Elderly patients or patients with NDMM who are ‘not' eligible to receive HDT and autologous transplantation

DR FATEMEH NEJATIFAR

HEMATOLOGIST & MEDICAL ONCOLOGIST

GUILAN UNIVERSITY OF MEDICAL SCIENCES

Updated IMWG Criteria for Diagnosis of Multiple Myeloma

MGUS

- M protein < 3 g/dL
- Clonal plasma cells in BM < 10%
- No myeloma defining events

Smoldering Myeloma

- M protein ≥ 3 g/dL (serum) or ≥ 500 mg/24 hours (urine)
- Clonal plasma cells in BM ≥ 10% to 60%
- No myeloma defining events

Multiple Myeloma

- Underlying plasma cell proliferative disorder

AND

- 1 or more myeloma defining events including either:

✓≥ 1 **CRAB** feature(s)

OR

✓≥ 1 **Biomarker Driven**

C: Calcium elevation (> 11 mg/dL or > 1 mg/dL above ULN)
R: Renal insufficiency (creatinine clearance < 40 mL/min or serum creatinine > 2 mg/dL)
A: Anemia (Hb < 10 g/dL or 2 g/dL < normal)
B: Bone disease (≥ 1 lytic lesions on skeletal radiography, CT, or PET-CT)

Biomarker driven

- Sixty-percent (≥ 60%) clonal PCs by BM
- Serum free light chain ratio involved:uninvolved ≥ 100
- > 1 focal lesion detected by MRI

BM, bone marrow; CT, computed tomography; Hb, hemoglobin; IMWG, International Myeloma Working Group; MGUS, monoclonal gammopathy of undetermined significance; PET, positron emission tomography; ULN, upper limit of normal.

Rajkumar SV, et al. Lancet Oncol. 2014;15:e538-e548.

These materials are provided to you solely as an educational resource for your personal use. Any commercial use or distribution of these materials or any portion thereof is strictly prohibited.

General eligibility requirements

- **Eligibility for autologous HCT in MM varies across countries and institutions.**
- In most European countries, transplantation for MM is offered primarily to patients younger than 65 years of age.
- In the United States (US), a strict age limit is not used. Instead, decisions are made on a case-by-case basis based on "physiologic age" and vary across institutions

abidi Oncology

What Drives the Approach to Frontline Therapy?

Risk Stratification

- Standard risk
  - Trisomic, t(11;14)
- High risk
  - t(4;14), t(14;16), t(14;20)
  - Gain(1q), del(17p), p53*mut*
  - Double/triple hit

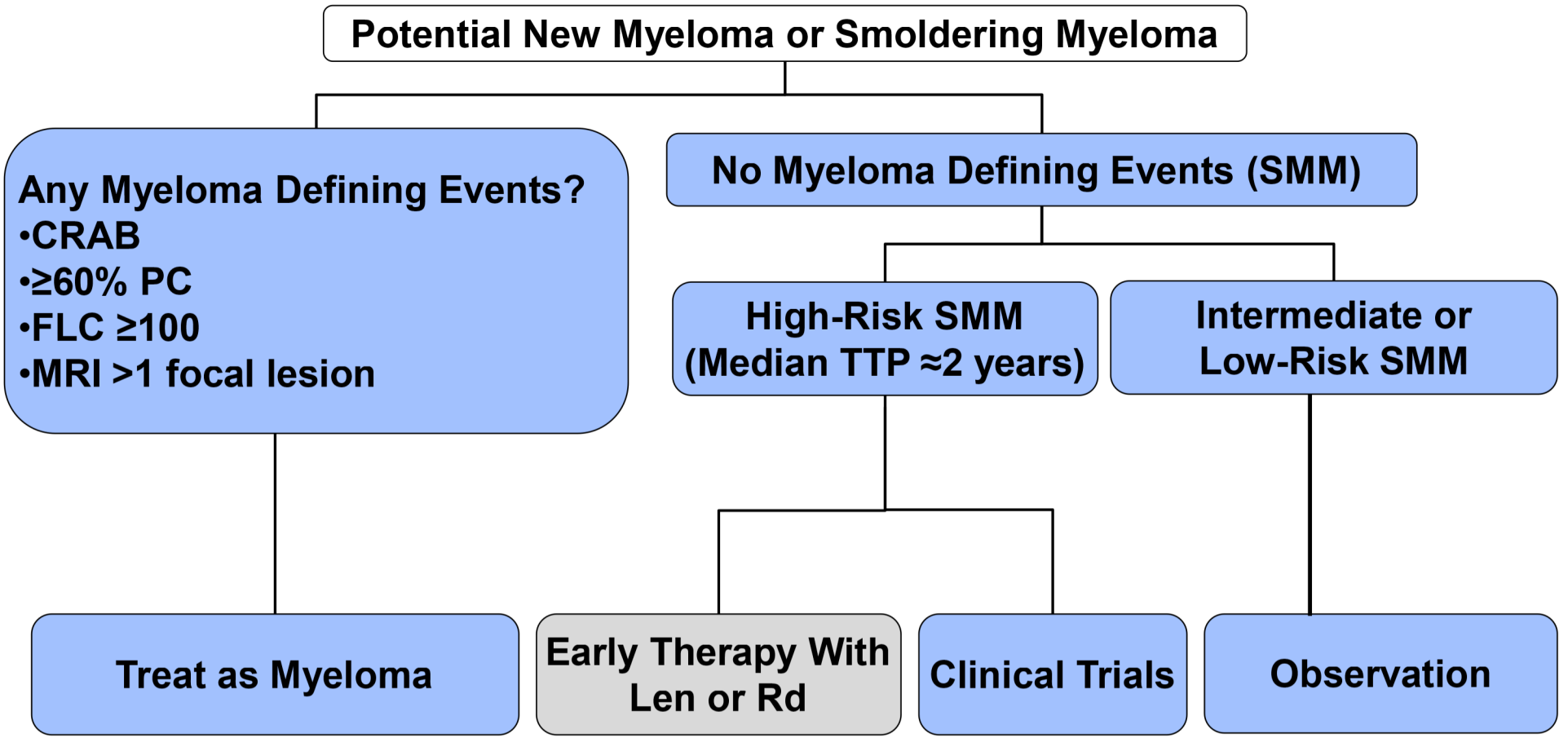
Transplant Eligibility

- Age
- Performance status
- Comorbidities

Rajkumar SV, et al. *Blood Cancer J.* 2020;10:94.

abidi Oncology

When Should Treatment Be Initiated?



Rajkumar SV © 2021

Selecting Treatment for MM: General Principles

Patient	Disease	Treatment	Regimen
▪ Age/frailty ▪ Performance status ▪ Lifestyle ▪ Patient preference ▪ Caregiver support ▪ Comorbidities – Renal status – Neuropathy – Cardiac – Diabetes – Cytopenias	▪ Disease burden: ISS – Rate of progression – Marrow burden – CRAB symptoms – Extramedullary disease ▪ Biology – LDH – Cytogenetics: • t(4;14) • del(17p) • t(14;16) • amp(1q) • t(11;14)	▪ Toxicity – Myelosuppression – Infections – Neuropathy – Secondary cancers – Ocular toxicity ▪ Cost ▪ Administration route ▪ Relapsed vs refractory ▪ Depth/duration of response to any prior treatment	▪ Triplet* (eg, VRd) is preferred over doublet ▪ Include ≥1 agent from a new or nonrefractory class ▪ Previously used agents may be effective in different combinations ▪ Treat to maximum response ▪ Maintain on ≥1 agent until progression or intolerability

*2 active classes plus dexamethasone.

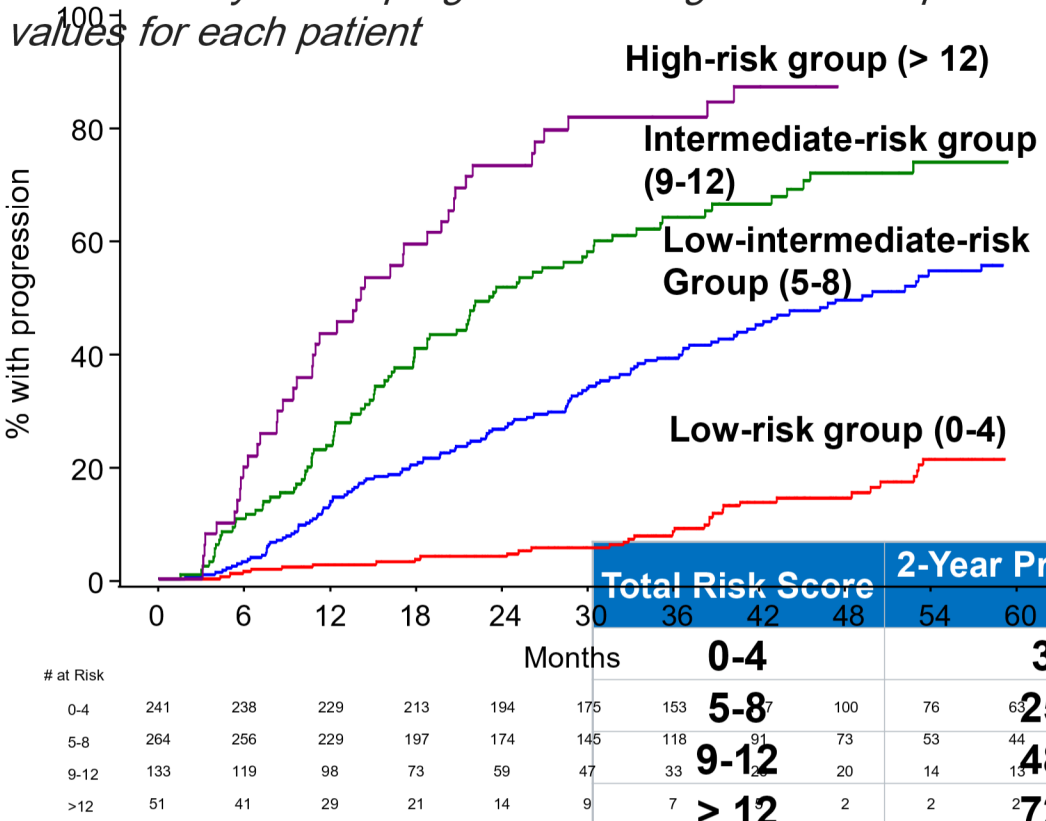
Slide credit: clinicaloptions.com

Laubach. Leukemia. 2016;30:1005. NCCN. clinical practice guidelines in oncology: multiple myeloma (v6.2021).
Sanchez. Expert Rev Hematol. 2020;13:943. Sonneveld. 2016;101:396.

abidi Oncology

IMWG: Risk Score to Predict Progression Risk at 2 Years

A more precise and individualized scoring tool to classify individuals by risk of progression using the entire spectrum of values for each patient



Total Risk Score	2-Year Progression, n (%)
0-4	3.7%
5-8	25.4%
9-12	48.9%
> 12	72.6%

Risk Factor	Coefficient	P-value	Score
FLC Ratio			
0-10 (reference)	-	-	0
> 10-25	0.69	0.014	2
> 25-40	0.96	0.004	3
> 40	1.56	<0.0001	5
M protein (g/dL)			
0-1.5 (reference)	-	-	0
> 1.5-3	0.95	0.0002	3
> 3	1.30	<0.0001	4
BMPC%			
0-15 (reference)	-	-	0
> 15-20	0.57	0.04	2
> 20-30	1.01	0.0002	3
> 30-40	1.57	<0.0001	5
> 40	2.00	<0.0001	6
FiSH abnormality	0.83	<0.0001	2

MyeRisk Calculator

San Miguel. ASCO 2019. Abstr 8000. Mateos. Blood Cancer J. 2020;10:102.

abidi Oncology

Goals of Therapy in the Setting of Newly Diagnosed MM

Goal: Achieve deepest and most durable response possible

- More aggressive therapy upfront
- Consider risk status, transplant eligibility

Goal: Optimize quality of life

- Balance efficacy with tolerability
- Provide supportive care
- Engage in shared decision making

MM, multiple myeloma.

abidi Oncology

- MRD negativity in the BM, defined as the absence of tumor plasma cells within 1 000 000 BM cells (<106)shows the best results for the prediction of both PFS and OS compared with higher cut-off values (i.e. 105).

- Outside the BM, PET-CT is able to recognize hypermetabolic areas in approximately 15%-20% of patients with MRD negativity in the BM and is considered the best method for imaging MRD to date

abidi Oncology

MYLODEQ®
Lenalidomide

Important issues :

1 – Combinations with CD38 antibodies upfront ?

