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Managing Newly Diagnosed Multiple Myeloma and Waldenstrom's Macroglobulinemia in 2023

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Disclosures

- Research funding: Amgen, Array Biopharma, BMS, Celgene, GSK, Janssen, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, Takeda.
- Consulting: Abbvie, Amgen, BMS, Celgene, EdoPharma, Genentech, Gilead, GSK, Janssen, Oncopeptides, Sanofi, Seattle Genetics, SecuraBio, SkylineDX, Takeda, TeneoBio.
- Speaker: Amgen, BMS, Janssen, Sanofi.

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Learning Objectives

- Discuss recent updates to clinical practice guidelines reflecting changes in best practices for treatment of newly diagnosed Multiple Myeloma.

- Discuss recent updates to clinical practice guidelines reflecting changes in best practices for treatment of newly diagnosed Waldenstrom's Macroblobulinemia.

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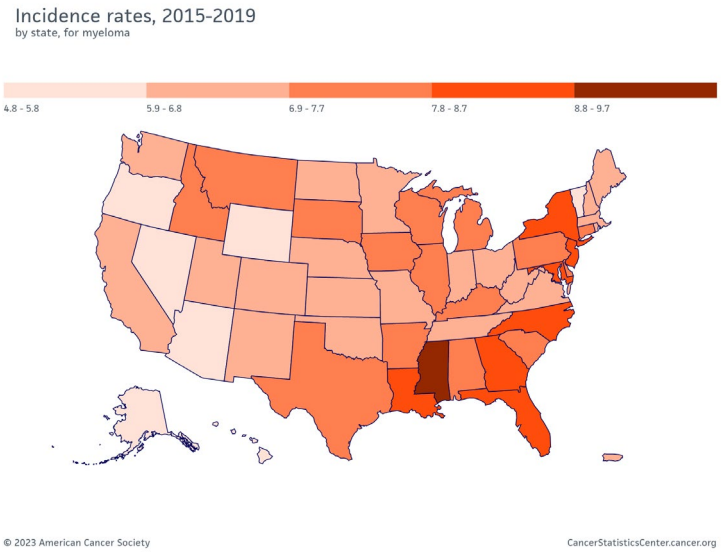
Multiple Myeloma: A Systemic Plasma Cell Malignancy

- Estimated new cases and deaths in 2022 in the United States[1]
  - New cases: 34,470
  - Deaths: 12, 640
- Percentage of patients surviving 5 years: 57.9%[1]
- Median age at diagnosis: 69 years[2]
- MM is most common in men and Black adults[2]



1. https://seer.cancer.gov/statfacts/html/mulmy.html 2. Myeloma at a glance. American Cancer Society Cancer Statistics Center. American Cancer Society website. https://cancerstatisticscenter.cancer.org/?_ga=2.47184933.325832967.1600196335-611855784.1581698489#!/cancer-site/Myeloma.

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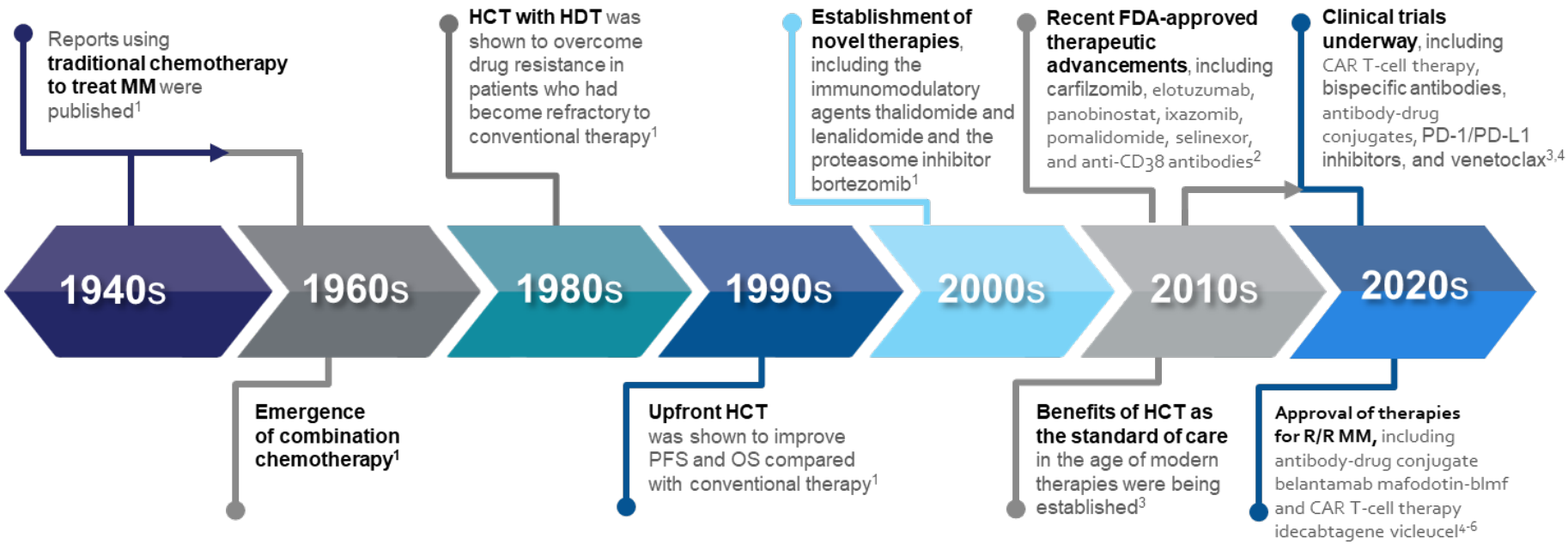
History of MM Treatments



CAR, chimeric antigen receptor; HCT, hematopoietic cellular therapy; HDT, high-dose therapy; OS, overall survival; PD-1, programmed cell death 1; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; R/R, relapsed/refractory.

1. Laubach J, et al. *Annu Rev Med.* 2011;62:249-264. **2.** Rajkumar SV. *Am J Hematol.* 2020;95(5):548-567. **3.** Palumbo A, et al. *N Engl J Med.* 2014;371(10):895-905. **4.** Zanwar S, et al. *Blood Cancer J.* 2020;10(8):84. doi: 10.1038/s41408-020-00350-x. **5.** US Food and Drug Administration. FDA granted accelerated approval to belantamab mafodotin-blmf for multiple myeloma. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-granted-accelerated-approval-belantamab-mafodotin-blmf-multiple-myeloma. Updated August 6, 2020. Accessed May 6, 2021. **6.** US Food and Drug Administration. FDA approves first cell-based gene therapy for adult patients with multiple myeloma. https://www.fda.gov/news-events/press-announcements/fda-approves-first-cell-based-gene-therapy-adult-patients-multiple-myeloma. Updated March 27, 2021. Accessed May 17, 2021.

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Staging and Cytogenetic Risk-Assessment

Stage[1]	R-ISS[1]
I	Serum albumin ≥3.5 g/dL^{-1} Serum β2M <3.5 mg/L^{-1} No high-risk cytogenetics Normal LDH level
II	Not stage I or III
III	Serum β2M >5.5 mg/L^{-1} High-risk cytogenetics: t(4;14), t(4;16), or del(17p) or elevated LDH

Risk[2]	Features
Standard	Trisomies t(11;14) t(6;14)
High	t(4;14) t(14;16) t(14;20) Del(17p) *p53* mutation Gain/Amp 1q High plasma cell S-phase GEP high-risk signatures Circulating Plasma Cells

1. Palumbo A, et al. *J Clin Oncol*. 2015;33:2863-2869; 2. Costa LJ, Usmani SZ. J Natl Compr Canc Netw. 2020;18(12):1730-1737.

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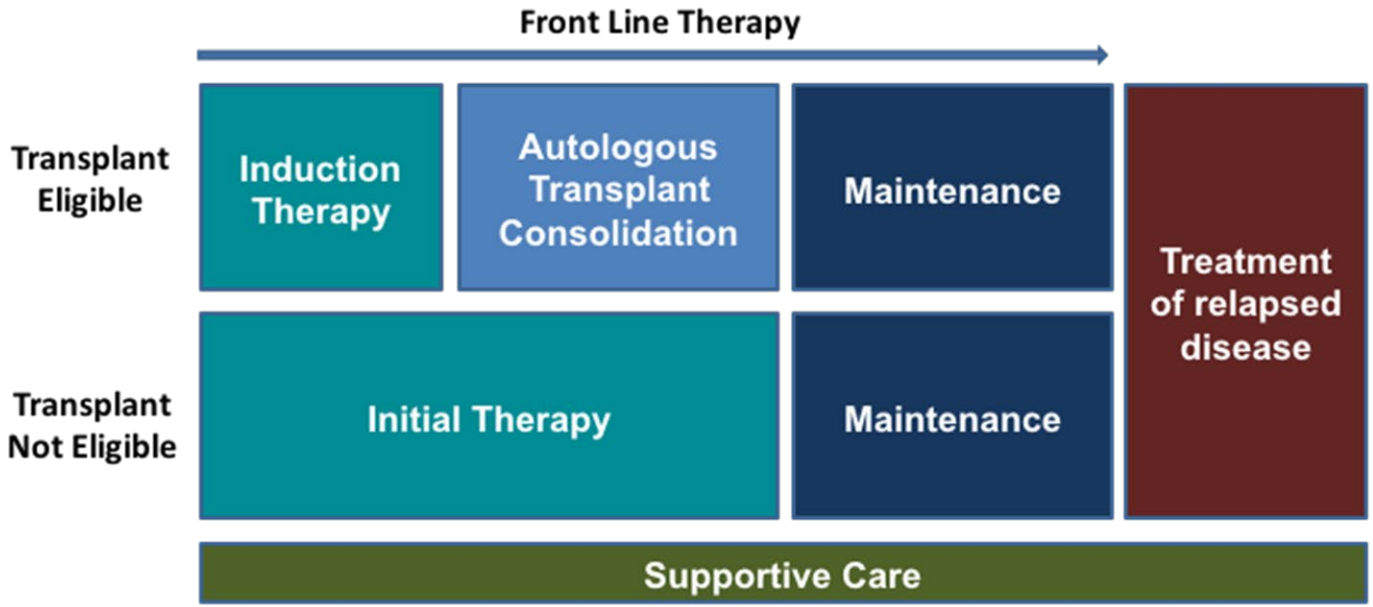
Treatment Paradigm For Newly Diagnosed Multiple Myeloma (NDMM)



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Approach to NDMM

Transplant eligible

- Induction : Dara-RVd, Dara-KRd, Dara-VTd, RVd, KRd, CyBorD
- Maintenance: R, VR, Dara-R, Dara
- Expected PFS/OS:
  - Standard Risk: 80 months/130+ months
  - High Risk: 40 months/80+ months

Transplant Ineligible

- DRd, VRd-lite/RVd-lite
- Expected PFS/OS:
  - Standard Risk: 36-60+ months/90+ months
  - High Risk: 24-30 months/60-72 months

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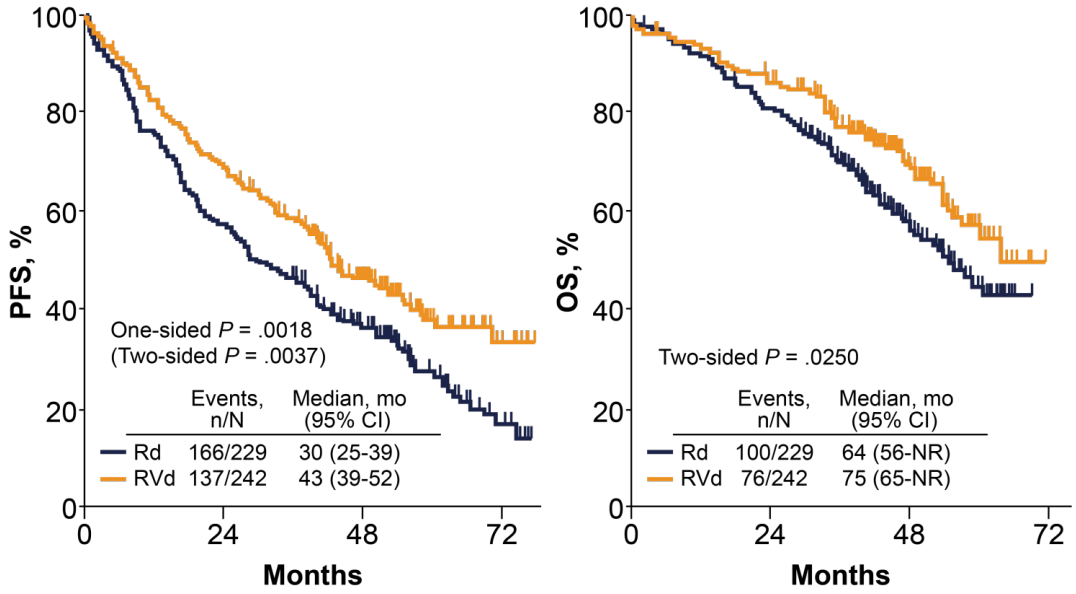
SWOG S0777: RVd Versus Rd in Patients Without Immediate Intent for ASCT



