Newly Diagnosed Multiple Myeloma

Board Review
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Andrew J. Portuguese, MD
Assistant Professor, Clinical Research Division, FHCC
Assistant Professor, Division of Heme and Onc, UWSOM
aportugu@fredhutch.org

Agenda

Newly Diagnosed Multiple Myeloma

- Initial diagnosis
- Risk stratification
- Current treatment paradigm
- Other considerations
- Questions

Vignette

A 50-year-old woman with back pain…

- **Jan:** Works as a CNA. First developed back pain after helping move a patient.
- **Feb:** Presented to ED with lumbar pain. Labs: Cr 0.76 mg/dL, Hgb 8.6 g/dL. D/c'ed with prednisone 50 mg daily x5 days and cyclobenzaprine 5 mg BID x10 days.
- **June:** Re-presented to ED with worsening lumbar pain. D/c'ed with more cyclobenzaprine, methylprednisolone 4 mg daily x21 days, and also diazepam and lidocaine patches.

Vignette

A 50-year-old woman with back pain…

- **July:** Presented to ED with worsening pain.
  - Imaging: acute-to-subacute L5 biconcave compression fracture, chronic L2 biconcave compression fracture, and questionable chronic compression deformity of L4 vertebral body.
  - Labs: AKI (Cr 1.57 mg/dL), hypercalcemia (13.4 mg/dL), anemia (Hgb 7.2 g/dL), thrombocytopenia (110k/µL), total protein 11.1 g/dL, albumin 3.0 g/dL.
  - Hypercalcemia: Given 2L IVFs, started on NS gtt 150 ml/hr, then zoledronic acid 4 mg IV

Multiple Myeloma Diagnostic Criteria

Since 2014

- **CLASSIC:** Clonal bone marrow plasma cells ≥10% *OR* biopsy proven plasmacytoma + “CRAB” criteria
  - Hyper**C**alcemia — Ca >11 mg/dL
  - **R**enal failure — CrCl <40 mL/min or Cr >2 mg/dL
  - **A**nemia — Hgb <10 g/dL
  - **B**one lesions — 1 or more lytic lesions ≥5 mm in size
- **NEW (“SLiM” CRAB):** additional paths to diagnosis (per IMWG)
  - **S**ixty percent or more clonal plasma cells in the bone marrow
  - **Li**ght chain ratio (involved/uninvolved) of 100 or more
  - **M**RI with more than 1 focal lesion ≥5 mm in size

Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol*. 2014;15(12):e538-e548. doi:10.1016/S1470-2045(14)70442-5

What else could it be?

Differential diagnosis

- **Monoclonal gammopathy of undetermined significance (MGUS)**
  - Serum monoclonal protein <3 g/dL
  - AND clonal bone marrow plasma cells <10%
  - AND absence of lytic lesions, anemia, hypercalcemia, and renal insufficiency (that can be attributed to the plasma cell disorder)
- **Smoldering multiple myeloma (SMM)**
  - M protein ≥3 g/dL and/or 10-60% bone marrow plasma cells
  - No end-organ damage or other myeloma-defining events
  - No amyloidosis

What else could it be?

Differential diagnosis

- **Waldenström macroglobulinemia**
  - Lymphoplasmacytic lymphoma (LPL) in the bone marrow
    - Presence of a clonal lymphocytic component
  - IgM monoclonal gammopathy in the blood
  - *MYD88* L265P gene mutation seen in ~90% of cases

Treon SP, Xu L, Yang G, et al. MYD88 L265P somatic mutation in Waldenström's macroglobulinemia. *N Engl J Med*. 2012;367(9):826-833. doi:10.1056/NEJMoa1200710

What else could it be?

Differential diagnosis

- **Solitary plasmacytoma**
  - Tumors composed of plasma cells
  - Must have:
    - Biopsy-proven solitary lesion of the bone or soft tissue
    - Normal bone marrow
    - Cross-sectional imaging (either MRI or PET/CT) without other lesions
    - Absence of lytic lesions, anemia, hypercalcemia, and renal insufficiency

What else could it be?

Differential diagnosis

- **AL amyloidosis**
  - Underlying plasma cell dyscrasia with abnormal light chain production
  - Amyloid deposition can lead to nephrotic syndrome, **heart failure**, hepatomegaly
  - Usually <20% marrow plasma cells
  - Diagnosis requires biopsy of affected tissue or surrogate site (eg, abdominal fat pad, salivary gland, or bone marrow)

What else could it be?

Differential diagnosis

- **Plasma cell leukemia**
  - Rare, aggressive form of multiple myeloma
  - Very poor prognosis — median survival historically 6-11 months, many die within first month
  - Peripheral blood plasma cells ≥5% of the peripheral white cells (by manual count, *not* flow cytometry)*

*As of the 2021 IMWG consensus definition, previously 20% threshold

Fernández de Larrea C, Kyle R, Rosiñol L, et al. Primary plasma cell leukemia: consensus definition by the International Myeloma Working Group according to peripheral blood plasma cell percentage. *Blood Cancer J*. 2021;11(12):192. Published 2021 Dec 2. doi:10.1038/s41408-021-00587-0

Vignette

A 50-year-old woman with back pain…

- **Pertinent labs:**
  - IgG **7861**
  - IgA 14
  - IgM 14
  - Kappa FLC 87.03
  - Lambda FLC 0.57
  - K/L FLC ratio **152.68**
  - SPEP with IF: IgG kappa monoclonal, **6.9 g/dL**
  - Peripheral smear: occasional plasma cells, rouleaux

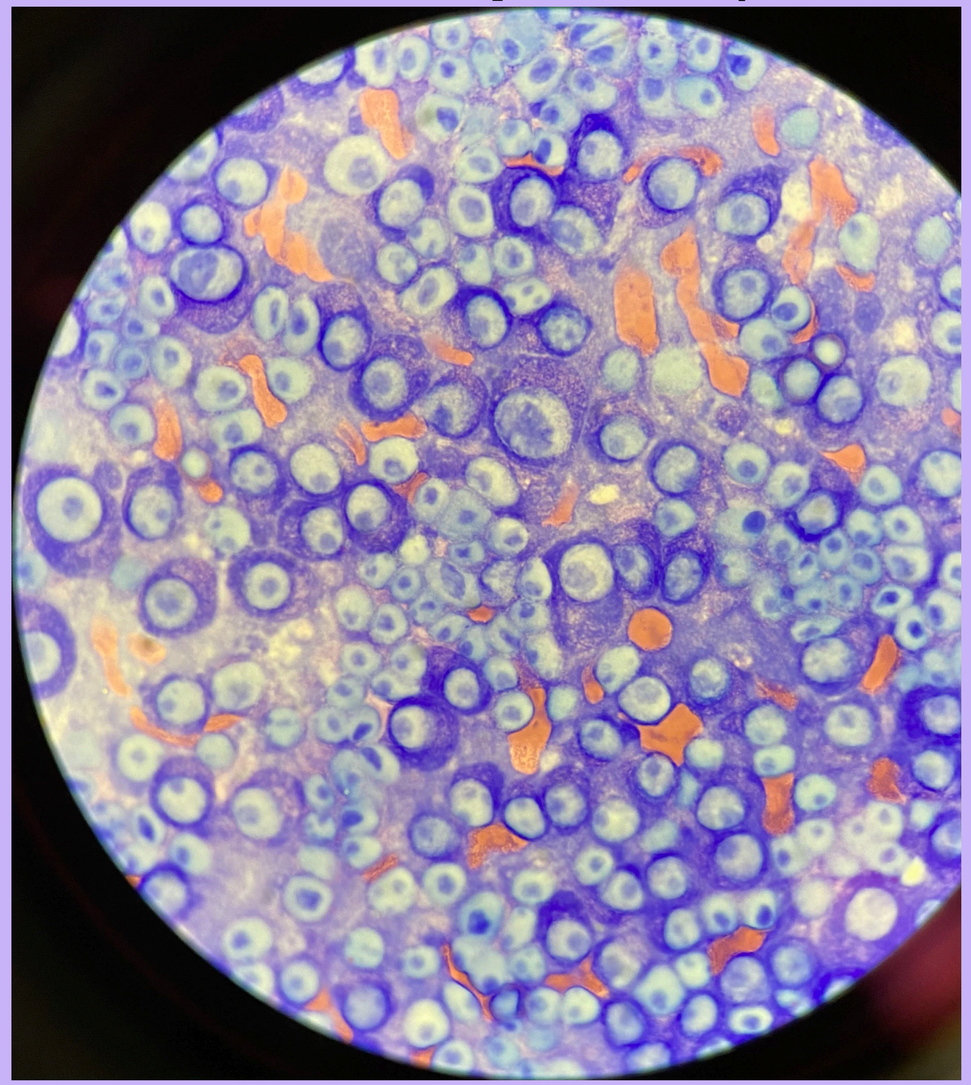
Vignette

A 50-year-old woman with back pain…

- **Additional workup:**
  - Peripheral flow: abnormal plasma cell population, 0.22% of the total white cells
  - Peripheral smear diff: **12.5% plasma cells**

