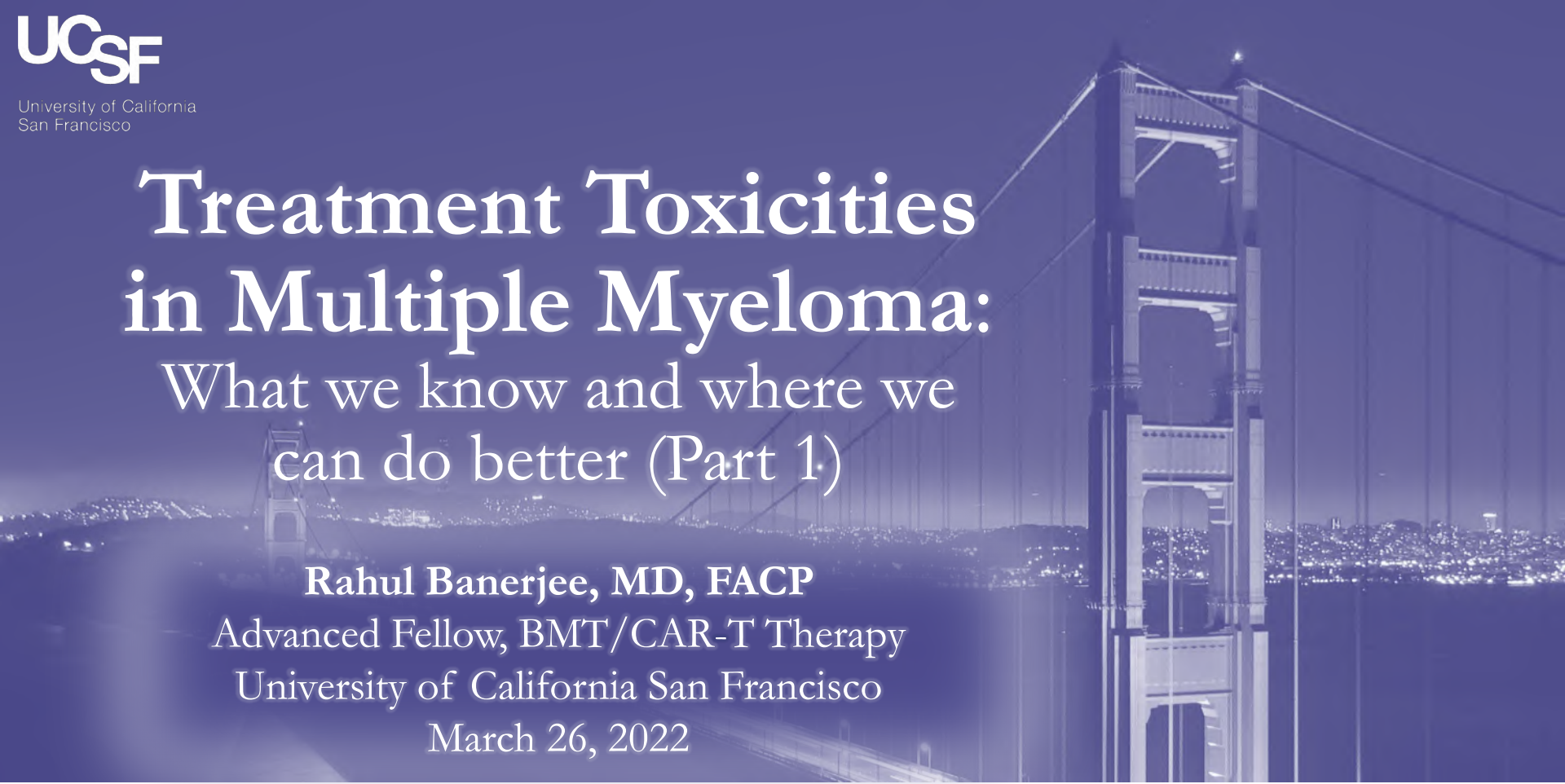

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Treatment Toxicities in Multiple Myeloma:
What we know and where we can do better (Part 1)

Rahul Banerjee, MD, FACP
Advanced Fellow, BMT/CAR-T Therapy
University of California San Francisco
March 26, 2022

Treatment Toxicities in Multiple Myeloma:
What we know and where we can do better (Part 1)

Rahul Banerjee, MD, FACP
Assistant Professor (Medical Oncology)*
University of Washington / SCCA
March 26, 2022

* As of August 2022.

Disclosures

- **Financial:**
  - Consulting: Eradigm Consulting, Guidepoint Global, Sanofi Pasteur, SparkCures; Honoraria: Curio Science; Research funding: Pack Health
- **Personal:**
  - Physicians generally under-quantify patients' symptoms, impairments in quality of life (QOL), levels of physical activity, and more
  - As such: I hope to learn a lot from all of you today!

PMID = Pubmed identification. Can search at pubmed.gov.

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Quinn B, Ludwig H, Bailey A. Pain Manag. 2022; 12(1):59-74. PMID: 34139887.
Schnadig ID, Fromme EK, Loprinzi CL, et al. Cancer. 2008; 113(8): 2205-14. PMID: 18780322.
Abbreviation: QOL, quality of life.

Outline for today's talk

- Complexity of symptom & toxicity management in MM
- Management of treatment-related **fatigue**
- Management of treatment-related **neuropathy**
- Management of treatment-related **'time toxicity'**

Abbreviations: MM, multiple myeloma.

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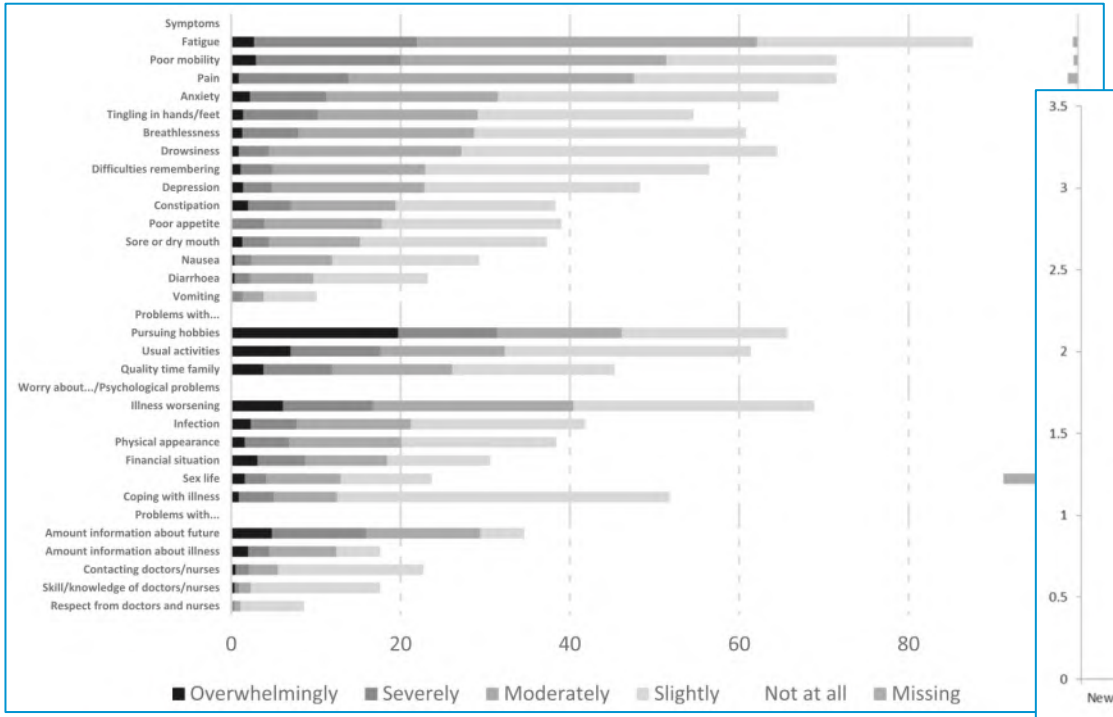
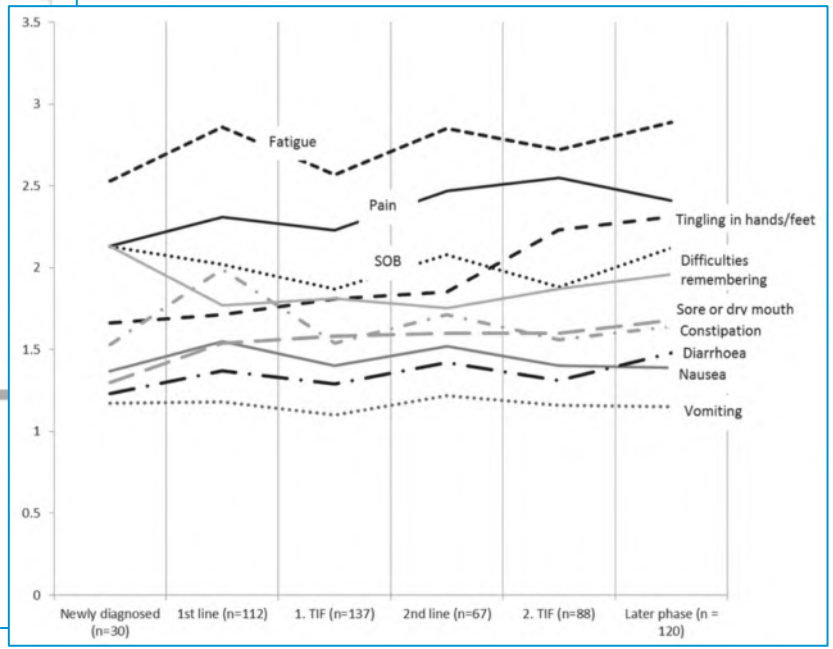
Abbreviations: MM, multiple myeloma.