Initial Therapy

RVd for eight 21-d cycles vs Rd for six 28-d cycles in patients not intending to proceed to upfront transplant, followed by Rd in both arms (N = 525)

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

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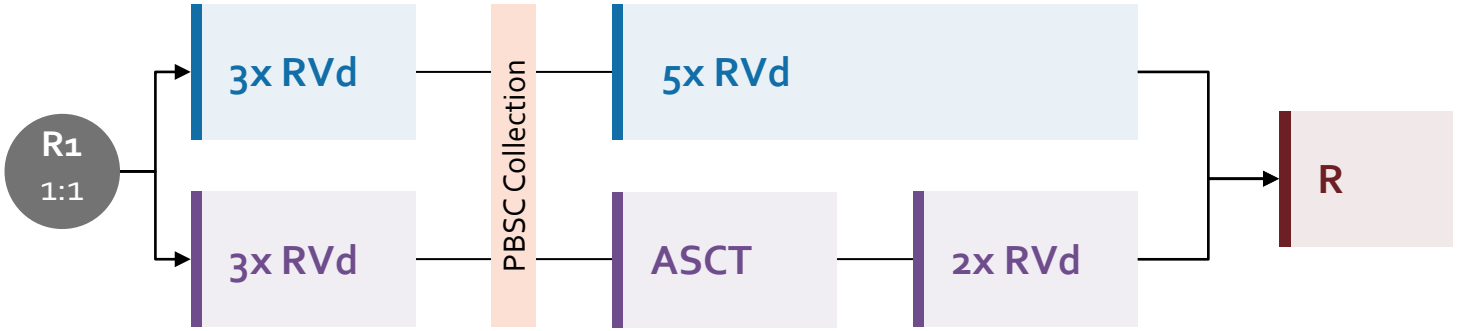
IFM 2009 Study: Early vs Late ASCT



RVd 21-day Cycles
R: 25 mg d 1 – 14
V: 1.3 mg/m² d 1, 4, 8, 11
d: 20 mg d 1, 2, 4, 5, 8, 9, 11, 12

R Maintenance
R: 10-15 mg/d for 13 cycles

Primary endpoint: PFS
Secondary endpoints:
ORR, MRD, TTP, OS, safety

Attal M, et al. N Engl J Med. 2017;376:1311-1320.

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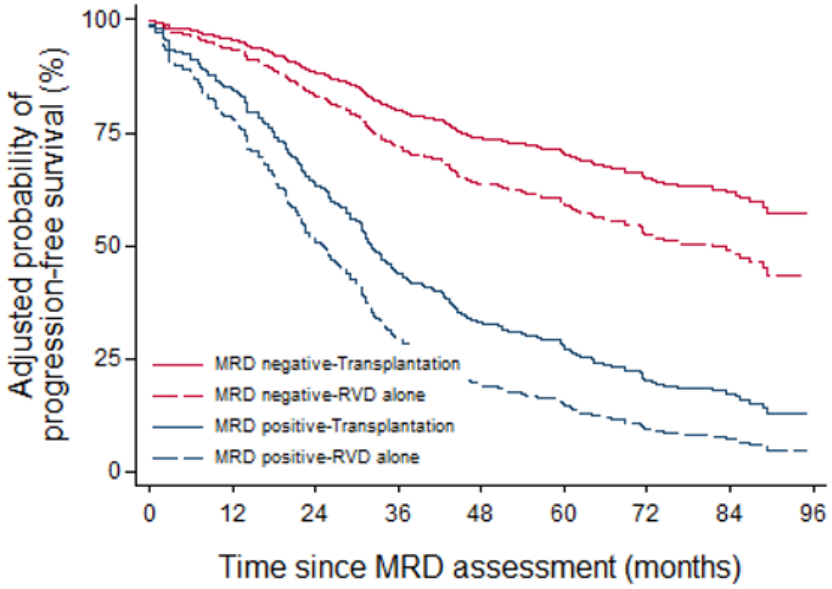
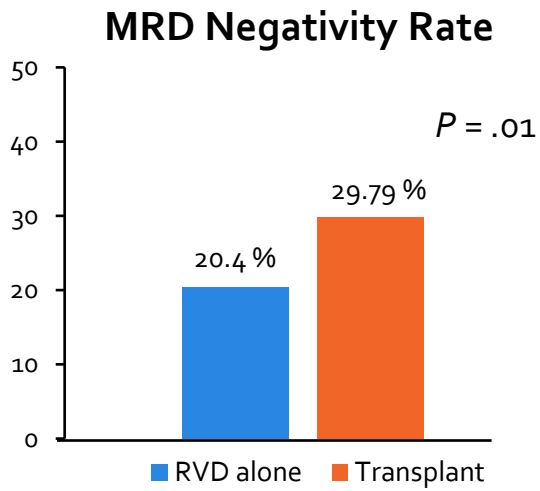
Superior PFS With ASCT vs RVd Alone





RVd + transplant was superior to RVd alone, even with undetectable MRD at 10^{-6}

MRD, minimal residual disease.

Perrot A. Presented at: 62nd ASH Annual Meeting and Exposition; December 5-8, 2020; Abstract 143.

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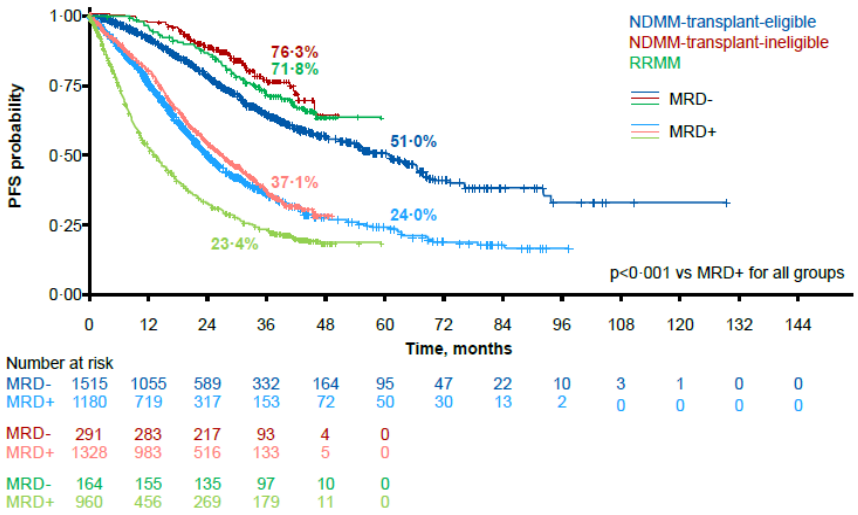
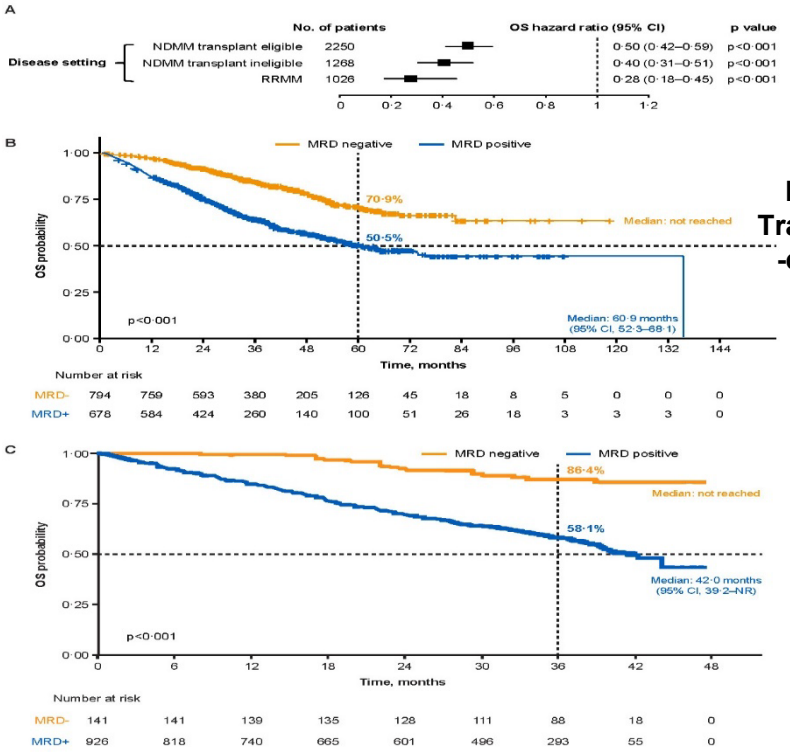
MRD Negativity and Survival Outcomes

PFS



OS



NDMM Transplant -eligible

RRMM

Munshi et al., Blood Adv 2020; 4: 5988-99.

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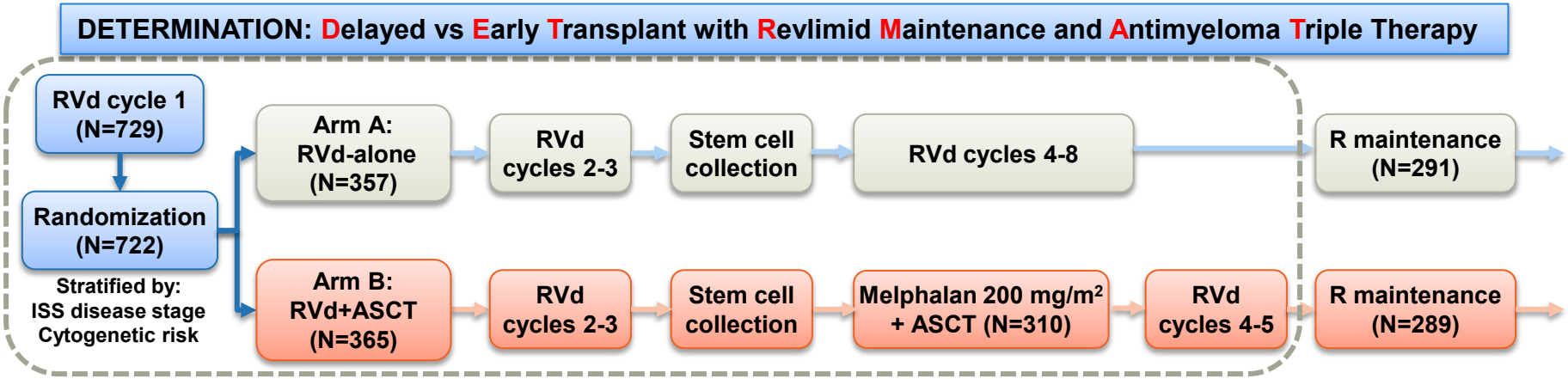
DETERMINATION: study design and patient disposition



Each RVd cycle (21 days):
R 25 mg/day PO, days 1-14
V 1.3 mg/m^2 IV/SC, days 1, 4, 8, 11
Dex 20/10 mg PO, days 1, 2, 4, 5, 8, 9, 11, 12

Induction ± ASCT + consolidation treatment duration = ~6 months

Lenalidomide maintenance
Months 1-3: 10 mg/day
Month 4 onwards: 15 mg/day

Primary endpoint: PFS

Secondary endpoints: response rates; DOR; TTP; OS; QoL; safety

- d/Dex, dexamethasone; DOR, duration of response; ISS, International Staging System; IV, intravenous; PO, orally; R, lenalidomide; SC, subcutaneous; TTP, time to progression; V, bortezomib

