MYELOMA: TREATING BLOOD CANCER AS A CHRONIC DISEASE

DERIVED FROM THE LIVE ACTIVITY WHICH OCCURRED ON APRIL 28, 2023

Held in conjunction with the
Oncology Nursing Society's 48th Annual Congress

LEUKEMIA & LYMPHOMA SOCIETY®

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WELCOME AND INTRODUCTIONS

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The Leukemia & Lymphoma Society
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Meeting space has been assigned to provide a Symposia supported by The Leukemia & Lymphoma Society during the Oncology Nursing Society's (ONS) 48th Annual Congress, April 26 – April 30, 2023 in San Antonio,TX. The Oncology Nursing Society's assignment of meeting space does not imply product endorsement.

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EDUCATIONAL OBJECTIVES

Upon completion, participants should be better able to:

- Identify disparities in diagnosing myeloma and access to treatment
- Explain treatment options and side-effect management, including newly approved and treatments in clinical trials
- Describe the factors to consider when initiating and/or changing treatment, including challenges in adherence to treatment for myeloma as a chronic blood cancer
- Explain goals of coordination among medical specialties to follow a plan of care throughout survivorship for myeloma and other chronic blood cancers
- List resources to support patients and their caregivers

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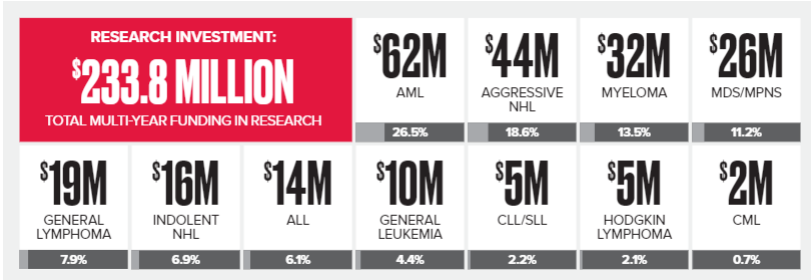
Our Mission:
Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

5

Breakthrough Research: Improving Treatments and Enhancing Quality of Life

LLS HAS INVESTED MORE THAN
$1.6 BILLION
IN RESEARCH FOR ALL TYPES OF BLOOD CANCER SINCE OUR FOUNDING

LLS HELPED ADVANCE
3 OF EVERY 4
BLOOD CANCER TREATMENTS APPROVED BY THE FDA IN THE LAST 6 YEARS



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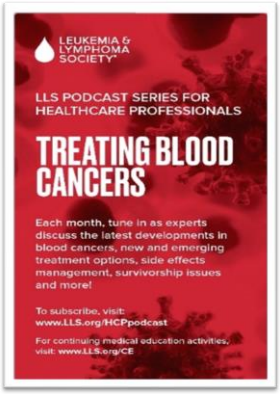
FREE LLS RESOURCES FOR HEALTHCARE PROVIDERS

- CME & CE courses: www.LLS.org/CE
- Fact Sheets for HCPs: www.LLS.org/HCPbooklets
- Videos for HCPs: www.LLS.org/HCPvideos
- Podcast series for HCPs: www.LLS.org/HCPpodcast



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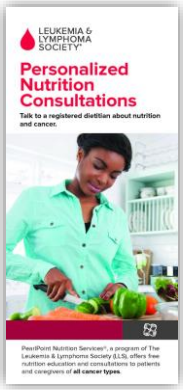
FREE LLS RESOURCES FOR PATIENTS

- **Information Specialists** – Personalized assistance for managing treatment decisions, side effects, and dealing with financial and psychosocial challenges (IRC).
- **Clinical Trial Nurse Navigators** – RNs provide a personalized service for patients seeking treatment in a clinical trial, sift through the information and provide information to bring back to their HC team (CTSC).
  - www.LLS.org/CTSC
- **Registered Dieticians** – (LLS) provides PearlPoint Nutrition Services® to patients/caregivers of all cancer types, free nutrition education and one-on-one consultations by phone or email.
  - www.LLS.org/nutrition
- **Reach out Monday–Friday, 9 am to 9 pm ET**
  - Phone: (800) 955-4572
  - Live chat: www.LLS.org/IRC
  - Email: infocenter@LLS.org
  - HCP Patient Referral Form: www.LLS.org/HCPreferral



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FREE LLS RESOURCES FOR PATIENTS AND CAREGIVERS

- **Webcasts, Videos, Podcasts, booklets**:
  - www.LLS.org/Webcasts
  - www.LLS.org/EducationVideos
  - www.LLS.org/Podcast
  - www.LLS.org/Booklets
- **www.LLS.org/myeloma**
- **Support Resources**
  - Financial Assistance: www.LLS.org/Finances
    - Urgent Need
    - Patient Aid
    - Travel Assistance
  - Other Support: www.LLS.org/Support
    - LLS Regions
    - Online Weekly Chats Facilitated by Oncology SW
    - LLS Community Social Media Platform
    - First Connection Peer to Peer Program

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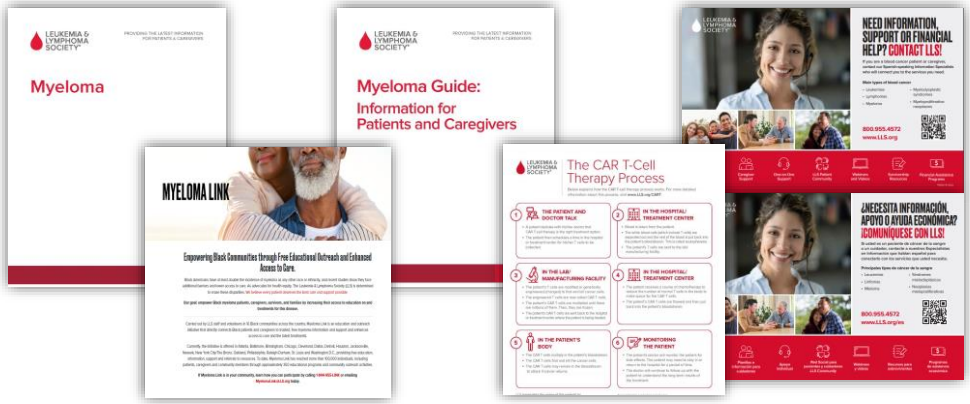
FREE LLS RESOURCES FOR YOUR PATIENTS



- www.LLS.org/Myelomalink

BOOKLETS AND FACT SHEETS

English – www.LLS.org/Booklets
Spanish – www.LLS.org/Materiales

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FACULTY

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FACULTY DISCLOSURES

Krina K. Patel, MD, MSc has a financial interest/relationship or affiliation with one or more ineligible companies in the form of:

- Honoraria/Consultation Fee and Grant Support with Janssen, BMS, Takeda, Caribou Bio
- Honoraria/Consultation Fee with Astra Zeneca, GSK, Karyopharm
- Honoraria/Consultation Fee and Grant Support with Precision Bio, Cellectis

Rhonda Hewitt, MSN, ANP, AOCNP® has a financial interest/relationship or affiliation with one or more ineligible companies in the form of:

- Honoraria/Consultation Fee with Janssen, Amgen, GSK, Sanofi, Pharmacyclics

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Myeloma Incidence

- Second most common hematologic malignancy[1]
- Estimated 34,000 new cases and 13,000 deaths annually in the US[2]
- Annual incidence in the US, Canada, UK, & Europe → 7:100,000[2]
- Incidence is stable but may appear to be increasing due to increased use of lab tests, greater awareness, and more people seeking care[2]

1. SEER stat fact sheet: myeloma. 2020
2. UpToDate accessed 9/16/22

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Age, Sex, & Ethnic Distribution

- Median age at diagnosis is 69 yrs & death is 75 yrs[1]
- More common in men > women[1]
- More common in African American > Caucasian >Asians/Mexicans[1]
- 5 yr survival rate 57.9% 2012-2018[1]
- Sensitive to treatment but not curable

1. SEER stat fact sheet: myeloma. 2020

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Disparities in Disease Characteristics

- Black patients have a lower frequency of high-risk disease but higher rates of anemia.
- The survival rate is higher among Black patients versus among White patients with MM (1973-2005).
- However, improvement in OS has been more dramatic among White patients over time.
- Surveillance Epidemiology and End Results (SEER)–based analysis reported differences in the median age at MM diagnosis
  - Hispanic pts: 65 years
  - African Americans pts: 66 years
  - Whites: 71 years
  - Hispanic patients had lower OS than other races/ethnicities

Baker A, et al. *Blood*. 2013;121(16):3147-3152.
Ailawadhi S, et al. *Blood Cancer J*. 2018;8(7):67.
Waxman AJ, et al. *Blood*. 2010;116(25):5501-5506.
Ailawadhi S, et al. Blood Adv. 2019; 3(20): 2986-94.