Common symptoms in MM (abridged)

Symptoms and issues reported by patients with MM



Longitudinal symptom burden



Ramsenthaler C, Osborne TR, Gao W, et al. BMC Cancer. 2016;16:427. PMID: 27387201.

Even if "patient tolerating treatment well"…

Issues reported by patients with MM (0-4 scale)

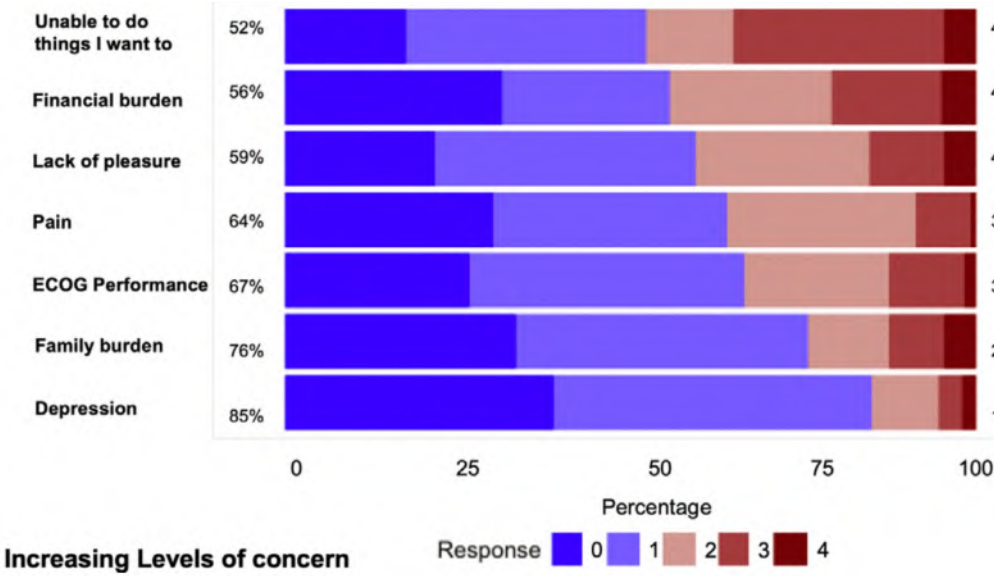


Table 3: Patient-reported financial coping strategies used during multiple myeloma treatment

Strategy	Entire cohort (max n = 100)	COST score < 21 (n = 50)	COST score ≥ 21 (n = 50)	P value
Decrease spending on:				
Food and clothing	55 (55%)	7 (14%)	43 (86%)	<0.001
Leisure activities	63 (64%)	15 (31%)	48 (96%)	<0.001
Use savings for myeloma treatment	43 (46%)	8 (16%)	35 (78%)	<0.001
Borrow money for myeloma treatment	21 (21%)	1 (2%)	20 (41%)	<0.001
Delay starting a myeloma treatment	17 (17%)	3 (6%)	14 (29%)	0.003
Fill part of prescription due to cost:				
Non-cancer medication	16 (16%)	2 (4%)	14 (28%)	0.002
Myeloma therapy	11 (12%)	1 (2%)	10 (21%)	0.01
Stop prescription due to cost:				
Non-cancer medication	11 (11%)	1 (2%)	10 (20%)	0.01
Myeloma therapy	10 (11%)	0	10 (22%)	0.001
Refuse test due to cost	10 (10%)	1 (2%)	9 (18%)	0.02
Skip clinic visit to save on money	6 (6%)	0	6 (12%)	0.03
Apply for financial assistance	36 (36%)	14 (28%)	22 (44%)	0.14
Discuss costs with their oncologist				0.15
Already have or very likely	34 (34%)	13 (26%)	21 (42%)	
Moderately likely to discuss	25 (25%)	12 (24%)	13 (26%)	
Unlikely or would not discuss	41 (41%)	25 (50%)	16 (32%)	
Self-reported level of financial burden				<0.001
Not a financial burden	29 (29%)	24 (49%)	5 (10%)	
Minor financial burden	34 (34%)	22 (45%)	12 (24%)	
Moderate financial burden	17 (17%)	3 (6%)	14 (28%)	
Significant financial burden	19 (19%)	0	19 (38%)	
Patient view of treatment costs				0.001
Lower than expected	4 (4%)	4 (8%)	0	
As expected	37 (37%)	25 (50%)	12 (24%)	
Higher than expected	59 (59%)	21 (42%)	38 (76%)	

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Richter J, Sanchez L, Biran N. CLML. 2021;21(3):e284-e289. PMID: 33358693.
Huntington SF, Weiss BM, Vogl DT, et al. JCO. 2015;33(suppl):6600. [#ASCO15 poster.]

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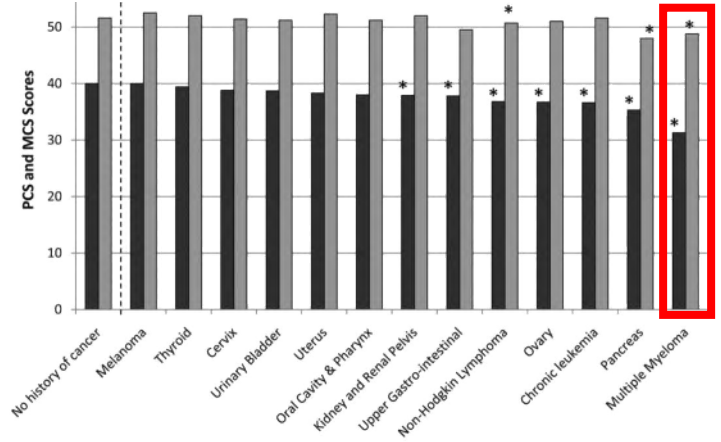
Consequences of symptoms in MM

- Symptoms and toxicities drive worsened QOL (quality of life)
  - QOL worse with patients with MM than with other types of cancer
- More symptoms mean more Emergency Dept (ED) visits

QOL in ambulatory patients with cancer



Symptom score in MM and risk of ED visits

Individual Symptom ESAS Scores (0-10)	0	1	2	3	4	5	6	7	8	9	10
Pain	8%	7%	10%	11%	12%	15%	15%	17%	23%	29%	36%
Tiredness	6%	6%	7%	9%	10%	14%	14%	16%	22%	23%	41%
Drowsiness	8%	9%	9%	11%	14%	13%	17%	20%	24%	26%	45%
Nausea	10%	11%	11%	17%	16%	20%	22%	29%	23%	25%	23%
Lack of appetite	7%	9%	11%	12%	13%	14%	17%	18%	23%	32%	40%
Shortness of breath	8%	9%	9%	12%	15%	19%	18%	20%	26%	25%	37%
Anxiety	9%	9%	10%	12%	13%	17%	16%	18%	22%	23%	31%
Depression	9%	11%	11%	19%	16%	16%	15%	17%	19%	19%	34%
Well-being	7%	5%	8%	11%	12%	13%	18%	17%	25%	25%	50%
Total ESAS score (0-90)	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	**71-80**	**81-90**		
t-ESAS	5%	8%	11%	14%	17%	24%	22%	34%	31%		

*Note higher numerical ESAS score is indicative of worse symptoms compared to a lower score.