Vignette

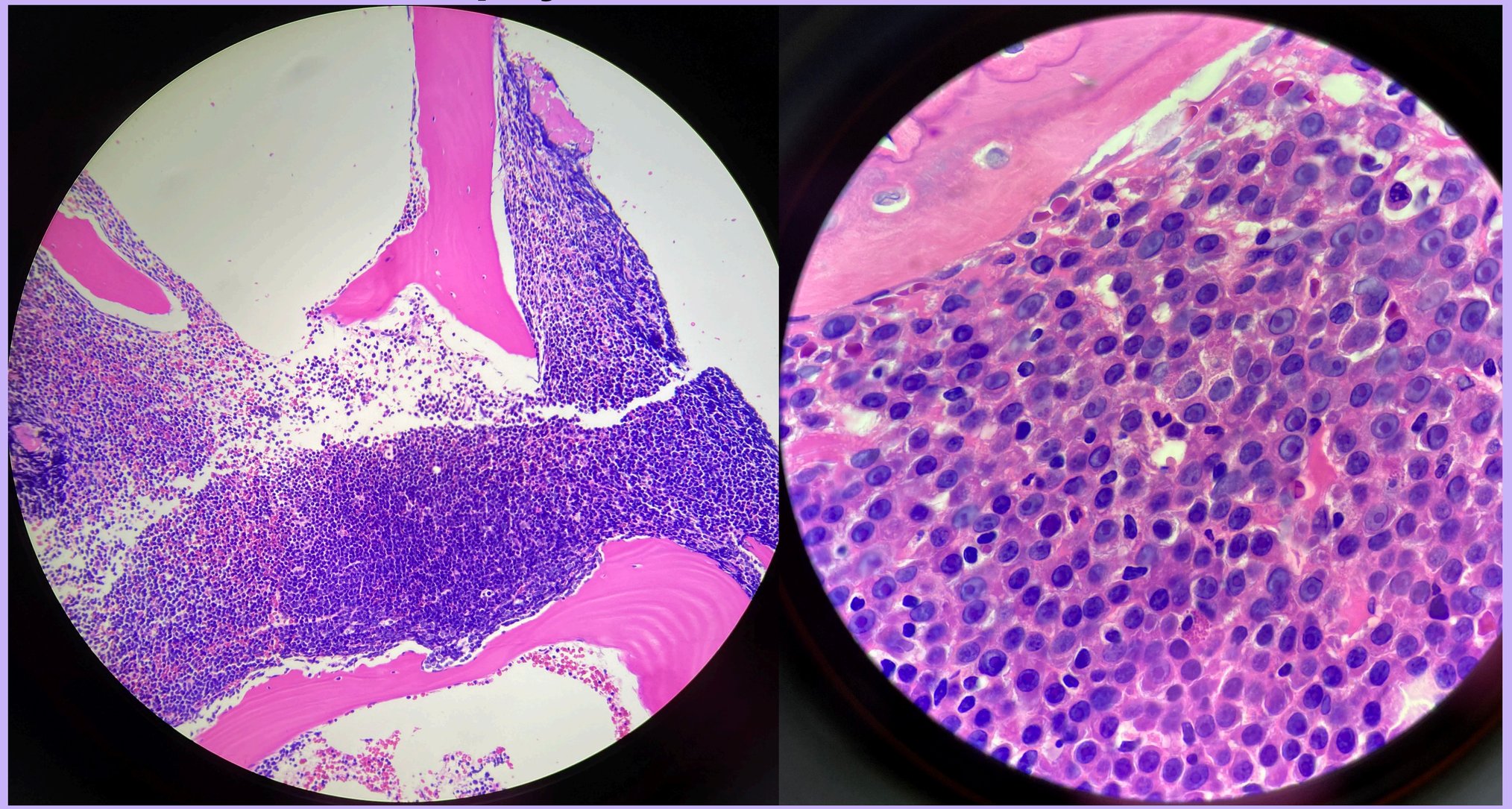
Bone marrow aspirate: particle prep



- **Flow cytometry:** abnormal plasma cell population, 28.6% of the total white cells

Vignette

Bone marrow core biopsy



How do I risk stratify?

Revised international staging system for myeloma

ISS or R-ISS stage	ISS criteria	R-ISS criteria	Median survival
I	Serum beta-2 microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL	ISS Stage I AND standard risk CA by iFISH and normal LDH	**62-66 mo**
II	Not ISS stage I or III	Not R-ISS stage I or III	**42-44 mo**
III	Serum beta-2 microglobulin ≥ 5.5 mg/L	ISS Stage III AND either high-risk CA by iFISH or high LDH	**29 mo**

Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised International Staging System for Multiple Myeloma: A Report From International Myeloma Working Group. *J Clin Oncol*. 2015;33(26):2863-2869. doi:10.1200/JCO.2015.61.2267

How do I risk stratify?

High risk cytogenetic abnormalities

- **Genetic abnormalities**
  - **IgH translocations:** – 40% of cases
    - **t(4;14):** 4p16 – *FGFR3* – deregulation of fibroblast growth factor
    - **t(14;16):** 16q23 – *MAF* – deregulation of c-MAF proto-oncogene
    - **t(14;20):** 20q11 – *MAFB* – deregulation of MAFB oncogene
  - **del(17p):** *p53* – clonal immortalization, resistance to apoptosis
  - **1q amplification (i.e., <u>4 or more copies</u>):** *CKS1B* – activation of cyclin dependent kinase leading to deregulation of cell cycle control

Sonneveld P, Avet-Loiseau H, Lonial S, et al. Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group. *Blood*. 2016;127(24):2955-2962. doi:10.1182/blood-2016-01-631200

How do I risk stratify?

Other risk factors

- R-ISS Stage III
- Circulating plasma cells (≥5%)
- Extramedullary disease
- Gene Expression Profiling (GEP) high risk signature
- Complex karyotype
  - 2 or more cytogenetic abnormalities

Sonneveld P, Avet-Loiseau H, Lonial S, et al. Treatment of multiple myeloma with high-risk cytogenetics: a consensus of the International Myeloma Working Group. *Blood*. 2016;127(24):2955-2962. doi:10.1182/blood-2016-01-631200

Dabedochukwu Obiekwe et al., The impact of complex karyotype identified by conventional cytogenetics on survival outcomes of 1,000 patients with newly diagnosed myeloma (NDMM)..JCO 40, 8063-8063(2022).DOI:10.1200/JCO.2022.40.16_suppl.8063

Vignette

A 50-year-old woman with back pain…

- **Karyotype:**
  - One-copy gain of chromosomes 3, 5, 7, 9, 18, 19 and 21
  - Two-copy gain of chromosome 15, three-copy gain of chromosome 11, and a derivative chromosome 9;16 consisting of 16p and 9q
- **FISH:**
  - PRESENCE of 4-5 copies of CCND1 in 37% of cells
  - PRESENCE of 1 copy loss of MAF in 20% of cells

What imaging should I get?

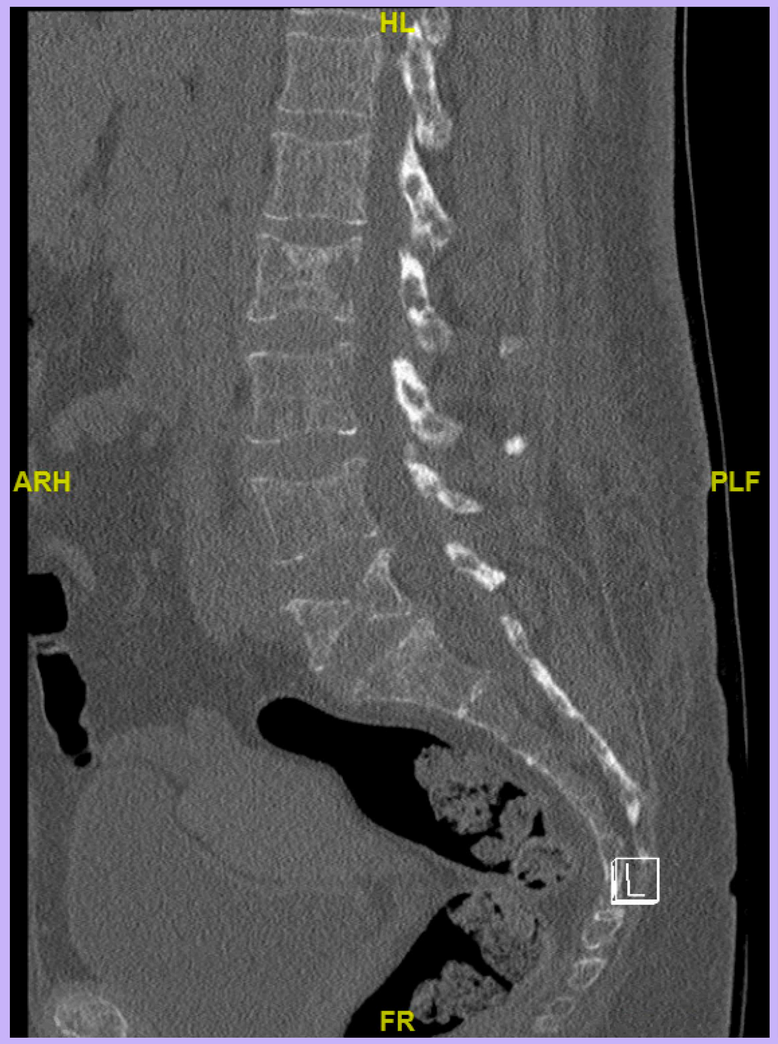
Skeletal survey vs CT vs PET/CT vs BM MRI

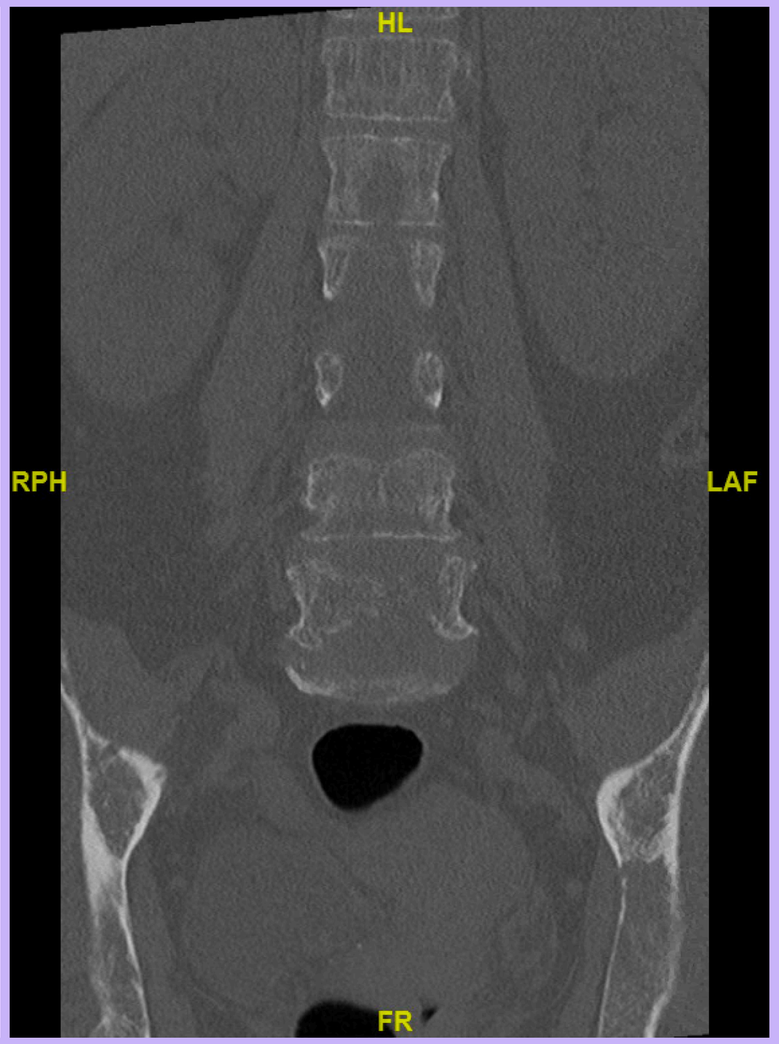
- Cross-sectional imaging is (*strongly*) preferred over plain radiographs
- Three acceptable options:
  - Whole body low dose CT without contrast
  - Whole body ^{18}F-FDG PET/CT
  - Whole body MRI (bone marrow or DWI)
- Skeletal survey ONLY for patients who are unable to undergo CT, MRI, or PET