Richardson PG, et al. N Engl J Med. 2022 Jun 5. doi: 10.1056/NEJMoa2204925

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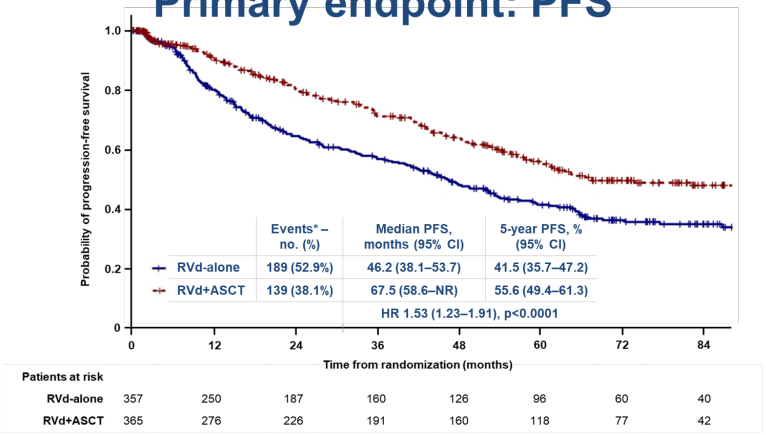
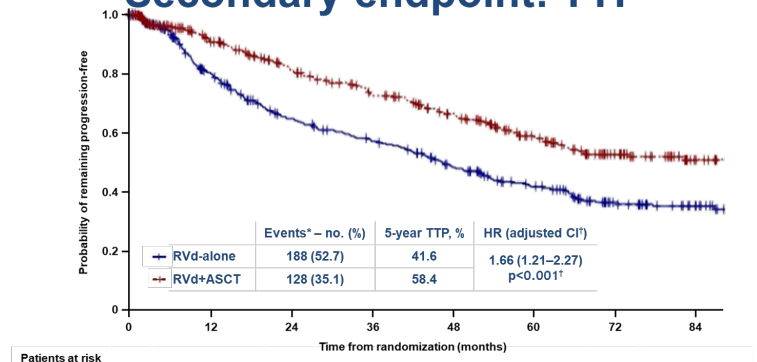
DETERMINATION: Endpoint Readouts
(Median follow-up 70 months)

Primary endpoint: PFS



Patients at risk								
RVd-alone	357	250	187	160	126	96	60	40
RVd+ASCT	365	276	226	191	160	118	77	42

Secondary endpoint: TTP



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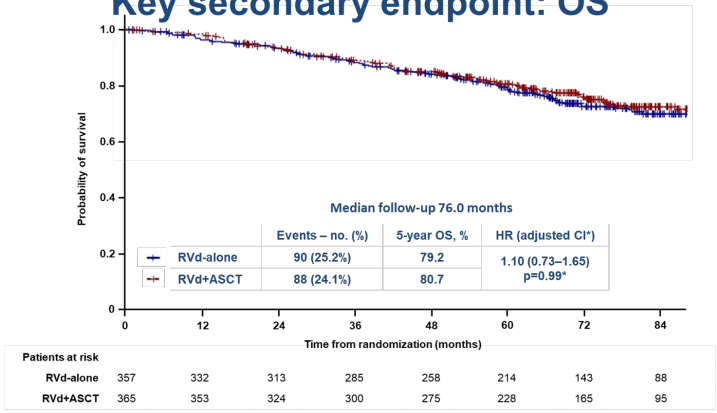
DETERMINATION: Endpoint Readouts
(Median follow-up 70 months)

Key secondary endpoint: OS



Second primary malignancies

5-year cumulative incidence of SPMs (RVd-alone vs RVd+ASCT):

- All : 9.7% vs 10.8%
- Invasive: 4.9% vs 6.5%
- Hematologic: 1.59% vs 3.52%

At time of data cutoff, among patients on the RVd-alone and RVd+ASCT arms who had hematologic SPMs, respectively:

- 6/7 vs 2/3 patients with ALL alive
- 6/10 patients with AML/MDS alive
- 1/2 patients with CLL/CML alive
- Overall, 7/9 RVd-alone vs 8/13 RVd+ASCT alive

SPMs	RVd-alone (N=357)	RVd+ASCT (N=365)
Any, %	10.4	10.7
Any invasive SPM, %	5.3	6.8
Any hematologic SPM, %	2.5	3.6
ALL, n	7	3
AML/MDS, n	0	10
CLL/CML, n	2	0
Any solid tumor SPM, %	3.4	3.3
Any non-invasive solid tumor SPM, %	0	0.5
Any non-melanoma skin cancer, %	5.9	4.1

Richardson PG, et al. N Engl J Med. 2022 Jun 5. doi: 10.1056/NEJMoa2204925

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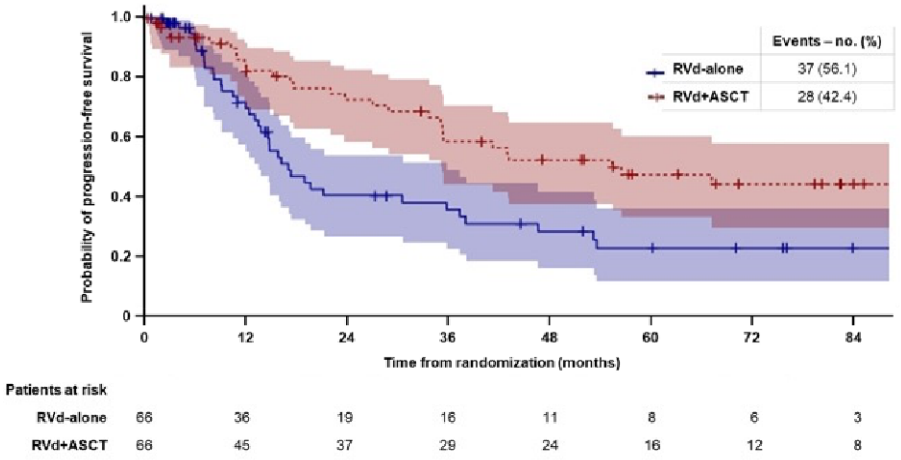
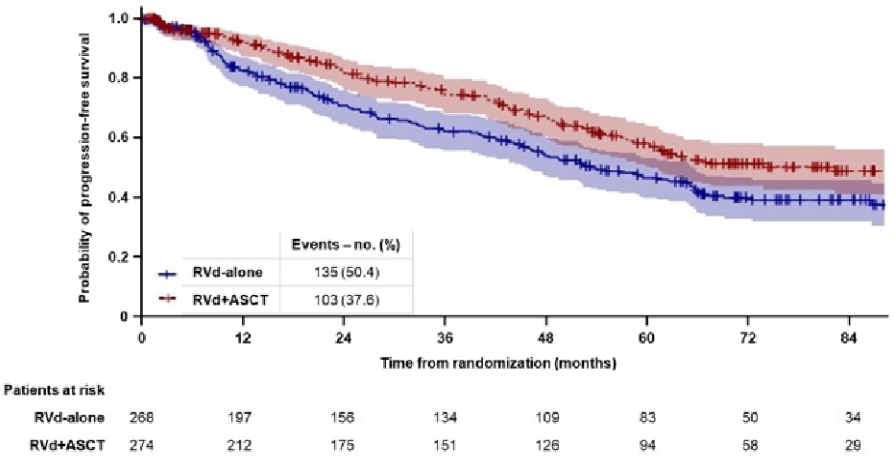
DETERMINATION Trial: PFS by Risk





Median PFS, months	RVd-alone	RVd+ASCT
High-risk	17.1	55.5
	HR 1.99 (95% CI 1.21–3.26)	

Median PFS, months	RVd-alone	RVd+ASCT
Standard-risk	53.2	82.3
	HR 1.38 (95% CI 1.07–1.79)	

Richardson PG, et al. N Engl J Med. 2022 Jun 5. doi: 10.1056/NEJMoa2204925

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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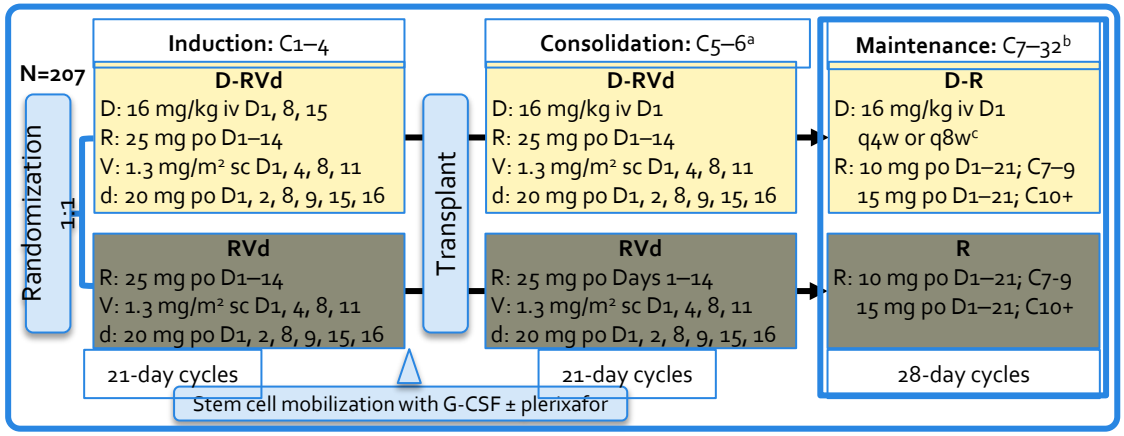
GRIFFIN: Daratumumab Plus Lenalidomide, Bortezomib, and Dexamethasone in Transplant-Eligible NDMM – 24 Months of Maintenance

Study design

Key eligibility criteria: TE NDMM; 18–70 years; ECOG PS 0–2; CrCl ≥30 mL/min[2]



- **Primary endpoint:** sCR by end of consolidation
- **Secondary endpoints:** MRD negativity (NGS 10^{-5}), ORR, ≥VGPR, CR, PFS, OS

Patient disposition

n (%)	D-RVd (n=104)	RVd (n=103)
Treated with maintenance therapy	90 (87)	70 (68)
Completed maintenance therapy	67 (64)	44 (43)
Discontinued treatment during maintenance therapy	21 (20)	21 (20)
Adverse event	8 (8)	7 (7)
Progressive disease	3 (3)	7 (7)
Patient withdrawal	2 (2)	4 (4)
Lost to follow-up	2 (2)	0
Death	1 (1)	1 (1)
Other	5 (5)	2 (2)

[a]Consolidation initiated 60–100 days post transplant; [b]Patients who complete maintenance cycles 7–32 may continue single-agent lenalidomide thereafter; [c]Protocol amendment allowed q4w dosing option. Phase 2 trial – patient enrollment between December 2016 and April 2018

Laubach JP, et al. ASH 2021, Virtual Meeting. Abstract 79

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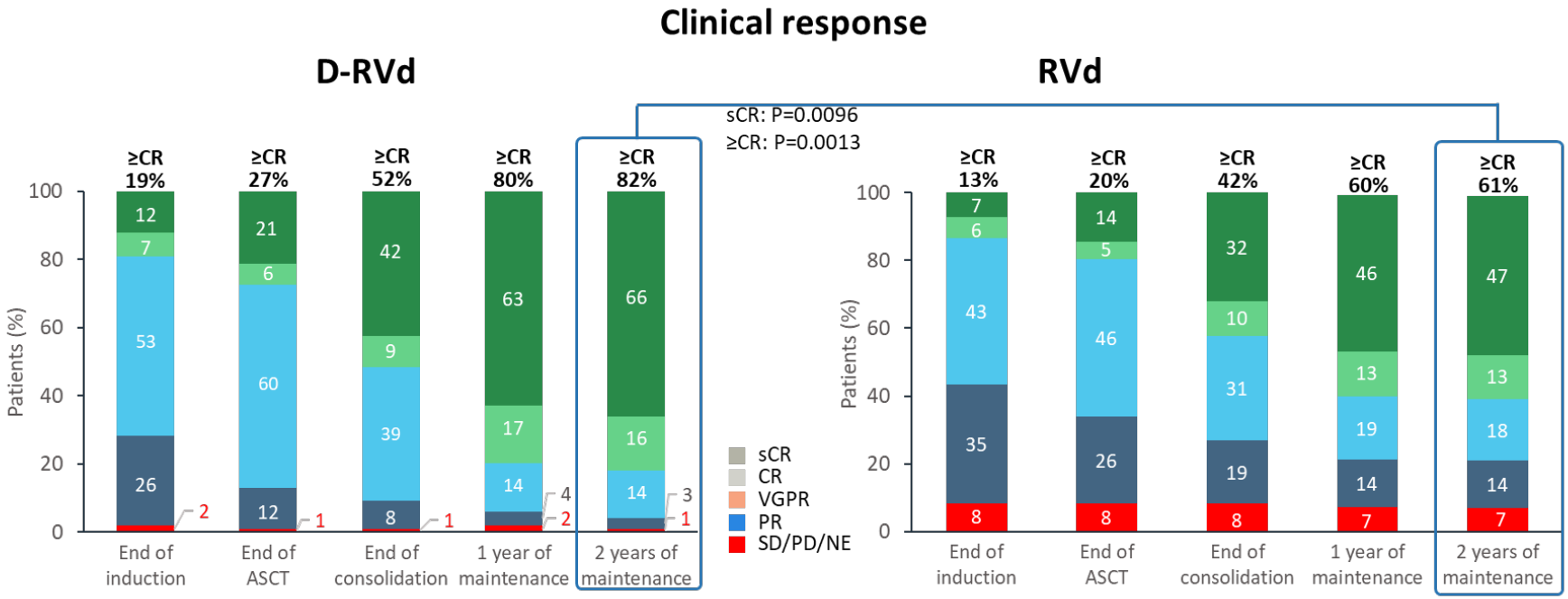
GRIFFIN: Daratumumab Plus Lenalidomide, Bortezomib, and Dexamethasone in Transplant-Eligible NDMM – 24 Months of Maintenance