Proportion of patients in the cohort who presented to the emergency department/hospitalization within 14 days following symptom assessm
the ESAS score*.

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Kent EE, Ambs A, Mitchell SA et al. Cancer. 2015; 121(5):758-65. PMID: 25369293.
Mian H, Sutradhar R, Pond GR, et al. Blood Cancer J. 2022;12(1):17. PMID: 35087029.
Abbreviations: ED, Emergency Department; QOL, quality of life.

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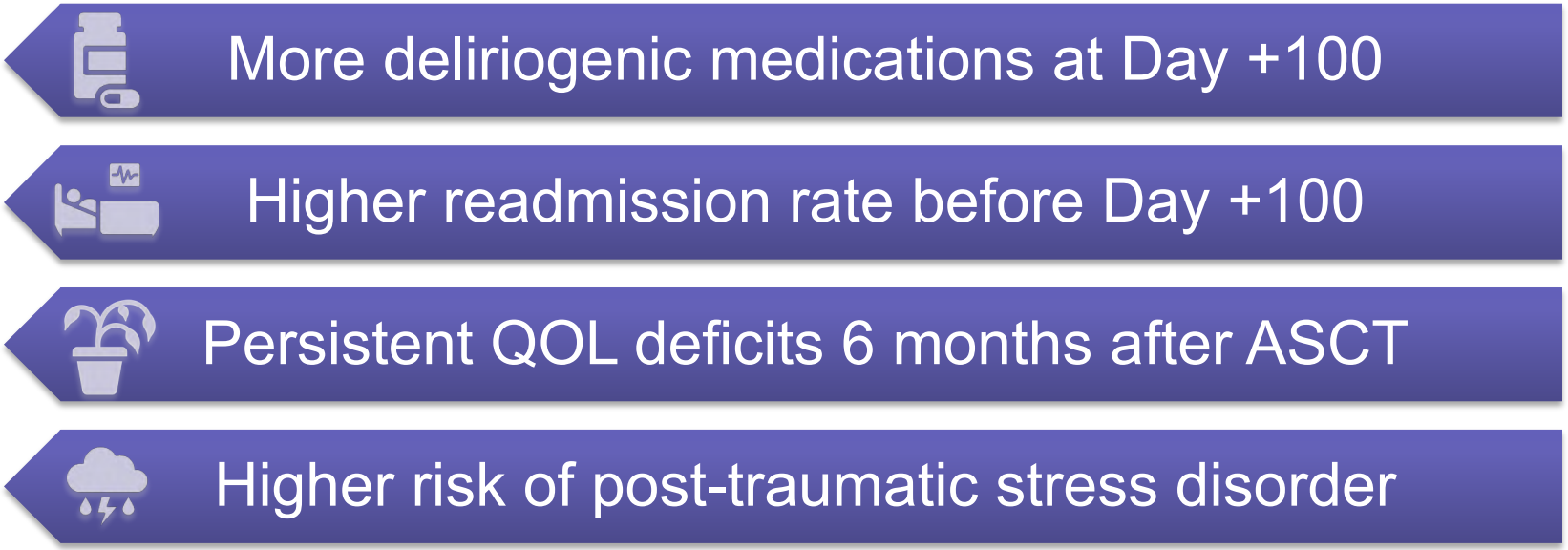
Even ‘temporary’ symptoms matter in MM

- Selected long-term consequences of the expected short-term rise in anxiety after stem cell transplantation in MM



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Banerjee R, Lazar AA, Dunn L et al. ejHaem (British Society for Haematology). 2021. 2(2):276-279.
Johnson PC, Bhatt S, Reynolds MJ, et al. Johnson PC et al. TCT. 2021;27(6):496.e1-496.e5. PMID: 33789836.
El-Jawahri AR, Vandusen HB, Traeger LN et al. Cancer. 2016;122(5):806-812. PMID: 26650840.
Griffith S, Fenech AL, Nelson A, et al. Griffith S et al. JCO. 2020;38(15_suppl):7505.

Are symptoms from MM or treatment?

- Very difficult to say unless clear temporal trends
- Examples from ED-provoking symptoms* in prior study:

Symptom	MM-related cause	Tx-related cause
Painful neuropathy	Amyloidosis	PIs (proteasome inhibitors) or IMIDs (immunomodulatory drugs)
Fatigue	Anemia	IMIDs, dexamethasone
Insomnia	Pain & distress	Dexamethasone
Shortness of breath	Anemia, rib fractures	Carfilzomib-induced cardiac dysfunction

*Mian H, Sutradhar R, Pond GR, et al. Blood Cancer J. 2022;12(1):17. PMID: 35087029.
Abbreviations: PI, proteasome inhibitors; IMIDs, immunomodulatory drugs.

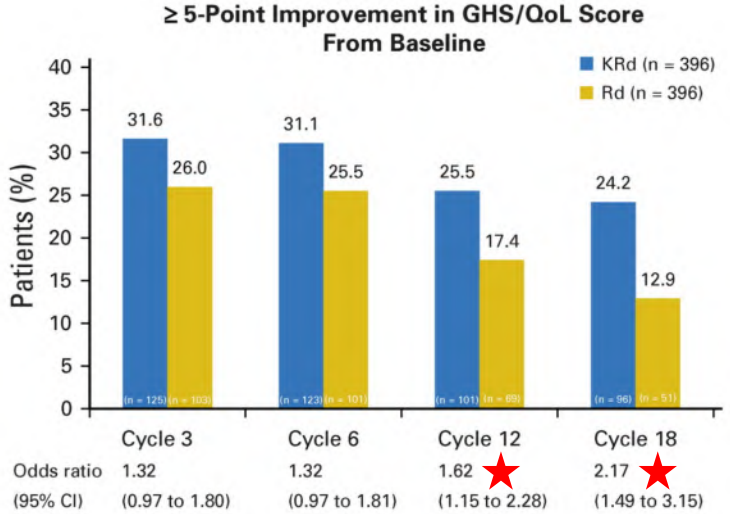
Does ↑Tx intensity always mean ↓QOL?

- Sometimes (e.g., short-term after transplant), but not always
- Two examples of triplets outperforming doublets for QOL:

MAIA trial of Dara-Rd versus Rd

	Improvement		
PRO	Rd	D-Rd	OR[a] (95% CI)
EQ-5D-5L			
VAS	50.4	54.3	1.17 (0.88 to 1.56)
Global health status/QoL			
Global health status	48.5	52.7	1.18 (0.89 to 1.58)
Functional scales			
Physical functioning	40.9	49.7	1.43 (1.07 to 1.91)
Role functioning	45.5	52.7	1.33 (1.00 to 1.78)
Emotional functioning	42.5	47.0	1.20 (0.90 to 1.60)
Cognitive functioning	34.4	36.1	1.08 (0.80 to 1.46)
Social functioning	38.5	45.4	1.33 (0.99 to 1.78)
Symptom scales			
Fatigue	52.0	62.2	1.52 (1.13 to 2.04)
Nausea and vomiting	18.2	18.8	1.04 (0.72 to 1.51)
Pain	59.6	65.2	1.27 (0.94 to 1.71)

ASPIRE trial of KRd versus Rd



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Perrot A, Facon T, Plesner T, et al. JCO. 39(3):227-237. PMID: 33326255.
Stewart AK, Dimopoulos MA, Masszi T, et al. JCO. 2016;34(32):3921-3930. PMID: 27601539.
Abbreviations: Dara-Rd, daratumumab, lenalidomide, dexamethasone; GHS, global health score; KRd, carfilzomib, lenalidomide, dexamethasone; Rd, lenalidomide, dexamethasone; Sx, symptoms; Tx, treatment.