Hillengass J, Usmani S, Rajkumar SV, et al. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders [published correction appears in Lancet Oncol. 2019 Jul;20(7):e346]. *Lancet Oncol*. 2019;20(6):e302-e312. doi:10.1016/S1470-2045(19)30309-2

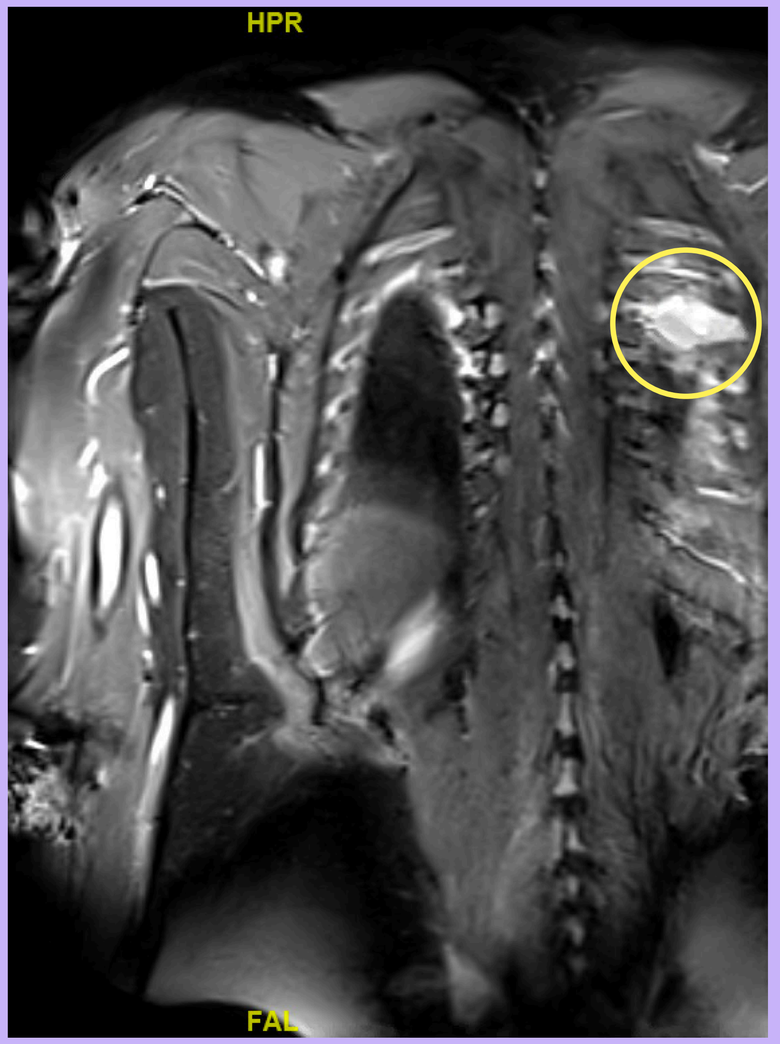
Vignette

CT L-spine: multiple compression fractures



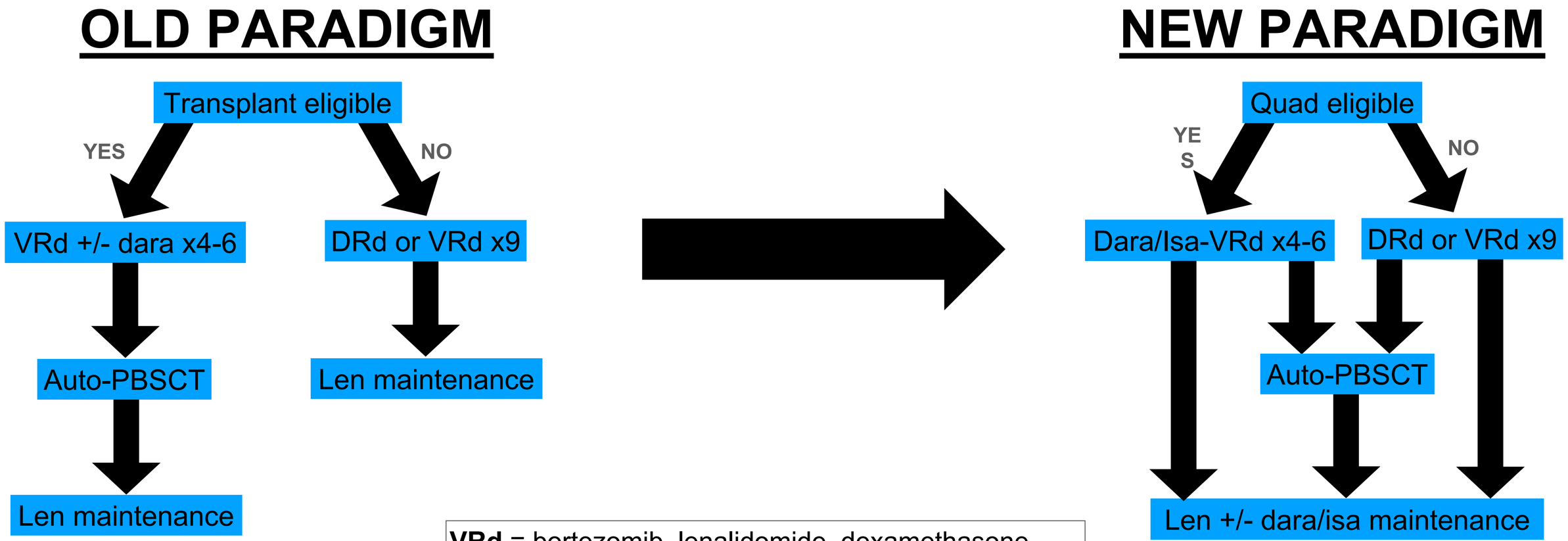


BM MRI: lesion in L posterior 6th rib (4.4 cm)



How do I treat newly diagnosed myeloma?

Old and new paradigms



VRd = bortezomib, lenalidomide, dexamethasone
DRd = daratumumab, lenalidomide, dexamethasone

Dispenzieri A, Rajkumar SV, Gertz MA, et al. Treatment of newly diagnosed multiple myeloma based on Mayo Stratification of Myeloma and Risk-adapted Therapy (mSMART): consensus statement. *Mayo Clin Proc*. 2007;82(3):323-341. doi:10.4065/82.3.323

How ma?