Laubach JP, et al. ASH 2021, Virtual Meeting. Abstract 79

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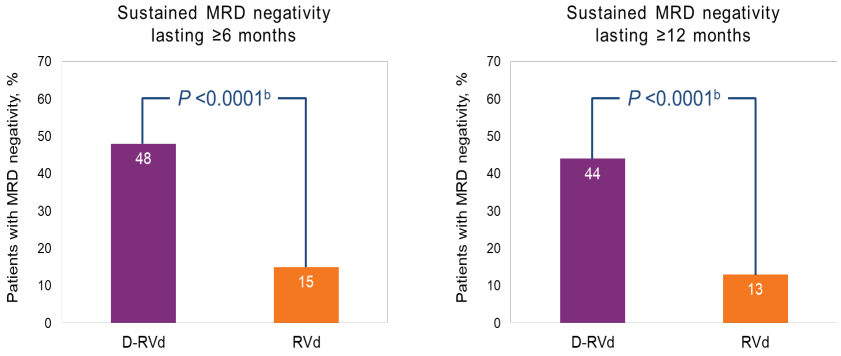
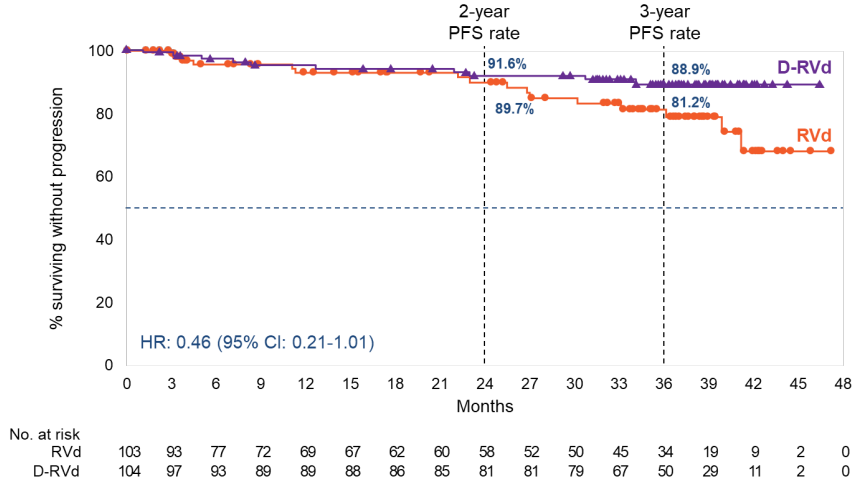
GRIFFIN Update: MRD and PFS Data

- D-RVd Improved Rates of Durable MRD Negativity[a] (10^{-5}) Lasting ≥6 Months or ≥12 Months Versus RVd





- Median follow-up: 38.6 months
- Median PFS was not reached in either group
- There is a positive trend toward improved PFS for D-RVd/DR versus RVd/R
- The separation of the PFS curves begins beyond 1 year of maintenance and suggests a benefit of prolonged DR therapy

[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status was based on BM aspirates by NGS per IMWG. [b]P values calculated by Fisher's exact test

Laubach et al. ASH 2021. Abstract 79.

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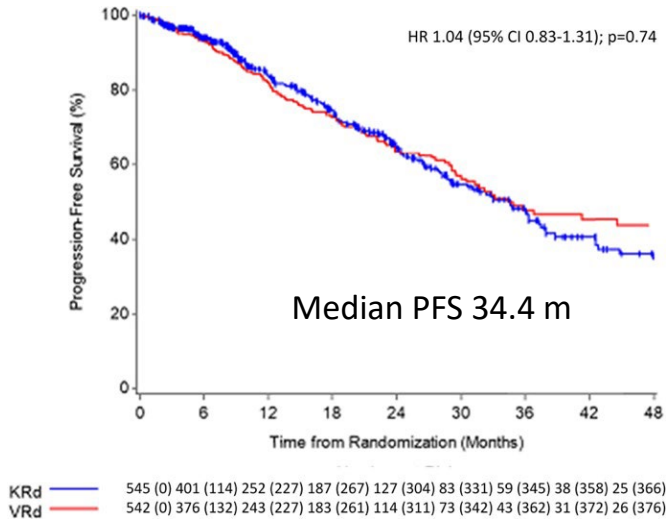
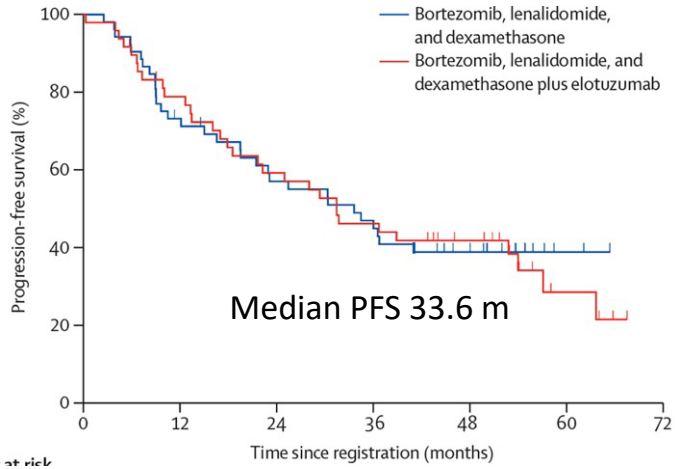
Impact of PI/IMiD Maintenance in High-Risk MM

Standard Risk



ENDURANCE: VRd or KRd with len maintenance
Kumar S et al Lancet Oncol 2021

High Risk



S1211: Elo VRd or VRd with VR maintenance
Usmani SZ et al Lancet Haematol 2021

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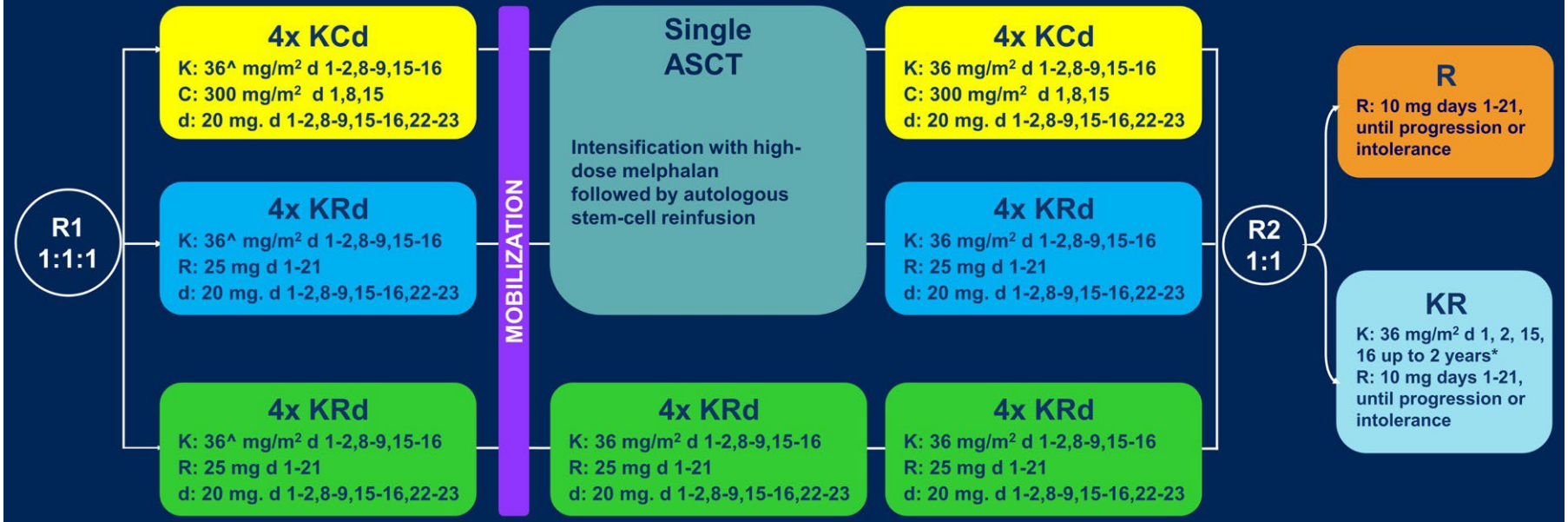
Trial design

474 NDMM patients, transplant-eligible and younger than 65 years



^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.

NDMM, newly diagnosed multiple myeloma, R1, first randomization (induction/consolidation treatment); R2, second randomization (maintenance treatment); ASCT, autologous stem-cell transplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd.

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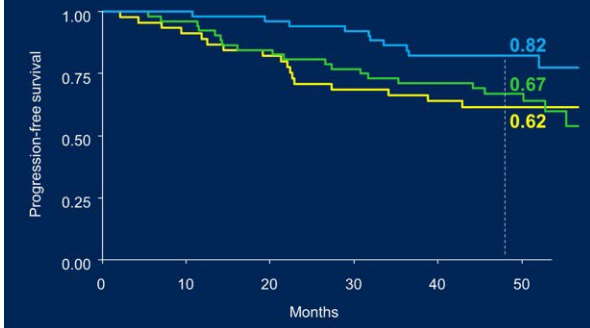
Progression-free survival: Random 1

KRd_ASCT vs. KRd12 vs. KCd_ASCT

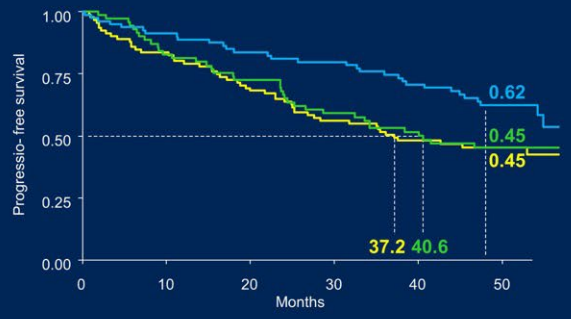
Median follow-up from Random 1: 51 months (IQR 46-55)

Standard risk (N=153)



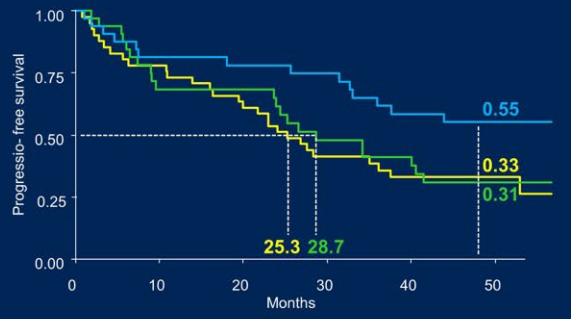
KRd_ASCT vs. KCd_ASCT: HR 0.44, p=0.04
KRd_ASCT vs. KRd12: HR 0.46, p=0.04
KRd12 vs. KCd_ASCT : HR 0.96, p=0.9

High risk (N=243)



KRd_ASCT vs. KCd_ASCT: HR 0.57, p=0.01
KRd_ASCT vs. KRd12: HR 0.6, p=0.04
KRd12 vs. KCd_ASCT: HR 0.95, p=0.8

Double hit (N=105)



KRd_ASCT vs. KCd_ASCT: HR 0.49, p=0.03
KRd_ASCT vs. KRd12: HR 0.53, p=0.07
KRd12 vs. KCd_ASCT: HR 0.91, p=0.75

Random 1, first randomization (induction/consolidation treatment); ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; HR, hazard ratio; CI, confidence interval; p, p-value; iQR, interquartile range.