Outline for today's talk

- Complexity of symptom & toxicity management in MM
- **Management of treatment-related fatigue**
- Management of treatment-related **neuropathy**
- Management of treatment-related **'time toxicity'**

Abbreviations: MM, multiple myeloma.

Cancer-related fatigue: what we know

- One of the most common symptoms (and determinants of QOL) across studies of patients with cancer
- Unique biochemical and symptomatic features:
  - Likely related to inflammation & meds (less likely infections)
  - More long-lasting and less likely to be relieved by sleep
- Other contributors:
  - Specific toxicities, e.g. anemia and impaired nutrition
  - Broader issues, e.g. emotional distress and time toxicity

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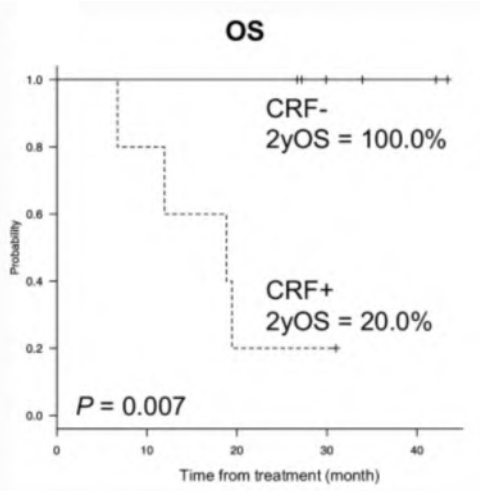
Rogers W, Rennoldson M. Cancer Nurs. 2020;43(3):E121-E131. PMID: 32108706.
Catamero D, Noonan K, Richards T, et al. Clin J Onc Nurs. 2017;21(5 Suppl):7-18. PMID: 28945731.
Suzuki K, Kobayashi N, Ogasawara Y, et al. Int J Hematol. 2018;108(6):580-587. PMID: 30155589.

Myeloma-related fatigue: why it matters

- Significant predictor of ED visits in newly diagnosed MM even after adjusting for pain, anemia, and treatment
- Major driver of why patients don't return to work after diagnosis (e.g., 70% of patients after transplant)
- In one study, 2-year survival in MM was 100% in patients without fatigue, versus 0% in patients with cancer-related fatigue
  - ⚠ Many confounders here



Mian H, Sutradhar R, Pond GR, et al. Blood Cancer J. 2022;12(1):17. PMID: 35087029.
Bennink C, van der Klift M, Scheurer H. Eur J Cancer Care. 2021;30(6):e13481. 34152665.
Granell M, Senín A, Barata A. Bone Marrow Transplant. 2021;56(12):2904-2910. PMID: 34404917.
Suzuki K, Kobayashi N, Ogasawara Y, et al. Int J Hematol. 2018;108(6):580-587. PMID: 30155589.

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Myeloma-related fatigue: what we know

- Multifactorial symptom requires multifactorial solutions.

Step	Notes
Optimizing care	Hemoglobin goal 8, nephrology referral, etc.
Adjusting MM meds	See next slides
New non-MM meds	Modafinil only for severe fatigue
New supplements	? Ginseng (no myeloma-specific data)
Exercise	? Most helpful in patients with baseline fatigue
Acupuncture	Fairly robust evidence base across oncology
Psychotherapy or life coaching	Cognitive behavioral therapy: Lots of evidence Life coaching: Trial coming to UW/SCCA!

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Rogers W, Rennoldson M. Cancer Nurs. 2020;43(3):E121-E131. PMID: 32108706.
Koutoukidis DA, Land J, Hackshaw A. Br J Cancer. 2020;123(2):187-195. PMID: 32435057.
Sadeghian M, Rahmani S, Zendehdel M, et al. Nutr Cancer. 2021;73(8):1270-1281. PMID: 32691627.
Abbreviations: CBT, cognitive-behavioral therapy.

IMID-related fatigue: what we know

- IMIDs = thalidomide, lenalidomide, or pomalidomide
- Generally the most common non-🩸 adverse event in trials of lenalidomide or pomalidomide (~40-50% of patients)
  - Depending on trial, 0-10% incidence of Grade 3 fatigue (unable to take care of 'activities of daily living' like eating or walking)
- **No great data for a dose-toxicity curve** for fatigue or QOL*
  - In other words, unclear if lenalidomide 25mg → 5mg daily or pomalidomide 4mg → 3mg daily makes a difference

Note: There is definitely an impact of IMID dose intensity on cytopenias.

Richardson PG, Siegel D, Baz R, et al. Blood. 2013;121(11):1961-1967. PMID: 23243282.
Fenk R, Giagounidis A, Goldschmidt H, et al. Clin Cancer Res. 2020; 26(22):5879-5886. PMID: 32817078.

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IMID-related fatigue: what we don't know

- **Does taking the IMID in the evenings help?** Worth a shot.
- **If ↓ IMID dose doesn't help, what about spacing out doses?**
  - For patients with Grade 3+ toxicities or renal issues, lenalidomide 25mg every other day has comparable efficacy
- **Or how about on/on/off instead of on/on/on/off weeks?**
  - No good data – but VRD21 (lenalidomide for 14/21 days) has better stem cell yields than VRD28 (len for 21/28 days)
  - Brief "IMID holidays" are probably fine, even if not studied

Merz M, Dechow T, Scheytt M, et al. Ann Hematol. 2020; 99(8):1709-1725. PMID: 32296915.
Cerchione C, Nappi D, Pareto AE. Anticancer Drugs. 2018;29(4):371-372. PMID: 29420336.
Popat R, Khan I, Dickson J. Br J Haematol. 168(1):148-151. PMID: 25103844.
Bal S, Landau HJ, Shah GL. BBMT. 2020;26(8):1394-1401. PMID: 32442725.

Can 'next-gen IMIDs' bypass these toxicities?

- CELMoDs (cerebron E3 ligase modulators) pills, such as CC-92480 and iberdomide, may replace IMIDs some day…

TEAEs of interest,[a] n (%)	Cohort D IBER + DEX (N = 107)		
	All grade	Grade 3	Grade 4
Hematologic TEAEs			
Neutropenia	64 (59.8)	27 (25.2)	21 (19.6)
Febrile neutropenia	5 (4.7)	4 (3.7)	1 (0.9)
Anemia	44 (41.1)	30 (28.0)	0
Thrombocytopenia	38 (35.5)	7 (6.5)	16 (15.0)
Leukopenia	30 (28.0)	11 (10.3)	11 (10.3)
Non-hematologic TEAEs			
Fatigue	25 (23.4)	2 (1.9)	1 (0.9)
Diarrhea	25 (23.4)	1 (0.9)	0
Constipation	23 (21.5)	0	0
Rash[b]	21 (19.6)	3 (2.8)	0
Infections	62 (57.9)	26 (24.3)	3 (2.8)
Pneumonia[c]	13 (12.1)	9 (8.4)	0
COVID-19[d]	10 (9.3)	5 (4.7)	2 (1.9)

Van de Donk NW, Popat R, Larsen J, et al. Blood (2020) 136 (Suppl_1):16-17. [#ASH21 poster]

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What about steroid-related fatigue?

- Dexamethasone (dex) causes fatigue in many ways: physiologic stress, insomnia, and more.
- On average, patients with MM sleep **81 fewer minutes** on dex days than other days.

