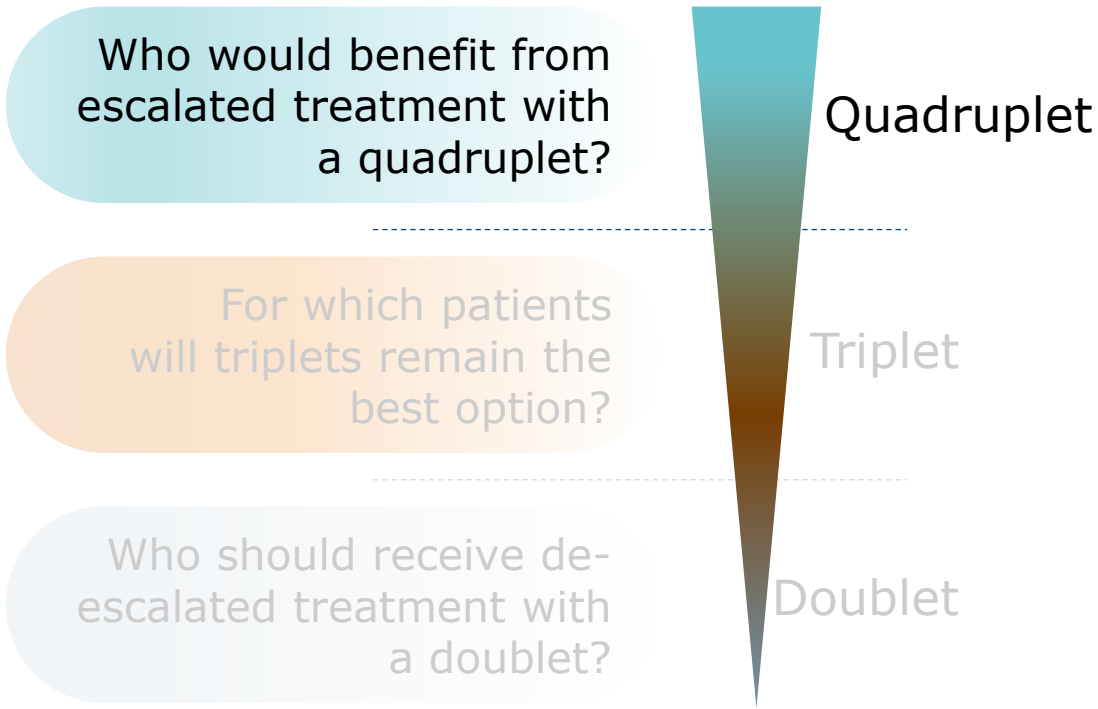
Sollten zukünftig alle TNE Patient:innen ein Quadruplet erhalten?



Te NDMM

TNE NDMM

While triplets are the current SOC regimens for Ti NDMM,[1,2] quadruplets may provide improved efficacy in the TNE setting while retaining acceptable tolerability for fitter patients[3,4]

NDMM, newly-diagnosed multiple myeloma; SOC, standard of care; Te, transplant eligible; Ti, transplant ineligible

1. Dimopoulos A, et al. Ann Oncol 2021;32:309-322; 2. NCCN v3 2023; 3. Orlowski RZ, et al. ASCO 2018; Abstract TPS8055; 4. Clinialtrials.gov NCT03652064

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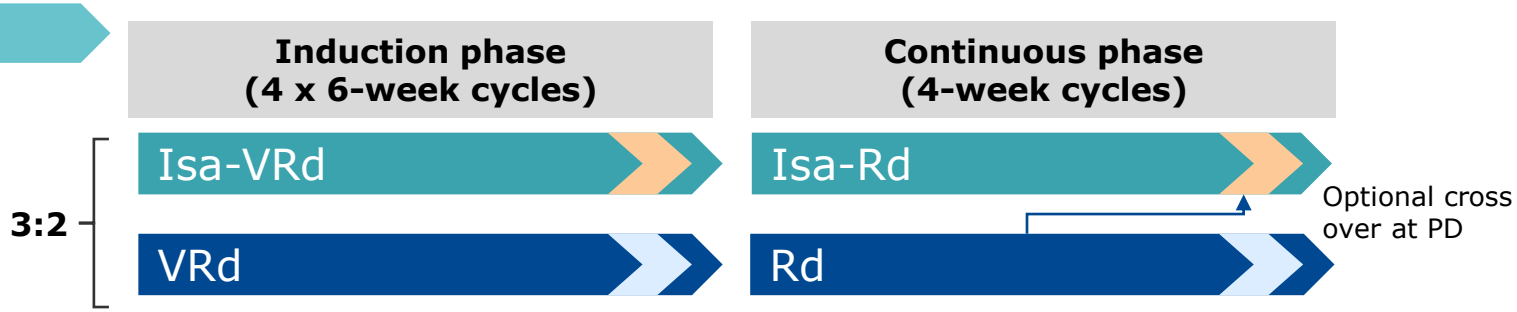
Aktuelle Quadruplet Studien in TNE Patient:innen

IMROZ[1]

- ✓ Age 18–80 years
- ✓ Not eligible for transplant due to age (≥65) or <65 with comorbidities impacting transplant
- × ECOG PS >2