Old anc

OLD P ADIGM

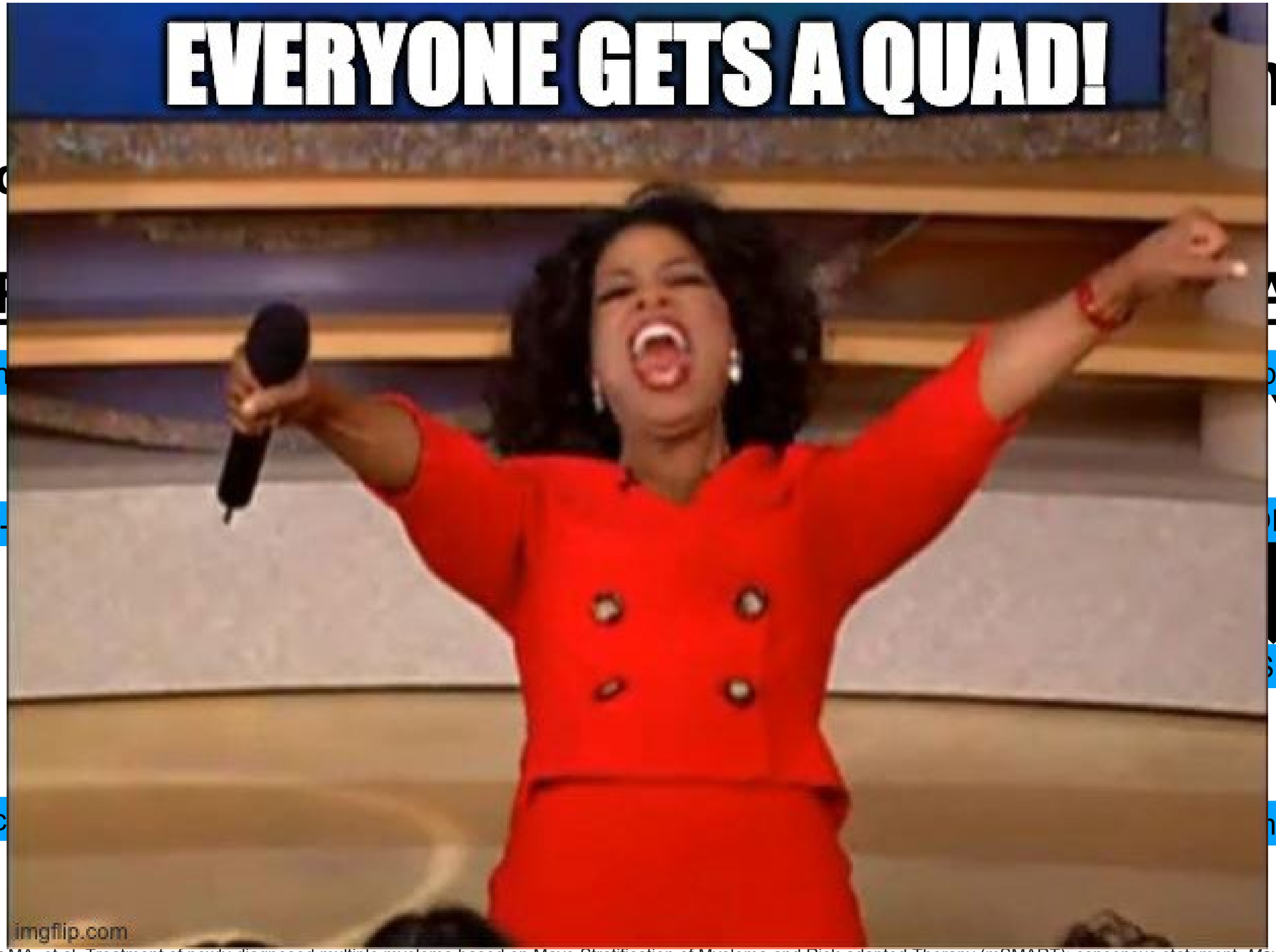
Tran ble

YES NO

VRd +/- dara x4- Rd or VRd x9

Auto-PBSCT SCT

Len maintenanc aintenance

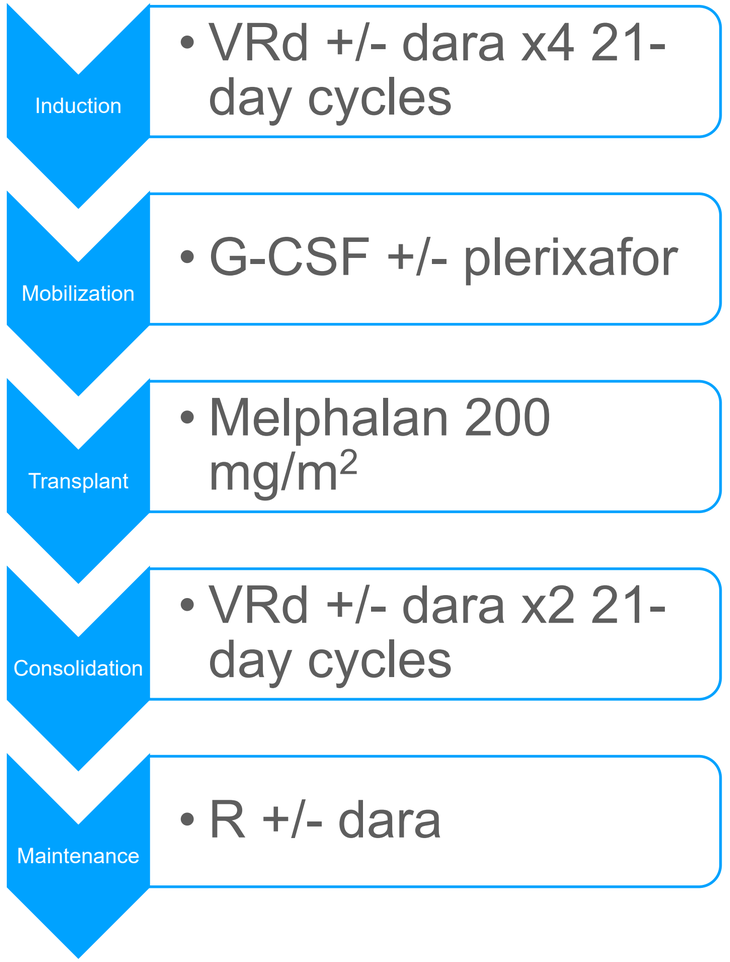


Dispenzieri A, Rajkumar SV, Gertz MA, et al. Treatment of newly diagnosed multiple myeloma based on Mayo Stratification of Myeloma and Risk-adapted Therapy (mSMART): consensus statement. *Mayo Clin Proc*. 2007;82(3):323-341. doi:10.4065/82.3.323

“Quad therapy” for transplant eligible NDMM

GRIFFIN study: Dara-VRd vs VRd in transplant-eligible patients

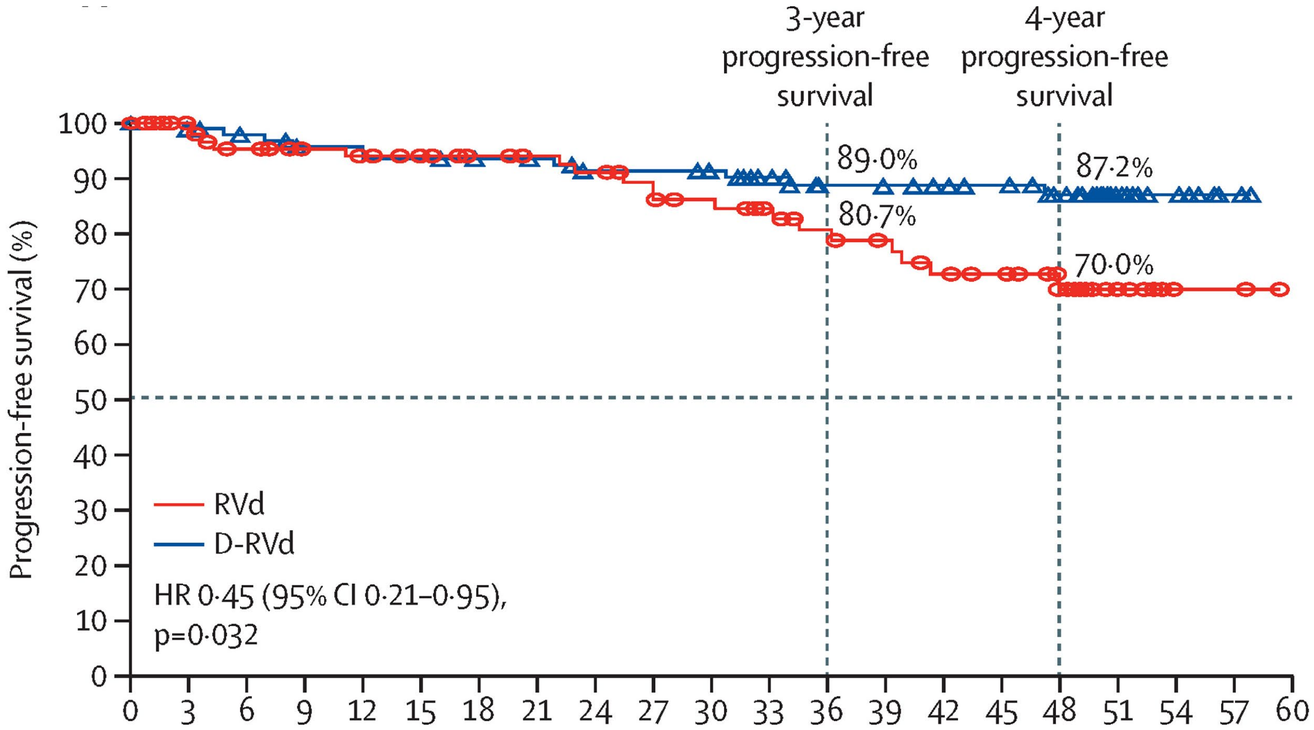
- **Phase 2 trial**, n=207, 14.5% high risk
- **Overall response rate:** 99.0% vs 91.8% (p=0.016)
  - *sCR after ASCT:* 42.4% vs 32% (p=0.068)
  - *MRD negativity:* 51.0% vs 20.4% (p<0.0001)
- **Serious adverse events:** 51.0% vs 39.4%
  - *Grade 3+:* 41.4% vs 21.6%



Voorhees PM, Kaufman JL, Laubach J, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*. 2020;136(8):936-945. doi:10.1182/blood.2020005288

“Quad therapy” for transplant eligible NDMM

GRIFFIN study: Superior PFS in the daratumumab arm



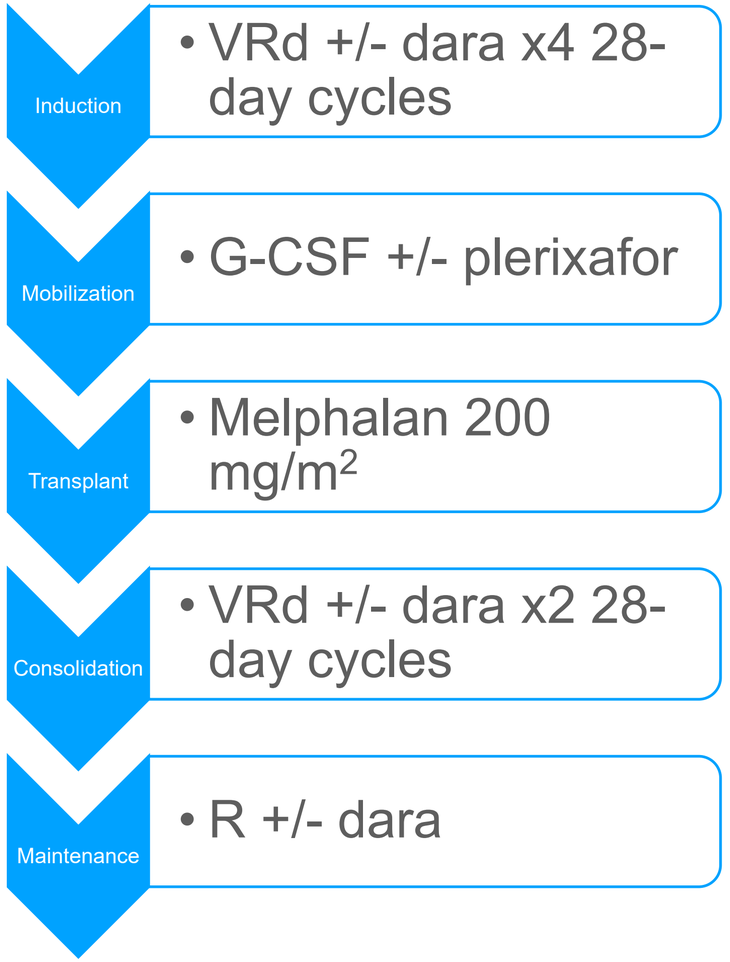
Number at risk (number censored)																					
RVd	103	93	77	72	70	68	63	61	59	53	51	46	42	39	35	33	25	12	3	3	0
	(0)	(9)	(22)	(27)	(28)	(30)	(35)	(37)	(37)	(40)	(42)	(46)	(48)	(50)	(51)	(53)	(60)	(73)	(82)	(82)	(85)
D-RVd	104	98	94	90	90	89	86	85	81	81	79	68	59	58	56	54	45	23	12	3	0
	(0)	(5)	(8)	(10)	(10)	(10)	(12)	(13)	(15)	(15)	(17)	(27)	(35)	(36)	(38)	(40)	(48)	(70)	(81)	(90)	(93)