2 – Use of frailty score

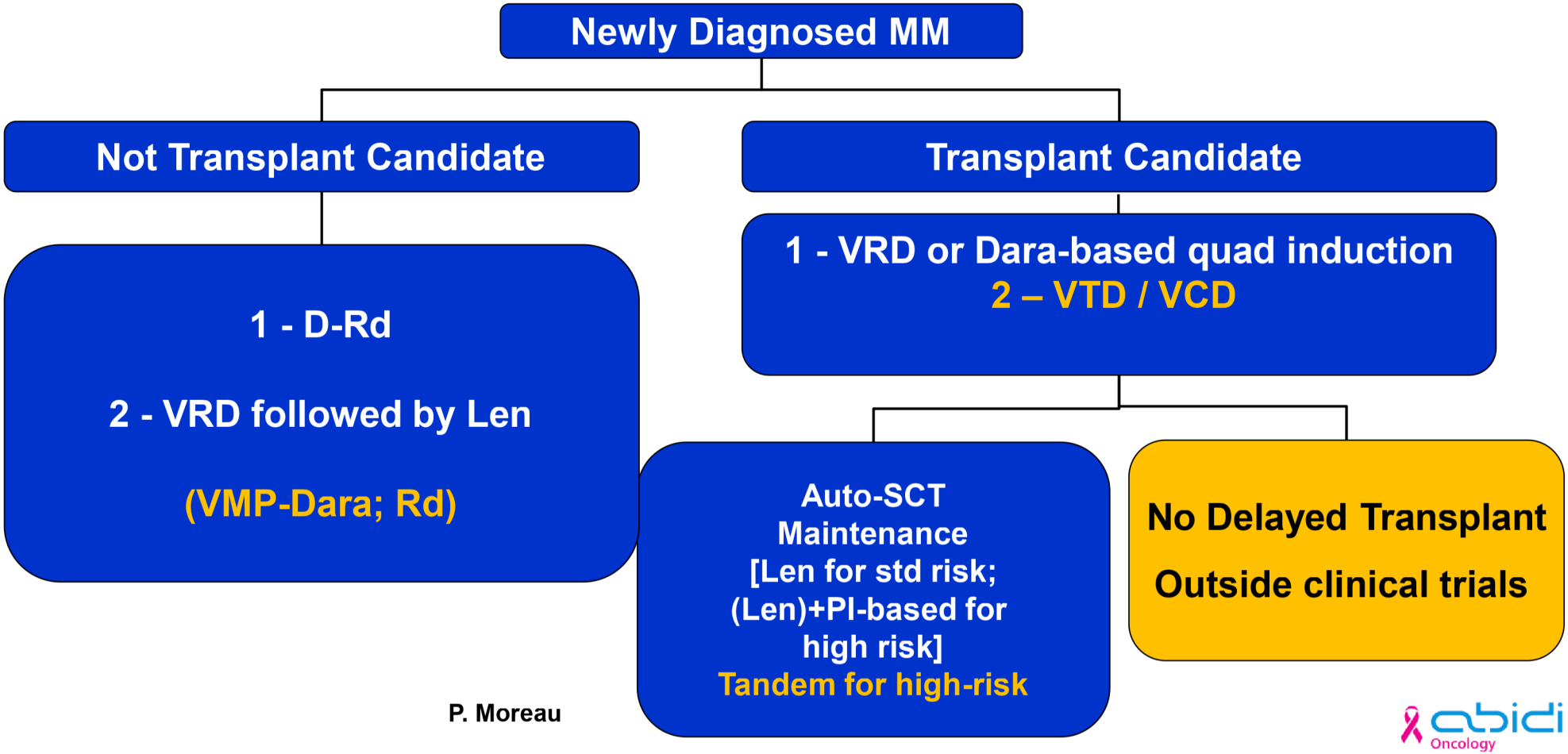
3 – Management of AEs

4 – Fixed duration of treatment until progression

abidi Oncology

MYLODEQ®
Lenalidomide

Myeloma: Frontline Treatment

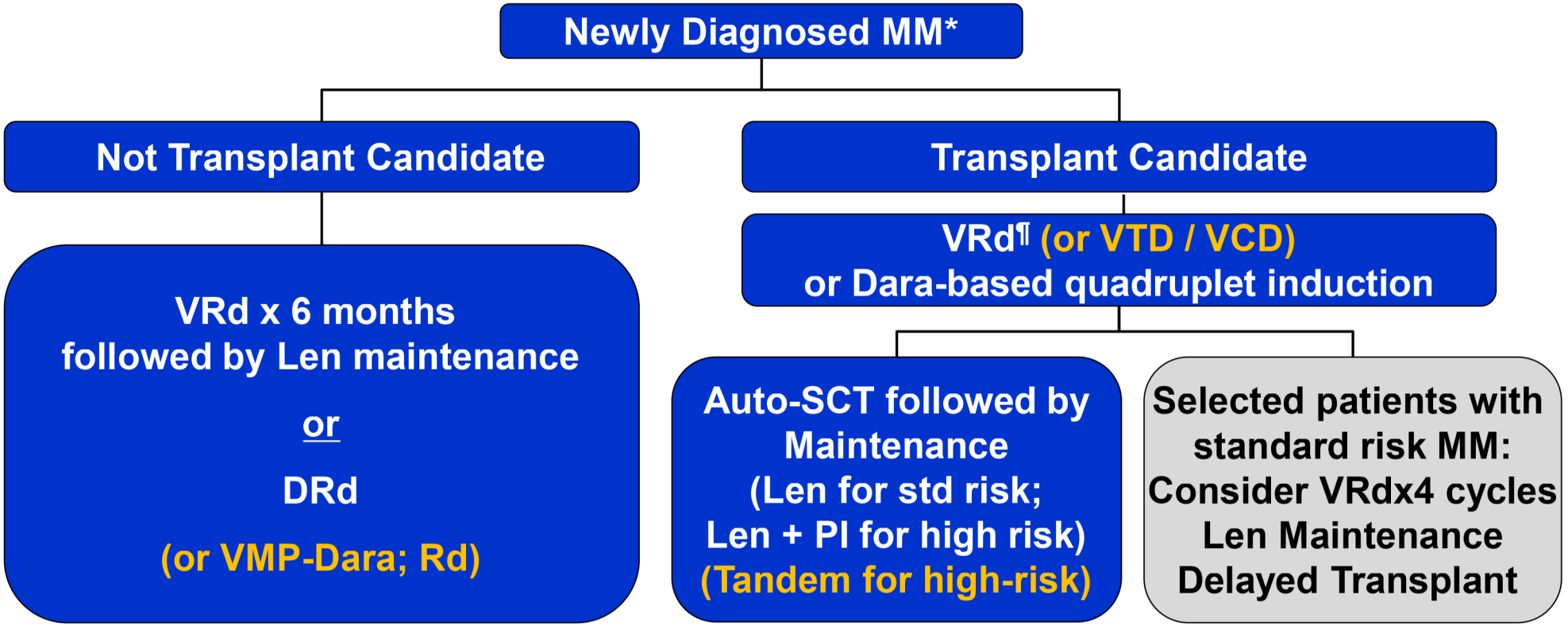


P. Moreau

abidi Oncology

MYLODEQ®
Lenalidomide

Myeloma: Frontline Treatment

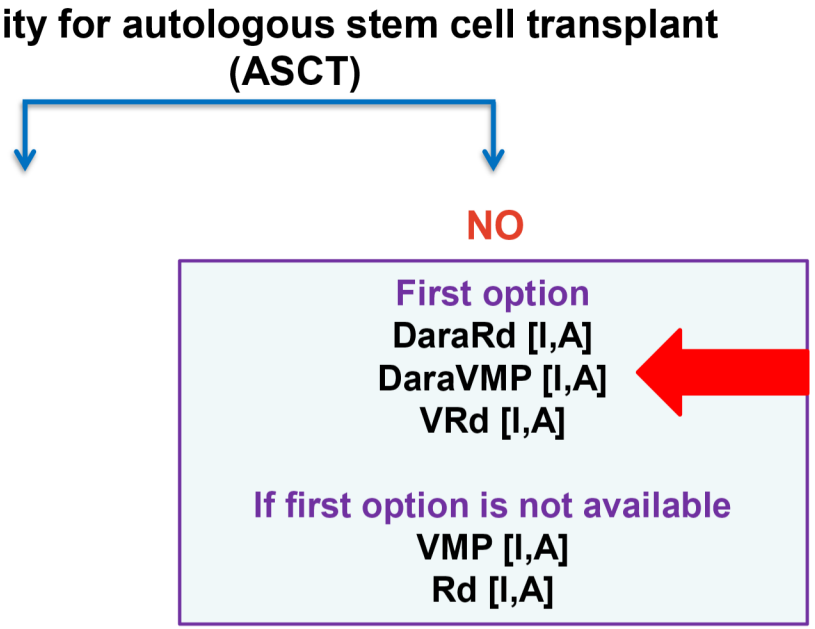


*Based on CALGB 100104, S0777, IFM-2009, CTN 0702, HOVON, MAIA, CASSIOPEIA
¶ VTd/VCd if VRd not available

Rajkumar SV © 2021 and P. Moreau

abidi Oncology

Frontline treatment of symptomatic multiple myeloma outside clinical trials (EHA-ESMO guidelines 2021)

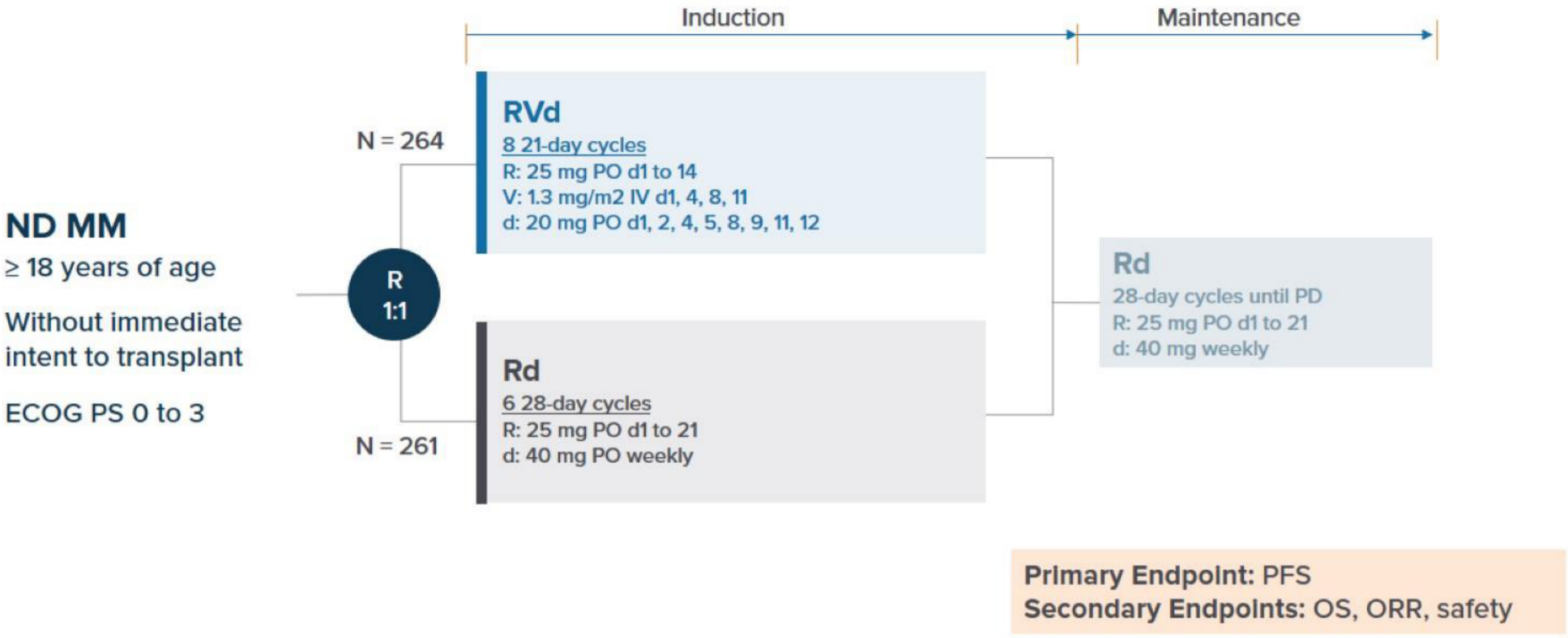


Dimopoulos MA, *et al.* Ann Oncol 2021; 32(3):309-322.