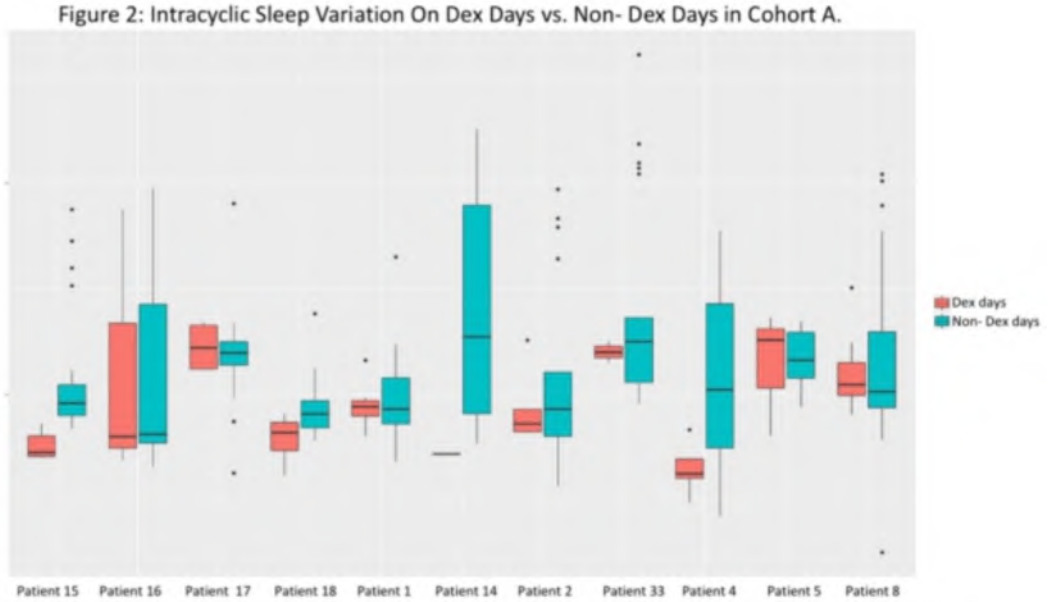

Figure 2: Difference in sleep on dex days compared to all other days during the sample cycle period for cohort A was 81.4 min/24 hr (p = 0.004, 95% CI 26, 135), indicating a significant decrease in intracyclic sleep variation on dex days vs. non- dex days. For Cohort B, the difference in sleep was 37.4 min/24 hr (p=0.35, 95% CI -41, 115), indicating no significant difference in intracyclic sleep variation on dex vs. non-dex days.

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Rogers W, Rennoldson M. Cancer Nurs. 2020;43(3):E121-E131. PMID: 32108706.
Hevroni G, Mastey D, Tavitian E, et al. JCO. 2021;39(15_suppl):8040. [#ASCO21 poster].

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Does everyone need dex 40mg weekly?

- **Steroid-related fatigue is definitely dose-dependent:**
  - Rd with dex 40mg once weekly *versus* 40mg 12/28 days:
    Grade 3+ fatigue 9% vs 15%. (Weekly dex also better survival).
  - Rd x9 cycles → R *versus* Rd continuously in pts aged >65:
    Grade 3+ fatigue 2% vs 7%. (No difference in survival).
- **Dex 40 → 20mg recommended only if age ≥75. My takes:**
  - Dex ≥12mg weekly might be okay if dex 40mg not tolerated
  - Can try dex 20mg twice-weekly to minimize 'withdrawal' effects
  - Can try methylpred instead of dex (shorter half-life)

Rajkumar SV, Jacobus S, Callander NS, et al. Lancet Oncol. 2010;11(1):29-37. PMID: 19853510.
Larocca A, Bonello F, Gaidano G, et al. Blood. 2021;137(22):3027-3036. PMID: 33739404.
Abbreviations: dex, dexamethasone; methylpred; methylprednisolone.

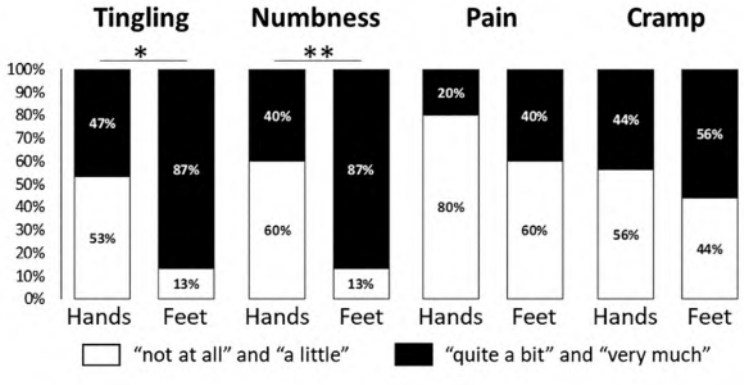
Outline for today's talk

- Complexity of symptom & toxicity management in MM
- Management of treatment-related **fatigue**
- **Management of treatment-related neuropathy**
- Management of treatment-related **'time toxicity'**

Abbreviations: MM, multiple myeloma.

Treatment-related neuropathy in MM

- **Most common offenders:**
  1. PIs: Bortezomib (~30%) more than carfilzomib (~5%)
  2. IMIDs: Thalidomide (~25%) more than lenalidomide (~5%)
- **Manifestations:** most commonly abnormal tingling in legs



> Leuk Lymphoma. 2022 Mar;63(3):722-728. doi: 10.1080/10428194.2021.1992758. Epub 2021 Oct 26.

Foot drop in patients treated with bortezomib – a case series and review of the literature

Iuliana Vaxman [1 2 3], Michelle L Mauerman [4], Moshe L Gatt [5], Tamar Berger [2 3], Morie A Gertz [1]

Affiliations + expand

PMID: 34702127 DOI: 10.1080/10428194.2021.1992758

Richardson PG, Delforge M, Beksac M, et al. Leukemia. 2012;26:595-608. PMID: 22193964.
LeBlanc R, Bergstrom DJ, Côté J, et al. CLML. 2021;22(1):e41-e56. PMID: 34456159.
Selvy M, Kerckhove N, Pereira P, et al. Front Pharmacol. 2021;12. PMID: 33967771.

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Bortezomib-related neuropathy in MM

- **Established risk factors:**
  1. Pre-existing peripheral neuropathy from another cause
  2. Specific gene or non-coding mutations
  3. [In most studies] Twice-weekly vs once-weekly bortezomib
- **Established non-risk factors:**
  1. Peripheral neuropathy from AL amyloidosis
  2. Pre-existing diabetes, either by history or hemoglobin A1C
  3. Age (although possibly related to thalidomide-related neuropathy)

Richardson PG, Delforge M, Beksac M, et al. Leukemia. 2012;26:595-608. PMID: 22193964.
LeBlanc R, Bergstrom DJ, Côté J, et al. CLML. 2021;22(1):e41-e56. PMID: 34456159.

Managing bortezomib-related neuropathy

- **What we know about bortezomib-related neuropathy:**
  - Some evidence of a dose-toxicity curve (so ↓ dose might help)
  - Consider lowering dose of concurrent IMID as well
  - Less 'cross-reactivity' if switched to carfilzomib
    - Still happens with ixazomib, but we don't really use this anymore
- **How we generally treat bortezomib-related neuropathy:**
  - Nerve-specific Rx: gabapentin (Neurontin®), pregabalin (Lyrica®)
  - Other pain medications: narcotics or acetaminophen

Richardson PG, Delforge M, Beksac M, et al. Leukemia. 2012;26:595-608. PMID: 22193964.
LeBlanc R, Bergstrom DJ, Côté J, et al. CLML. 2021;22(1):e41-e56. PMID: 34456159.

Other options for bortezomib neuropathy

- **Other oral medications**:
  - Antidepressants, e.g. duloxetine (Cymbalta®) / amitryptaline (Elavil®)
- **Topical medications**, e.g. lidocaine, menthol, CBD [cannabis]
- **Integrative medicine**, e.g. acupuncture
- **Electrical devices:** *(e.g., TENS = transcutaneous electrical nerve stimulation)*
  - TENS unit: Patient-applied, readily available, worth a try
  - Scrambler unit (Calmare®): Provider-applied. Probably better efficacy than TENS, but I'm not sure if anyone offers this in Seattle.

Richardson PG, Delforge M, Beksac M, et al. Leukemia. 2012;26:595-608. PMID: 22193964.
LeBlanc R, Bergstrom DJ, Côté J, et al. CLML. 2021;22(1):e41-e56. PMID: 34456159.
Miceli TS, Gonzalves WI, Buadi FK. Cancer Treat Res Comm. 2021;29:100476. PMID: 34653748.
Abbreviations: CBD, cannabidiol; TENS, transcutaneous electrical nerve stimulation.

What about vitamins and neuropathy?