Frail patients were not excluded

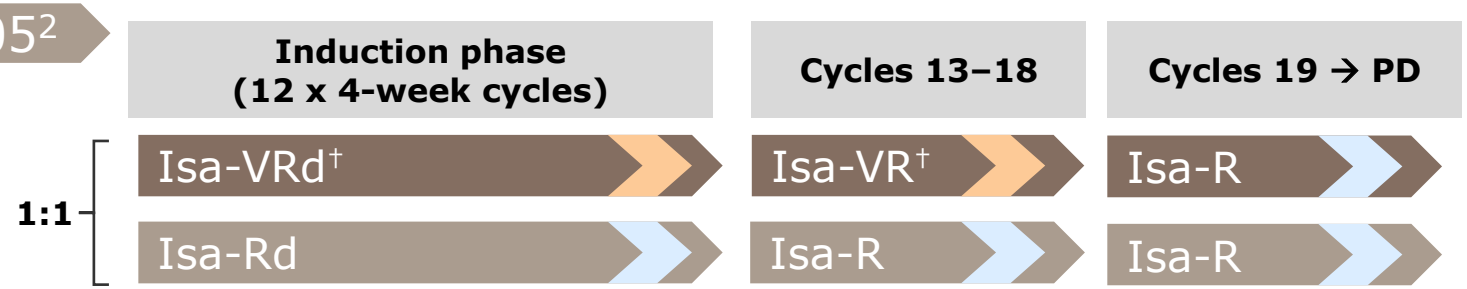


Primary endpoint
PFS

Treatment until PD, unacceptable toxicities, or patient withdrawal

BENEFIT – IFM 2020-05[2]

- ✓ Age ≥65–<80 years
- ✓ Not eligible for transplant and non-frail
- × ECOG PS >2

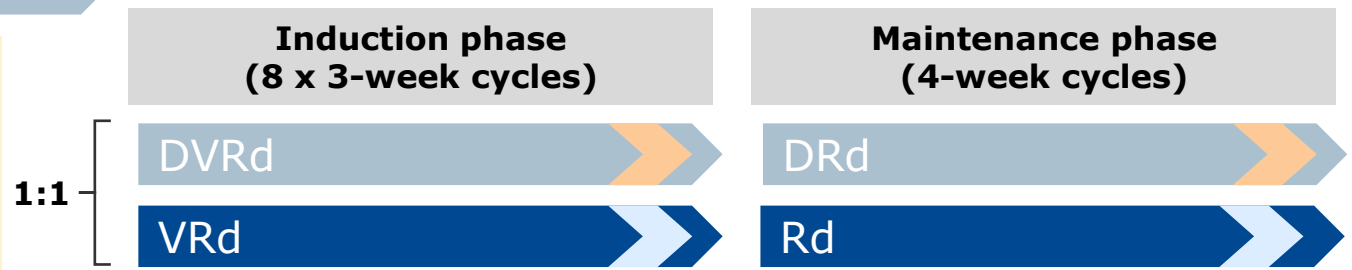


Primary endpoint
MRD– rate

Treatment until PD, unacceptable toxicities, or patient withdrawal

CEPHEUS[2]

- ✓ Age ≥18 years
- ✓ No intent for transplant: ≥65 or <65 with comorbidities impacting transplant
- × ECOG PS >2
- × Frailty index ≥2*



Primary endpoint
MRD– rate

Treatment until PD or unacceptable toxicities

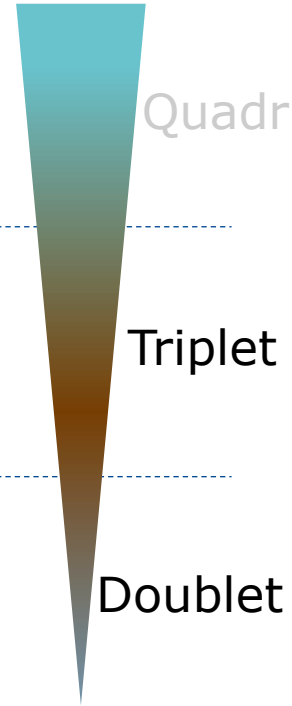
1. Orlowski RZ, et al. ASCO 2018; Abstract TPS8055;
2. Clinialtrials.gov NCT04751877 3. Clinialtrials.gov NCT03652064

Rolle von Triplets und Doublets?

Who would benefit from escalated treatment with a quadruplet?

For which patients will triplets remain the best option?

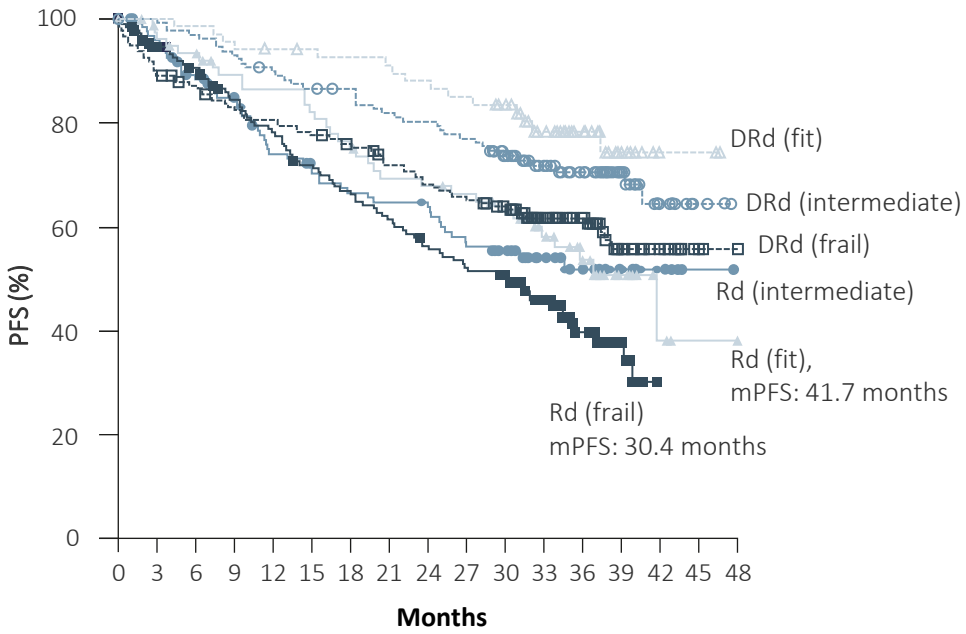
Who should receive de-escalated treatment with a doublet?