DaraRd, daratumumab/lenalidomide/dexamethasone; DaraVMP, daratumumab/bortezomib/melphalan/prednisone; DaraVTD, daratumumab/bortezomib/thalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; VMP, bortezomib/melphalan/prednisone; VRd, bortezomib/lenalidomide/dexamethasone

abidi Oncology

Superiority of Triplet RVd vs Rd Established in Phase 3 SWOG S0777 Study

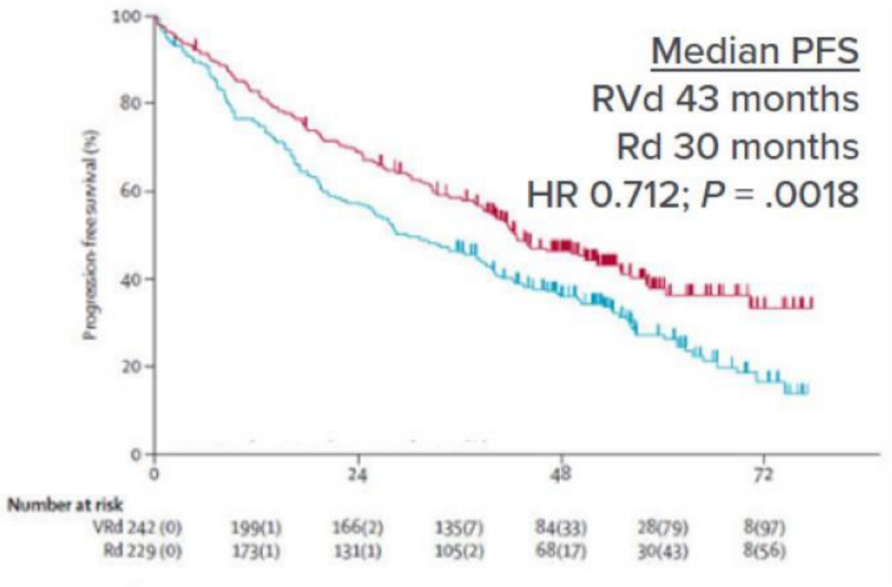


ECOG, Eastern Cooperative Oncology Group; ND, newly diagnosed; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PS, performance status.
Durie B, et al. Lancet. 2017;389:519-527.

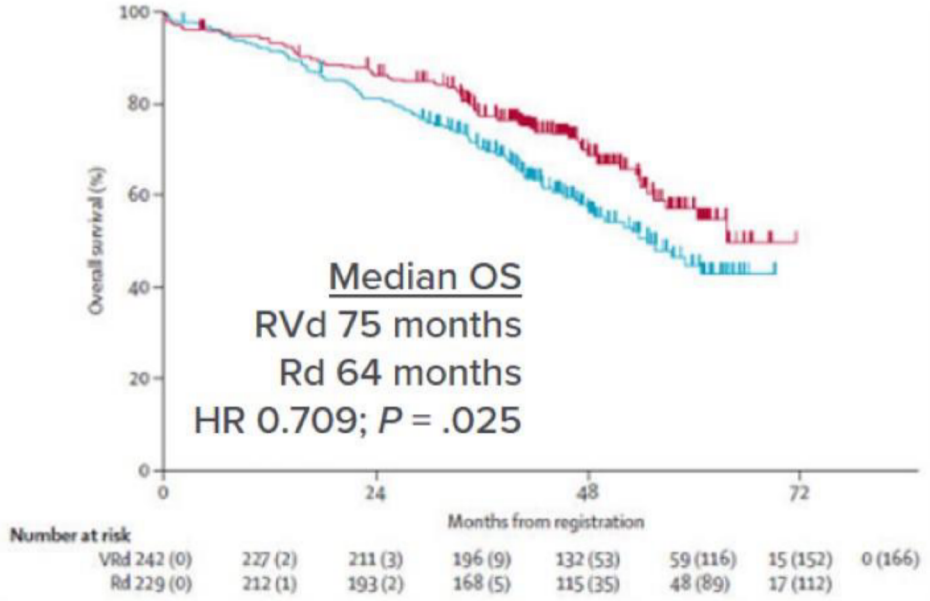
abidi Oncology

Superiority of Triplet RVd vs Rd Established in Phase 3 SWOG S0777 Study

PFS – Primary Endpoint



OS



Durie B, et al. Lancet. 2017;389:519-527.

abidi Oncology

Updated analysis SWOG777 – Durie et al Blood Cancer J 2020

Adverse event description	Revlimid/dexamethasone (*N* = 222)					Velcade/Revlimid/dexamethasone (*N* = 234)				
	1	2	3	4	5	1	2	3	4	5
Allergy/immunology	12 (5%)	5 (2%)				10 (4%)	4 (2%)	2 (<1%)		
Auditory/ear	1 (<1%)	16 (7%)				1 (<1%)	8 (3%)			
Blood/bone marrow	22 (10%)	53 (24%)	68 (31%)	39 (18%)		27 (12%)	52 (22%)	70 (30%)	44 (19%)	
Cardiac arrhythmia	5 (2%)	4 (2%)	4 (2%)			10 (4%)	3 (1%)	3 (1%)		
Cardiac general	13 (6%)	9 (4%)	8 (4%)			15 (6%)	17 (7%)	21 (9%)		
Coagulation	1 (<1%)		3 (1%)					5 (2%)		
Constitutional symptoms	61 (27%)	77 (35%)	38 (17%)			60 (26%)	84 (36%)	51 (22%)		
Death					1 (<1%)					2 (<1%)
Dermatology/skin	60 (27%)	23 (10%)	9 (4%)			50 (21%)	41 (18%)	7 (3%)	1 (<1%)	
Endocrine	11 (5%)	8 (4%)				7 (3%)	12 (5%)			
Gastrointestinal	77 (35%)	71 (32%)	19 (9%)			64 (27%)	79 (34%)	51 (22%)	2 (<1%)	1 (<1%)
Hemorrhage/bleeding	13 (6%)	2 (<1%)				9 (4%)	3 (1%)	8 (3%)		
Hepatobiliary/pancreas			2 (<1%)							
Infection	1 (<1%)	31 (14%)	27 (12%)	4 (2%)		1 (<1%)	33 (14%)	34 (15%)	7 (3%)	1 (<1%)
Lymphatics	58 (26%)	19 (9%)	1 (<1%)			73 (31%)	26 (11%)	4 (2%)		
Metabolic/laboratory	56 (25%)	58 (26%)	51 (23%)	13 (6%)		50 (21%)	58 (25%)	57 (24%)	8 (3%)	
Musculoskeletal/soft tissue	25 (11%)	25 (11%)	16 (7%)	1 (<1%)		15 (6%)	31 (13%)	24 (10%)		
Neurology	78 (35%)	44 (20%)	21 (9%)	3 (1%)	1 (<1%)	42 (18%)	70 (30%)	77 (33%)	4 (2%)	
Ocular/visual	21 (9%)	8 (4%)	11 (5%)			39 (17%)	17 (7%)	6 (3%)		
Pain	44 (20%)	29 (13%)	10 (5%)			55 (24%)	43 (18%)	28 (12%)		
Pulmonary/upper respiratory	42 (19%)	27 (12%)	9 (4%)	1 (<1%)		56 (24%)	17 (7%)	15 (6%)	5 (2%)	
Renal/genitourinary	3 (1%)	2 (<1%)	9 (4%)	1 (<1%)		10 (4%)	3 (1%)	6 (3%)		
Secondary malignancy			5 (2%)	1 (<1%)				5 (2%)	2 (<1%)	
Sexual/reproductive function	1 (<1%)	1 (<1%)	1 (<1%)			3 (1%)	1 (<1%)			
Syndromes			2 (<1%)			1 (<1%)	2 (<1%)	4 (2%)		
Vascular		7 (3%)	15 (7%)	6 (3%)		1 (<1%)	9 (4%)	20 (9%)	4 (2%)	

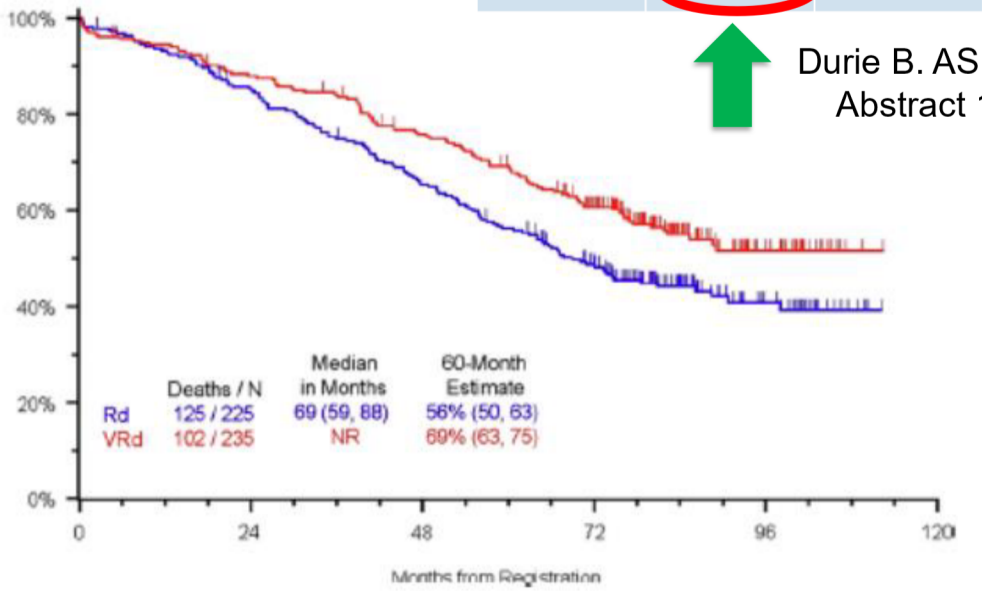
abidi Oncology

Updated analysis SWOG777 – Durie et al Blood Cancer J 2020

Median PFS (months)

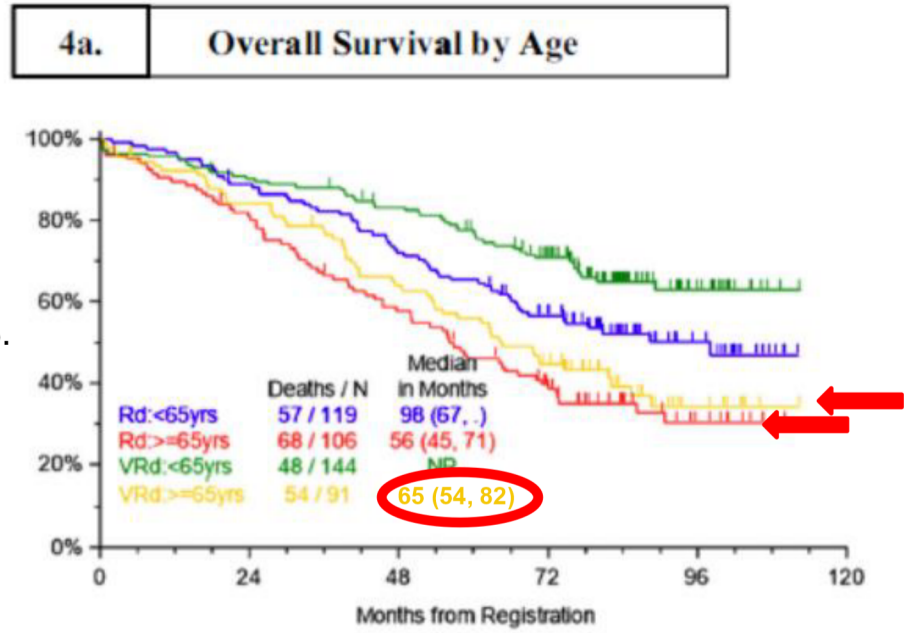
Age (years)	VRd	Rd
<65	48	34
≥65	34	24
>75	34	17

Durie B. ASH 2018. Abstract 1992.