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Etiology

- Unknown
- Risk Factors[1,2]
  - Increasing age
  - Male
  - Family history → if 1st degree relative with MM, 3.7 times more likely to get MM
  - African/African American
  - MGUS or plasmacytoma
  - Obesity
  - Radiation
  - Agent Orange exposure

1. American Cancer Society: Myeloma. What are the Risk Factors for Myeloma Feb 2018
2. UpToDate accessed 9/16/2022

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Pathophysiology

- Myeloma is a blood cancer that develops in the bone marrow[1]
- It is a cancer of the plasma cells
- Normally plasma cells produce immunoglobulins (antibodies) as part of an immune response[1]
- Myeloma results in an excess secretion of one type of dysfunctional antibody (immunoglobulin) known as the monoclonal (M) protein or paraprotein[1,3]

1. Munshi NC et al. In: DeVita VT Jr et al, eds. *Cancer: Principles & Practice of Oncology.* Vol 2. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:2305-2342.
2. SEER stat fact sheet: myeloma. 2020. 3. Kyle RA et al. *Leukemia.* 2009;23(1):3-9

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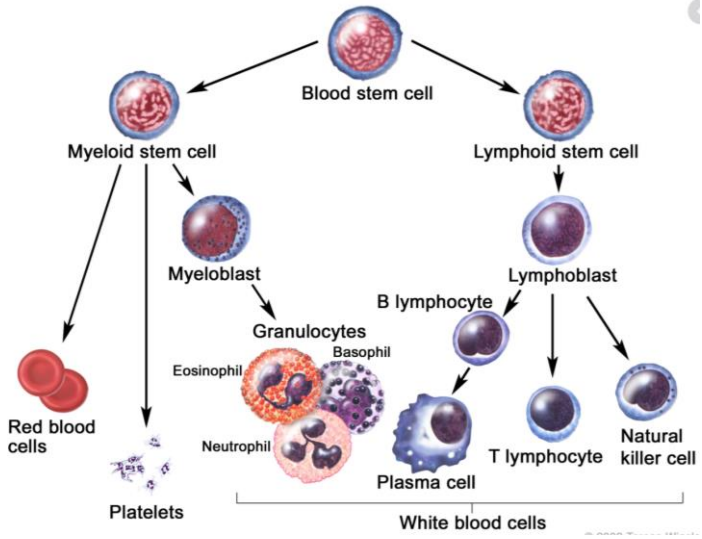
Pathophysiology



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ARS Question 1

Risk factors associated with developing myeloma include:

A. Younger age
B. Female sex
C. Having MGUS
D. Being Caucasian

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ARS Question 1

Risk factors associated with developing myeloma include:

A. Younger age
B. Female sex
C. Having MGUS
D. Being Caucasian

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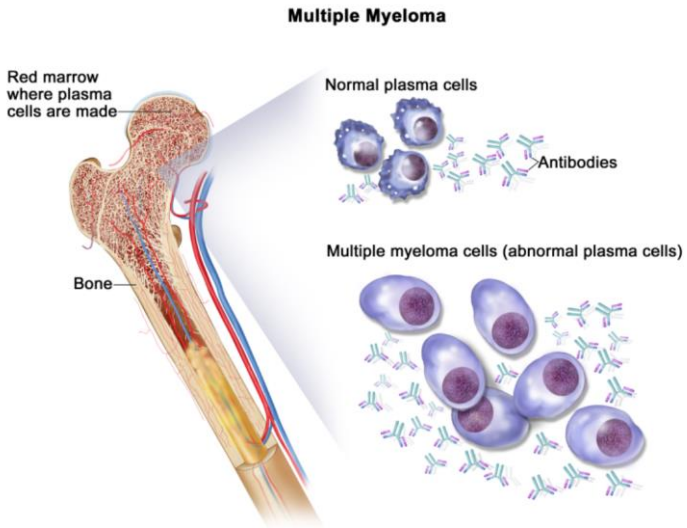
Pathophysiology



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*In healthy bone marrow (A), **B-cells** develop into antibody-producing plasma cells when foreign substances (antigens) enter the body. Normally, plasma cells make up less than 1 percent of the cells in the bone marrow. In multiple myeloma (B), genetic damage to a developing B cell transforms the normal plasma cell into a malignant multiple myeloma cell. The malignant cell multiplies, leaving less space for normal blood cells in the bone marrow, and produces large quantities of M protein.*

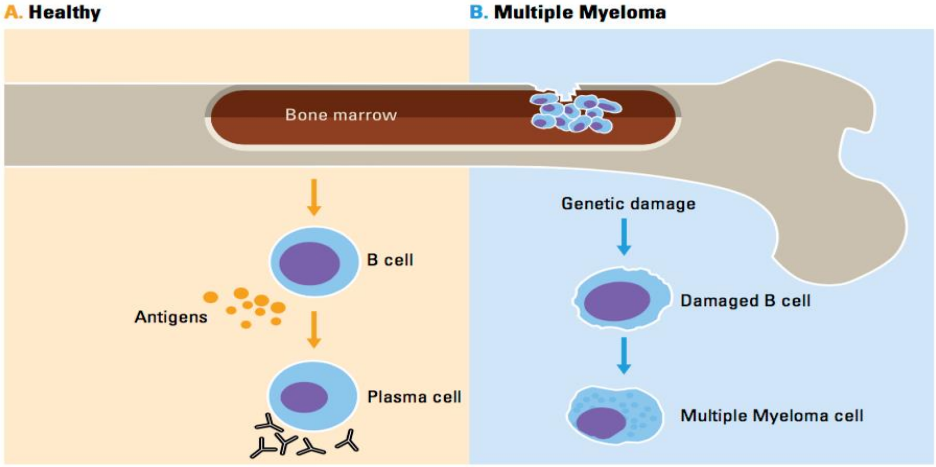

Figure 1

https://www.themmrf.org/assets/mmrf-disease-overview.pdf

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Pathophysiology

- The myeloma cell secretes a number of osteoclast activating factors → leads to bone destruction or osteolytic lesions (Figure 2)
- Can lead to hypercalcemia

Esteve and Roodman 2007, 613-624

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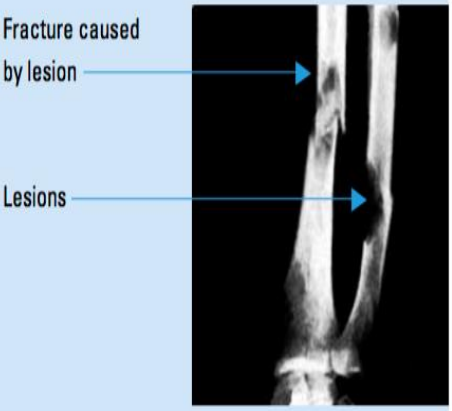
Pathophysiology

Figure 2.