Voorhees PM, Sborov DW, Laubach J, et al. Addition of daratumumab to lenalidomide, bortezomib, and dexamethasone for transplantation-eligible patients with newly diagnosed multiple myeloma (GRIFFIN): final analysis of an open-label, randomised, phase 2 trial. Lancet Haematol. 2023;10(10):e825-e837. doi:10.1016/S2352-3026(23)00217-X

“Quad therapy” for transplant eligible NDMM

PERSEUS study: Dara-VRd vs VRd in transplant-eligible patients

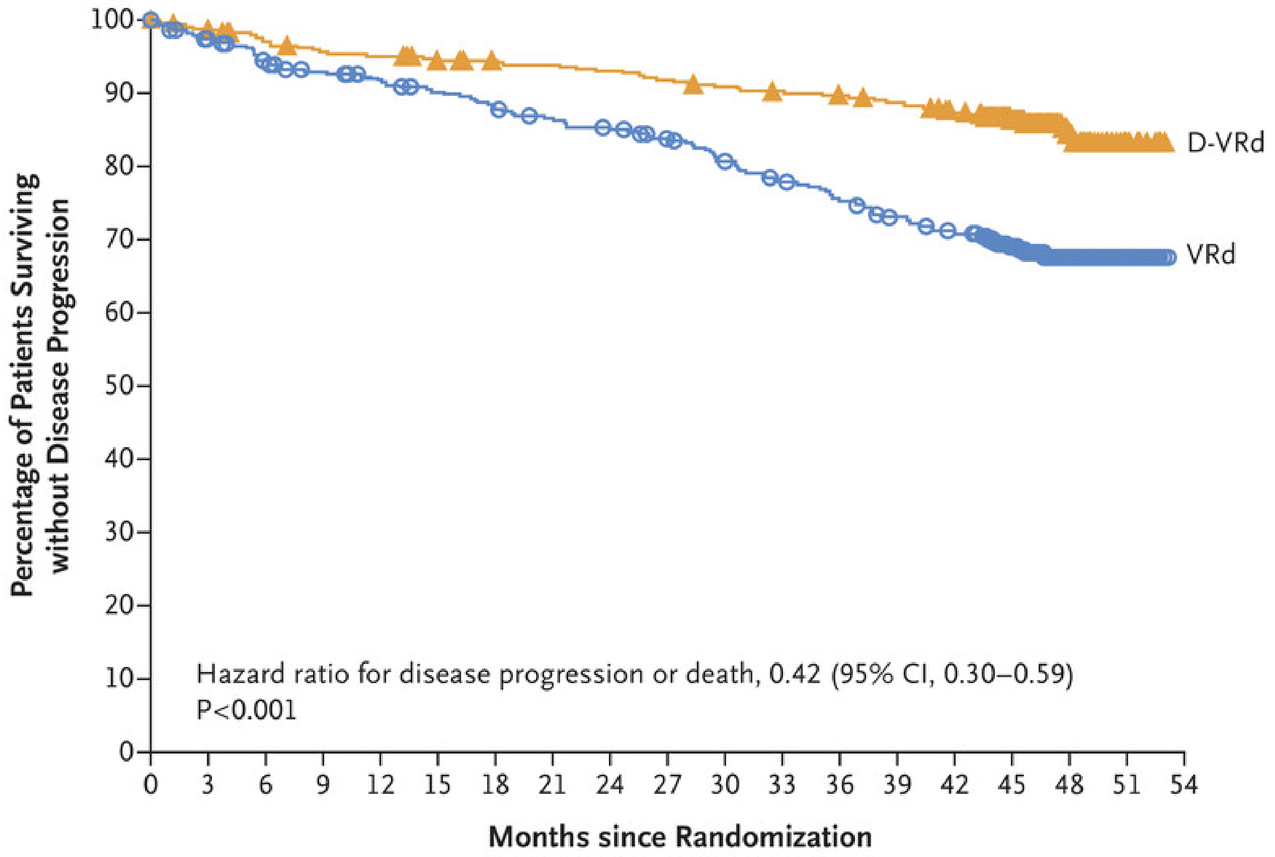
- **Phase 3 trial**, n=709, 21.7% high risk
- **Overall response rate:** 96.6% vs 93.8%
- **CR or better:** 87.9% vs 70.1% (p<0.001)
- **MRD-neg (10^{-5}):** 75.2% vs 47.5% (p<0.001)
- **Serious adverse events:** 57.0% vs 49.3%



Voorhees PM, Kaufman JL, Laubach J, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. *Blood*. 2020;136(8):936-945. doi:10.1182/blood.2020005288

“Quad therapy” for transplant eligible NDMM

PERSEUS study: Superior PFS in the daratumumab arm



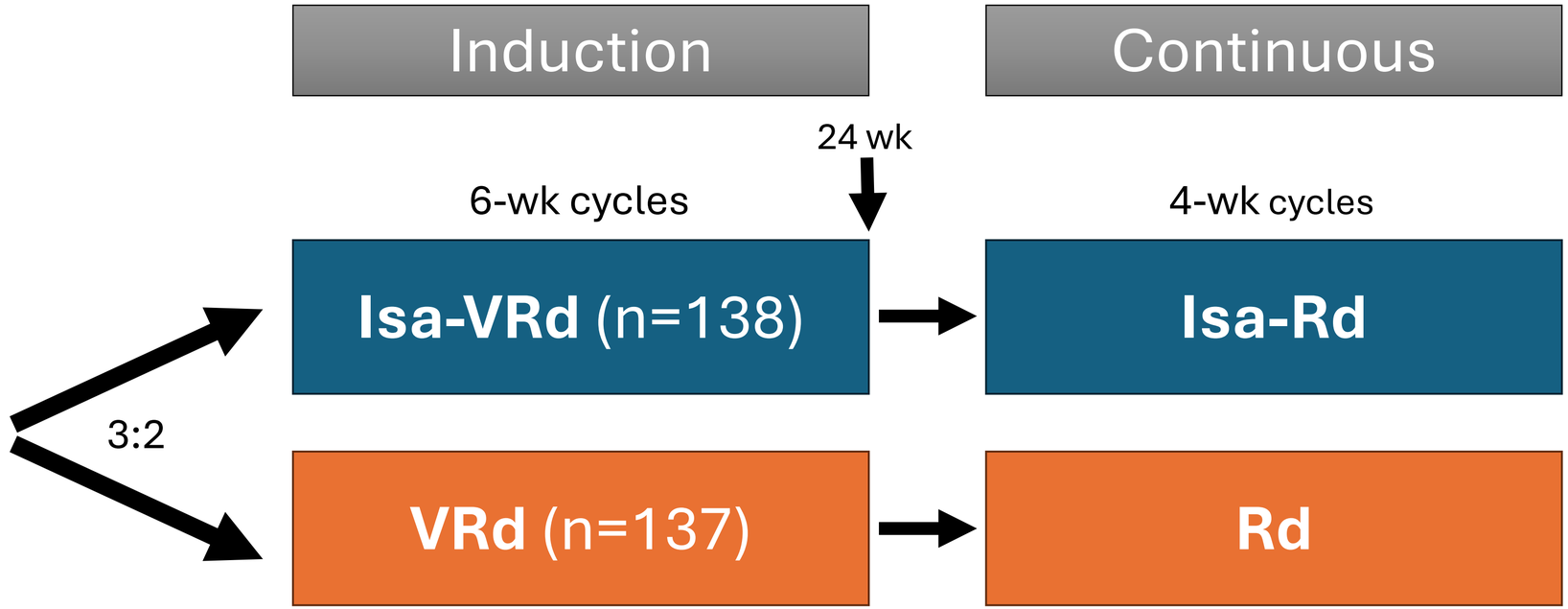
Sonneveld P, Dimopoulos MA, Boccadoro M, et al. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. *N Engl J Med*. 2024;390(4):301-313. doi:10.1056/NEJMoa2312054

“Quad therapy” for transplant *ineligible* NDMM

IMROZ study: Isa-VRd vs VRd in transplant-eligible patients

International, open-label, phase 3 trial
- Median f/u: 59.7 months; data cutoff: March 2019

Patients aged ≥18 yr with symptomatic previously untreated myeloma and measurable disease; ineligible to undergo transplantation due to age ≥65 or coexisting conditions; ECOG PS 0/1