OS at 5 years

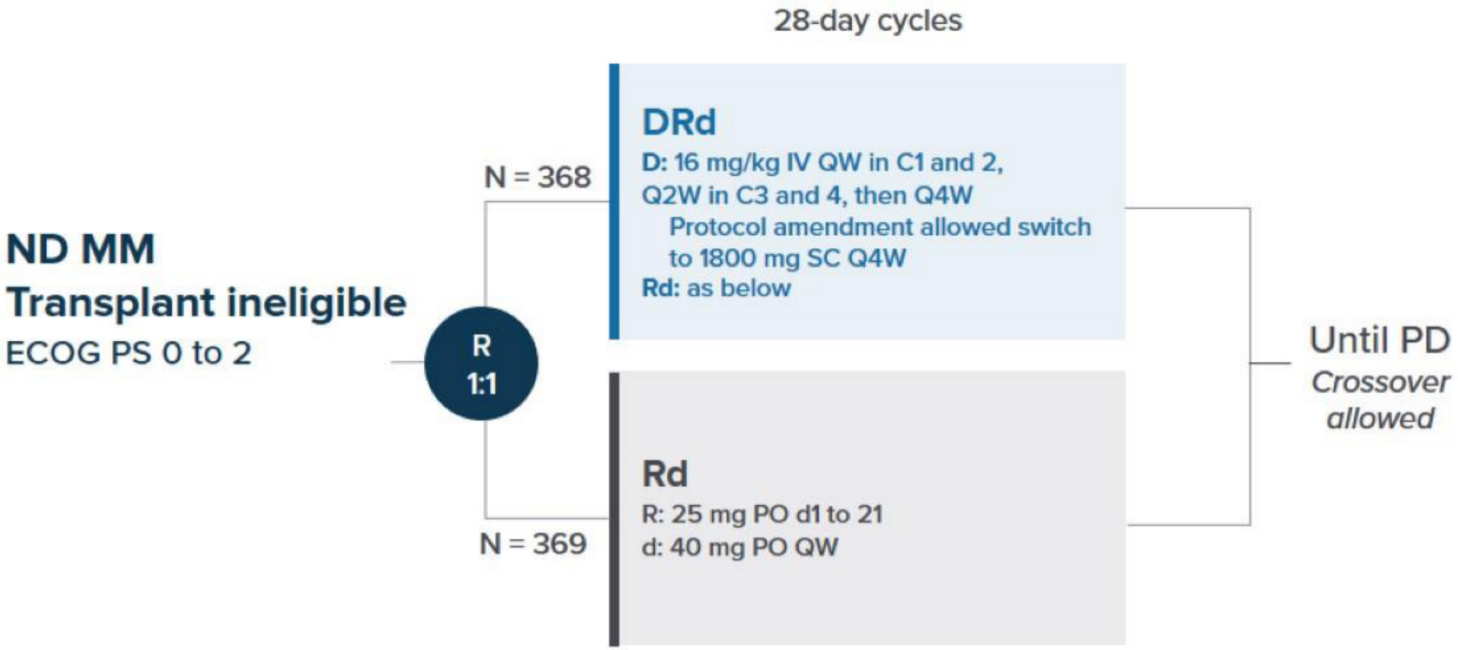
Median follow-up 84 months



Age < 65 years: HR= 0.640 (0.421,0.973);
stratified, two-sided p= 0.028

Age ≥ 65 years: HR= 0.769 (0.520,1.138);
stratified, two-sided p= 0.168

MAIA Evaluated Anti-CD38-Based Triplet DRd vs Rd in Transplant-Ineligible ND MM



Primary Endpoint: PFS

Secondary Endpoints:
OS, PFS2, ORR, ≥ CR, MRD (10^{-5})

- *78% of patients were ≥ 70 years of age*

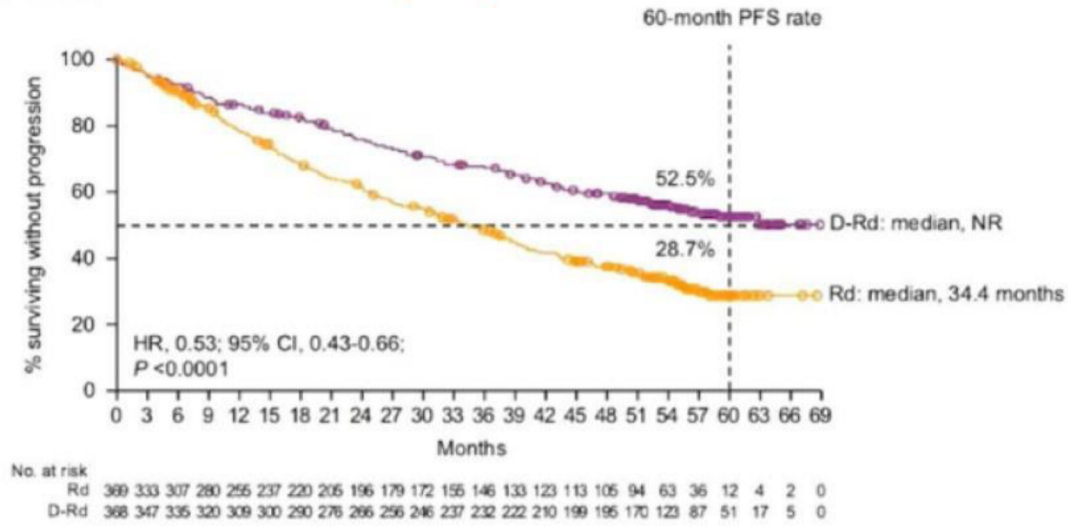
CR, complete response; MRD, minimal residual disease; PFS2, time to second progression or death.
Facon T, et al. Lancet Oncol. 2021;22:1582-1596.

abidi Oncology

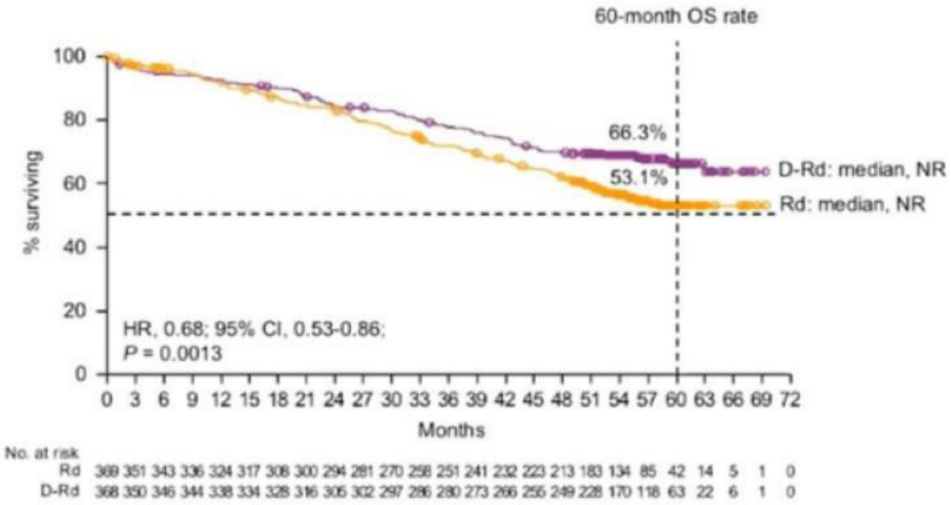
DRd Triplet Set PFS Benchmark in Transplant-Ineligible MM

PFS

Primary endpoint



OS



Median PFS remains not yet reached with DRd after ~ 5 years follow-up

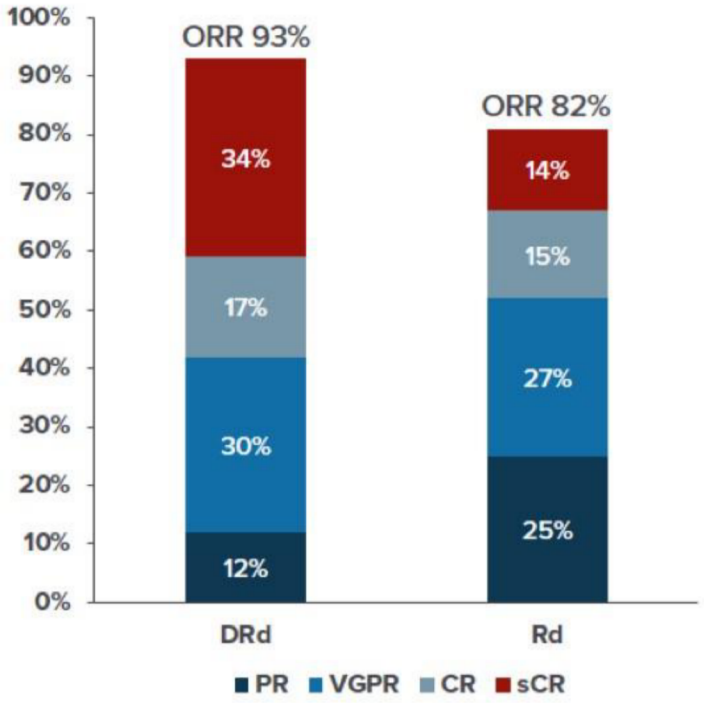
NR, not reached.

Facon T, et al. HemaSphere. 2021;5:LB1901.

abidi Oncology

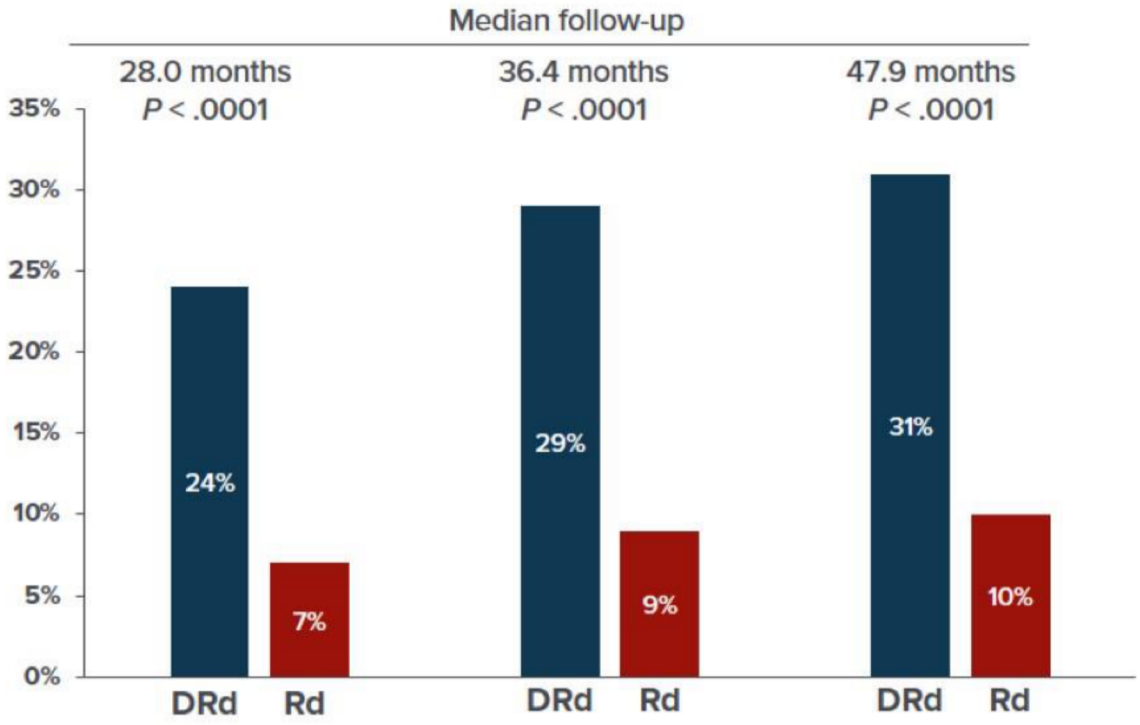
Significantly Higher Rates of MRD Negativity With DRd Triplet

Overall Response



sCR, stringent complete response; VGPR, very good partial response.
Kumar SK, et al. Blood. 2020;136:24-26.