Myeloma cells in the bone marrow cause osteolytic lesions, which appear as "holes" on an x-ray. Weakened bones increase the risk of fractures, as shown in this x-ray of a forearm. DeVita VT Jr, Hellman S, Rosenberg SA, eds. Cancer: Principles and Practice of Oncology. 5th ed. 1997:2350. Adapted with permission from Lippincott Williams & Wilkins.



https://www.themmrf.org/assets/mmrf-disease-overview.pdf

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ARS Question 2

The class of drugs used to help reset the balance between osteoclasts & osteoblasts is called:

A. Proteosome inhibitors
B. Immunomodulatory agents
C. Bisphosphonates
D. Steroids

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ARS Question 2

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Pathophysiology

- The proteins produced and secreted by the malignant plasma cells can cause kidney damage, especially when light chains become deposited in the kidneys, causing Light Chain Deposition Disease (LCDD).
- Can lead to renal failure and the need for dialysis

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Case Study

- Brittany is a 47 yr old African American woman, mom to 2 girls (11 & 14 yrs old) who presents to her primary care doctor with 3 months of worsening back pain & fatigue.
- PMH: type 1 DM
- Meds: insulin, prn acetaminophen
- SH: single mom with good support system. Parents live nearby & has wonderful group of friends. Works FT as a speech pathologist. Lives 2hr from the medical center.
- Work up reveals mild anemia & imaging concerning for metastatic process → referred to oncology

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Diagnosis

- Clonal BM plasma cells >/=10% or plasmacytoma
- Plus one of the following:
  - S sixty percent BM plasma cells
  - Li involved/uninvolved FLC ratio of 100 or more
  - M MRI with > one focal lesion involving bone or bone marrow

  - C calcium >11 mg/dL (>2.75 mmol/L)
  - R renal insufficiency
  - A HGB <10 g/dL (<100 g/L) or >2 g/dL below normal
  - B one or more lytic lesions on imaging

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ARS Question 3

How many bone marrow plasma cells are present in a healthy individual who does not have a plasma cell disorder?

A. <1%
B. <5%
C. <10%
D. <20%

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ARS Question 3

How many bone marrow plasma cells are present in a healthy individual who does not have a plasma cell disorder?

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D. <20%

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Clinical Presentation

- Most patients present with signs or symptoms related to the myeloma burden
- Clinical presentation is usually subacute, but a small percentage of patients present acutely with findings that require rapid attention and intervention
  - eg spinal cord compression, kidney failure, hyperviscosity

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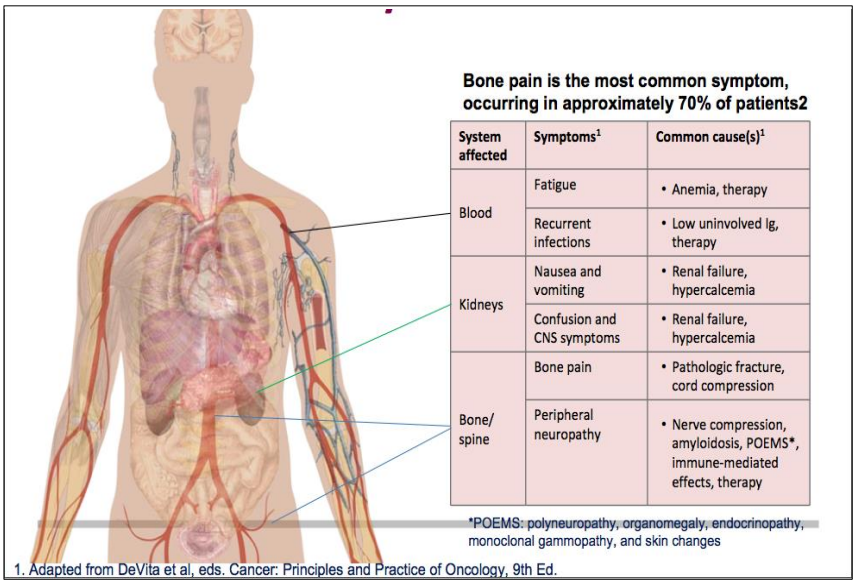
Clinical Presentation



Bone pain is the most common symptom, occurring in approximately 70% of patients2

System affected	Symptoms[1]	Common cause(s)[1]
Blood	Fatigue	• Anemia, therapy
	Recurrent infections	• Low uninvolved Ig, therapy
Kidneys	Nausea and vomiting	• Renal failure, hypercalcemia
	Confusion and CNS symptoms	• Renal failure, hypercalcemia
Bone/ spine	Bone pain	• Pathologic fracture, cord compression
	Peripheral neuropathy	• Nerve compression, amyloidosis, POEMS*, immune-mediated effects, therapy

*POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes

1. Adapted from DeVita et al, eds. Cancer: Principles and Practice of Oncology, 9th Ed.

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Clinical Presentation

- The natural history of myeloma is one of progressive end-organ damage, including bone destruction, refractory cytopenia's, renal dysfunction[1]
- Delays in diagnosis and the initiation of treatment place patients at risk of an exacerbation of symptoms & have the potential to result in irreversible organ damage & morbidity

1. Kyle RA et al. *Leukemia.* 2009;23(1):3-9

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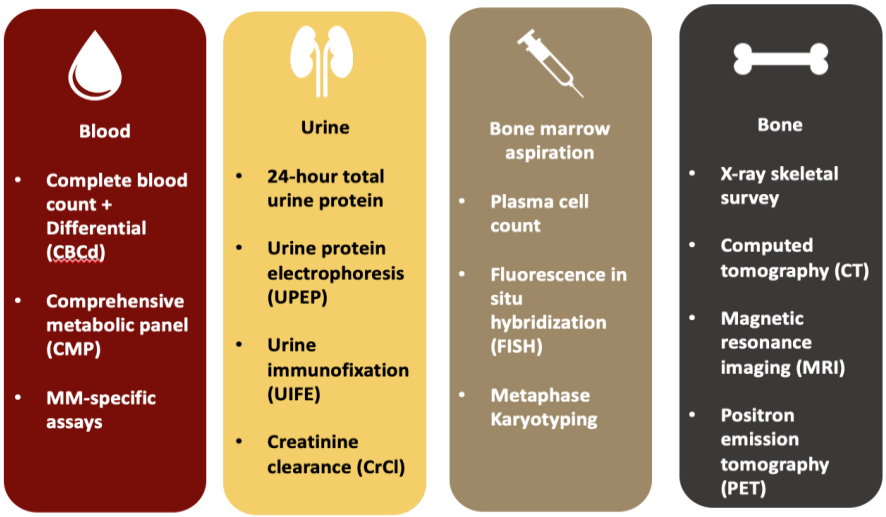
Myeloma Work-up



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Myeloma Labs

- CBCD, CMP
- B2-microglobulin, albumin, & lactate dehydrogenase → nonspecific markers of metabolic activity
- B2M & albumin used in staging → although, in general cytogenetics are more important in heme malignancies

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Myeloma Labs

- Serum protein electrophoresis (SPEP)
  - There is a monoclonal spike.
- Immunofixation (SPI)
  - What type it is?
- Quantitative immunoglobulins
  - How much?
- Free light chains

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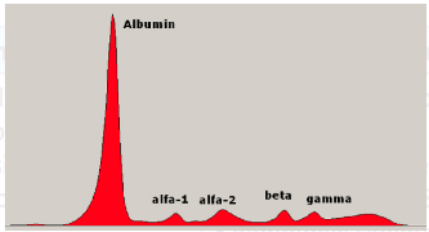
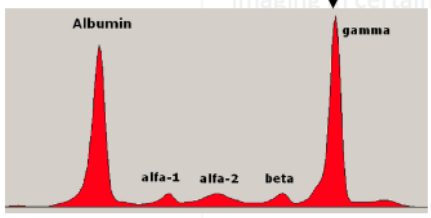
Protein Electrophoresis



Normal SPEP



Abnormal SPEP showing
M-spike of myeloma (arrow)

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ARS Question 4

Which test identifies the involved immunoglobulin?