Category	Score
Age	
≥75	0
76–80	1
>80	2
CCI	
≤1	0
≥2	1
Sum of scores	
Fit	0
Intermediate	1
Frail	2

PFS according to frailty status in the Phase III MAIA trial[1]

Post-hoc analysis; median FU 36.4 months



Evidence shows that frail patients can benefit from a triplet over a doublet without adverse impact on tolerability*

*Serious TEAEs were seen in 74.4% and 72.9% of frail patients with DRd and Rd, respectively

Facon T, et al. Leukemia 2022;36:1066–77

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D-Rd vs Rd: Frailty subgroup analysis of MAIA

	Total Non-frail (n=395)		Frail (n=334)	
n (%)	D-Rd (n=196)	Rd (n=199)	D-Rd (n=168)	Rd (n=166)
Patients with a TEAE with outcome of death	7 (4)	7 (4)	20 (12)	20 (12)
Patients with a serious TEAE	123 (63)	126 (63)	125 (74)	121 (73)
Treatment discontinuations due to TEAEs	13 (7)	31 (16)	17 (10)	32 (19)
Deaths	26 (13)	46 (23)	57 (34)	57 (34)

	Total–non-frail[b] (54.2%[c]; *n* = 395/729)		Frail (45.8%[c]; *n* = 334/729)	
	D-Rd (53.8%[d]; *n* = 196/364)	Rd (54.5%[e]; *n* = 199/365)	D-Rd (46.2%[d]; *n* = 168/364)	Rd (45.5%[e]; *n* = 166/365)
Lenalidomide permanent discontinuation, *n* (%)	37 (18.9)	25 (12.6)	45 (26.8)	23 (13.9)
Reason for discontinuation, *n* (%)				
AE	30 (15.3)	11 (5.5)	37 (22.0)	14 (8.4)
Other	7 (3.6)	14 (7.0)	8 (4.8)	9 (5.4)
Lenalidomide dose delay, *n* (%)	28 (14.3)	18 (9.0)	31 (18.5)	13 (7.8)
Reason for delay, *n* (%)				
AE	15 (7.7)	8 (4.0)	14 (8.3)	8 (4.8)
Other	14 (7.1)	12 (6.0)	21 (12.5)	7 (4.2)
Lenalidomide dose skipped, *n* (%)	151 (77.0)	125 (62.8)	140 (83.3)	109 (65.7)
Reason for skipping, *n* (%)				
AE	124 (63.3)	98 (49.2)	117 (69.6)	77 (46.4)
Other	84 (42.9)	72 (36.2)	81 (48.2)	66 (39.8)
Lenalidomide dose reduced, *n* (%)	136 (69.4)	110 (55.3)	118 (70.2)	88 (53.0)
Reason for reduction, *n* (%)				
AE	125 (63.8)	101 (50.8)	108 (64.3)	73 (44.0)
Other	16 (8.2)	15 (7.5)	22 (13.1)	24 (14.5)

Facon et al., Leukemia 2022

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Kann man Steroide einsparen?

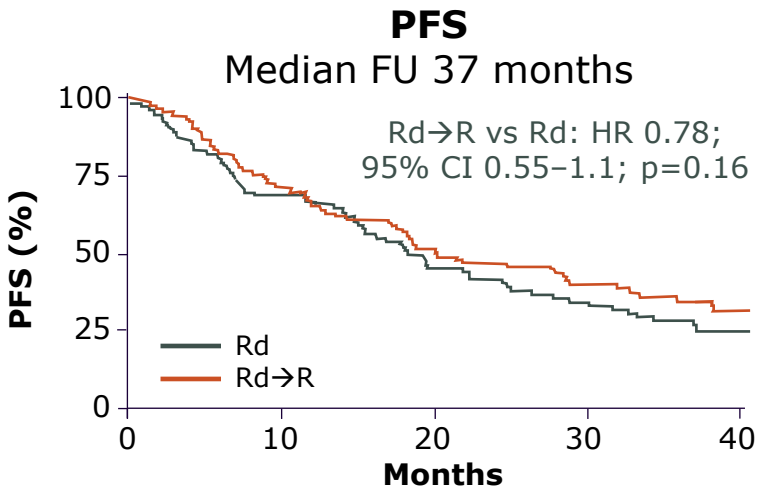
Phase III study of continuous Rd→R vs Rd in elderly intermediate-fit patients with Ti NDMM[1]

Rd→R (n=101)* **Rd x9 cycles** → **R until PD**

Rd (n=98)* **Rd until PD**

*R: 25 mg D1–21 and d: 20 mg of D1, 8, 15, 22

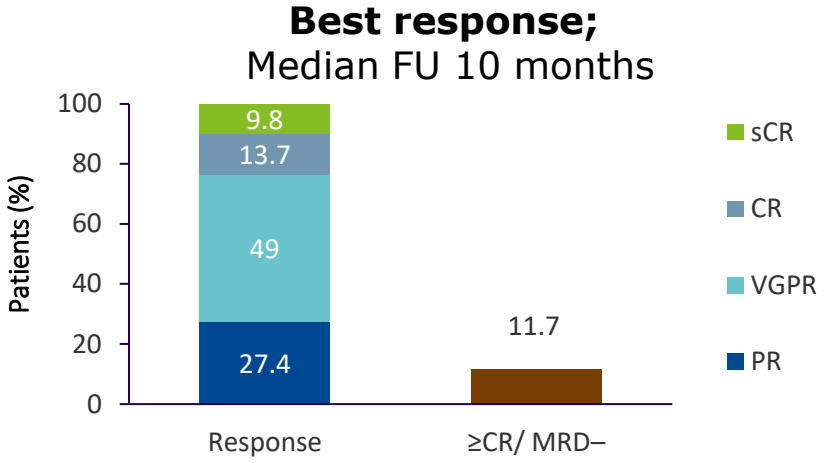
Primary endpoint: Event-free survival



REST study: Phase II open-label study of Isa-VRd in Ti NDMM (N=50)[2]

Isa-VRd x2 cycles → **Isa-VR x6 cycles** → **Isa-R x10 cycles** → **R until PD**

Primary endpoint: MRD– (NGF 10^{-5}) CR during and/or after 18 cycles of study treatment