Presented By: Francesca Gay

2021 ASCO ANNUAL MEETING

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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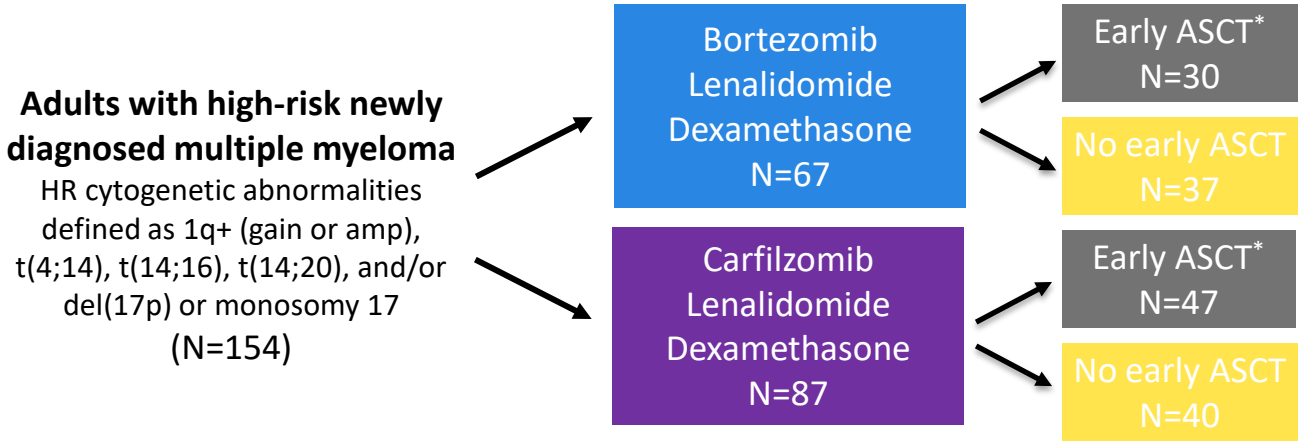
Carfilzomib, Lenalidomide, and Dexamethasone (KRd) vs Bortezomib, Lenalidomide, and Dexamethasone (VRd) as Induction Therapy in Newly Diagnosed HR-NDMM

- **We conducted a retrospective chart review study with 154 consecutive HR-NDMM patients treated with KRd and VRd at Memorial Sloan Kettering Cancer Center.**
- **Time period: January 1, 2015 to December 31, 2019**
- **Date of last follow-up: Sept. 30, 2022**



Primary endpoint:
Progression Free Survival
Secondary endpoints:
- Overall response rate
- MRD negativity rate
- Event Free Survival
- Overall Survival

*Early ASCT: ASCT within 12 months of start of induction therapy without progressive disease
HR: high risk; NDMM: newly diagnosed multiple myeloma; VRd: Bortezomib, lenalidomide, dexamethasone; KRd: Carfilzomib, lenalidomide, dexamethasone; ASCT: Autologous stem cell transplant

Tan C et al, ASH 2022

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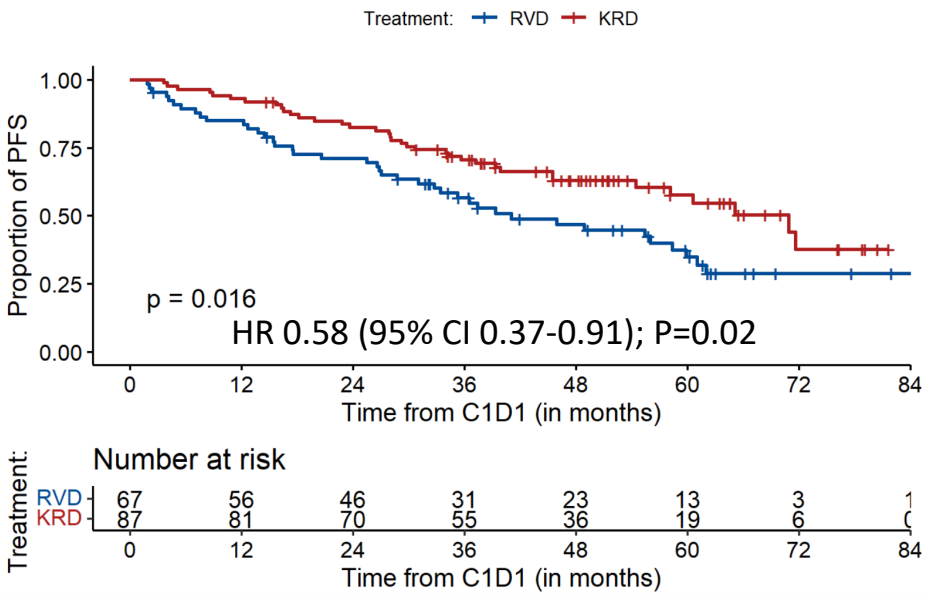
Progression Free Survival



Median f/u for all patients: 55.8 mos (95%CI 50.9-62.6)

Median f/u VRd 61.7 mos (95%CI 53-67.1)

Median f/u KRd 51.6 mos (95%CI 49.1-63.5)

PFS	VRd (N=67)	KRd (N=87)
Median, mo (95%CI)	41 (32.8 – 61.1)	70.9 (58.2 – NR)*
5-yr estimate (95%CI)	35% (24% - 51%)	58% (47% - 71%)

*Median PFS is an estimate

Tan C et al, ASH 2022

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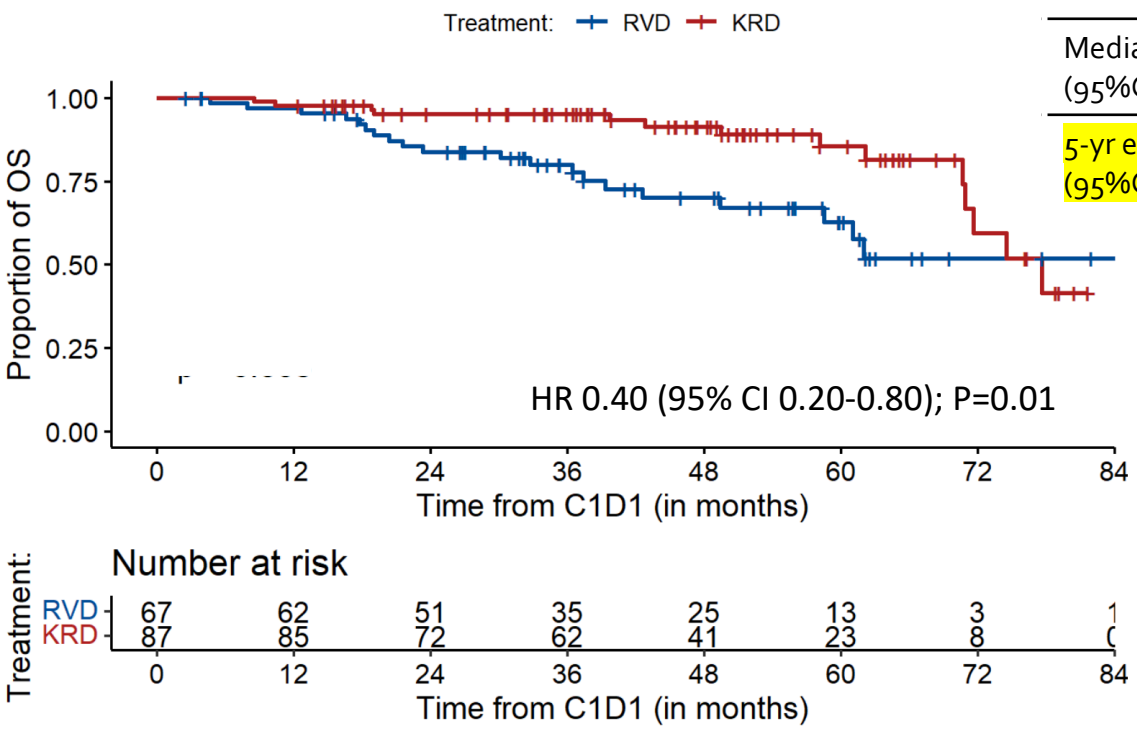
Overall Survival



OS	VRd (N=67)	KRd (N=87)
Median, mo (95%CI)	NR	77.7 (70.9-NR)
5-yr estimate (95%CI)	63% (49%-80%)	85% (76%-96%)

Median f/u for all patients: 48.9 mos (95%CI 44.9-53)

Median f/u VRd: 49.3 mos (95%CI 36.6-59.8)

Median f/u KRd: 48.6 mos (95%CI 44.9-52.6)

Tan C et al, ASH 2022

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Daratumumab-KRd for NDMM

Study/Phase	Patient Characteristics	Responses	PFS data	Safety (Grade ¾)
Landgren O et al JAMA Onc 2021 Phase II 8 cycles	N=41 High-risk = 49% (included gain 1q) Median age: 60 years	ORR = 100% ≥CR rate = 95% MRD-ve at 10^{-5} = 71%	1-year PFS rate 100%	Neutropenia 27%, Rash 9% Lung infection 7% Increased ALT 4% No TRM
Costa LJ et al JCO 2022 Phase II 4 cycles	N=123 High-risk = 57% (included gain 1q) Median age: 60 years	ORR = 100% ≥CR rate = 39% MRD-ve at 10^{-5} = 80%	2-year PFS rate 87%	Lung infection 6% VTE 3% No TRM
Bhutani M et al ASH 2022 Phase II 8 cycles	N=23 (of 39) High-risk = 43% (included gain 1q) Median age:	ORR = 100% ≥CR rate = 65% MRD-ve at 10^{-5} = 70%	Not reported	Hypophosphatemia 30% Neutropenia 13%, HTN 13% COVID19 7% No TRM

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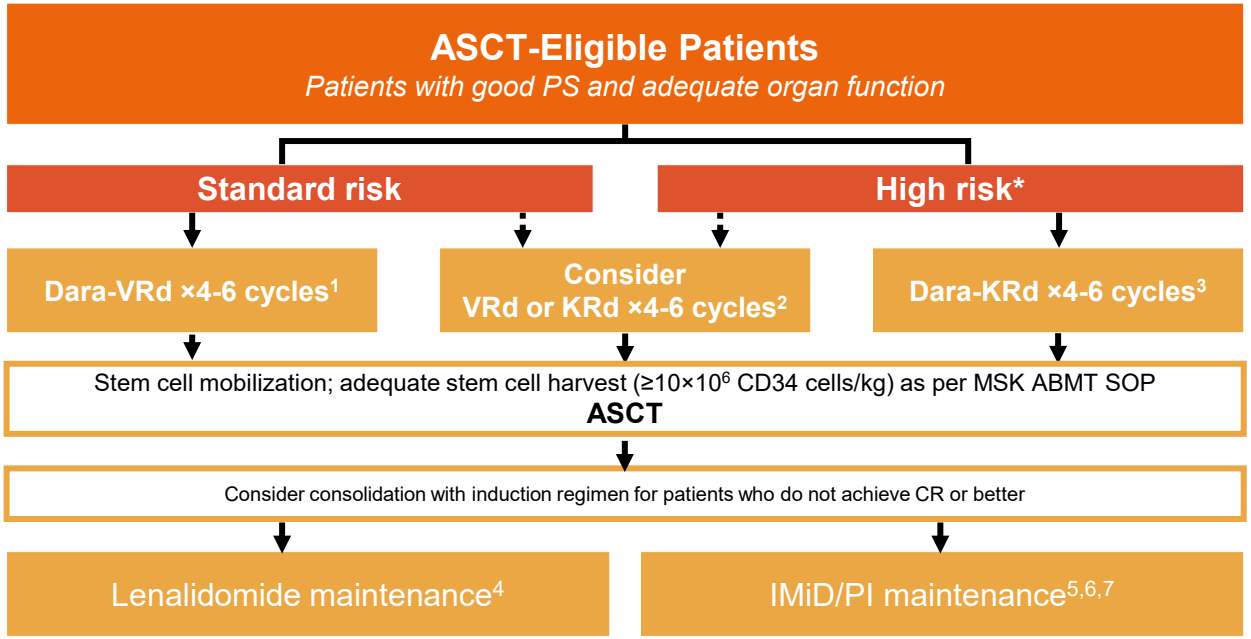
MSK Approach to Transplant Eligible NDMM



- ASCT, autologous stem cell transplant; CR, complete response; DVRd, daratumumab, bortezomib, lenalidomide, and dexamethasone; IMiD, immunomodulatory drug; PI, proteasome inhibitor; PS, performance status; Tx, treatment.
- *By R-ISS staging (R-ISS II/III) and/or cytogenetics (t[4;14], t[14;16], or del[17p]), elevated LDH, primary plasma cell leukemia
- 1. Attal. *NEJM*. 2017;376:1311. 2. Voorhees PM. Blood 2020. Gay. ASH 2020. Abstr 294. 4. McCarthy. *J Clin Oncol*. 2017;35:3279. 5. Nooka. *Leukemia*. 2014;28:690. 6. Dimopoulos. ASH 2018. Abstr 301. 7. Usmani. *Lancet Haematol*. 2021 Jan;8(1):e45-e54.