A. Protein electrophoresis
B. Quantitative immunoglobulins
C. Free light chain ratio
D. Immunofixation

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ARS Question 4

Which test identifies the involved immunoglobulin?

A. Protein electrophoresis
B. Quantitative immunoglobulins
C. Free light chain ratio
D. Immunofixation

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Bone Marrow Assessment

- BMBx to determine plasma cell percentage & clonality
- BM Aspirate:
  - Cytogenetics
  - FISH analysis – t(4;14), t(14;16), t(11;14), del 17p, Amp 1q21, del 1p
  - Flow cytometry (what's on the surface of those cells?)

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Imaging

- Need more sensitive testing than x-rays for skeletal survey
  - MRI
  - CT
  - PET/MRI
  - PET/CT

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Staging & Prognosis is R2-ISS

Table 1. Multivariate analysis on OS and PFS of the most impacting prognostic variables in the overall population (n=7077). Score calculation and stratification into 4 risk groups according to the total additive score in pts with complete data (n=2227) is shown as well.

Risk feature	OS Hazard ratio*	PFS Hazard ratio*	Score value**
ISS II	1.55 (1.42-1.69)	1.35 (1.26-1.44)	1
ISS III	2.02 (1.83-2.24)	1.53 (1.42-1.66)	1.5
del(17p)	1.74 (1.56-1.94)	1.41 (1.29-1.55)	1
High LDH	1.65 (1.50-1.83)	1.33 (1.23-1.45)	1
t(4;14)	1.56 (1.40-1.74)	1.49 (1.36-1.63)	1
1q CNAs	1.45 (1.29-1.63)	1.37 (1.25-1.50)	0.5

Group	Number of patients (%)	Total additive score
Low	429 (19.3%)	0
Low-Intermediate	686 (30.8%)	0.5-1
Intermediate-High	917 (41.2%)	1.5-2.5
High	195 (8.8%)	3-5

*Cox model adjusted for age, sex, therapy, performance status, isotype, t(14;16) and renal function.
**Calculated on the risk of death in patients with complete data only (n=2227), value rounded at the nearest 0.5 with ISS II vs. I comparison as reference (score = 1).
Abbreviations. OS, overall survival; PFS, progression-free survival; pts, patients; ISS, International Staging System stage; LDH, lactate dehydrogenase; CNAs, copy-number abnormalities.

ISS staging is based on B2M, albumin, LDH and cytogenetics. R2ISS adds 1q CNA

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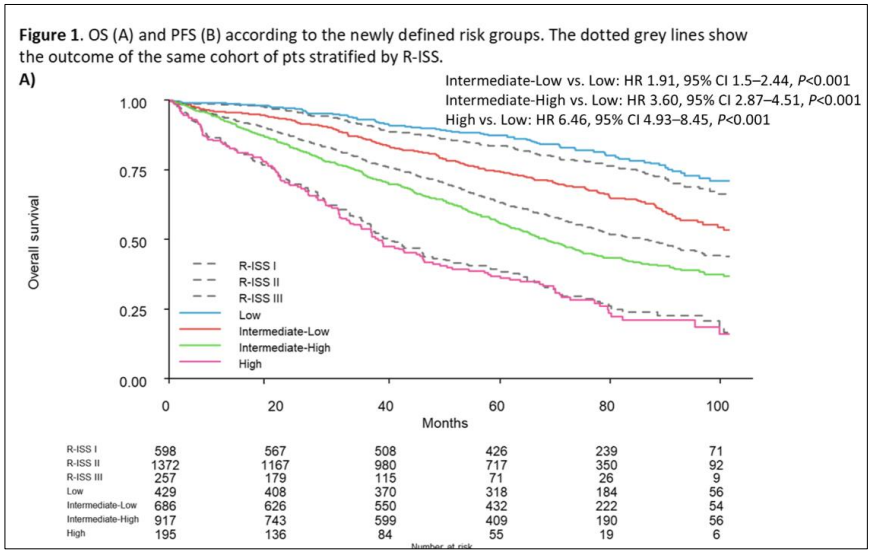
Staging & Prognosis is R2-ISS



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Why Is It "High Risk"?

- May be characterized by deep remissions early on, however **early relapse** is universal, especially if treatment is interrupted
- Often need high dose alkylating chemotherapy to achieve a remission once the patient relapses which can have higher risk of complication, especially when given repetitively
- Subgroup of patients that should be enrolled onto clinical trials, or have access to novel therapies like CAR T or bispecifics early, when available, since optimal therapy resulting in long term survival is needed

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Disease Trajectory

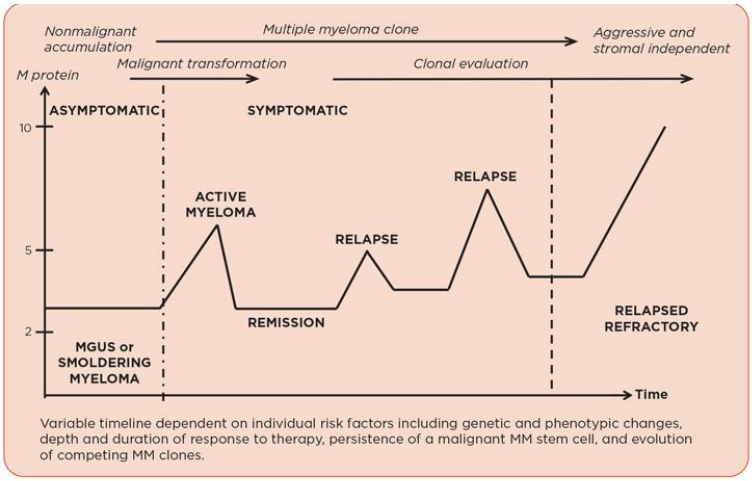

Figure 2. Multiple myeloma disease trajectory characterized by malignant transformation; serial cycles of response, remission, and relapse in the presence of treatment; and clonal evolution with diminished depth and duration of response over time. Information from Aagarwal & Ghobrial (2013). Borrello (2012). Durie et al. (2003). Keats et al. (2012).

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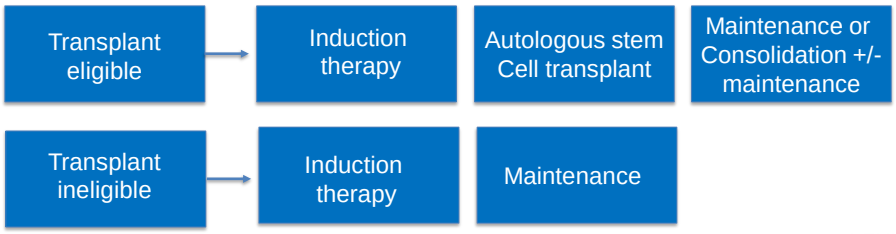
Systemic Therapy: Induction

- Goals:
  - Prolong life
  - Improve quality of life
- Combination therapies
  - To achieve quick, deep remission with limited toxicity



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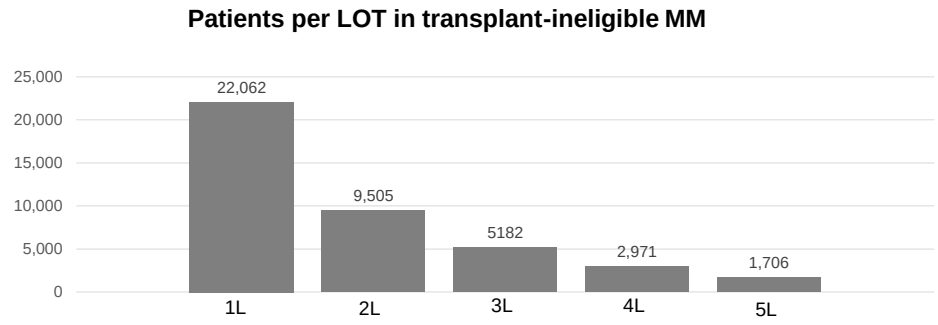
Attrition in Patients with Multiple Myeloma Leads to Fewer Opportunities to Use an Effective Treatment Over Time



The proportion of patients* who received the subsequent line of therapy decreased by approximately 50% between each line

The analysis utilized patient-level data from the years 2000 to 2018.