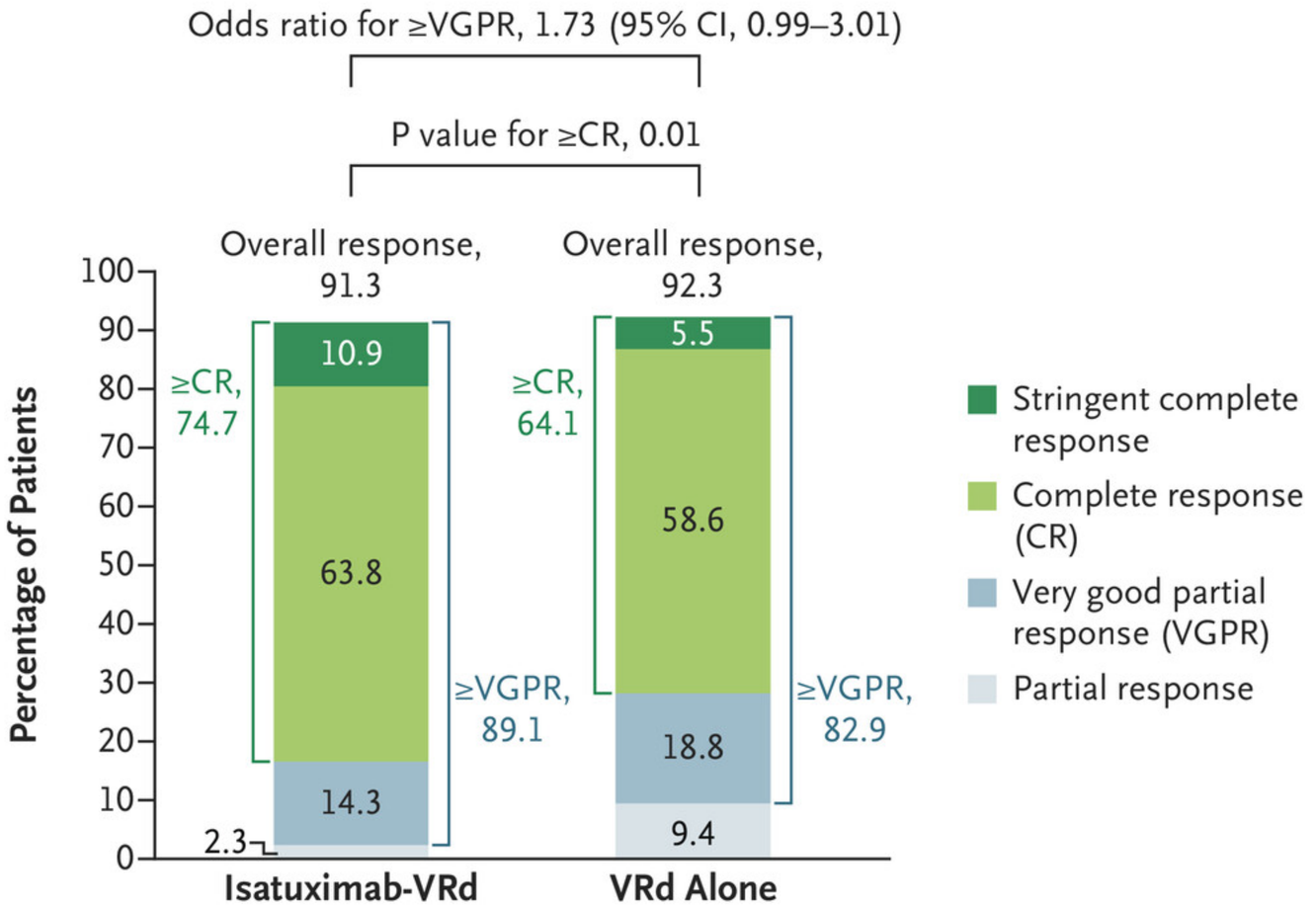


- Primary endpoint: progression-free survival
- Secondary endpoints: CR or better, MRD-neg status

Facon T, Dimopoulos MA, Leleu XP, et al. Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. Published online June 3, 2024. doi:10.1056/NEJMoa2400712

“Quad therapy” for transplant *ineligible* NDMM

IMROZ study: Deeper responses in the ixatuximab arm



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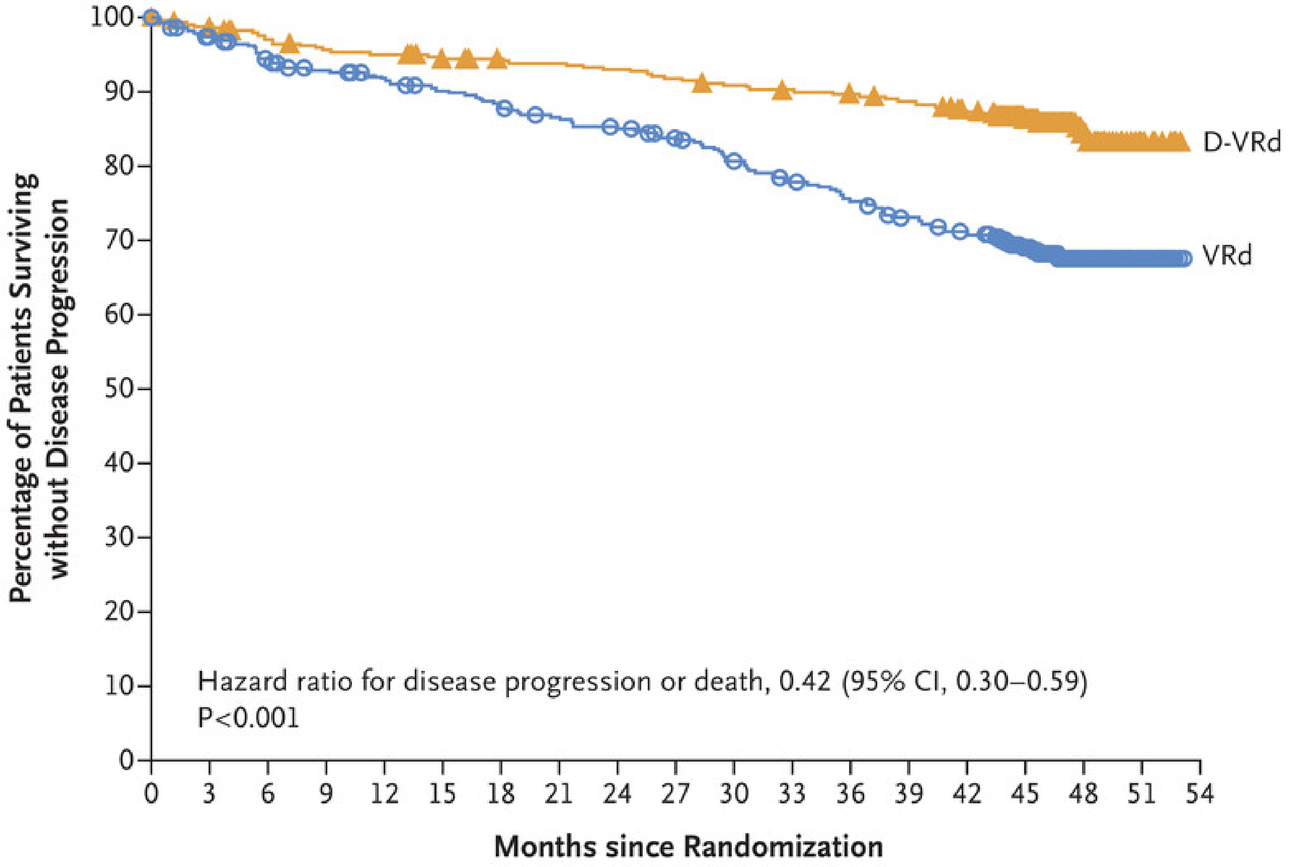
“Quad therapy” for transplant *ineligible* NDMM

IMROZ study: Superior PFS in the ixatuximab arm



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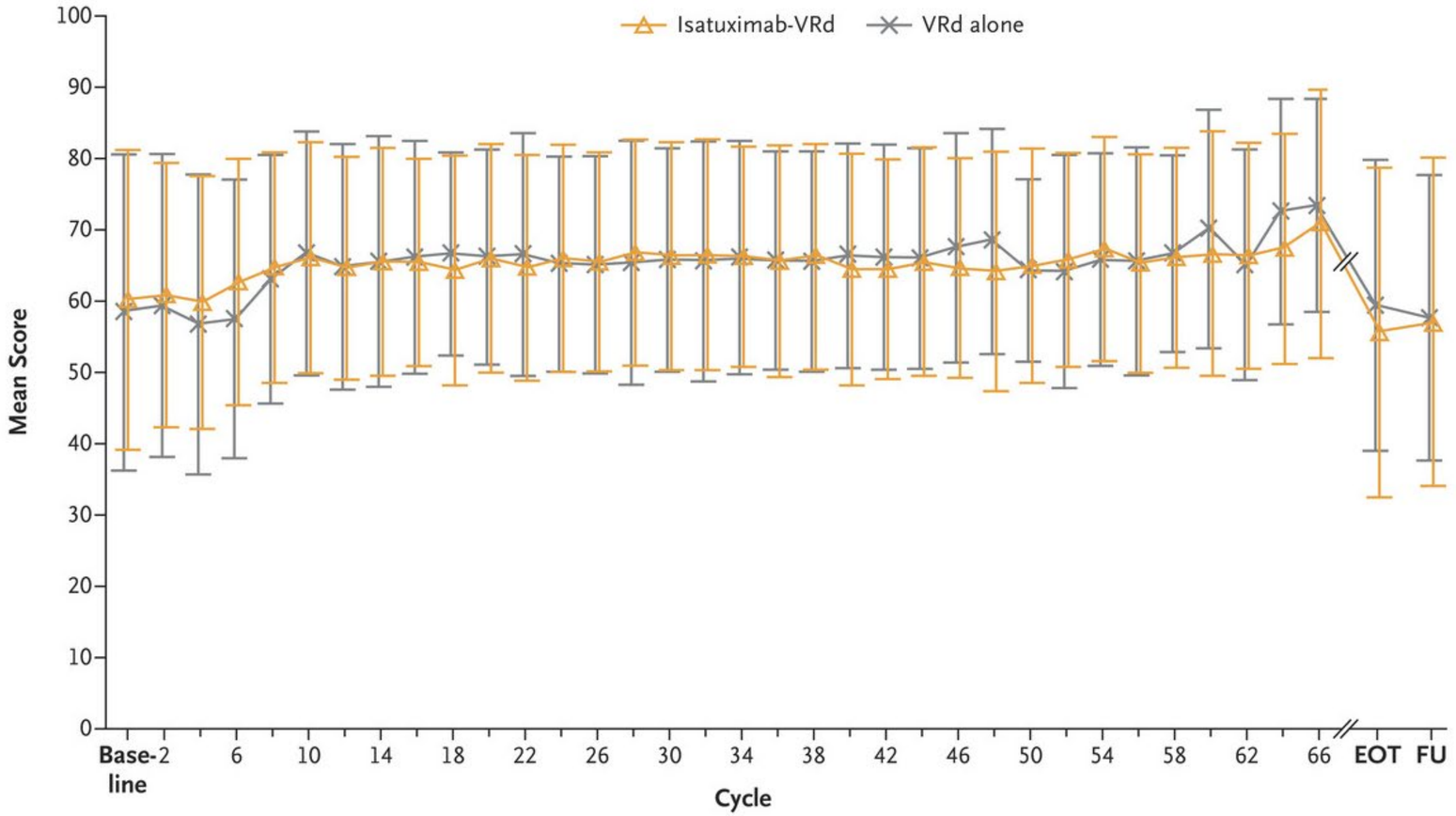
“Quad therapy” for transplant *ineligible* NDMM

IMROZ study: Similar quality of life (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire)



No. of Patients																			
Isatuximab-VRd	243	237	231	221	201	190	190	181	173	162	152	148	140	130	119	90	54	20	81	52
VRd alone	171	159	145	135	121	104	92	87	84	79	72	65	67	56	40	31	16	5	89	44