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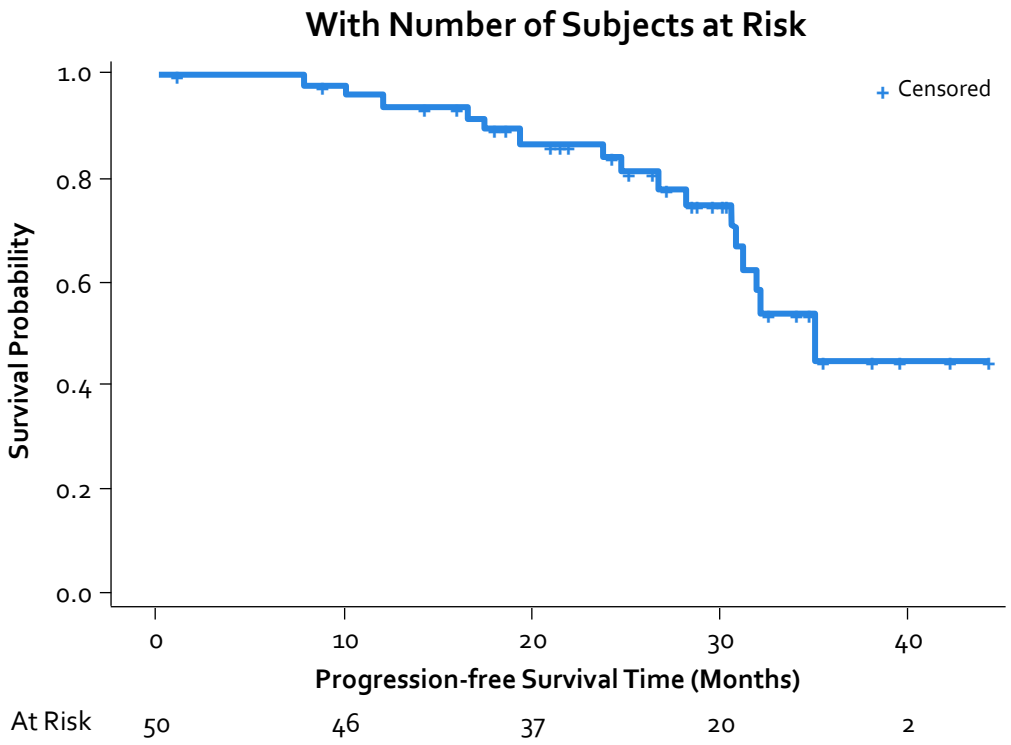
RVd-Lite

- Regimen (N=53)
  - Lenalidomide: 15 mg po days 1 to 21
  - Bortezomib: 1.3 mg/m2 subcutaneous 1× weekly on days 1, 8, 15, 22
  - Dexamethasone
    - If ≤75 years, 20 mg 2× weekly
    - If >75 years, 20 mg 1× weekly
- Results
  - 86% ORR
  - 66% ≥VGPR
  - Median PFS: 35.1 months
  - Median OS: NR
  - Median follow-up: 30 months
  - Median age: 73 years (range: 65-91)
  - PN: 62%
  - Only 1 patient had grade 3 symptoms



- PN, peripheral neuropathy.

O'Donnell et al. *Br J Haematol*. 2018;182:222-230.

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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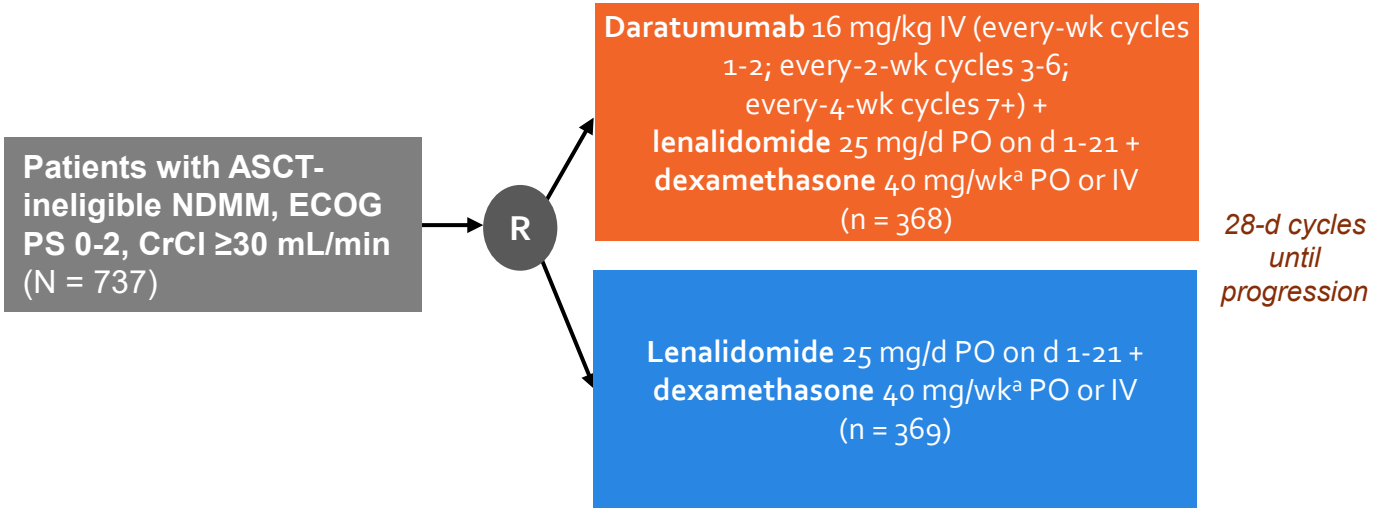
Phase 3 MAIA Study: Daratumumab Plus Rd in NDMM

- Stratified by ISS (I vs II vs III), region (North America vs other), and age (<75 vs ≥75 y)
- **Primary endpoint:** PFS
- **Secondary endpoints:** ≥ CR rate, ≥ VGPR rate, MRD negativity, ORR, OS, and safety



[a] Reduced to 20 mg/wk if aged >75 y or BMI <18.5.

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

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Demographics and Baseline Characteristics (ITT)

	D-Rd (n = 368)	Rd (n = 369)
Age		
Median (range), y	73 (50-90)	74 (45-89)
Distribution, n (%)		
<65 y	4 (1)	4 (1)
65-<70 y	74 (20)	73 (20)
70-<75 y	130 (35)	131 (36)
≥75 y	160 (43)	161 (44)
Male, n (%)	189 (51)	195 (53)
ECOG PS score,[a] n (%)		
0	127 (35)	123 (33)
1	178 (48)	187 (51)
2[b]	63 (17)	59 (16)
ISS stage,[c] n (%)		
I	98 (27)	103 (28)
II	163 (44)	156 (42)
III	107 (29)	110 (30)

	D-Rd (n = 368)	Rd (n = 369)
Type of measurable disease, n (%)		
IgG	225 (61)	231 (63)
IgA	65 (18)	66 (18)
Other[d]	9 (2)	10 (3)
Detected in urine only	40 (11)	34 (9)
Detected as serum-free light chain only	29 (8)	28 (8)
Cytogenetic profile,[e] n/total n (%)		
Standard risk	271/319 (85)	279/323 (86)
High risk	48/319 (15)	44/323 (14)
Median time since initial diagnosis of MM (range), months	0.95 (0.1-13.3)	0.89 (0-14.5)

Demographics and baseline characteristics were well balanced between arms

ITT, intention-to-treat.

[a]ECOG PS is scored on a scale from 0 to 5, with 0 indicating no symptoms and higher scores indicating increasing disability. [b]2 patients had an ECOG PS score >2 (1 patient each with an ECOG PS score of 3 and 4). [c]ISS stage is derived based on the combination of serum β_2-microglobulin and albumin; higher stages indicate more severe disease. [d]Includes IgD, IgE, IgM, and biclonal. [e]Cytogenetic abnormalities were identified by fluorescence in situ hybridization or karyotype testing; high risk was defined as having a t(4;14), t(14;16), and/or del17p abnormality.

Note: percentages may not add up to 100% due to rounding.

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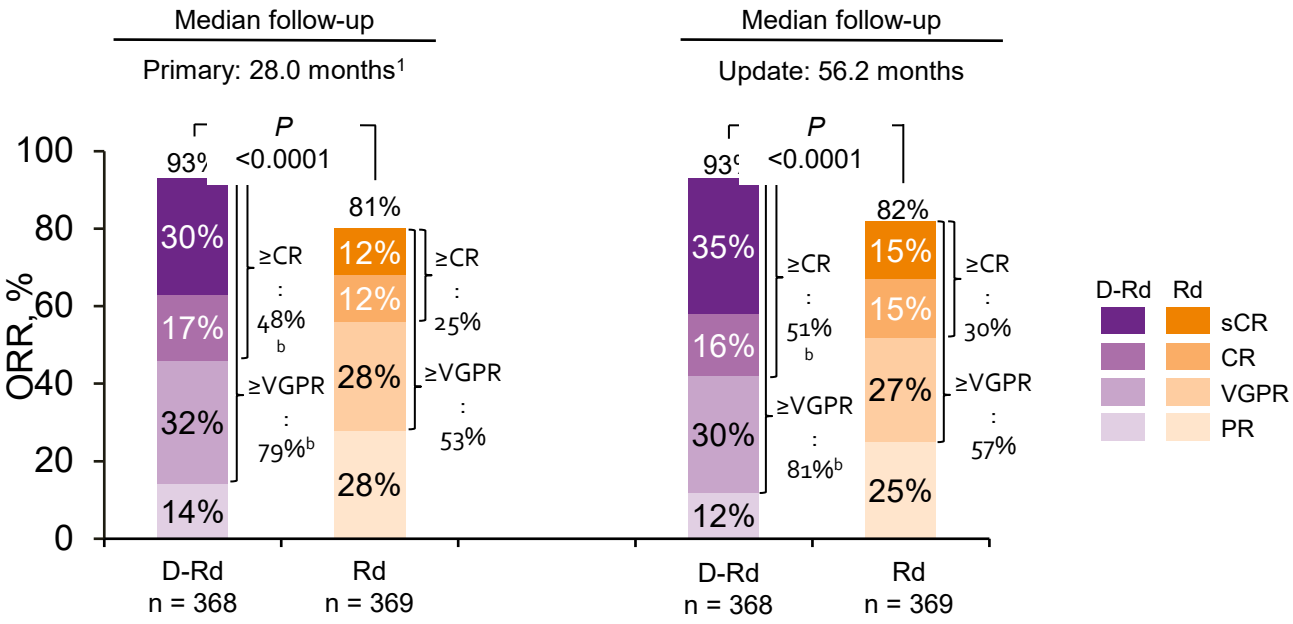
MAIA Phase III ORR[a]



- **D-Rd induced deeper responses, with significantly higher rates of ≥CR and ≥VGPR, compared with Rd**
- **With >28 months of additional follow-up, responses deepened with continued daratumumab therapy**

VGPR, very good partial response; PR, partial response; OR, odds ratio.
[a]ITT population. [b]*P* <0.0001; *P* values were calculated from the Cochran-Mantel-Haenszel Chi-Squared test.
1. Facon T, et al. *N Engl J Med*. 2019;380(22):2104-2115.
Note: percentages may not add up to the total due to rounding.