- Lots of no-evidence or weak-evidence statements, but reasonable to try vitamins or supplements if safe and affordable

Prophylaxis

On the basis of trials and anecdotal evidence in MM, potential PN prophylaxis in MM patients could include: vitamin supplements, including multi-B complex with B1, B6 and B12, folic acid and vitamin E; magnesium supplement; increased dietary potassium intake; amino acid supplements, fish oils, omega-3 fatty acids, evening primrose oil, and flax seed oil; medications as indicated, including gabapentin, pregabalin, amitriptyline and duloxetine; and topical creams such as cocoa butter.[5] Daily vitamins, gabapentin and nortryptiline have been combined in a step-wise cocktail for frontline MM patients experiencing grade ⩾1 PN or neuropathic pain treated at the Dana–Farber Cancer Institute (Supplementary Table 2).[5] There remains a need for prospective evaluation of the effects of these interventions in the prevention of PN specifically associated with different MM therapies. Additionally, neuro-rehabilitation through physical and occupational therapy might be considered for prospective evaluation in patients developing TiPN or BiPN.

Supplementary Table 2. Potential supplemental interventions used at DFCI

Supplement	Dose
Multi B-complex vitamins	Approximately 50 mg/day with B1, B6, B12, folic acid, and other B6, not to exceed 100 mg/day. Folic acid 1 mg/day
Vitamin E	400 IU/day
Vitamin D	400–800 IU/day
Magnesium	250 mg twice-daily (over-the-counter); or 400 mg/day by prescription, with frequency dependent on serum levels
Potassium	As provided by treating physician or increased intake of foods rich in potassium (such as bananas, oranges, potatoes)
Acetyl-L-carnitine	500 mg twice-daily with food; can take up to 2000 mg/day
Alpha-lipoic acid	300 –1000 mg/day with food
Glutamine	1 g up to three times daily with food

Supplements should be taken with food unless otherwise indicated.
It is currently advised that patients do not take supplements on days of bortezomib infusion and all supplements must be discussed with and approved by the treating physicians concerned.
The effectiveness of the use of the above supplemental interventions is not proven in prospective studies.

Richardson PG, Delforge M, Beksac M, et al. Leukemia. 2012;26:595-608. PMID: 22193964.

Which vitamins do I recommend against?

Magnesium (causes 💩)

> Blood. 2014 Oct 9;124(15):2467-8. doi: 10.1182/blood-2014-06-583302.

Lenalidomide-induced diarrhea in patients with myeloma is caused by bile acid malabsorption that responds to treatment

Charlotte Pawlyn [1], Mohid S Khan [2], Ann Muls [3], Priya Sriskandarajah [4], Martin F Kaiser [1], Faith E Davies [1], Gareth J Morgan [1], H Jervoise N Andreyev [3]

653. MYELOMA: THERAPY, EXCLUDING TRANSPLANTATION | DECEMBER 6, 2014

Colesevelam Hydrochloride for the Treatment of Lenalidomide Induced Diarrhea

Melanie Watson, RN, OCN, Ajay K. Nooka, MD MPH, Charise Gleason, MSN, ANP-BC, AOCNP, Kelly Valla, PharmD, BCOP, Jonathan L. Kaufman, MD, Sagar Lonial, MD

Check for updates

Blood (2014) 124 (21): 5779.

https://doi.org/10.1182/blood.V124.21.5779.5779

lenalidomide/cyclophosphamide/dexamethasone: 1 pt). Median age of the patients was 60 year (range: 44-77 yrs). Median prior lines of therapy were 1 (range: 1-6). Median time from initiation of lenalidomide to Colesevelam hydrochloride is 44 months (0-64 months). Eighty-five percent of patients have noted improvement and 30% experienced total resolution of symptoms. Median time from initiation of Colesevelam hydrochloride to symptomatic response is 4 weeks (range, 0-17). In one patient response was seen in less than a week.

CONCLUSION: Multiple Myeloma patients on lenalidomide therapy with chronic diarrhea noted improvement or total resolution of symptoms with the addition of colesevelam, thus allowing patients to stay on therapy, improving survival as well as quality of life.

L-carnitine (often $$$)

Purpose: Retreatment with bortezomib (B) is often considered for patients with relapsed multiple myeloma (MM), but this strategy is hindered by uncertainty of response and emergence of B-induced peripheral neuropathy (PN). We incorporated acetyl-L-carnitine (ALCAR) to prevent PN and all

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Clinical Trial > Cancer Chemother Pharmacol. 2014 Oct;74(4):875-82.

doi: 10.1007/s00280-014-2550-5. Epub 2014 Aug 29.

Acetyl-L-carnitine (ALCAR) for the prevention of chemotherapy-induced peripheral neuropathy in patients with relapsed or refractory multiple myeloma treated with bortezomib, doxorubicin and low-dose dexamethasone: a study from the Wisconsin Oncology Network

Natalie Callander [1], Stephanie Markovina, Jens Eickhoff, Paul Hutson, Toby Campbell, Peiman Hematti, Ronald Go, Robert Hegeman, Walter Longo, Eliot Williams, Fotis Asimakopoulos, Shigeki Miyamoto

study examining constitutive bortezomib-inducible NF-κB activity in primary subject-specific MM cells, the presence of NF-κB activation correlated with lower likelihood of response.

Conclusions: Addition of ALCAR to BDD did not alter the incidence or severity of PN in relapsed MM patients receiving a B-based regimen. Bortezomib-inducible NF-κB activation in patient-derived primary MM cells may be associated with poorer response.

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Which vitamin <u>do</u> I recommend repleting?

Multicenter Study > Support Care Cancer. 2016 Jul;24(7):3105-10.
doi: 10.1007/s00520-016-3126-1. Epub 2016 Feb 23.

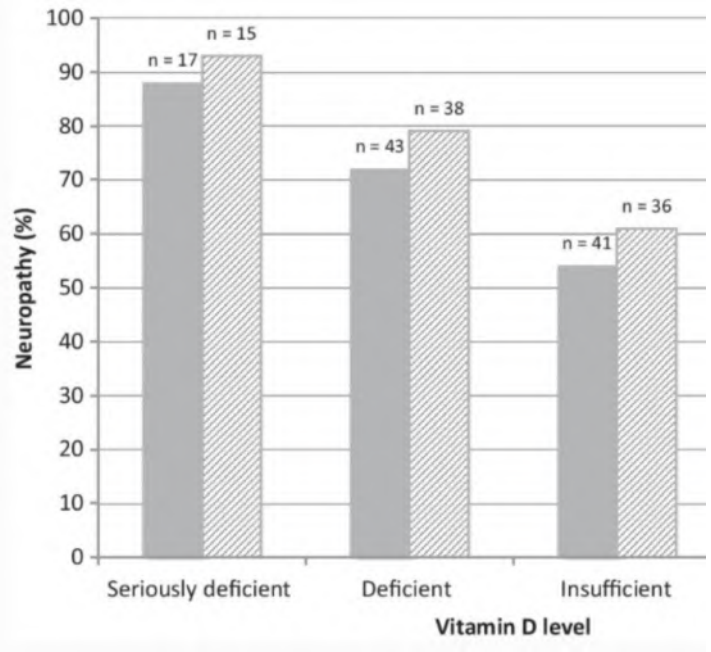
Low serum vitamin D occurs commonly among multiple myeloma patients treated with bortezomib and/or thalidomide and is associated with severe neuropathy

James Wang [1], Kyle A Udd [1], Aleksandra Vidisheva [2], Regina A Swift [1], Tanya M Spektor [2],

Multicenter Study > Support Care Cancer. 2022 Jan;30(1):271-278.
doi: 10.1007/s00520-021-06414-3. Epub 2021 Jul 17.