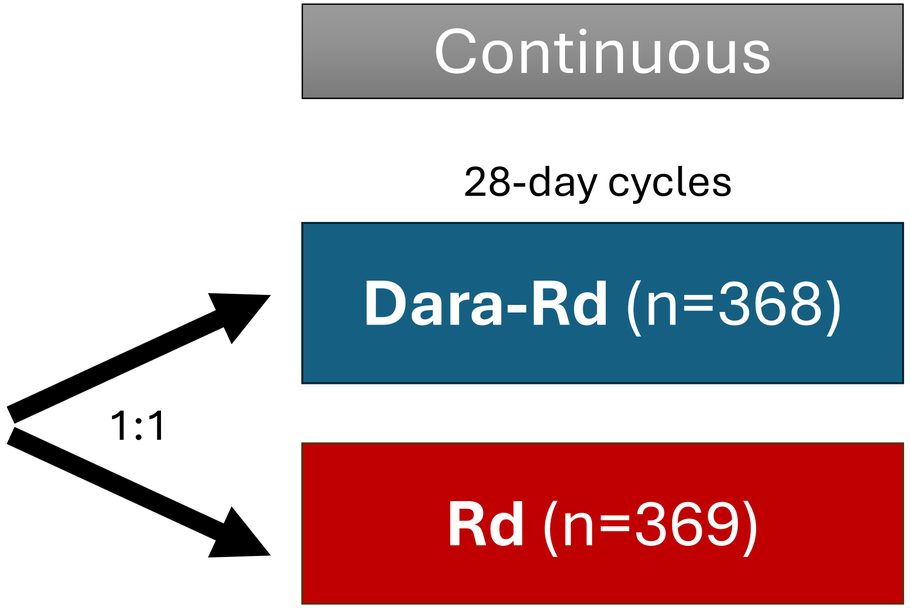
Facon T, Dimopoulos MA, Leleu XP, et al. Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. N Engl J Med. Published online June 3, 2024. doi:10.1056/NEJMoa2400712

“Triplet therapy” for transplant *ineligible* NDMM

MAIA study: Dara-Rd vs Rd in transplant-ineligible patients

International, open-label, phase 3 trial
- Median f/u: 56.2 months; data cutoff: February 2021

Patients aged ≥18 yr with symptomatic previously untreated myeloma; ECOG PS 0-2; ineligible for ASCT due to age (≥65 yrs) or comorbidities



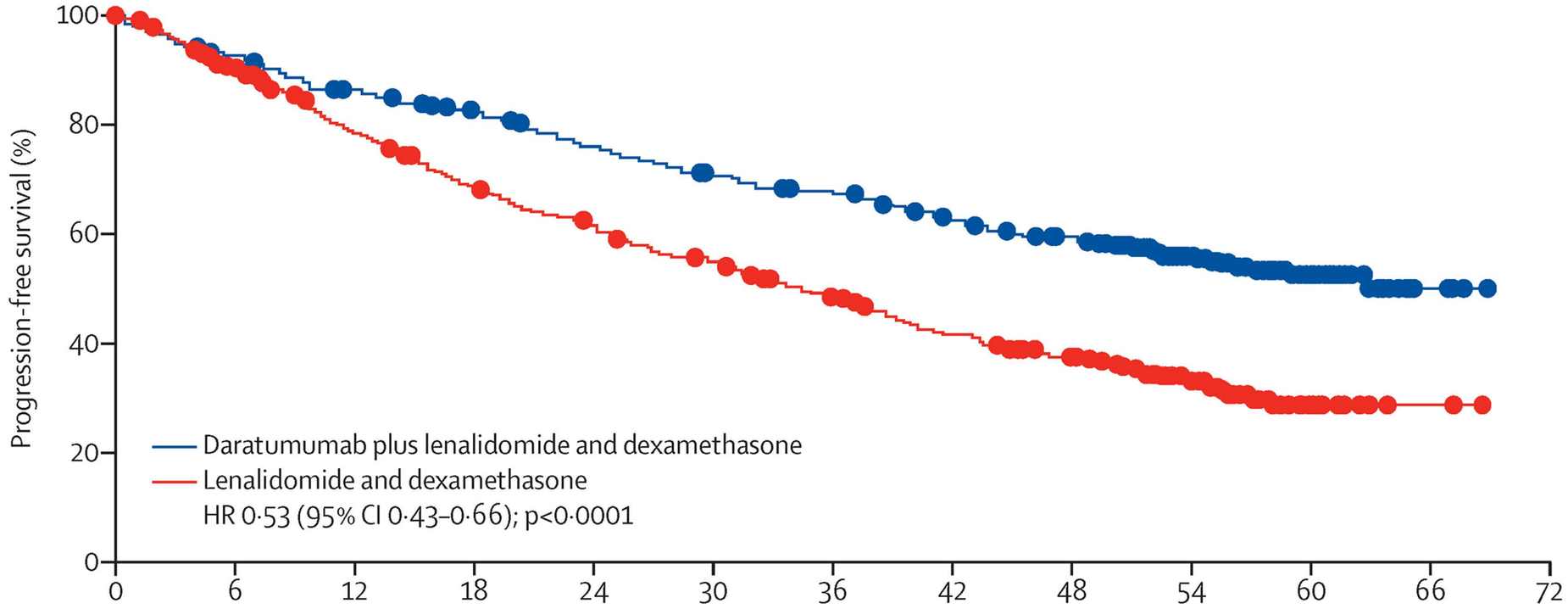
	Dara-Rd	Rd
Median age, yrs	73	74
ECOG 2	17%	16%
HRCA	15%	14%
ISS III	29%	30%

- Primary endpoint: progression-free survival
- Key secondary endpoints: OS, CR and MRD-neg rates, ORR, DOR

Facon T, Kumar SK, Plesner T, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(11):1582-1596. doi:10.1016/S1470-2045(21)00466-6

“Triplet therapy” for transplant *ineligible* NDMM

MAIA study: Superior PFS in the daratumumab arm

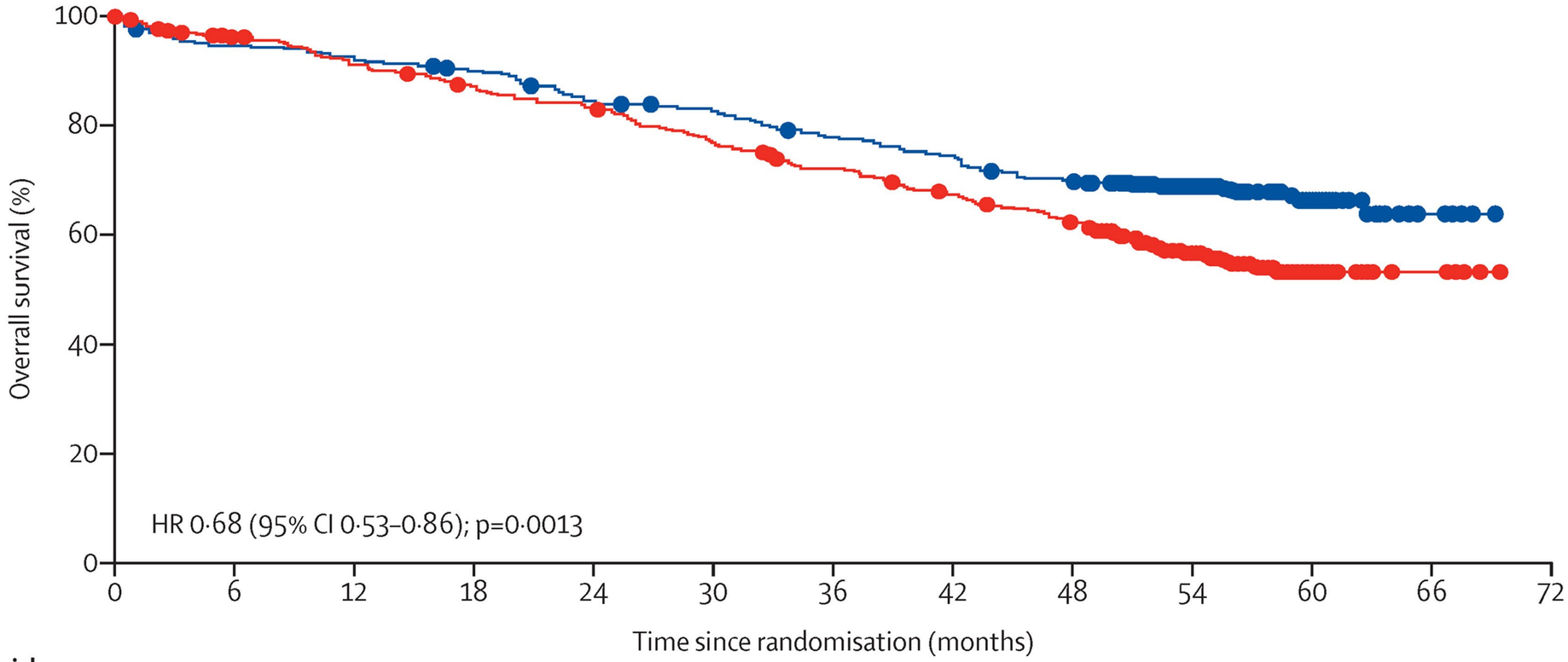


Number at risk (number censored)													
Lenalidomide and dexamethasone	369 (0)	307 (29)	255 (41)	220 (44)	196 (46)	172 (49)	146 (55)	123 (58)	105 (64)	63 (95)	12 (140)	2 (150)	0 (152)
Daratumumab plus lenalidomide and dexamethasone	368 (0)	335 (6)	309 (9)	290 (14)	266 (16)	246 (18)	232 (20)	210 (25)	195 (30)	123 (92)	51 (158)	5 (203)	0 (208)

Facon T, Kumar SK, Plesner T, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(11):1582-1596. doi:10.1016/S1470-2045(21)00466-6

“Triplet therapy” for transplant *ineligible* NDMM

MAIA study: Superior OS in the daratumumab arm



Number at risk (number censored)													
Lenalidomide and dexamethasone	369 (0)	343 (13)	324 (14)	308 (16)	294 (16)	270 (17)	251 (20)	232 (22)	213 (24)	134 (85)	42 (171)	5 (208)	0 (213)
Daratumumab plus lenalidomide and dexamethasone	368 (0)	346 (3)	338 (3)	328 (5)	305 (6)	297 (8)	280 (9)	266 (9)	249 (10)	170 (86)	63 (189)	6 (245)	0 (251)

Facon T, Kumar SK, Plesner T, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(11):1582-1596. doi:10.1016/S1470-2045(21)00466-6