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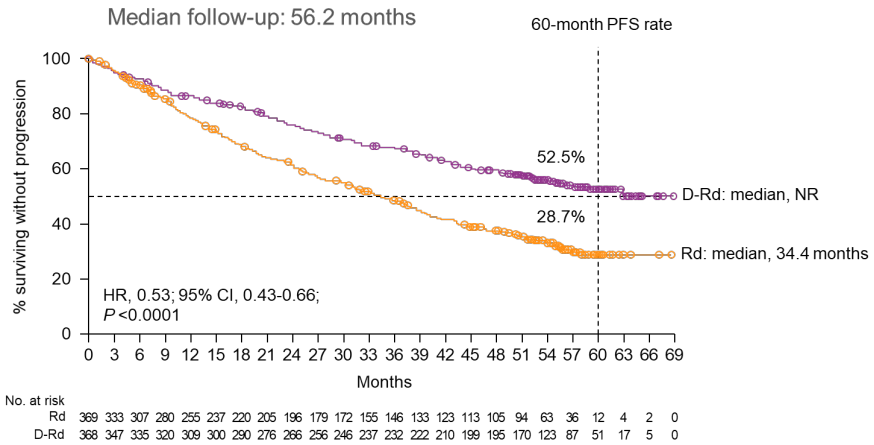
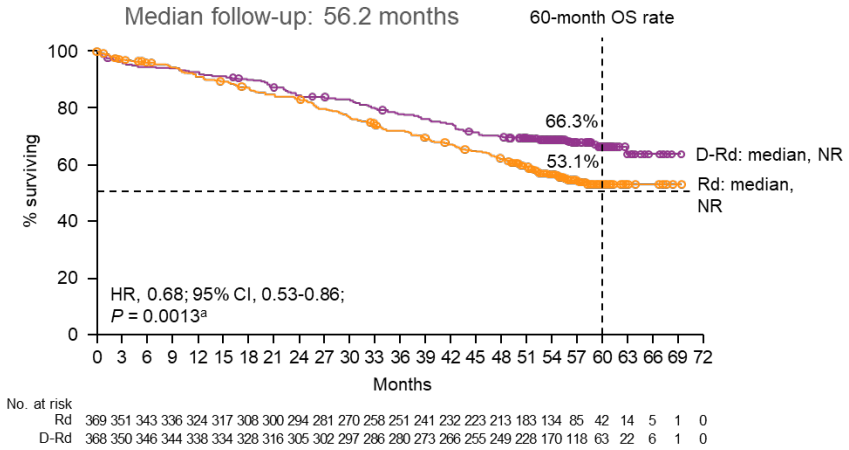
MAIA Phase III Updated PFS/OS





[a]*P* = 0.0013 is statistically significant, crossing the prespecified stopping boundary of *P* = 0.0414.

NR, not reached; CI, confidence interval.

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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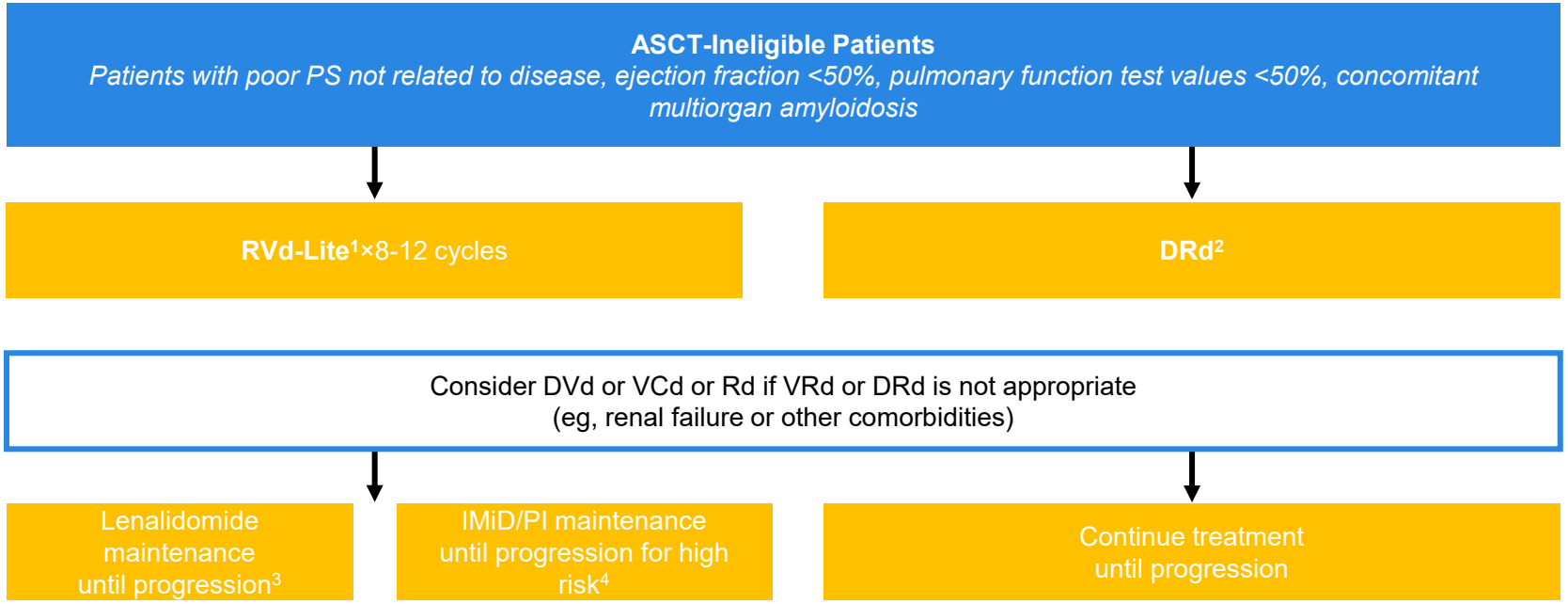
MSK Approach to Transplant Ineligible NDMM



- DRd, daratumumab, lenalidomide, and dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; VRd-Lite, modified VRd regimen.
- Adjust dosing of lenalidomide based on renal function. Consider empiric age-adjusted dose reductions for all regimens, as needed.[4]
- 1. O'Donnell. Br J Haematol. 2018;182:222. 2. Facon. ASH 2018. Abstr LBA-2. 3. Larocca. ASH 2018. Abstr 305. 4.Usmani. *Lancet Haematol*. 2021 Jan;8(1):e45-e54.

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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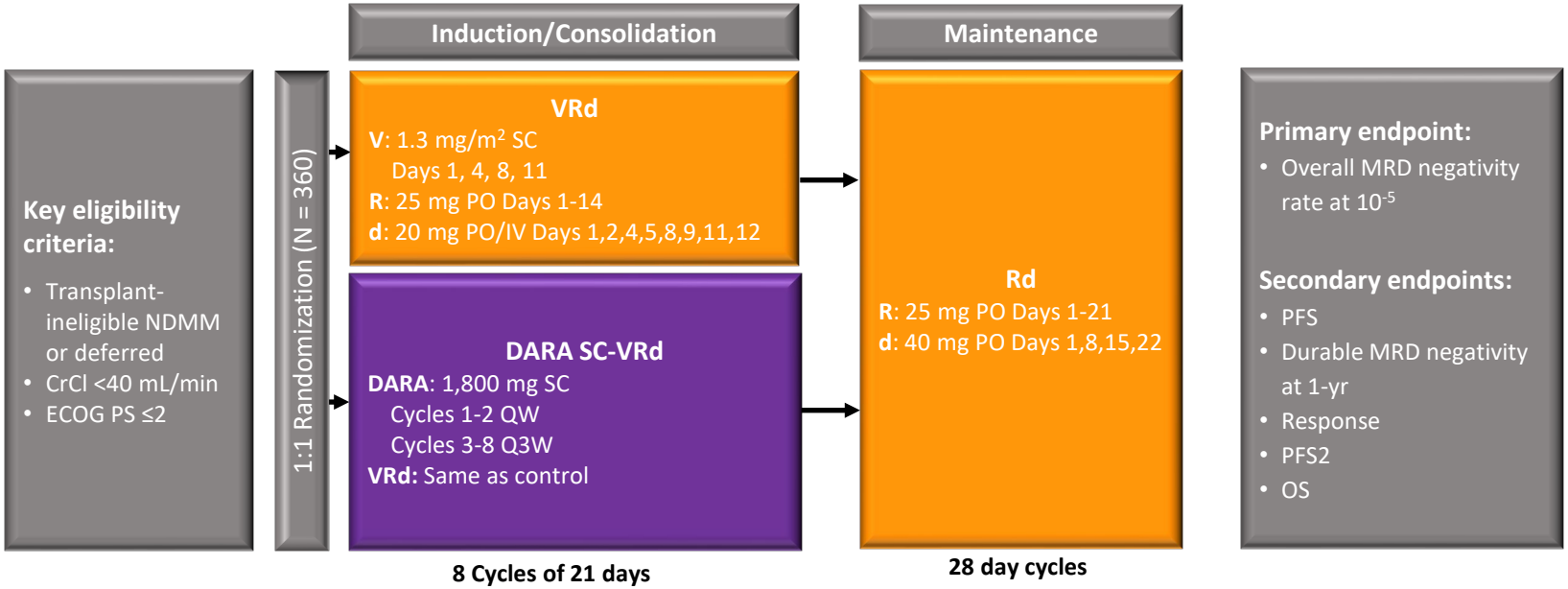
CEPHEUS: Study Design

- **Phase 3 study of DARA-VRd versus VRd in transplant-ineligible NDMM**



Zweegman S, et al. Trials in Progress Poster presented at ASCO Annual meeting. May 31-June 4, 2019. Chicago, IL. Abstract TPS8066.
ClinicalTrials.gov Identifier: NCT03652064. Accessed 24 February 2022

Presented by: Saad Z. Usmani, MD MBA FACP, @szusmani

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Waldenstrom's Macroglobulinemia

Incipient myelomatosis or «essential» hyperglobulinemia with fibrinogenopenia — a new syndrome?

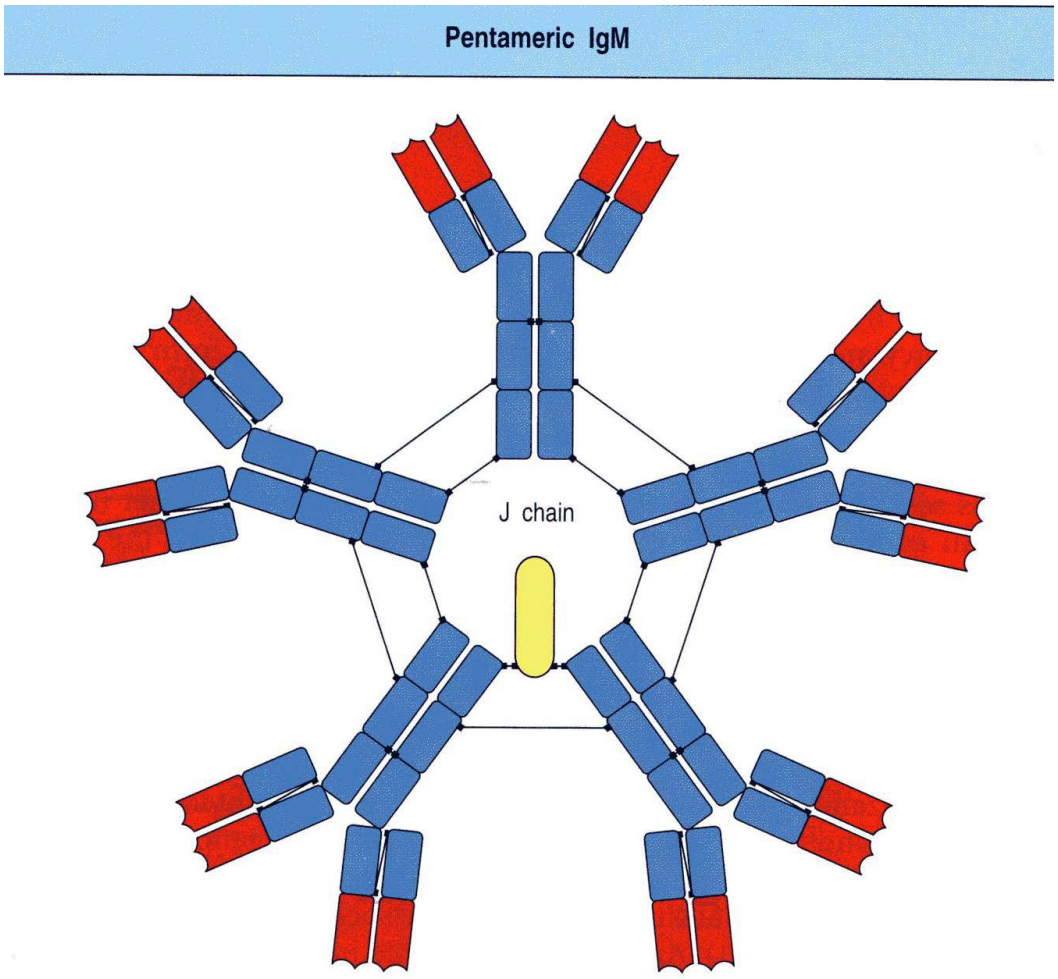
By

JAN WALDENSTRÖM.

Submitted for publication September 2, 1943.

The real nature of myelomatosis.