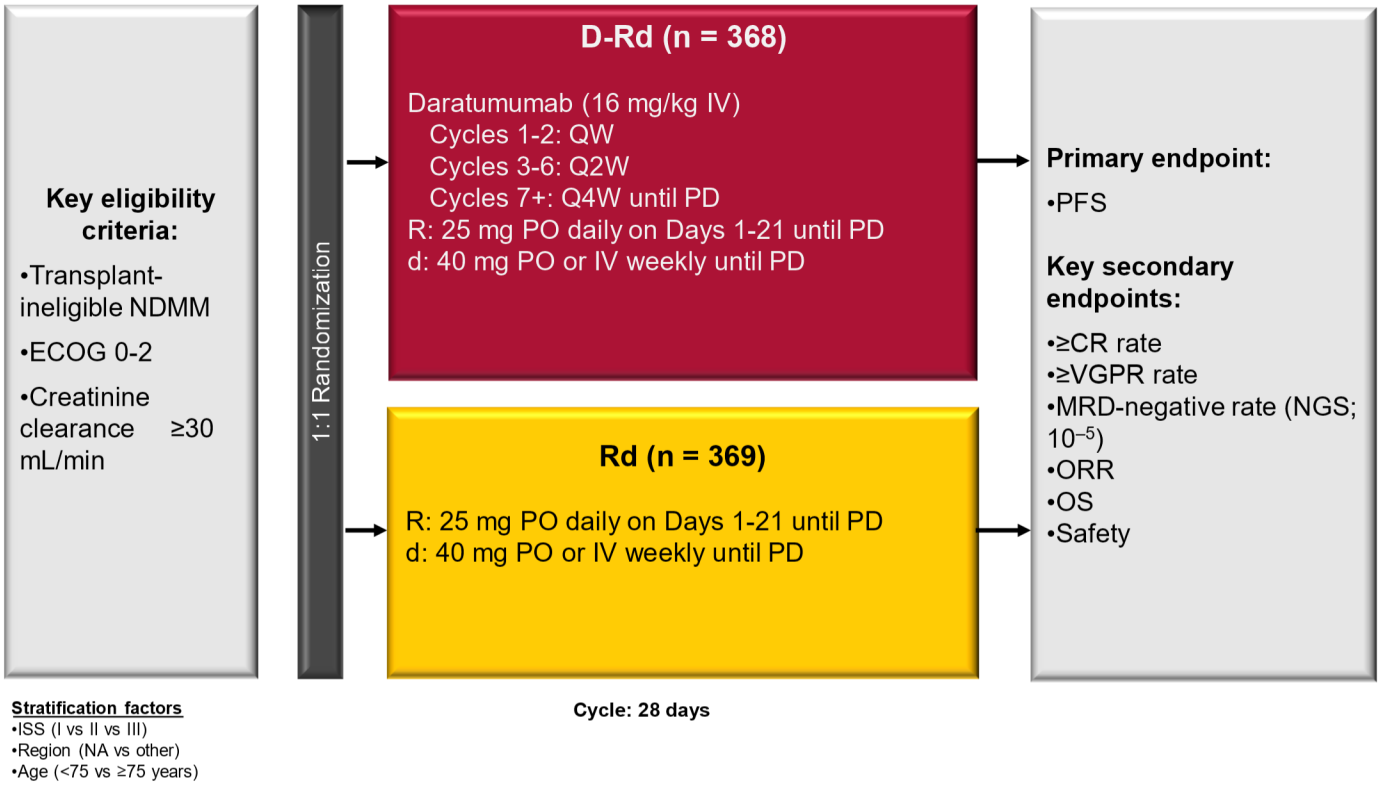
MRD Negativity



DRd was associated with higher rates of neutropenia and infection vs Rd, but less than half the rate of TRAE-related discontinuation

MAIA: study design

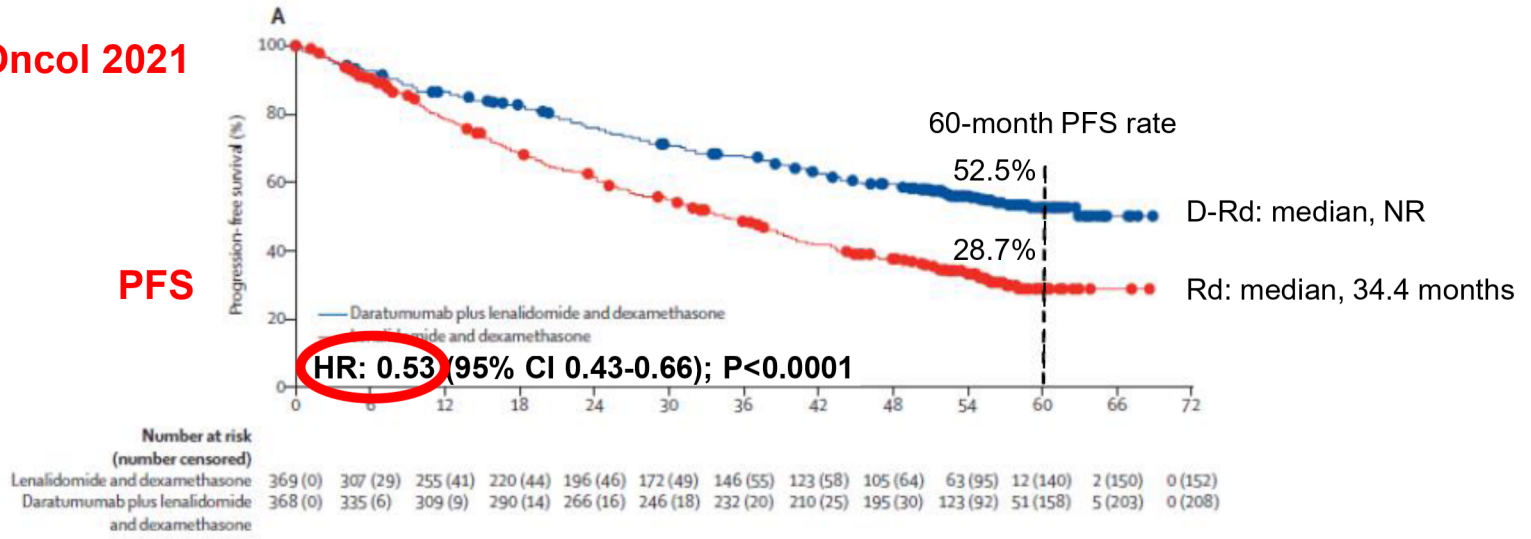
- Phase 3 study of D-Rd vs Rd in transplant-ineligible NDMM (N = 737)



Facon T et al. N Eng J Med 2019;380:2104-2115

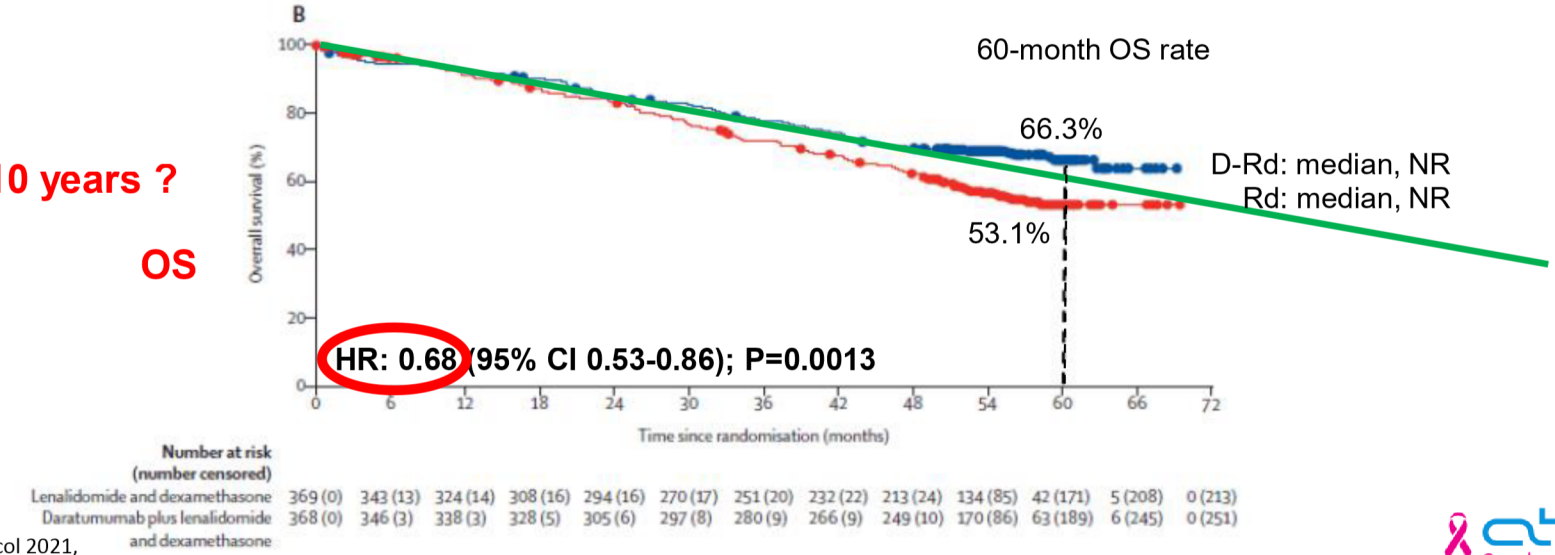
Facon et al. Lancet Oncol 2021

PFS



Median Survival : 10 years ?

OS



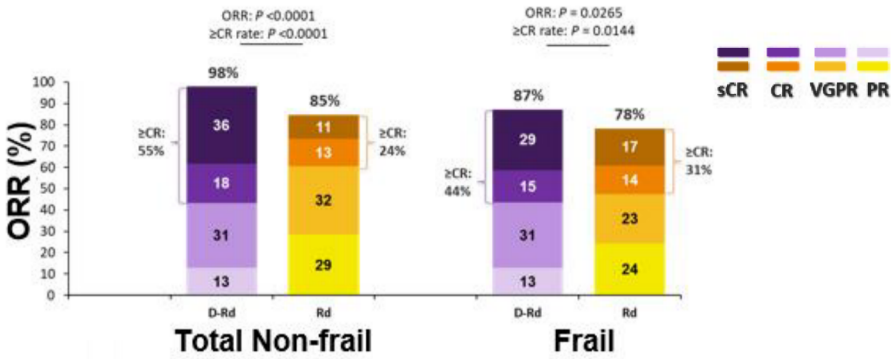
Thierry Facon et al., Lancet Oncol 2021,
https://doi.org/10.1016/ S1470-2045(21)00466-6

abidi Oncology

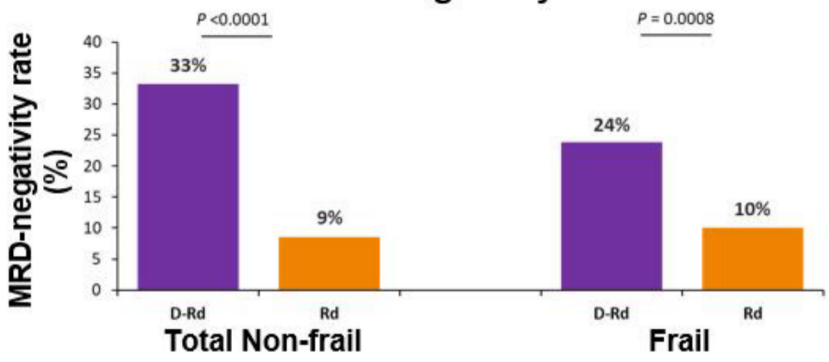
MYLODEQ®
Lenalidomide

Frailty subgroup analysis of MAIA

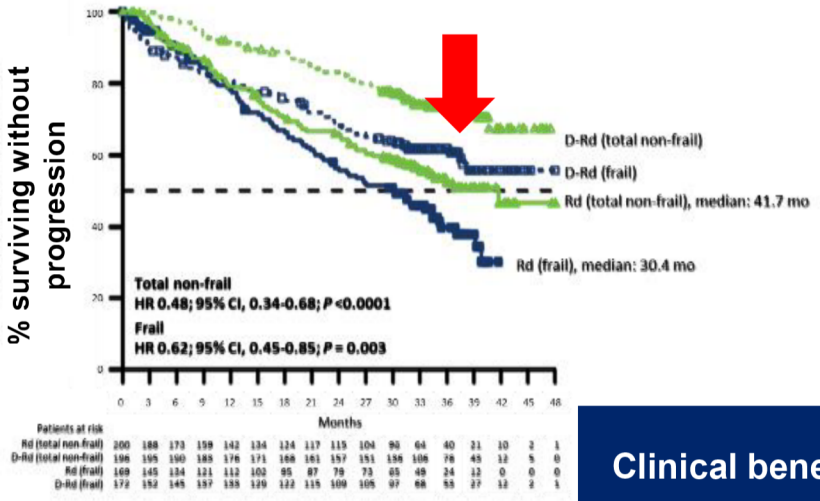
ORR and ≥CR rate



MRD-negativity



PFS in the total non-frail and frail subgroups



Safety

	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)

Clinical benefit of D-Rd, regardless of frailty status

Sonja Zweegman et al., Abstract B05, EMN 2021
Facon T et al. N Engl J Med. 2019;380:2104-15.