LOT=line of therapy.
*The analysis followed patients with NDMM who did not receive stem cell transplant at any time during follow-up.
Fonseca R, et al. *BMC Cancer*.202;20(1):1087.

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Case Study

- Brittany is diagnosed with myeloma based on BMPC 30% & multiple lytic lesions on bone imaging
  - HGB 10.2, Cr 1.1, Ca 10, ALB 4, B2M 3.2
  - High risk cytogenetics → t(4;14), del17
- What are going to be some of the challenges Brittany faces?

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Case Study

- What are going to be some of the challenges Brittany faces?
  - Single mom, only source of income
  - Lives a long way from treatment center
  - Type 1 DM
  - Steroids
    - Bortezomib
  - She's young, high-risk disease, living with a second chronic illness, concern for children

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Considerations for Myeloma Therapy

- Patients should receive at least a triplet
  - Deepest remissions are usually seen with first line of therapy
  - Increased tumor kill is associated with longer remissions
  - Many patients do not go on to next LOT
  - If patient frail, can start with doublet & add 3rd agent if performance status improves
- A new triplet should include drugs or drug classes the patient has not been exposed to
- Frailty assessment should be considered
- Consider dose modification based on functional status & age
- Avoid myelotoxic agents in HCT eligible patients
- Harvest stem cells in first remission

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Standard of Care Frontline Therapy

- Daratumumab, Bortezomib, Lenalidomide, Dexamethasone (D-VRD)
- **Bortezomib Lenalidomide Dexamethasone (VRD)**
- Carfilzomib Lenalidomide Dexamethasone (KRD)
- **Daratumumab Lenalidomide Dexamethasone (DRD)**

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NCCN Guidelines for Newly Diagnosed Myeloma Therapy

PRIMARY THERAPY FOR TRANSPLANT CANDIDATES[a-d]
Preferred Regimens • Bortezomib/lenalidomide/dexamethasone (category 1) • Carfilzomib/lenalidomide/dexamethasone
Other Recommended Regimens • Daratumumab/lenalidomide/bortezomib/dexamethasone
Useful In Certain Circumstances • Bortezomib/thalidomide/dexamethasone (category 1) • Bortezomib/cyclophosphamide/dexamethasone[e] • Bortezomib/doxorubicin/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone[f] • Cyclophosphamide/lenalidomide/dexamethasone • Daratumumab/bortezomib/thalidomide/dexamethasone • Daratumumab/carfilzomib/lenalidomide/dexamethasone • Daratumumab/cyclophosphamide/bortezomib/dexamethasone • Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide/bortezomib[g] (VTD-PACE) • Ixazomib/cyclophosphamide/dexamethasone[f] • Ixazomib/lenalidomide/dexamethasone (category 2B)

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

NCCN guidelines from Multiple Myeloma Version 3.2023

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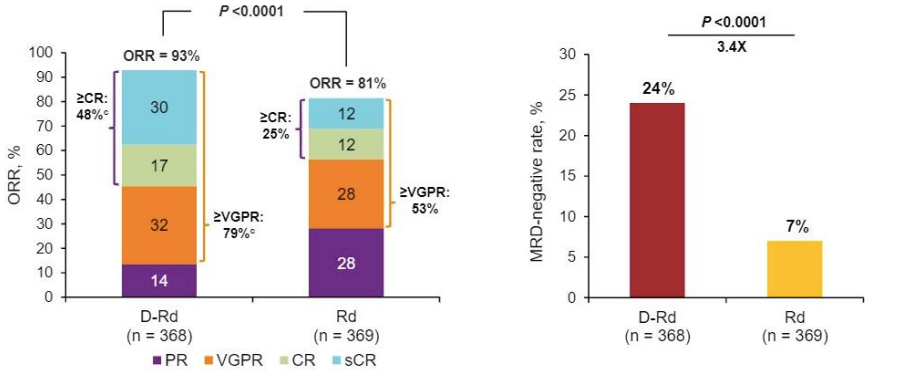
DRd vs RD

Efficacy: ORR[a] and MRD[b] (NGS; 10^{-5} Sensitivity Threshold)



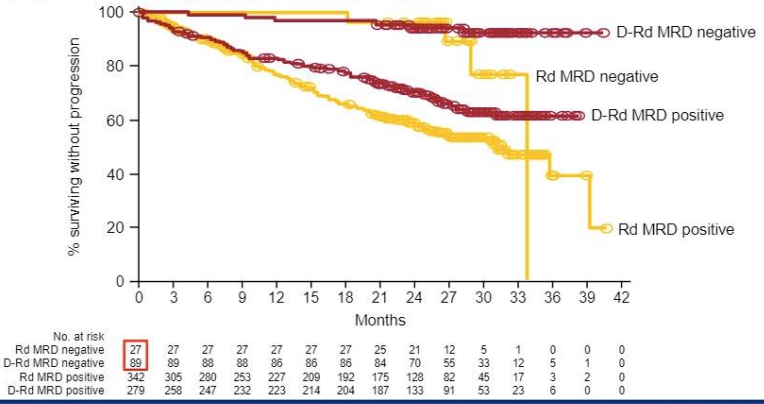
Significantly higher ORR, ≥CR rate, ≥VGPR rate, and MRD-negative rate with D-Rd

Facon, et al. ASH 2018

55

DRd vs RD

Efficacy: PFS by MRD Status



- **>3-fold higher MRD negativity achieved with D-Rd**
- **Lower risk of progression or death with MRD negativity**

Facon, et al. ASH 2018

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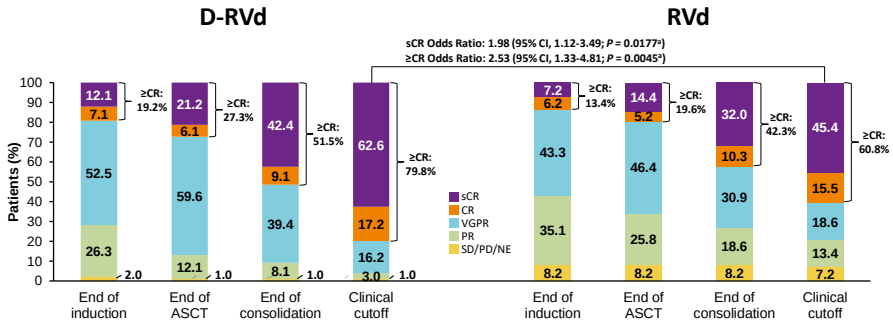
Responses Deepened Over Time



- Median follow up at primary analysis (end of consolidation) was 13.5 months; median follow up at clinical cutoff was 22.1 months

Response rates and depths were greater for D-RVd at all time points

[a]*P* values (2-sided) calculated using Cochran–Mantel–Haenszel chi-square test.