IFM 2017-3: Phase III study of DR vs Rd in Ti NDMM[3]

Rd (n=95)* **Rd until PD**

DR (n=200)† **DR until PD**

*R: 25 mg D 21/28 and d: 20 mg QW, 22/28; †D: 1800 mg SC QW for 8 weeks, Q2W for 16 weeks and then Q4W and R 25 mg D 21/28 (x2 cycles of d [QW 8wks])

Endpoints: ORR, ≥VGPR, MRD–

AE, adverse event; d, dexamethasone; D, daratumumab; FU, follow-up; Isa, isatuximab; NDMM, newly diagnosed multiple myeloma; NGF, next-generation flow; PD, disease progression; R, lenalidomide; Ti, transplant ineligible; V, bortezomib

1. Larocca A, et al. Blood 2021;137:3027-36;
2. Askeland FB, et al. EHA 2023; Poster P875;
3. Manier S, et al. Blood 2022;140:1369–70

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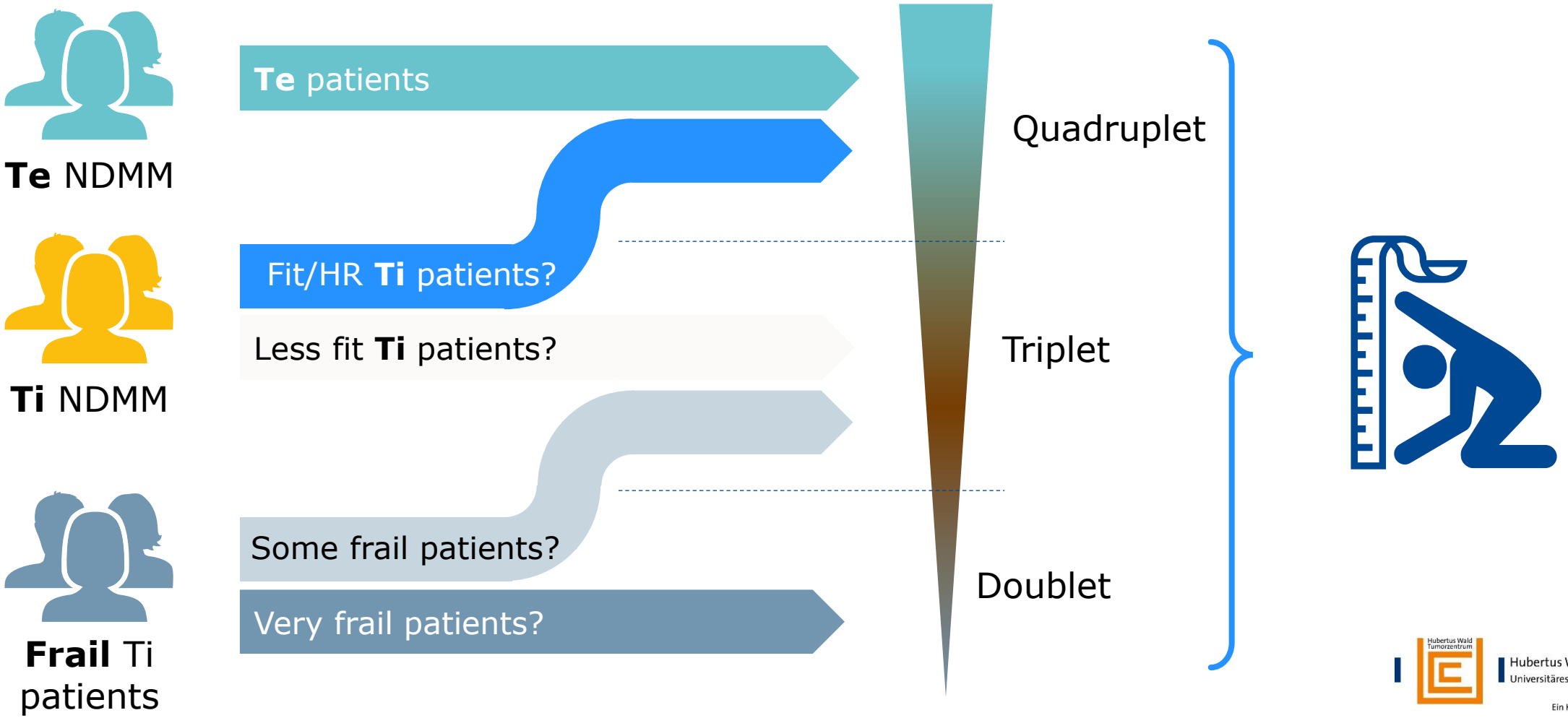
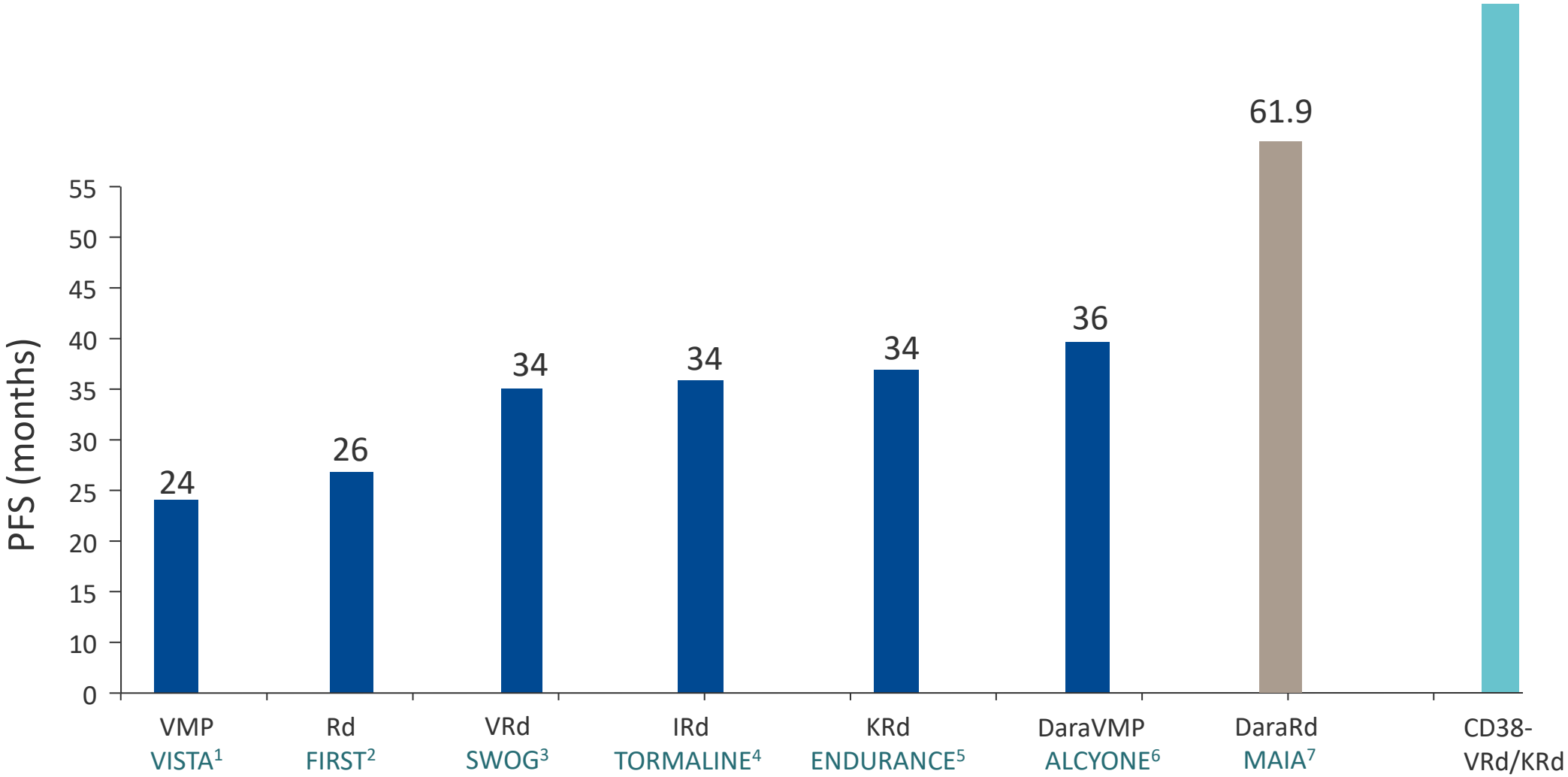
Zukünftige Erstlinientherapie?