MYLODEQ®
Lenalidomide

DRd vs Rd: adverse events

	D-Rd (n = 364)		Rd (n = 365)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Hematologic, n (%)				
Neutropenia	207 (57)	182 (50)	154 (42)	129 (35)
Anemia	126 (35)	43 (12)	138 (38)	72 (20)
Thrombocytopenia	68 (19)	27 (7)	69 (19)	32 (9)
Lymphopenia	66 (18)	55 (15)	45 (12)	39 (11)
Nonhematologic, n (%)				
Diarrhea	207 (57)	24 (7)	168 (46)	15 (4)
Constipation	149 (41)	6 (2)	130 (36)	1 (<1)
Fatigue	147 (40)	29 (8)	104 (28)	14 (4)
Peripheral edema	140 (38)	7 (2)	107 (29)	2 (<1)
Back pain	123 (34)	11 (3)	96 (26)	11 (3)
Asthenia	117 (32)	16 (4)	90 (25)	13 (4)
Nausea	115 (32)	5 (1)	84 (23)	2 (<1)
Pneumonia	82 (23)	50 (14)	46 (13)	29 (8)
Deep vein thrombosis, pulmonary embolism, or both	43 (12)	23 (6)	49 (13)	23 (6)

- Rate of IRRs for D-Rd was 41% (grade 3/4: 3%)
- Incidence of invasive SPMs was 3% for D-Rd and 4% for Rd
  - Hematologic SPM was 0.5% in each arm
- TEAEs with outcome of death were 7% for D-Rd and 6% for Rd

Facon et al., ASH 2018; abstract LB-2
Facon T et al. N Engl J Med. 2019;380:2104-15.

abidi Oncology

Expert Perspectives: Transplant-Ineligible ND MM

Considerations when selecting between preferred regimens: RVd and DRd

Expert Perspectives: Transplant-Ineligible ND MM

Considerations when selecting between preferred regimens: RVd and DRd

Efficacy

- Both regimens offer superior efficacy over the Rd doublet[a,b]

a. Durie B, et al. Lancet. 2017;389:519-527; b. Facon T, et al. Lancet Oncol. 2021;22:1582-1596.

abidi Oncology

Expert Perspectives: Transplant-Ineligible ND MM

Considerations when selecting between preferred regimens: RVd and DRd

Efficacy	Route of administration	Safety profile
▪ Both regimens offer superior efficacy over the Rd doublet[a,b]	▪ Subcutaneous formulations allow greater ease of administration and less logistical strain on patients	▪ PIs associated with risk of peripheral neuropathy[a] ▪ Anti-CD38s associated with risk of infection[b]

PI, proteasome inhibitor.
a. Durie B, et al. Lancet. 2017;389:519-527; b. Facon T, et al. Lancet Oncol. 2021;22:1582-1596.

abidi Oncology

Expert Perspectives: Transplant-Ineligible ND MM

Considerations when selecting between preferred regimens: RVd and DRd

Efficacy	Route of administration	Safety profile	Individual disease factors
▪ Both regimens offer superior efficacy over the Rd doublet[a,b]	▪ Subcutaneous formulations allow greater ease of administration and less logistical strain on patients	▪ PIs associated with risk of peripheral neuropathy[a] ▪ Anti-CD38s associated with risk of infection[b]	▪ PI + IMiD combination therapy recommended for aggressive, high-risk disease[c]

IMiD, immunomodulatory drug; PI, proteasome inhibitor.

a. Durie B, et al. Lancet. 2017;389:519-527; b. Facon T, et al. Lancet Oncol. 2021;22:1582-1596; c. Sonneveld P, et al. Blood. 2016;127:2955-2962.

abidi Oncology

Expert Perspectives: Transplant-Ineligible ND MM

Considerations when selecting between preferred regimens: RVd and DRd

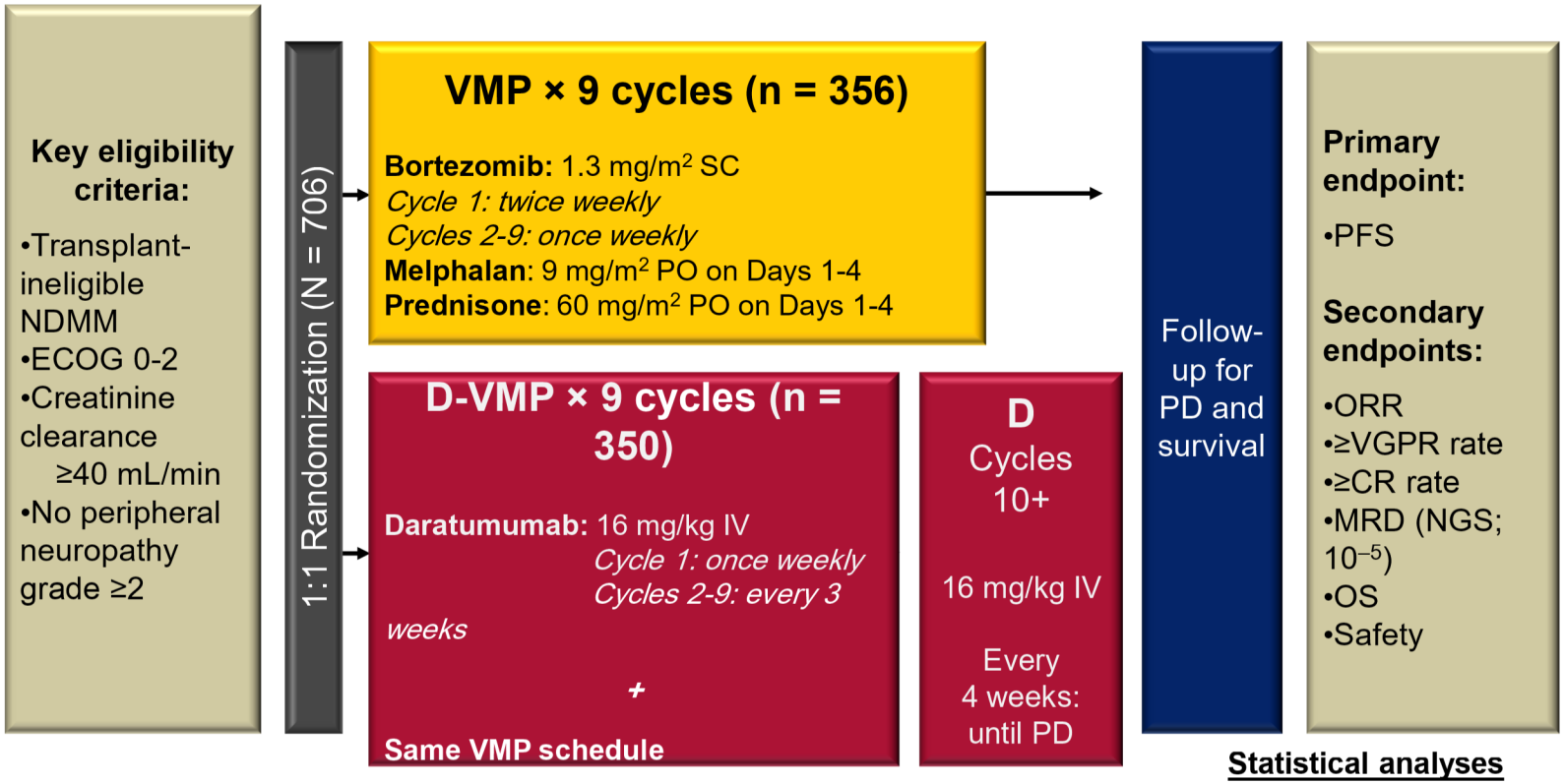
Efficacy	Route of administration	Safety profile	Individual disease factors
▪ Both regimens offer superior efficacy over the Rd doublet[a,b]	▪ Subcutaneous formulations allow greater ease of administration and less logistical strain on patients	▪ PIs associated with risk of peripheral neuropathy[a] ▪ Anti-CD38s associated with risk of infection[b]	▪ PI + IMiD combination therapy recommended for aggressive, high-risk disease[c] ▪ Addition of bortezomib has been shown to overcome adverse effects of t(4;14) and del17p[c]

IMiD, immunomodulatory drug; PI, proteasome inhibitor.

a. Durie B, et al. Lancet. 2017;389:519-527; b. Facon T, et al. Lancet Oncol. 2021;22:1582-1596; c. Sonneveld P, et al. Blood. 2016;127:2955-2962.

abidi Oncology

ALCYONE phase 3 study of daratumumab + VMP in NDMM



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

- Cycles 1-9: 6-week cycles
- Cycles 10+: 4-week cycles

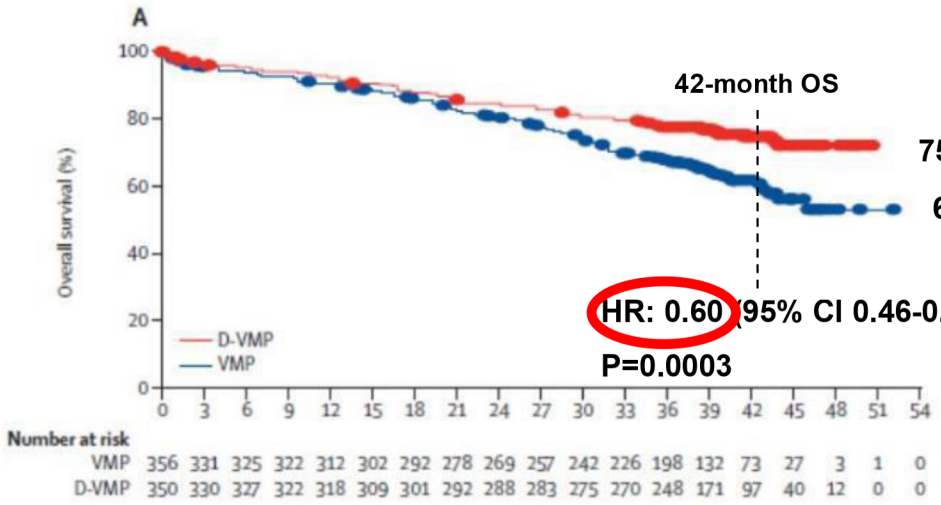
Statistical analyses
- 360 PFS events: 85% power for 8-month PFS improvement
- Interim analysis: ~216 PFS events

Mateos, M-V, et al. N Engl J Med. 2018;378:518:28

abidi Oncology

MYLODEQ®
Lenalidomide

OS



42-month OS

75% : D-VMP

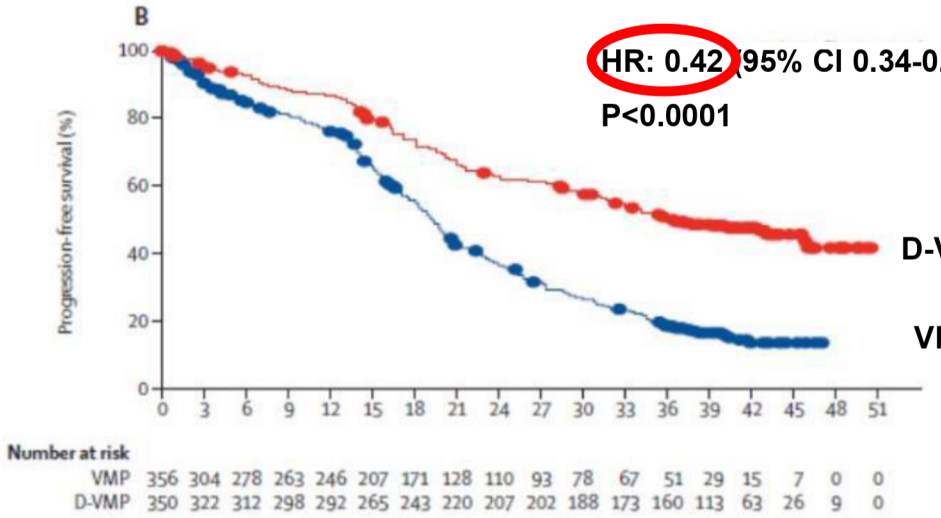
62% : VMP

HR: 0.60 (95% CI 0.46-0.80)

P=0.0003

Mateos et al Lancet 2020; 395: 132–41
Mateos et al. ASH 2019. Abstract 859.