The title of this paper may at first seem somewhat surprising. The myeloma has of old had a reputation as a well defined clinical entity. With the aid of the typical changes on the X-ray film and guided by the examination of the cells from a sternal puncture the diagnosis should therefore be easy and there ought not to be found any serious diagnostical troubles. In the following I am going to give a description of two cases, who have several symptoms suggesting myelomatosis but also show decided differences. They are very much alike even as regards details in the chemistry of the blood proteins and it seems probable according to my opinion, that they suffer from the same malady. A third case very much resembles these two patients but also shows other signs, that do not fit in



80-90% sIgM retained in intravascular space

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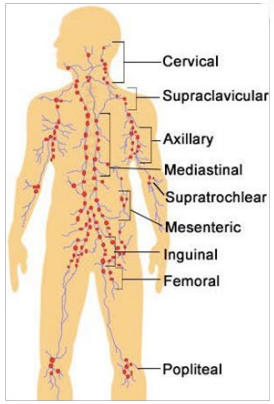
Manifestations of WM Disease

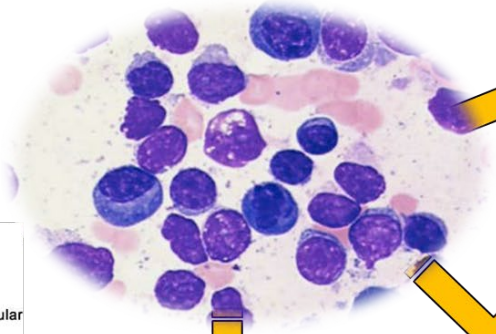
Bing Neel Syndrome

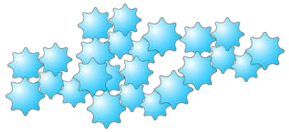


≤20% at diagnosis;
50-60% at relapse.

Bone Marrow

↓Hb>>> ↓PLT> ↓WBC





Hyperviscosity Syndrome:
Epistaxis, Headaches
Impaired vision
>6,000 mg/dL or >4.0 CP

Cold Agglutinemia (5%)
Cryoglobulinemia (10%)
IgM Neuropathy (22%)
Amyloidosis (10-15%)

Hepcidin
↓Fe Anemia

Treon S., Hematol Oncol. 2013; 31:76-80.

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NCCN Guidelines for Initiation of Therapy in WM

- Hb ≤10 g/dL on basis of disease
- PLT <100,000 mm^3 on basis of disease
- Symptomatic hyperviscosity
- Moderate/severe peripheral neuropathy
- Symptomatic cryoglobulins, cold agglutinins, auto-immune related events, amyloid.

Kyle RA, et al. Semin Oncol. 2003;30(2):116-120; Anderson et al, JNCCN 2012; 10(10):1211-9.

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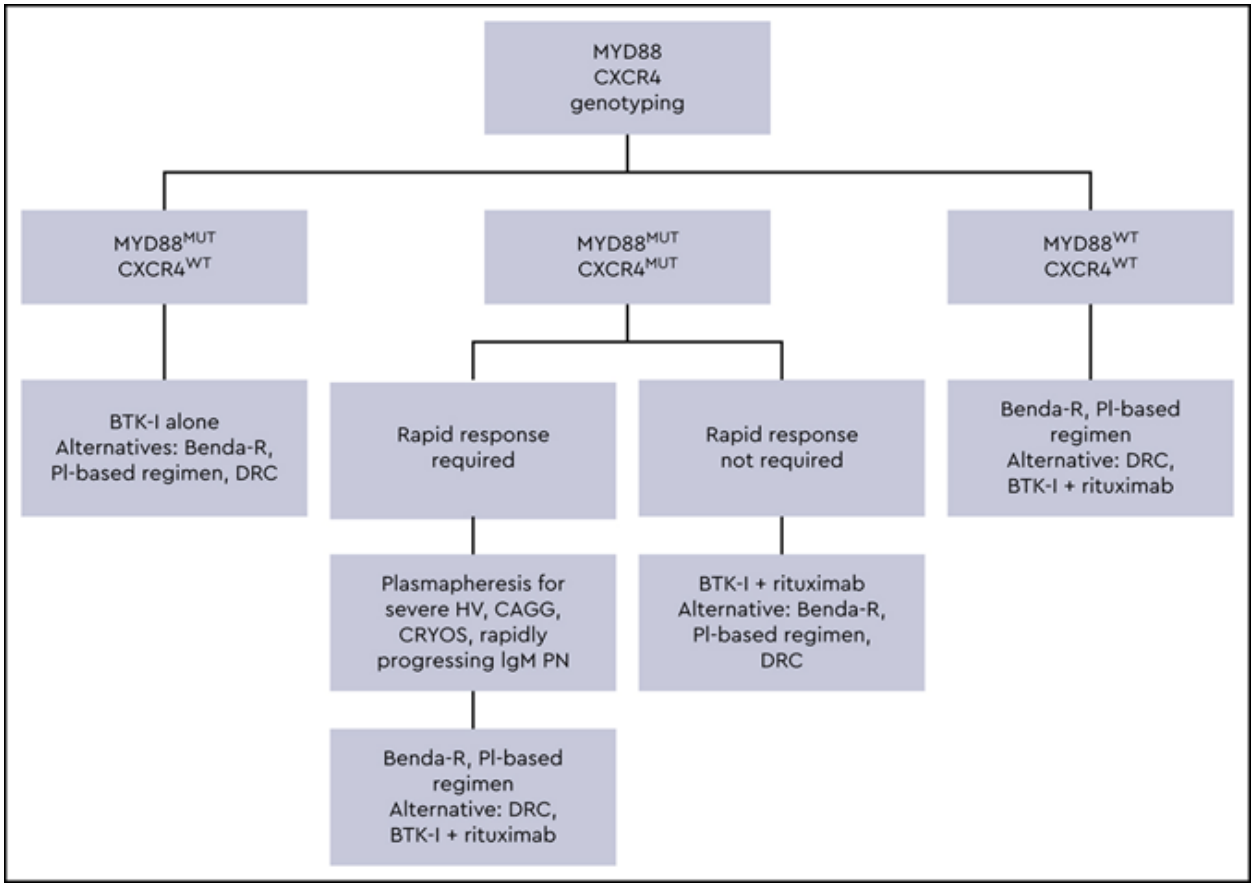
Front Line Therapy



Jorge J. Castillo,Steven P. Treon, Management of Waldenström macroglobulinemia in 2020, Hematology Am Soc Hematol Educ Program, 2020,

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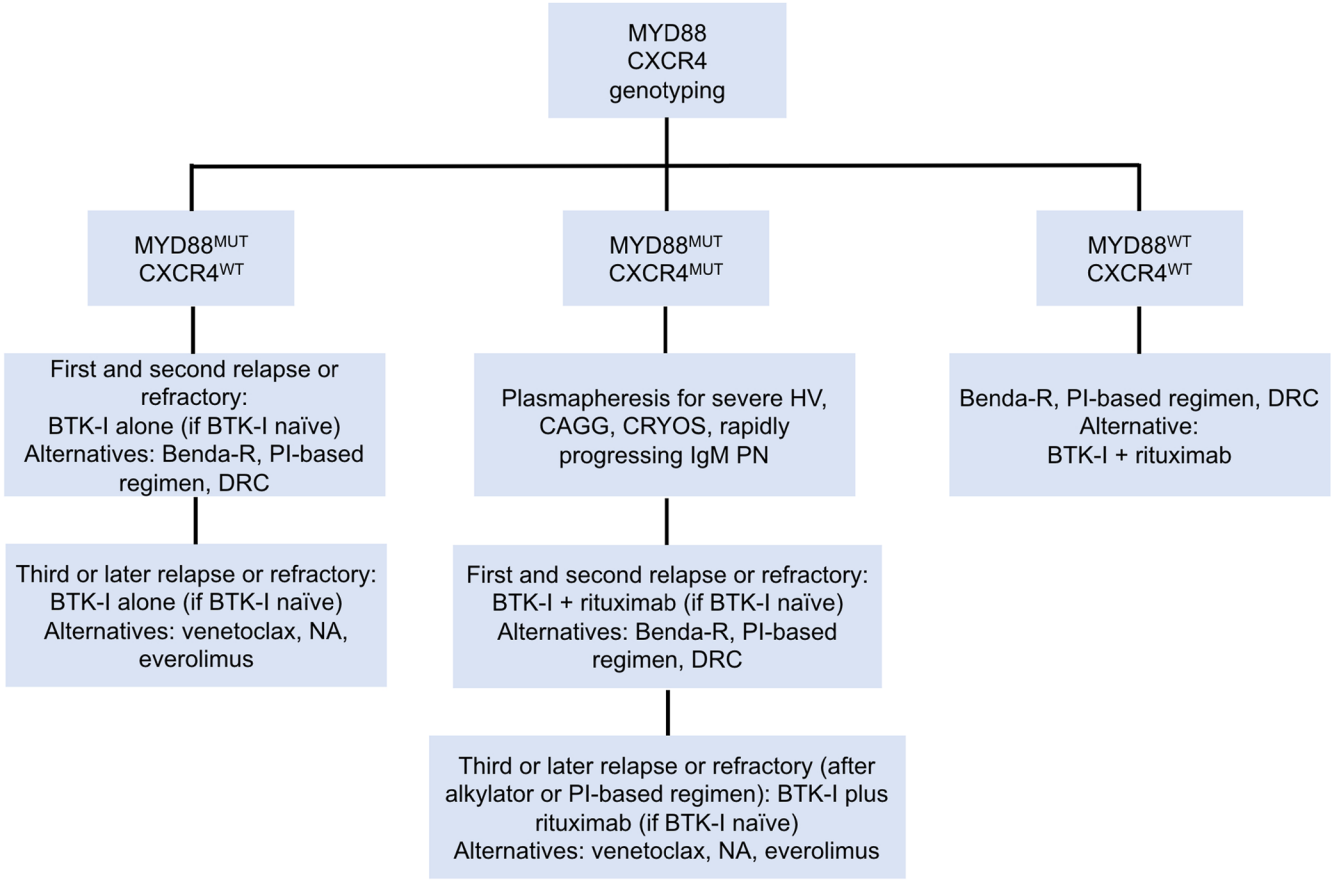
Therapy at Relapse



Jorge J. Castillo,Steven P. Treon, Management of Waldenström macroglobulinemia in 2020, Hematology Am Soc Hematol Educ Program, 2020,

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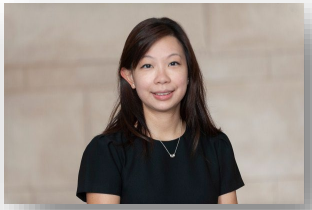
MSKCC Myeloma Service

Saad Z. Usmani (Chief)
High-Risk Disease , Disparities
TCE, CAR T Cells
Checkpoint Inhibitors
Developmental Therapeutics

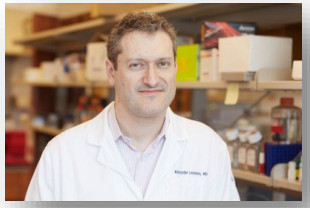


Carlyn Tan
MM Precursor diseases
Supportive Care
Bone Health

Urvi Shah
MM Precursor Disease
Nutrition & Modifiable
Risk Factors
Early Relapse

Kylee Maclachlan
MM Precursor Disease,
NDMM Trials
Genomics, Immune
Profiling

Neha Korde
NDMM Clinical Trials
Digital Wearables
Supportive Care



Alex Lesokhin
RRMM Immunotherapy
TCE, Checkpoints Inhibitors
Neoantigens
Microbiota, Immune
Profiling

Hani Hassoun
MM Supportive Care
Alliance Liaison
NDMM/RRMM Trials
Elderly and Frail

Sham Mailankody
RRMM Trials with
CAR T Cells
High-Risk Disease

Malin Hultcrantz
RRMM Trials in TCR
Antibody drug conjugates
Epidemiology

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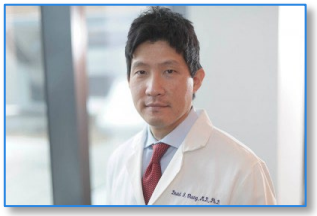
MSKCC Myeloma TCT Program

Sergio Giralt
Allo/Auto HCT for MM
New Regimens
CAR T Cells



David Chung
T Cell exhaustion
Auto HCT + Vaccines
MM Immunotherapies

Gunjan Shah
HCT Toxicities
Precision Drug Dosing
CAR T Cells
Salvage Auto and Allo HCT

Saad Z. Usmani
High-Risk Disease Biology/Trials
CAR T Cells
Auto HCT for MM

Michael Scordo
HCT Toxicities
Precision Drug Dosing
CAR T Cells

Heather Landau
Amyloidosis
HCT Toxicities
Homebound HCT
Precision Drug Dosing
Novel Regimens for Salvage Auto

Oscar Lahoud
Auto HCT and CAR T Cells
Post HCT Therapies