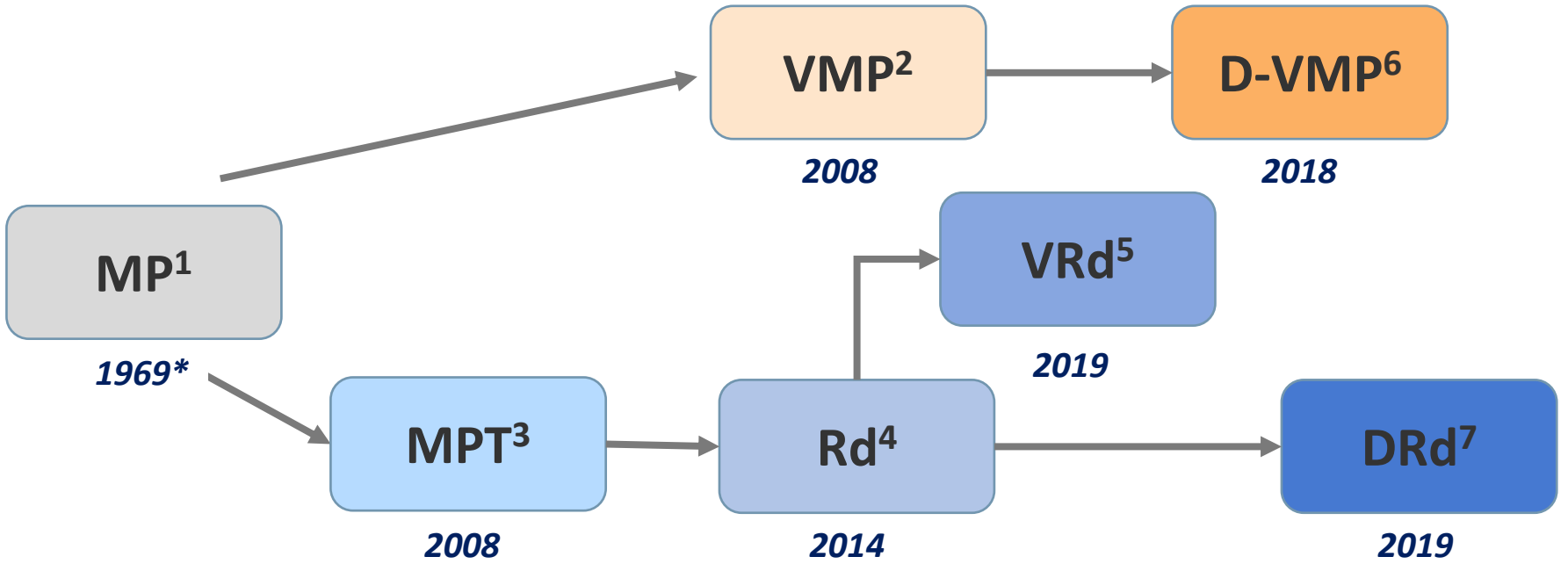


The data presented are provided for ease of viewing information from multiple trials. Direct comparison between trials is not intended and should not be inferred.

DaraRd, daratumumab + lenalidomide + dexamethasone; DaraVMP, daratumumab + bortezomib + melphalan + prednisolone; VMP, bortezomib + melphalan + prednisolone.