PFS



HR: 0.42 (95% CI 0.34-0.51)

P<0.0001

D-VMP: median 36.4

VMP: median 19.3

Median follow-up: 40.1 months

abidi Oncology

Table 3. Most Common Adverse Events during Treatment in the Safety Population.*

Event	Daratumumab Group (N=346)		Control Group (N=354)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Hematologic adverse events				
Neutropenia	172 (49.7)	138 (39.9)	186 (52.5)	137 (38.7)
Thrombocytopenia	169 (48.8)	119 (34.4)	190 (53.7)	133 (37.6)
Anemia	97 (28.0)	55 (15.9)	133 (37.6)	70 (19.8)
Nonhematologic adverse events				
Peripheral sensory neuropathy	98 (28.3)	5 (1.4)	121 (34.2)	14 (4.0)
Diarrhea	82 (23.7)	9 (2.6)	87 (24.6)	11 (3.1)
Pyrexia	80 (23.1)	2 (0.6)	74 (20.9)	2 (0.6)
Nausea	72 (20.8)	3 (0.9)	76 (21.5)	4 (1.1)
Infections	231 (66.8)	80 (23.1)	170 (48.0)	52 (14.7)
Upper respiratory tract infection	91 (26.3)	7 (2.0)	49 (13.8)	5 (1.4)
Pneumonia	53 (15.3)	39 (11.3)	17 (4.8)	14 (4.0)
Second primary cancer†	8 (2.3)	NA	9 (2.5)	NA
Any infusion-related reaction	96 (27.7)	17 (4.9)	NA	NA

Mateos, M-V, et al. N Engl J Med. 2018;378:518:28

Cost-Effectiveness Analysis of Adding Daratumumab to Bortezomib, Melphalan, and Prednisone for Untreated Multiple Myeloma

frontiers in Pharmacology

ORIGINAL RESEARCH
published: 01 March 2021
doi: 10.3389/fphar.2021.608685

Yaohua Cao[1†], Lina Zhao[2†], Tiantian Zhang[2,3] and Weiling Cao[1*]*

Conclusion: In the case that the upper limit of willingness to pay threshold was $150,000 per QALY from the perspective of US payers, D-VMP was not a cost-effective regimen compared to VMP.

Cost-Effectiveness of First-Line Versus Second-Line Use of Daratumumab in Older, Transplant-Ineligible Patients With Multiple Myeloma

2021 by American Society of Clinical Oncology

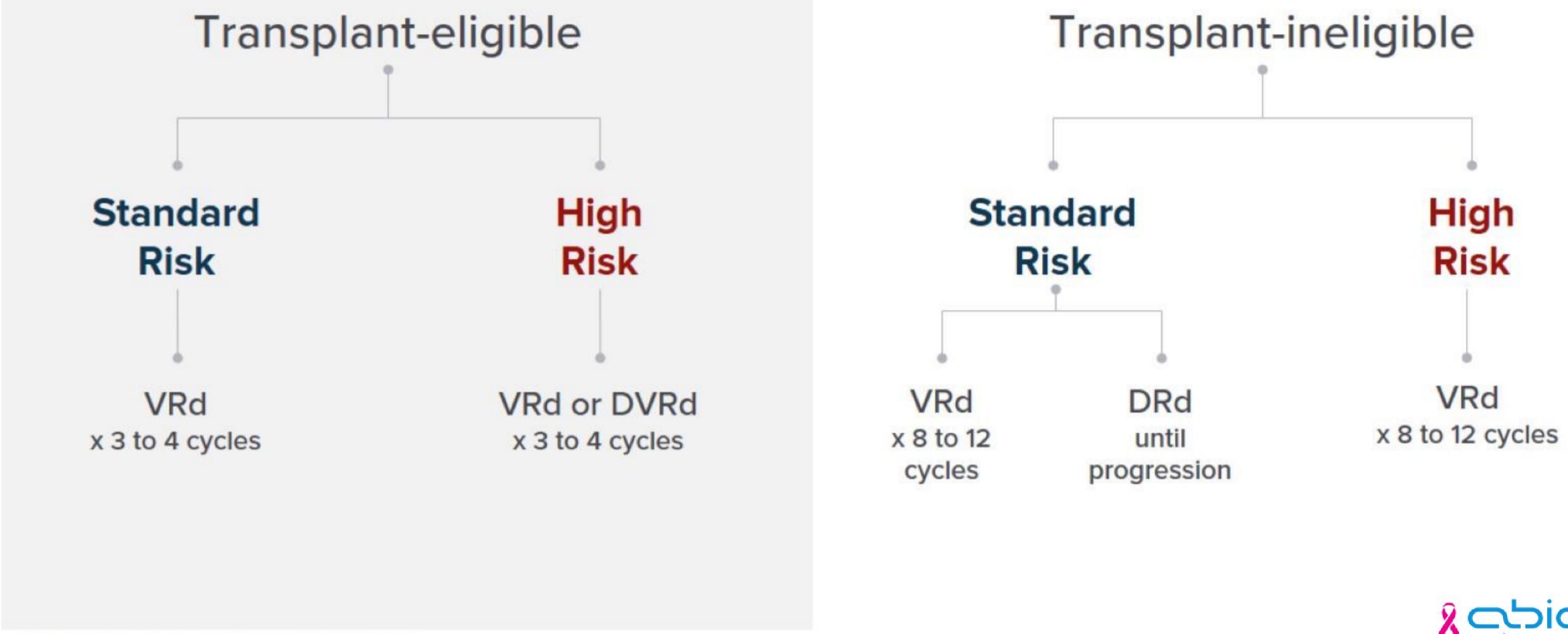
Journal of Clinical Oncology®

Kishan K. Patel, BS[1]; Smith Giri, MD, MHS[2]; Terri L. Parker, MD[1]; Noffar Bar, MD[1]; Natalia Neparidze, MD[1]; and Scott F. Huntington, MD, MPH, MSc[1,3]

CONCLUSION Using daratumumab in the first-line setting for transplant-ineligible patients may not be cost-effective under current pricing. Delaying daratumumab until subsequent lines of therapy may be a reasonable strategy to limit healthcare costs without significantly compromising clinical outcomes. Mature overall survival data are necessary to more fully evaluate cost-effectiveness in this setting.

abidi Oncology

Preferred Induction Therapies



Rajkumar SV, et al. *Blood Cancer J.* 2020;10:94.

abidi Oncology

VRd or DRd?
Factors for Consideration

Regulatory approval status, accessibility

abidi Oncology

VRd or DRd?
Factors for Consideration

Regulatory approval status, accessibility

Patient ability to tolerate the regimen

Shorter vs longer duration therapy?

abidi Oncology

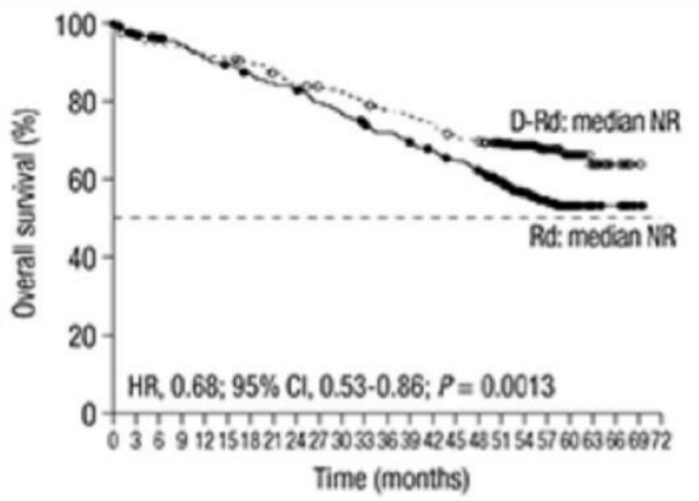
Patient-Specific Induction Strategies

DRd VRd-Intolerant; Neuropathy[a]

MAIA[b,c]

	DRd	Rd
MRD-, %	24	7
mPFS, mo	NR	34

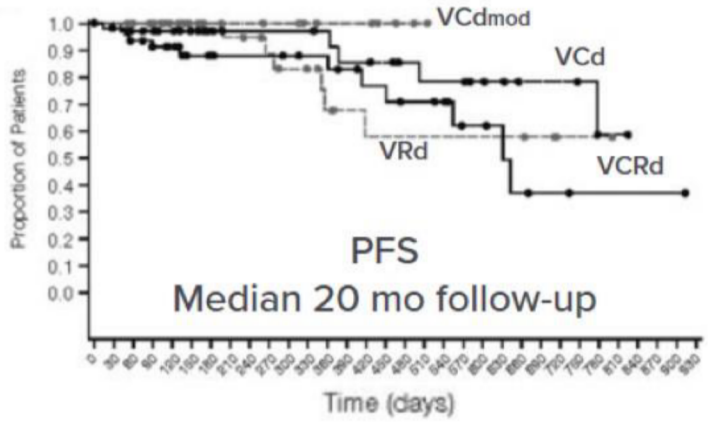
5-Year OS



VCd Acute renal insufficiency, VTE history[a]

EVOLUTION[d]

	VCd_{mod}	VCd	VRd	VCRd
ORR, %	100	75	85	88
CR, %	58	10	21	21
MRD-, %	29	0	85	50
1y PFS, %	100	93	83	93



a. Rajkumar SV, et al. *Blood Cancer J*. 2020;10:94; b. Facon T, et al. *N Engl J Med*. 2019;380:2104-2115; c. Facon T. EHA 2021. Abstract LB1901; d. Kumar S, et al. *Blood*. 2012;119:4375-4382.

Preferred Maintenance Therapies

Rajkumar SV, et al. *Blood Cancer J.* 2020;10:94.