57

Disparities in SCT Access/Use

Racial disparities in treatment for use for multiple myeloma

Approximately 54% of patients (11,269 patients) were eligible for the SCT use analysis	Overall SCT use was low; only 7% of patients underwent the procedure.	SCT use was found to be higher among white patients compared with black patients (8% vs 4%; chi-square = 34.37 [*P*<.0001]).
In the initial regression model, black patients were 49% less likely to use SCT than white patients (*P*<.0001).	After controlling overall health, there was no change noted; black individuals were 49% less likely to use SCT (*P*<.0001).	After also controlling for potential access barriers (MHI, Medicaid, and urban/rural status), black patients were found to be 37% less likely to undergo SCT (*P*<.0001).

Fiala M, et al. Cancer 2017; 123(9):1590-96

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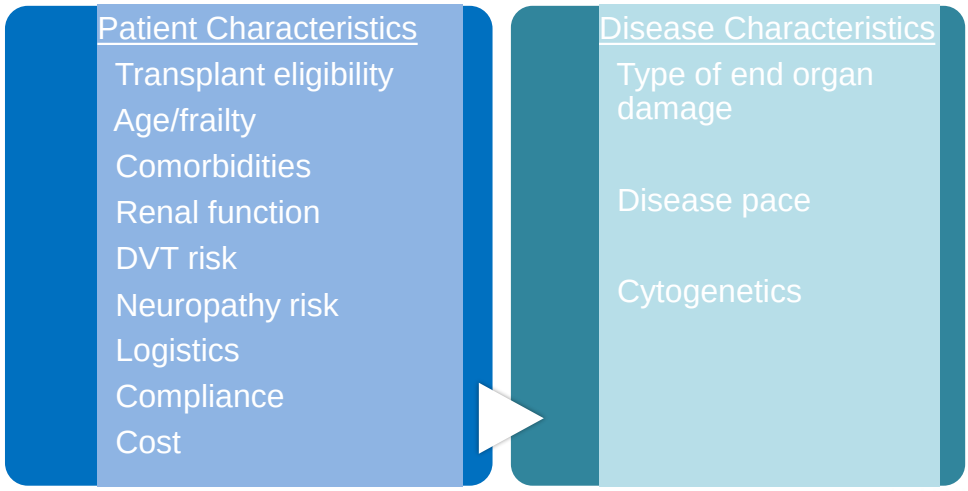
Consider…



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Case Study

- Given her high risk disease & young age, Brittany's oncologist starts her on therapy with Dara-RVd followed by autologous SCT, then Dara+len maintenance. She had a complete response CR to therapy.
  - Peripheral neuropathy with bortezomib cycle 3
    - → after discussion with team Brittany's bortezomib frequency is adjusted to match SQ daratumumab dosing days
  - Poorly controlled DM
    - Early on Brittany is referred to local endocrinologist & ultimately when MM markers improved the dexamethasone is completely discontinued
  - Psychosocial
    - Brittany has a really hard time being so far away from her kids during SCT. Her RN encourages frequent facetime calls & parents/friends bring kids to visit on weekends
    - Brittany has concerns about her kids' risk of MM/cancer. She is referred to genetic counselling

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Case Study

- After 2 years on maintenance and supportive medications, Brittany has new pain in her left leg and her m protein increases from 0 to 0.8. Imaging reveals a new lytic lesion with risk for pathological fracture and bone marrow biopsy reveals 20% CD138+ aberrant plasma cells.

- What do you treat with in second line?
  - Refractory to lenalidomide and daratumumab
  - Exposed to bortezomib
  - Triple class exposed
  - Double refractory

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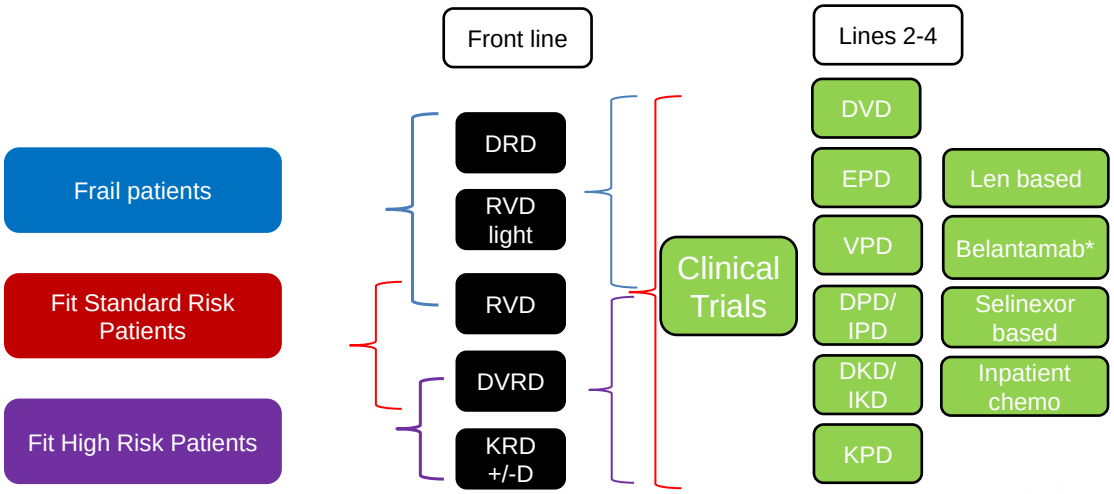
Upfront Rx and Fitness Affects Subsequent Rx



*currently off market, compassionate use available and combination trials ongoing

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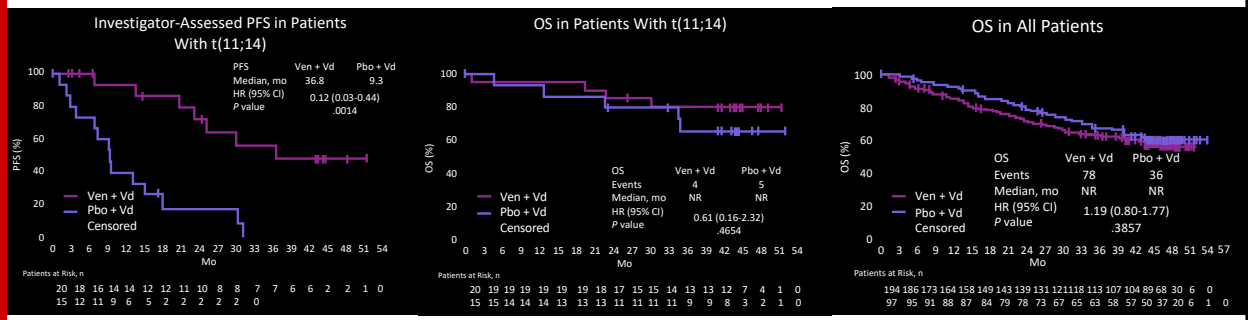
Venetoclax for t(11;14)



Kumar. ASH 2021. Abstr 84.