1. San Miguel J, et al. N Engl J Med 2008;359:906–17. 2. Benboubker L, et al. N Engl J Med 2014;371:906–17. 3. Durie BGM, et al. Lancet. 2017;389:519-27. 4. Facon T et al. Oral presented at ASH 2020; abstract 551.
5. Kumar S, et al. J Clin Oncol. 2020:38: abstract LBA3. 6. Mateos MV, et al. Blood 2019;138:abstract 859. 7. Facon T, et al. N Engl J Med. 2019;380:2104-15. 8. NCT03319667. Available at: https://clinicaltrials.gov/. Accessed May 2022.

Treatment Landscape and Perspective in ND TNE Patients



* Publication; OS Overall survival; **NCT03319667 et NCT03652064;
[1]MP, melphalan-prednisone; [2]VMP, bortezomib(Velcade)-melphalan-prednisone; [3]MPT, melphalan-prednisone-thalidomide; [4]Rd, lenalidomide(Revlimid)-dexamethasone; [5]VRd, bortezomib(Velcade)-lenalidomide (Revlimid)-dexamethasone; [6]D-VMP, daratumumab-bortezomib (Velcade)-melphalan-prednisone; [6]DRd, daratumumab-lenalidomide(Revlimid)-dexaméthasone; Isa = isatuximab; IMiDs = immunomodulateurs; BCMA = B cell maturation antigen; Ac = antibody; CAR-T cells = chimeric receptor T cells.

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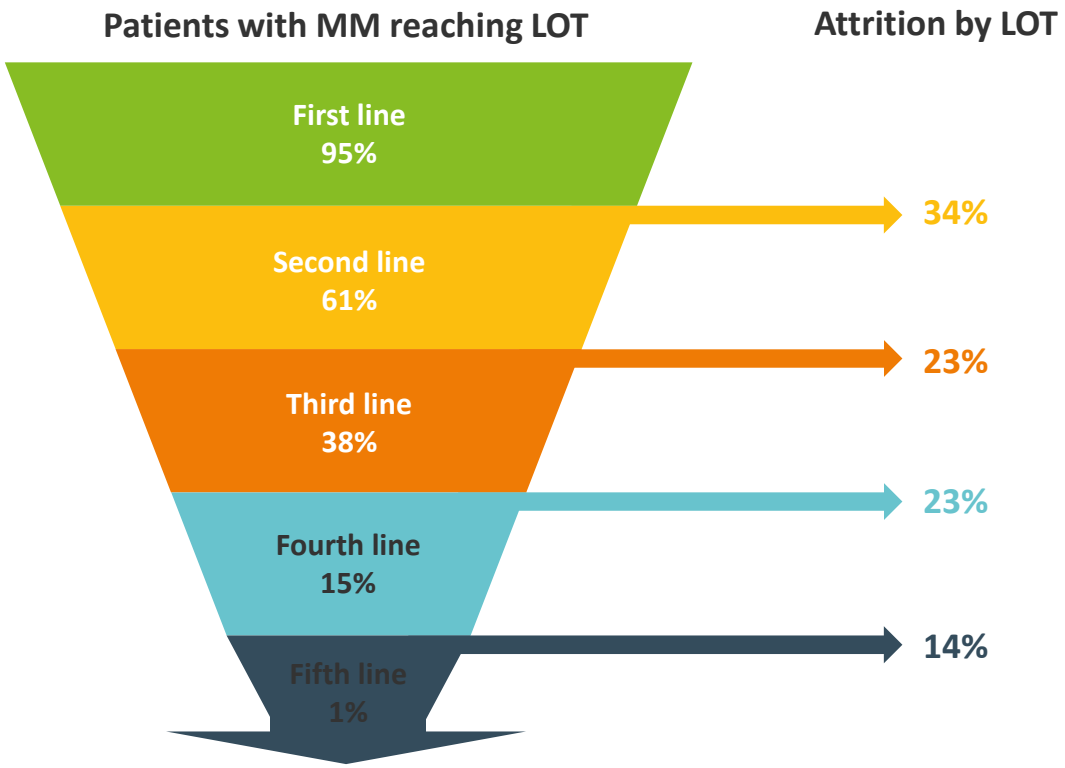
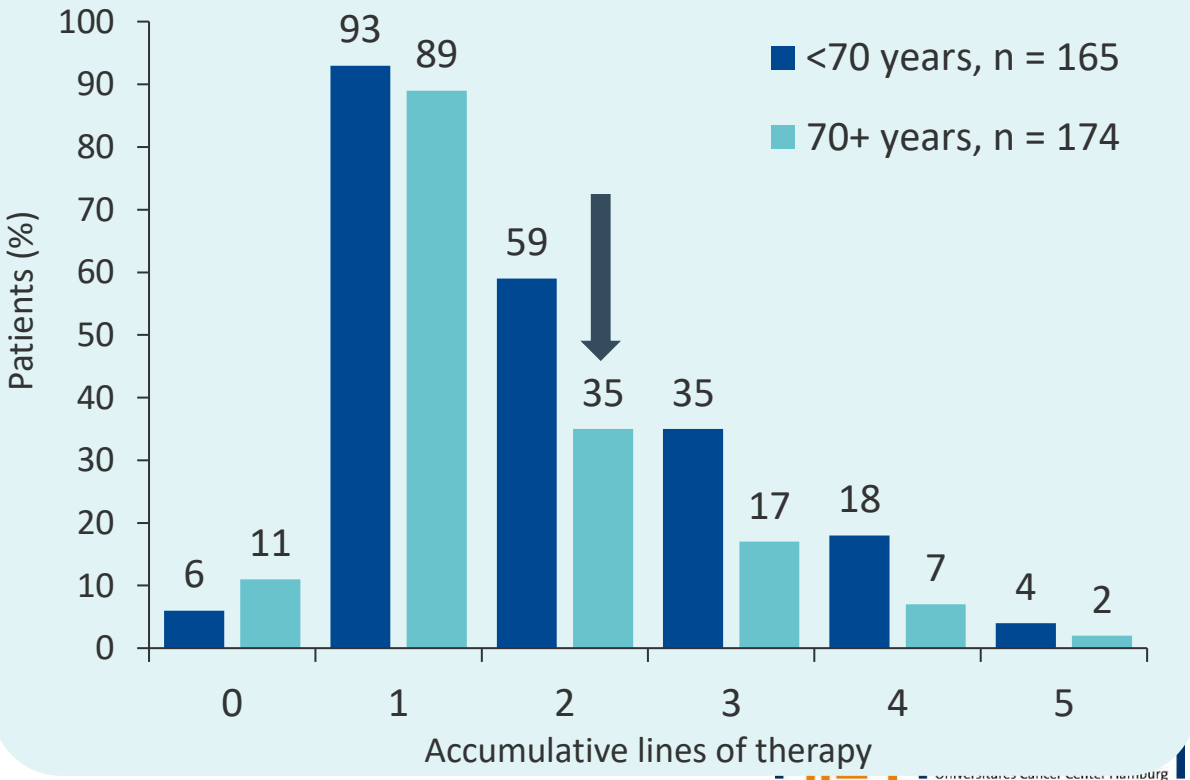
Courtesy of T Facon, IMW 2021