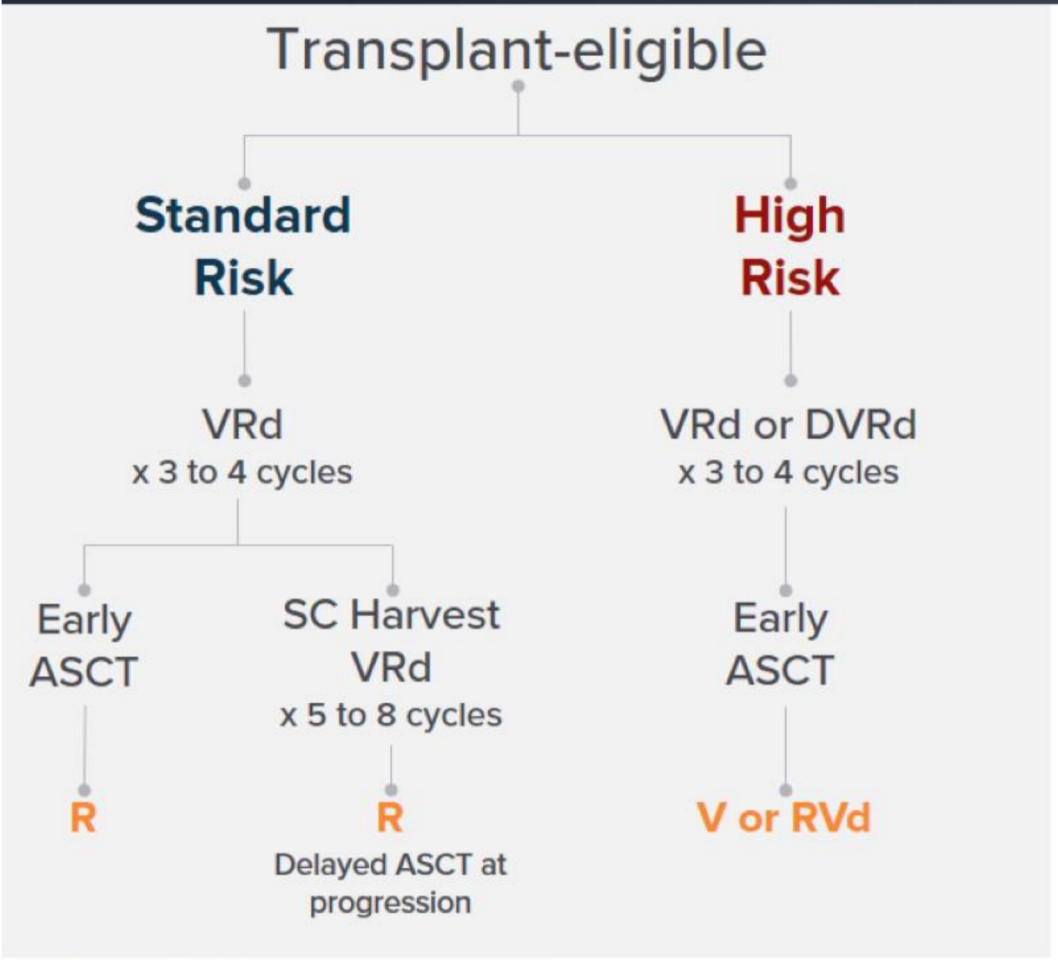
abidi Oncology

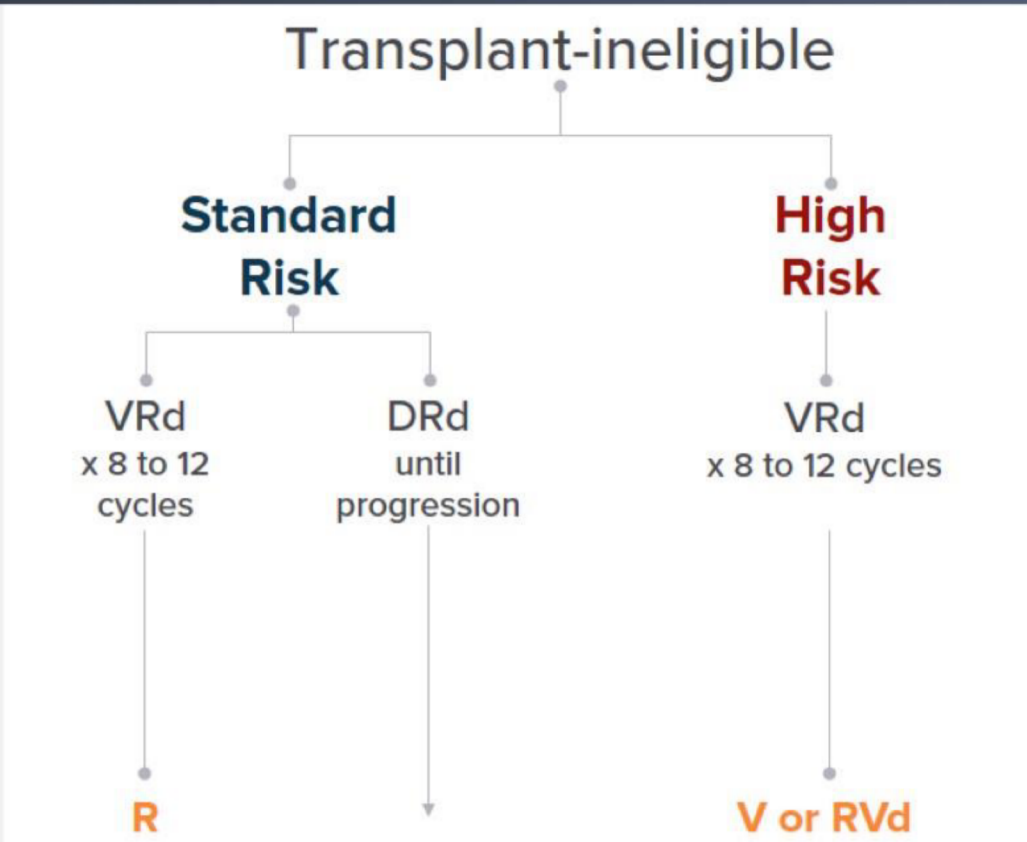
Preferred Maintenance Therapies

Rajkumar SV, et al. *Blood Cancer J.* 2020;10:94.

abidi Oncology

Preferred Maintenance Therapies



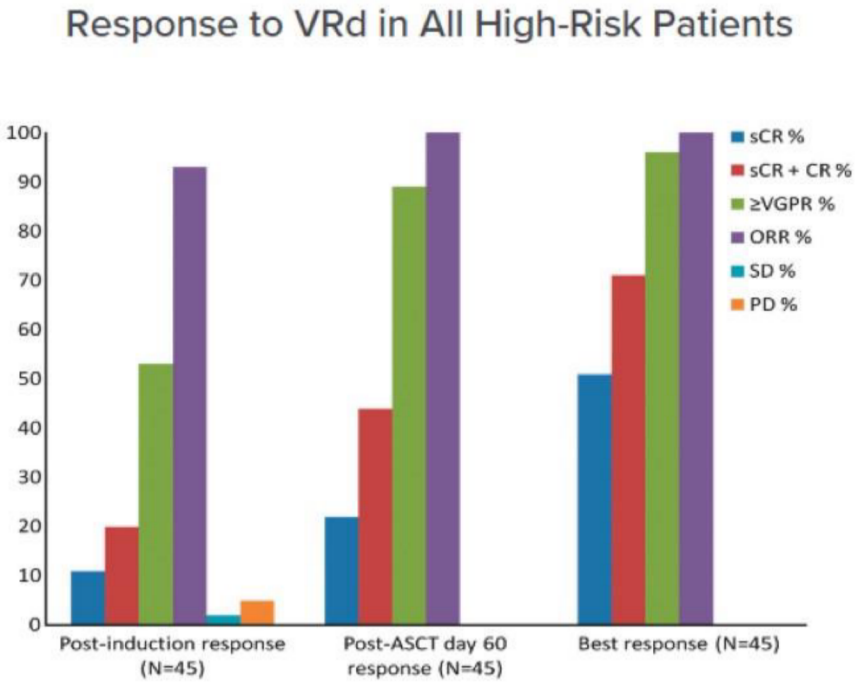


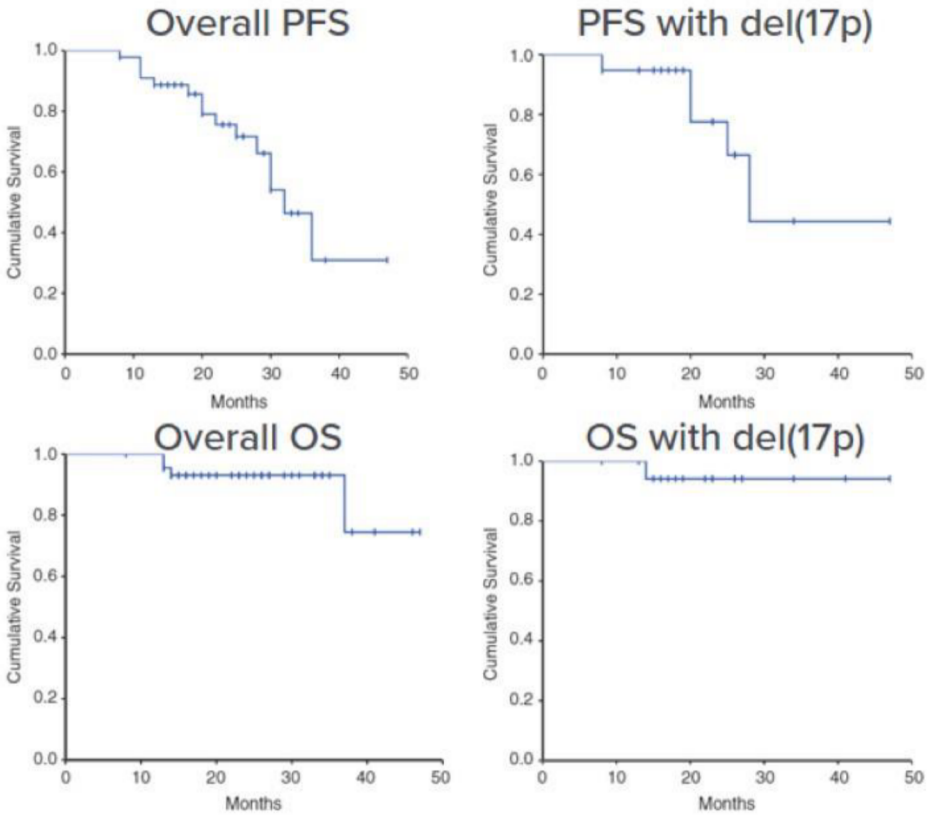
Rajkumar SV, et al. *Blood Cancer J.* 2020;10:94.

abidi Oncology

Maintenance Strategies in High-Risk MM: VRd

VRd improved survival in high-risk MM, particularly with del(17p)



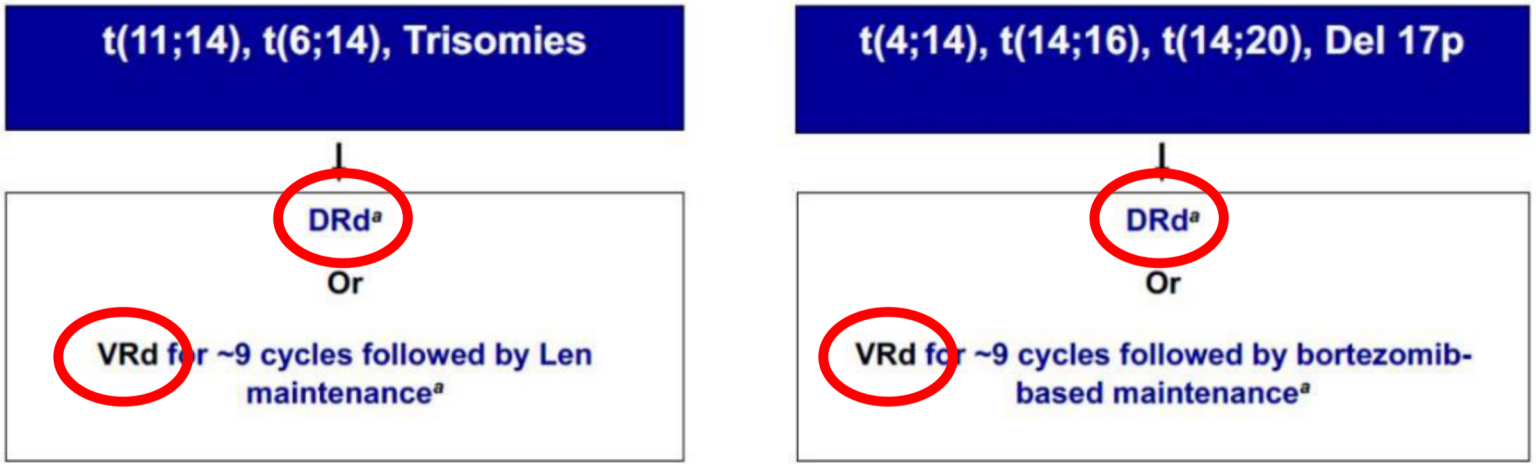


Nooka AK, et al. *Leukemia*. 2014;28:690-693.

MAYO CLINIC

mSMART – Off-Study

Transplant Ineligible



[a] *Duration is usually until progression, based on tolerance*

VRd, Bortezomib, lenalidomide, dexamethasone; DRd, daratumumab, lenalidomide, dexamethasone

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v19 //last reviewed Feb 2021

abidi Oncology

Maintenance therapy

- **High-risk MM** – Following 8 to 12 cycles of triplet therapy, we offer patients with high-risk MM proteasome-inhibitor-based maintenance until progression.

- **Standard-risk MM** – Following 8 to 12 cycles of triplet therapy, we offer patients with standard-risk MM lenalidomide-based maintenance until progression.

- **Frail patients** – Following 9 cycles of treatment with lenalidomide plus dexamethasone, we offer frail patients with standard-risk MM maintenance with single-agent lenalidomide until progression unless there is significant toxicity.

abidi Oncology

NCCN Guidelines Version 5.2022
Multiple Myeloma

PRIMARY THERAPY FOR NON-TRANSPLANT CANDIDATES[a-d]	
Preferred Regimens • Bortezomib/lenalidomide/dexamethasone (category 1) • Daratumumab/lenalidomide/dexamethasone (category 1)	
Other Recommended Regimens • Carfilzomib/lenalidomide/dexamethasone • Ixazomib/lenalidomide/dexamethasone	• Daratumumab/bortezomib/melphalan/prednisone (category 1) • Daratumumab/cyclophosphamide/bortezomib/dexamethasone
Useful In Certain Circumstances • Bortezomib/dexamethasone • Bortezomib/cyclophosphamide/dexamethasone[e] • Cyclophosphamide/lenalidomide/dexamethasone	• Carfilzomib/cyclophosphamide/dexamethasone[f] • Lenalidomide/low-dose dexamethasone (category 1)[k] • Bortezomib/lenalidomide/dexamethasone (VRD-lite) for frail patients

MAINTENANCE THERAPY
Preferred Regimens • Lenalidomide (category 1)
Other Recommended Regimens • Ixazomib (category 2B)[i] • Bortezomib
Useful In Certain Circumstances • Bortezomib/lenalidomide[j]

abidi Oncology

Thank you