High prevalence of peripheral neuropathy in multiple myeloma patients and the impact of vitamin D levels, a cross-sectional study

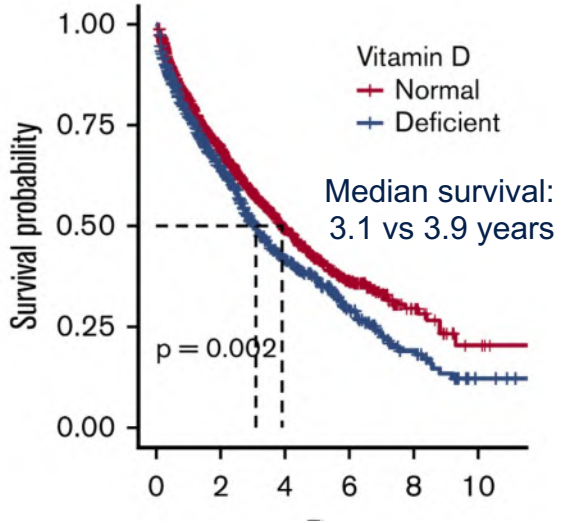
B E Oortgiesen [1], J A Kroes [2], P Scholtens [3], J Hoogland [3], P Dannenberg-de Keijzer [4], C Siemes [4], F G A Jansman [3 5], R E Kibbelaar [6], N J G M Veeger [7 8], M Hoogendoorn [9], E N van Roon [2 3]

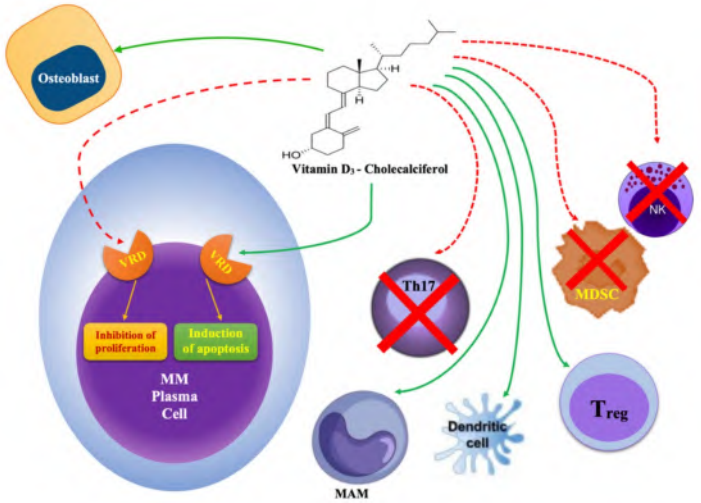


Oortgiesen BE, Kroes JA, Scholtens P, et al. Support Care CA. 2022;30(1);271-278. PMID: 34273034.

Another reason to consider vitamin D

- Provocative analysis of almost 2000 veterans: low vitamin D associated with worsened survival (esp. if Caucasian)
  - ? correlation vs causation; ? reversibility with supplementation





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Yellapragada SV, Fillmore NR, Frolov A, et al. Blood Adv. 2020; 4(8):1643-1646. PMID: 32315398.
Innao V, Allegra A, Ginaldi L. Inj J Mol Sci. 2021. doi: 10.3390/ijms22094922. PMID: 34066482.

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Outline for today's talk

- Complexity of symptom & toxicity management in MM
- Management of treatment-related **fatigue**
- Management of treatment-related **neuropathy**
- **Management of treatment-related 'time toxicity'**

Abbreviations: MM, multiple myeloma.

Barriers to ‘home time’ in myeloma

	Example #1	Example #2
Per cycle	Twice-weekly PI dosing	Bisphosphonates, scans, etc.
Per appt	Travel time for injections	Wait time for pre-appt labs to result*
Per dose	Pre-medications before infusion	Post-dose monitoring

* **54%** of time during an average VRd appointment

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Banerjee R, George M, Gupta A. JCO Oncol Pract. 2021;17(9):513-516. PMID: 33661703.
Inyang E, Atkas-Samur A, Munshi NC, et al. Blood. 2021;138(Suppl_1):666. [#ASH21 poster.]

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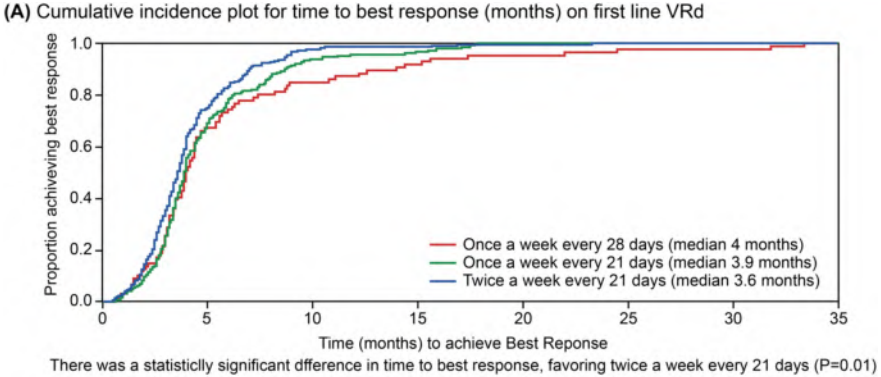
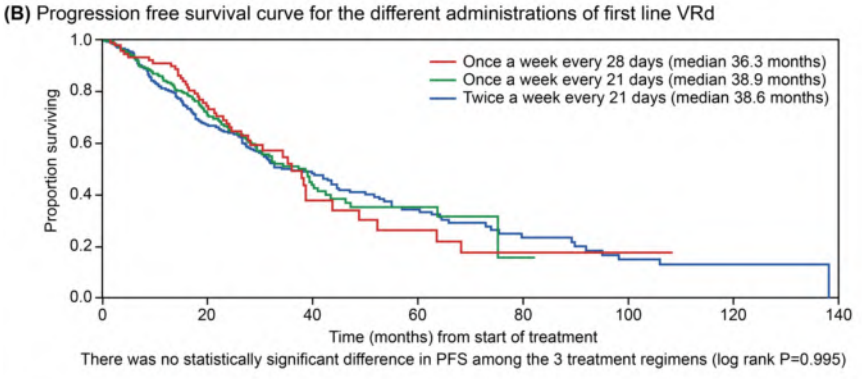
Strategy #1: Prescribe PIs once weekly

- Twice-weekly bortezomib in VRd doesn't add much except more neuropathy
  - Twice-weekly V may lead to best response 2 weeks faster, but no change in survival
- ARROW trial: survival lower with twice-weekly carfilzomib (by itself) than once-weekly





Cook J, Johnson I, Higgins A, et al. Am J Hematol. 2021;96(3):330-337. PMID: 33326116.
Moreau P, Mateos MV, Berenson JR, et al. Lancet Oncol. 2018;19(7):953-964. PMID: 29866475.
Abbreviations: OS, overall survival; PFS, progression-free survival.

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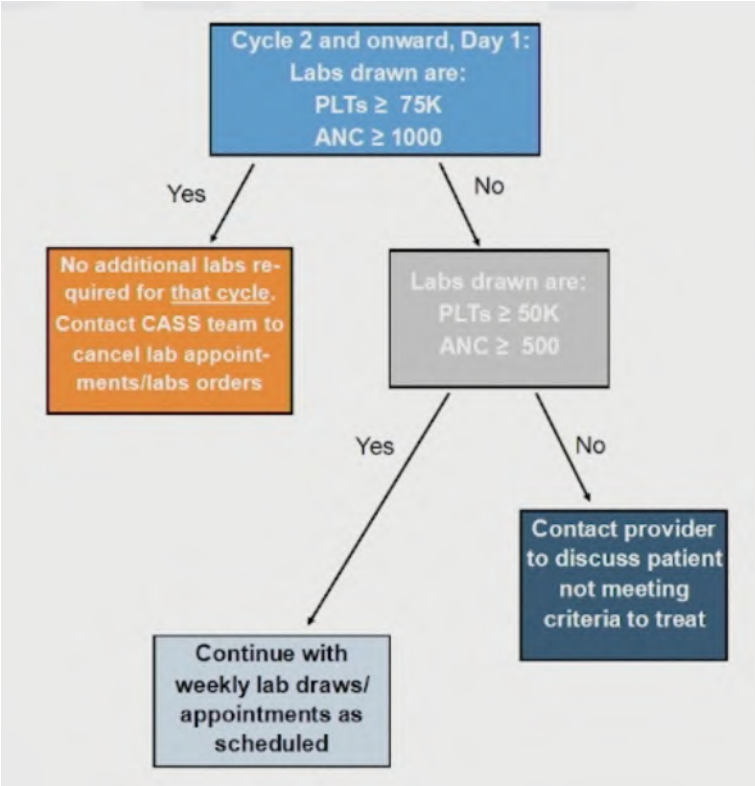
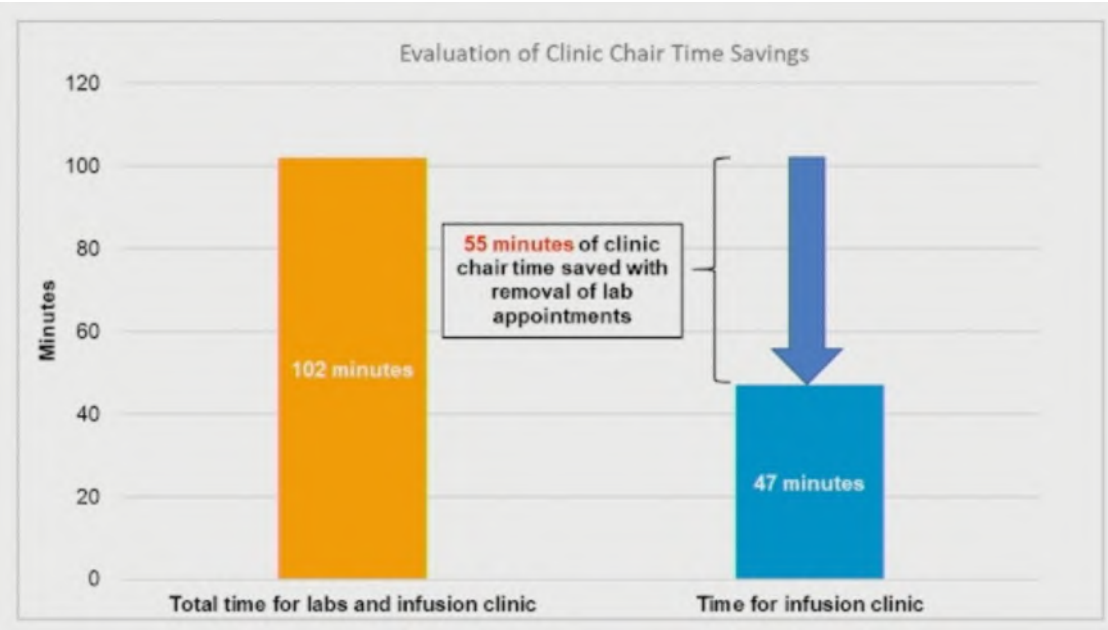
Strategy #2: Check all labs only once per cycle