There is a high attrition rate in MM treatment … front-line treatment is critical!

~ 15%–35% of patients are lost for every new line of treatment



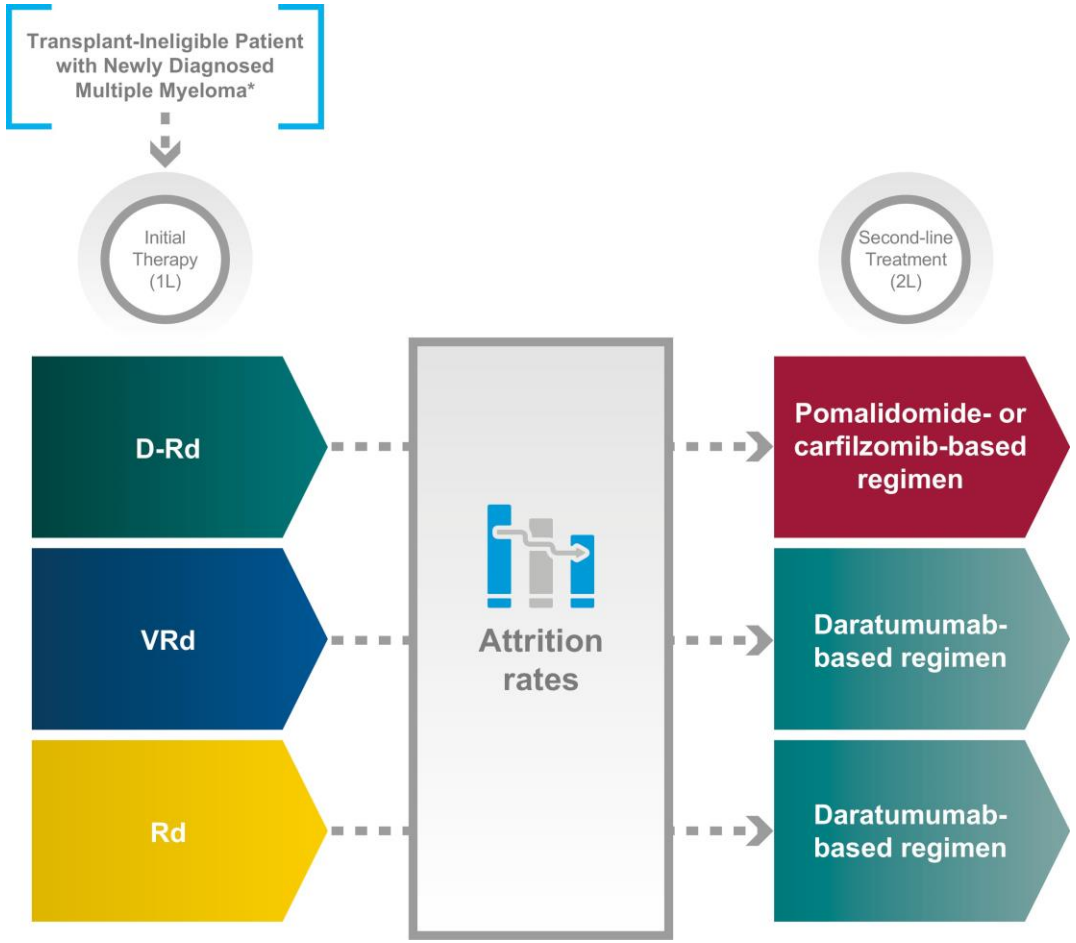
Attrition rate is particularly high in the elderly