63

ARS Question 5

Venetoclax improves ORR, PFS and OS for patients with the following FISH aberration:

A. 17p deletion
B. T(4;14)
C. T(11;14)
D. T(14;16)

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ARS Question 5

Venetoclax improves ORR, PFS and OS for patients with the following FISH aberration:

A. 17p deletion

B. T(4;14)

C. T(11;14)

D. T(14;16)

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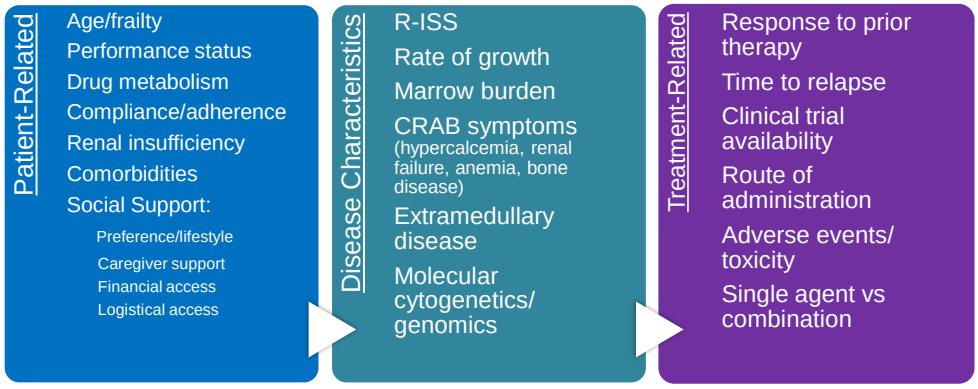
Why It's Not An Algorithm

Many variables change over time!!



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Nursing Considerations

- RNs & APPs play an important role in the management of multiple myeloma patients
  - Education
    - Disease
    - Therapy
  - Side effect management
  - Reinforcing expectations & helping patients and family with learning to live with a chronic disease

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Proteosome Inhibitors

- Bortezomib, Carfilzomib, Ixazomib
- MOA: proteosomes are responsible for protein degradation. Their function supports cell homeostasis by breaking down proteins into their individual constituents so that those can be reused by the cell. Proteosome inhibitors block this pathway which leads to increased ER stress & apoptosis
- Side effects:
  - Bortezomib – peripheral neuropathy
    - Assess PN at each visit & report changes
  - Carfilzomib – cardiotoxicity (increased if >75yr), pulmonary toxicity, VTEs
    - Report new cardiac symptoms
    - Monitor for hypertension

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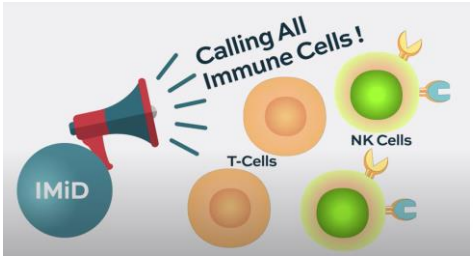
IMiDs

- Immunomodulatory Drugs
  - Lenalidomide, pomalidomide, thalidomide
- MOA
- Direct tumor kill
  - Work on the bone marrow microenvironment to strengthen the body's immune response
    - Activate T cells and NK cells
- Side Effects:
  - Diarrhea
  - Skin rash
  - Myelosuppression
  - VTEs
  - Secondary cancers
  - Renal dosing needed



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Steroids

- Dexamethasone, prednisone, solumedrol
- MOA: not well understood
- Side effects:
  - Associated with emotional lability, insomnia, hyperglycemia, hypertension, infections
- Really important early on for myeloma tumor kill
  - → Consider tapering/discontinuing once myeloma responds in order to minimize side effects related to long-term steroid use

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Monoclonal Antibodies

- Daratumumab & Isatuximab
- MOA: target CD38 on the cell surface of the myeloma cell
  - → kills myeloma cell directly & tags the CD38 which helps the patient's immune system to recognize & attack
- Side effects:
  - Interference with assessment of response & cross-matching
  - Infusion/administration reactions (premeds required)
  - Increases myelosuppression of background regimen
  - Hypogammaglobulinemia → infection risk & decreased response to vaccines
  - Consider PFTs for patients with lung pathology such as COPD; CD38 at low levels on lung tissue so can lead to exacerbations. Inhalers can be helpful
- Elotuzamab
- MOA: targets SLAMF7
  - → spurs the growth of the immune system's natural "killer" cells and tags myeloma cells with the SLAMF7 protein. This makes it easier for the natural killer cells to recognize and kill the myeloma cells
- Side effects:
  - Infusion reactions (premeds required)

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Prevention & Management of Complications

- Skeletal Lesions & Bone Health
  - Prevention: bone-modifying therapy with osteoclast inhibitors (bisphosphonates) or RANK ligand inhibitor (denosumab)
  - Spinal Cord Compression: true emergency → ER
  - Pathologic & impending fractures: long bones may require stabilization. Vertebral fractures may benefit from kyphoplasty or vertebroplasty
  - Pain: can usually be controlled with a combinations of analgesics & active myeloma therapy
  - Palliative XRT: ~40% of patients will require RT to control disease
    - Pain, SCC, plasmacytoma, local control
  - Notify provider for new bone pain or jaw pain
  - Hold bone-modifying therapy for ~3 months prior to dental work

UpToDate accessed 9/16/2022

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Prevention & Management of Complications

- Kidney Impairment:
  - Avoid nephrotoxins
  - Maintain adequate hydration
  - Renally dose meds
- Infections:
  - Antiviral ppx & PJP ppx (steroids)
  - Yearly influenza vaccination
  - Pneumococcal vaccine at time of diagnosis
  - Consider prophylactic antibiotics during the first months of induction
  - IVIG for select patients
  - These patients have a hard time with encapsulated bacteria & gram-negative organisms → education to report & urgent visits/treatment if infection suspected

UpToDate accessed 9/16/2022

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Prevention & Management of Complications

- Thromboembolism:
  - Myeloma patients are at high risk for VTE
    - Malignancy
    - iMID therapy (lenalidomide, pomalidomide)
    - Higher doses of Carfilzomib
  - VTE risk should be assessed
    - Low dose ASA
    - Apixaban or Rivaroxaban

UpToDate accessed 9/16/2022

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Prevention & Management of Complications

- Hypercalcemia
  - Anorexia, n/v, polyuria, polydipsia, constipation, weakness, confusion, stupor
  - Less of an issue with current supportive care; may see pts on Ca & Vit D supplements
- Anemia
  - From disease & the therapies
    - iMIDs, SQ daratumumab in small patient
    - → proceed with therapy vs hold depending on state of MM control
  - PRBC prn
  - ESAs prn (renal dosing vs for HGB)

UpToDate accessed 9/16/2022

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Prevention & Management of Complications

- Neutropenia & Thrombocytopenia
  - More likely due to therapy vs disease but can occur with packed marrow
  - iMIDs (lenalidomide, pomalidomide), SQ daratumumab
- Neuropathy
  - Can be from myeloma, therapy (bortezomib, thalidomide), or comorbidity (diabetes, alcoholism)
  - Needs to be assessed & documented at every interaction
  - Report change from baseline
  - Often requires dose modification &/or discontinuation

UpToDate accessed 9/16/2022

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Case Study

- Brittany gets the following therapies for early relapsed disease:
  - Line 2: Carfilzomib pomalidomide dexamethasone --> VGPR, 17 months
  - Line 3: Daratumumab carfilzomib dexamethasone --> PR 12 month PFS
  - Line 4: Bortezomib selinexor dexamethasone --> PR 9 month PFS

Now she has worsening clinical disease with multiple extramedullary lesions. Her LDH is elevated, creatinine is 1.6, Hgb 7.6 and calcium 12.6.

What do you treat with next in 4+ lines?