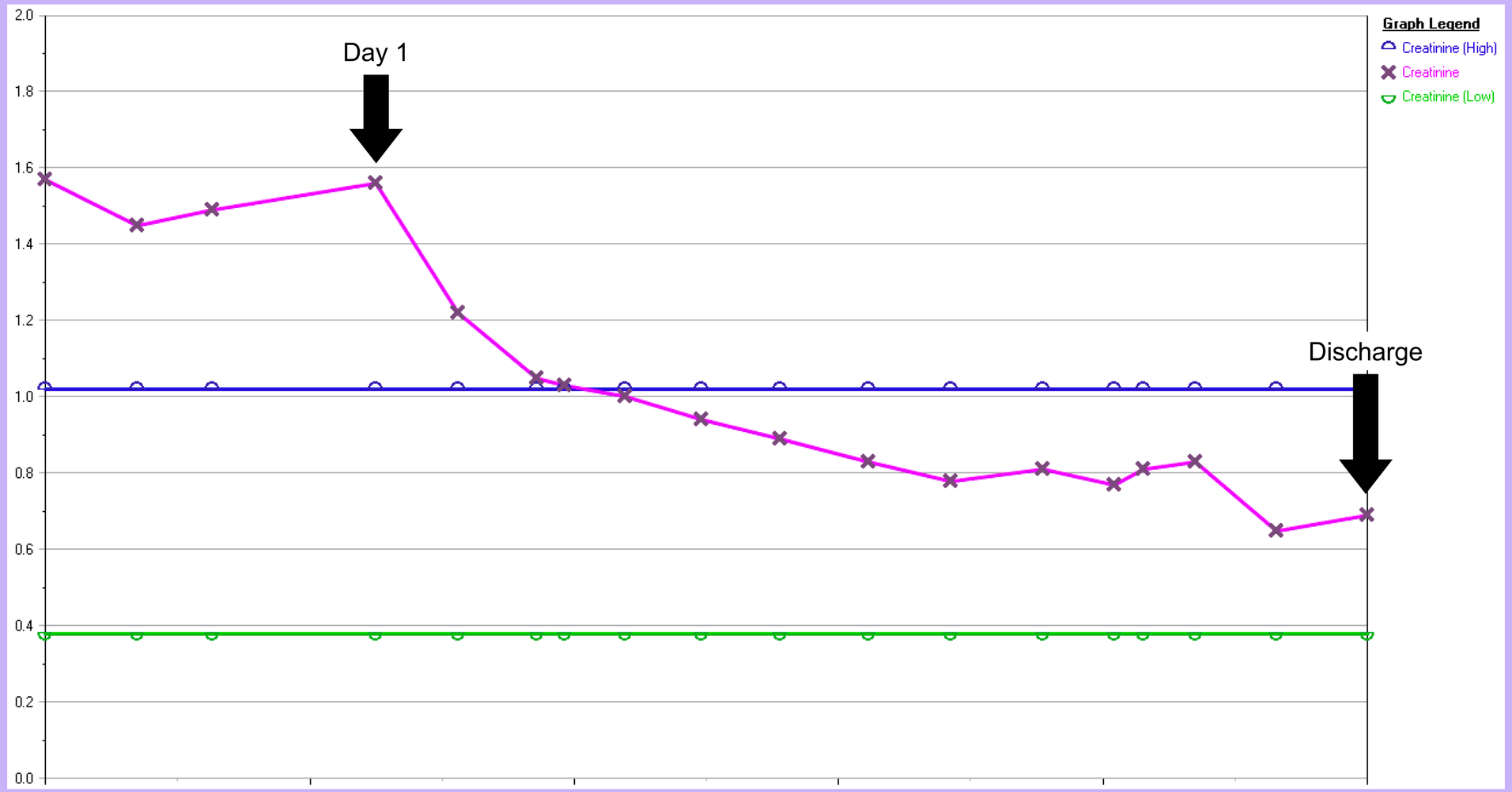
Vignette

A 50-year-old woman with back pain…

- **Hospital course:**
  - Compression fractures deemed non-operative
  - Stuck in the hospital due to poor mobility and pain
  - Started on **CyBorD** (cyclophosphamide, bortezomib, dex)

Vignette

Renal function rapidly improved with treatment



Vignette

Treatment course to date

- Completed induction therapy with **Daratumumab + Velcade / lenalidomide / dex (Dara-VRd) x4 cycles**, achieving a **partial response (50-90% reduction in M-spike)**
  - **M-spike** 6.9 → 3.0 g/dL & **K/L FLC ratio** 152.68 → 82.48
- Not an auto-PBSCT candidate due to lack of caregiver
- Switched to **dara/pom/dex** rather than maintenance due to suboptimal response
  - Now s/p 17 cycles
  - **M-spike** 3.0 → ~1.0 g/dL & **K/L FLC ratio** 82.48 → ~6-7

Newly diagnosed multiple myeloma

Other considerations

- **Bone Disease:** Bone-strengthening treatment (bisphosphonates or denosumab) improves OS[1]
- **VTE ppx:** aspirin 81 mg daily with lenalidomide
- **Viral ppx:** acyclovir 400-800 mg 2x daily with proteasome inhibitors
- **Common toxicities:**
  - Lenalidomide → Fatigue and VTE (consider dose-reduction)
  - Bortezomib → Peripheral neuropathy (consider stopping therapy)
  - Carfilzomib → Heart failure (must stop therapy)

1. Morgan GJ, Davies FE, Gregory WM, et al. Long-term follow-up of MRC Myeloma IX trial: Survival outcomes with bisphosphonate and thalidomide treatment. *Clin Cancer Res*. 2013;19(21):6030-6038. doi:10.1158/1078-0432.CCR-12-3211

Newly diagnosed multiple myeloma

Take home points

- **(Almost) everyone gets a quad (anti-CD38, PI, IMiD, dex [e.g., Dara-VRD])**
  - Regardless of transplant eligibility
- **Replace/hold lenalidomide if renal function is rapidly fluctuating**
  - e.g., CyBorD +/- Dara for 1 cycle if NDMM with acute renal failure
- **Triplet with Dara-Rd reasonable for frail or comorbid patients**
  - Improves OS compared to doublet
- **Everyone gets a bone-strengthening agent (bisphosphonate or denosumab)**
  - Improves OS

Questions

Question #1

A 54yo woman presents for a second opinion. Her prior Onc team recently diagnosed her with MM and are recommending treatment with RVd. Upon reviewing her records, you notice that her hemoglobin, creatinine and calcium are within normal limits. A PET/CT showed no evidence of plasmacytomas or skeletal lesions. Bone marrow biopsy revealed 17% plasma cells with diploid cytogenetics and FISH studies were unrevealing. SPEP with IF reveals an M-protein of 2.5 g/dL IgG kappa and her free kappa/lambda ratio is 50. What is her diagnosis?

A. Multiple myeloma

B. Smoldering myeloma

C. MGUS

D. Waldenstrom’s macroglobulinemia

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A. Multiple myeloma

B. Smoldering myeloma

C. MGUS

D. Waldenstrom's macroglobulinemia

Since she has >10% plasma cells in her BM, she at least has smoldering myeloma and not MGUS. However, there is no evidence of end organ dysfunction, lytic lesions, or other myeloma-defining features (ie, ≥60% plasma cells, free kappa/lambda >100, bone lesions).

Questions

Question #2

A 71yo man has routine yearly labs dran by his PCP. On his CMP, his total protein is 9.8 g/dL and albumin is 3.5 g/dL. Because of this high protein/albumin ratio, an SPEP with IF is ordered, which shows an IgG kappa M-protein of 2.5 g/dL. Free kappa/lambda light chain ratio is 35. A 24 hr urine collection reveals Bence-Jones protein levels of 400 mg/24 hrs.

The patient is referred to see a Hematologist/Oncologist. A bone marrow biopsy is performed and reveals 8% plasma cells and normal cytogenetics. His Hgb, creatinine, calcium, and PET/CT are all normal. What therapy would you offer?

A. Melphalan, bortezomib, prednisone

B. Lenalidomide, bortezomib, dexamethasone

C. Bortezomib and dexamethasone

D. Observation

Questions

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C. Bortezomib and dexamethasone

D. **Observation**

He meets the criteria for MGUS. Observation should be recommended.

MGUS is found in >3% of people who are ≥50 years old. Characterized by presence of M-protein, <10% plasma cells in the BM, and absence of myeloma-defining features. Annual risk of transformation to myeloma is ~1%.

Questions

Question #3

A 68yo man presents with a new diagnosis of myeloma. His creatinine is 3.9 mg/dL, calcium is 9 mg/dL, and Hgb is 9.8 g/dL. Skeletal survey shows lytic lesions throughout his body. SPEP shows an IgG lambda M-protein of 5.2 g/dL and 24 hr UPEP/IF reveals 365 mg of lambda Bence-Jones protein. His serum B2 microglobulin is 5.0 mg/dL.

A bone marrow biopsy shows 65% plasma cells. Cytogenetics/FISH reveals a 13q deletion. LDH is normal. What therapy do you offer?

A. Lenalidomide and dexamethasone

B. Bortezomib and dexamethasone +/- cyclophosphamide

C. Lenalidomide, melphalan, dexamethasone

D. Melphalan, prednisone, thalidomide

Questions

CyBorD is the preferred regimen in the treatment of myeloma patients presenting in renal failure.

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Questions

Question #4

A 76yo woman presents for a 2nd opinion. She was diagnosed with multiple myeloma 2 months prior after routine labs found an acute kidney injury. Serum markers showed an IgA kappa M-spike 1.14 g/dL, kappa FLCs 1,280 mg/dL, lambda FLCs 1.01 mg/dL. CT imaging identified compression deformities at L4 and L2. Bone marrow biopsy showed 80-90% plasma cells. Karyotype is complex. FISH shows t(14;16). Kidney biopsy showed light chain cast nephropathy. She started treatment with CyBorD (cyclophosphamide, bortezomib, dexamethasone) 1 month ago. She walks several miles per day and has no significant comorbidities.

Which of the following would you recommend as first-line therapy?

A. Continue CyBorD (cyclophosphamide, bortezomib, dex)

B. Switch to dara-Rd (daratumumab, lenalidomide, dex)

C. Switch to isa-VRd (isatuximab, bortezomib, lenalidomide, dex)

D. Switch to KRD-PACE (carfilzomib, lenalidomide, dex, cisplatin, doxorubicin, cyclophosphamide, etoposide)

Questions

Question #4

Quad therapy is preferred among transplant ineligible patients with NDMM

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Thank You!