Inyang E, Atkas-Samur A, Munshi NC, et al. Blood. 2021;138(Suppl_1):666. [#ASH21 poster.]
Abbreviations: ANC, absolute neutrophil count; PLT, platelets.

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Strategy #3: Give Zometa® every 3 months

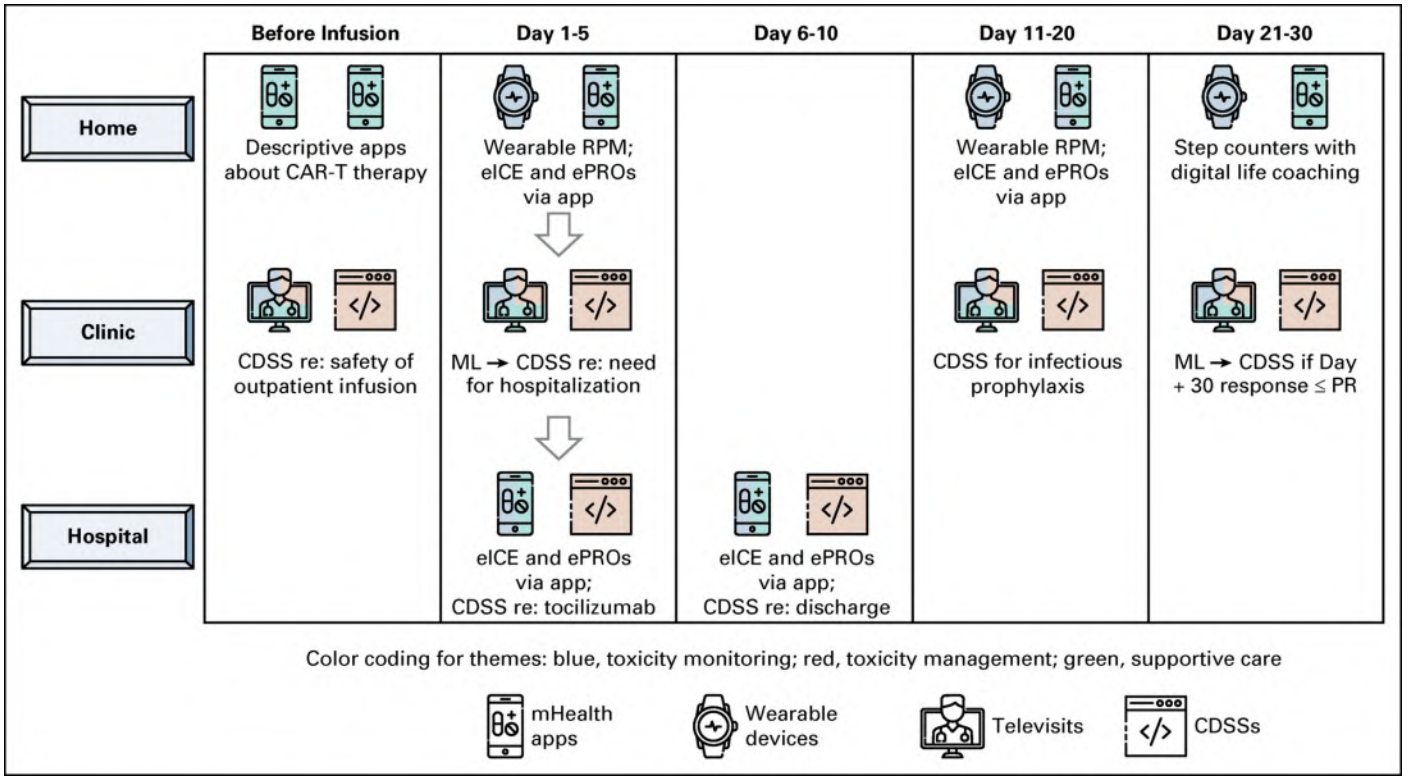
- Zoledronic acid (Zometa®): IV bisphosphonate infusion that helps to prevent fractures in myeloma
  - Has been shown to be superior to other IV bisphosphonates.
- Only randomized study of zoledronic acid dosing:
  - No difference in fractures with every-4-week dosing (26%) versus every-12-week dosing (21%) among patients with MM.
- ASCO guidelines: Consider dosing Zometa® every 12 weeks for patients "who do not have active myeloma."
  - My practice: Consider switching after 9-12 months.

Anderson K, Ismaila N, Flynn PJ, et al. JCO. 2018;36(8):812-818. PMID: 29341831.
Himelstein AL, Foster JC, Khatcheressian JL, et al. JAMA. 2017;317(1):48-58. PMID: 28030702.

Strategy #4: Use cell phones with cell therapies

Can we improve 'home time' following BCMA CAR-T?

Study coming to UW/SCCA!



Banerjee R, Shah N, Dicker AP. JCO Clin Cancer Inform. 2021;5:668-678. PMID: 34110929
Abbreviations: CDSS, clinical decision support software; ML, machine learning; PR, partial response; RPM, remote patient monitoring.

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Strategies #5-8 to discuss with doctors

5. Can my follow-up visits be done by video visits?
6. If I do need labs each week, can I get them done at a Quest® or Labcorp® closer to my home the day before?
   - Caveat: Labs need to readily cross over into our medical record
7. If I need pre-medications before daratumumab (Darzalex®), can I take them as pills right before I drive to clinic?
   - Caveat: Might not be advisable with diphenhydramine (Benadryl®)
8. If I'm in remission and need surveillance imaging every year, will a whole-body CT scan work instead of a PET scan?

And, of course, the most important point:

- **Physicians are only part of your treatment team for MM.**
- Other specialists for the topics I touched on in this presentation:
  - Nurses & pharmacists for everything
  - Social workers for financial toxicity
  - Nutritionists re: ginseng, etc.
  - Therapists & coaches re: fatigue
  - Acupuncturists and pain providers
  - **Other patients like you!**

Consider finding or becoming a myeloma coach (and let me know how it goes).
https://healthtree.org/myeloma/coach

Thank you for your time!

Questions? Comments?

PMID links for articles not working or asking you to pay $$$ for access?

- Email me: rahul.banerjee.md@gmail.com
- Follow or DM me: @RahulBanerjeeMD #MMsm #TcellRx

Looking forward to meeting many of you this summer and beyond!