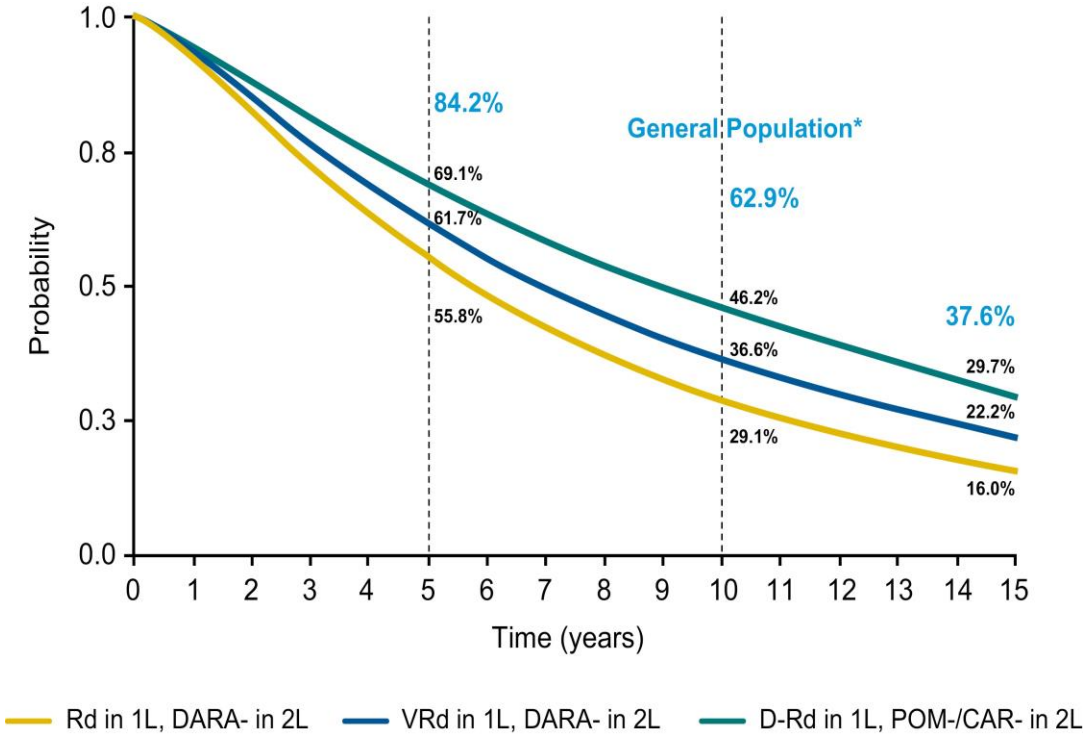


LOT, line of therapy.

Left figure adapted from: Yong K, et al. Br J Haematol. 2016;175:252-64. Right figure: courtesy of Spencer A (Monash University, Australia).

Does Sequence matters?

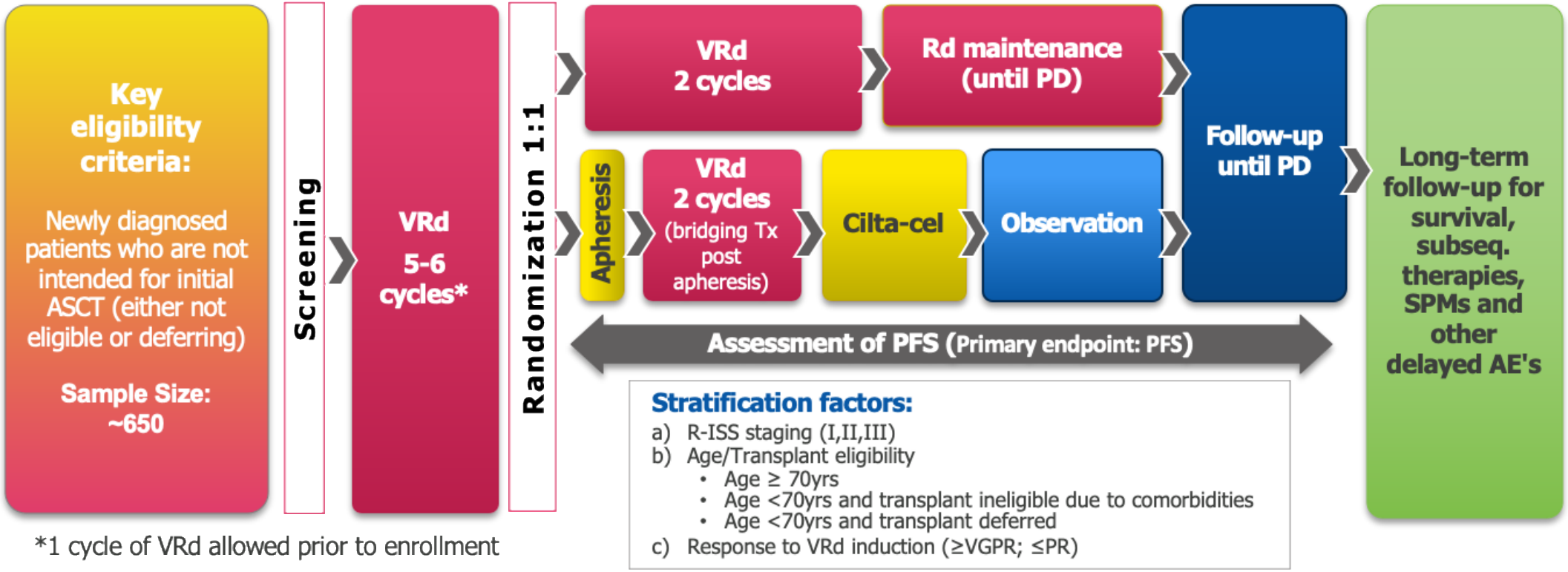




5-, 10-, and 15-year OS rates (base case).

* Median simulated age 86.7 years

Frontline CAR-T cells in transplant ineligible patients
CARTITUDE-5[1,2]



AE, adverse event; ASCT, autologous stem cell transplantation; PD, progressive disease; PFS, progression-free survival; PR, partial response; R-ISS, revised international staging system; Tx, treatment; VGPR, very good partial response; VRd, bortezomib, lenalidomide and dexamethasone.

1. NCT04923893. Available at https://clinicaltrials.gov/ct2/show/NCT04923893 (last accessed June 2023). 2. Dytfeld D, et al. (ASH 2021 – poster).

Zusammenfassung

TNE-Erstlinienbehandlung:

- Dara-Rd ist die führende leitliniengerechte Behandlungsoption, Dara-VMP und VRd stehen als Alternativen zur Verfügung
- Bei VRd kann auch das VRd-lite Regime gewählt werden
- Hochrisikopatient:innen profitieren von Quadruplet-Regimen
- Die Gesamtbedeutung von Quadrupletterapien bei TNE Patient:innen wird gegenwärtig geprüft
- In Studien wird die Rolle der primären CAR-T Zelltherapie sowie von bispezifischen Antikörpern evaluiert

Thank you!

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