77

NCCN Guidelines for Previously Treated Multiple Myeloma (late relapse, >4 prior LOT)

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,l-n]
Therapies for Patients with Late Relapses (>3 prior therapies)
• **Bendamustine** • **Bendamustine/bortezomib/dexamethasone** • **Bendamustine/carfilzomib/dexamethasone** • **Bendamustine/lenalidomide/dexamethasone** • **High-dose or fractionated cyclophosphamide**
After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD ‣ **Idecabtagene vicleucel** ‣ **Ciltacabtagene autoleucel** ‣ **Teclistamab-cqyv** ‣ **Useful in certain circumstances:** ◊ **Belantamab mafodotin-blmf (if available through compassionate use program)**
After at least four prior therapies and whose disease is refractory to at least two PIs, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody ‣ **Selinexor/dexamethasone**

NCCN guidelines from Multiple Myeloma Version 3.2023

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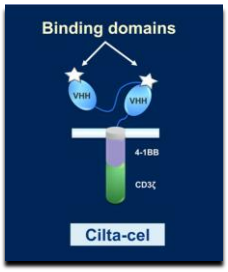
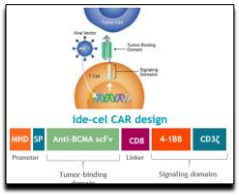
CAR-T





Characteristics	Ide-Cel (n=128)	Cilta-cel (n=97)
Target Cell Dose	300-350 million	0.75 million/kg
Median prior Lines of Therapy	6	6
Triple class refractory	84%	88%
Penta class refractory	26%	42%
Extramedullary disease	39%	13.4%
Bone marrow disease	>50% PC=51%	>60% PC=21.9%
High Risk cytogenetics	35%	23.7%

Efficacy	Ide-Cel (n=128)	Cilta-cel (n=97)
ORR	73%	98%
CR	33%	80%
MRD neg (10^{-5})	26%	58%
PFS	8.8 (CR=19 months)	NR at 2 years
OS	19 months	NR

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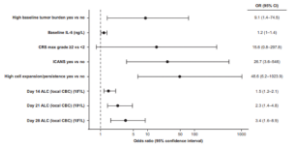
Safety for CAR T

Toxicity	Ide-Cel (n=128)	Cilta-cel (n=97)
CRS (all, g3/4)	84% (5%)	95% (5%)
Median onset CRS	1 day	7 days
ICANS (all, g3/4)	18% (3%)	17% (2%)
Infections (all; g3/4)	69% (22%)	58% (20%)
Grade 3/4 neutropenia > 1 month	41%	10%
Grade 3/4 thrombocytopenia > 1 month	48%	25%
Delayed neurotoxicity (all;g3/4)	None*	12% (9%)

Potential factors associated with MNTs in CARTITUDE-1



Management strategies

- Early and more aggressive supportive care (including steroids) for any-grade ICANS, especially in patients with high tumor burden
- Consider administration of tocilizumab for any grade of ICANS with concurrent CRS, and/or dexamethasone (grade 1–3) or methylprednisolone (grade 4)
- Use of other cytokine-targeting therapies (e.g., anti-IL-1) based on institutional practice, especially for cases of neurotoxicity that do not respond to tocilizumab and corticosteroids
- Consider non sedating, anti seizure medicines (e.g., levetiracetam) for seizure prophylaxis for any grade 2 or higher neurologic toxicities

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CAR T in Earlier Lines

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ide-cel or Standard Regimens in Relapsed and Refractory Multiple Myeloma

Paula Rodriguez-Otero, M.D., Ph.D., Sikander Ailawadhi, M.D., Bertrand Arnulf, M.D., Ph.D., Krina Patel, M.D., Michele Cavo, M.D., Ajay K. Nooka, M.D., M.P.H., Salomon Manier, M.D., Ph.D., Natalie Callander, M.D., Luciano J. Costa, M.D., Ph.D., Ravi Vij, M.D., Nizar J. Bahlis, M.D., Philippe Moreau, M.D., et al.

PFS Ide-cel vs SOC (DPd, EPd, Kd, IRd, DVd)

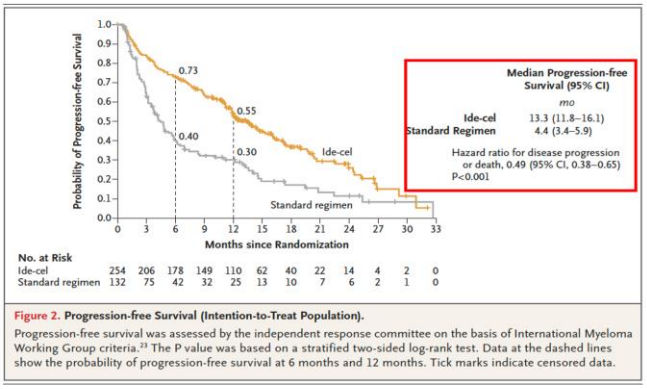

Figure 2. Progression-free Survival (Intention-to-Treat Population).

Progression-free survival was assessed by the independent response committee on the basis of International Myeloma Working Group criteria.[23] The P value was based on a stratified two-sided log-rank test. Data at the dashed lines show the probability of progression-free survival at 6 months and 12 months. Tick marks indicate censored data.

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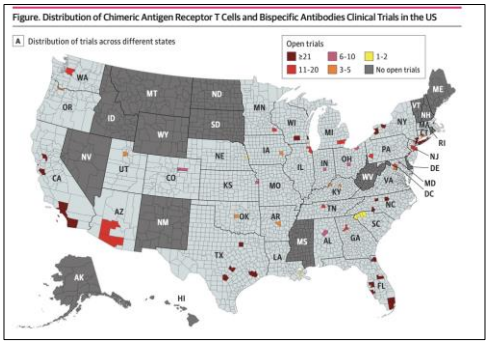
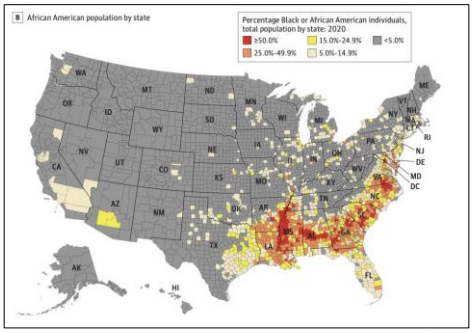
Disparities in Access to CAR T

Enrollment of Black patients in clinical trials that resulted in CAR-T product approvals in the US for all hematological malignant neoplasms including multiple myeloma is suboptimal.





Alqazaqi R, et al. Jama Network 2022

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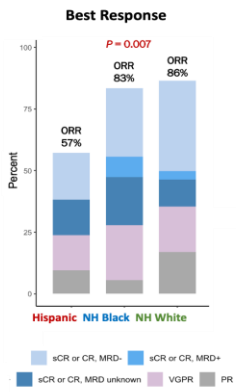
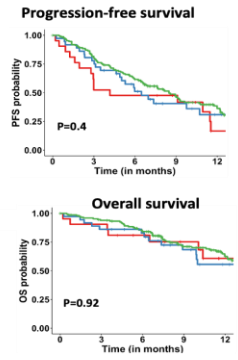
Real World Experience
Ide-cel Outcomes in Minority Patients

Racial and Ethnic Differences in Outcomes of RRMM Treated with Idecabtagene Vicleucel

- Compared to **Non-Hispanic (NH) White** patients, **Non-Hispanic Black** patients had:
  - Higher baseline systemic inflammatory markers (CRP, ferritin)
  - Higher incidence of CRS
  - A longer hospital stay
  - Persistent severe cytopenias ≥ 30 days
- Compared to **Non-Hispanic White** patients, **Non-Hispanic Black** and **Hispanic** patients had higher rates of infection

Despite racial and ethnic differences in safety profile and responses to ide-cel, survival was similar across groups, encouraging the use of ide-cel for all RRMM patients





Peres et al. Oral presentation at ASH 2022; abstract 252

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ARS Question 6

Enrollment of Black patients onto novel immunotherapy clinical trials is:

A. Adequate
B. Suboptimal
C. Higher than the proportion of black patients with MM

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ARS Question 6

Enrollment of Black patients onto novel immunotherapy clinical trials is:

A. Adequate
B. Suboptimal
C. Higher than the proportion of black patients with MM

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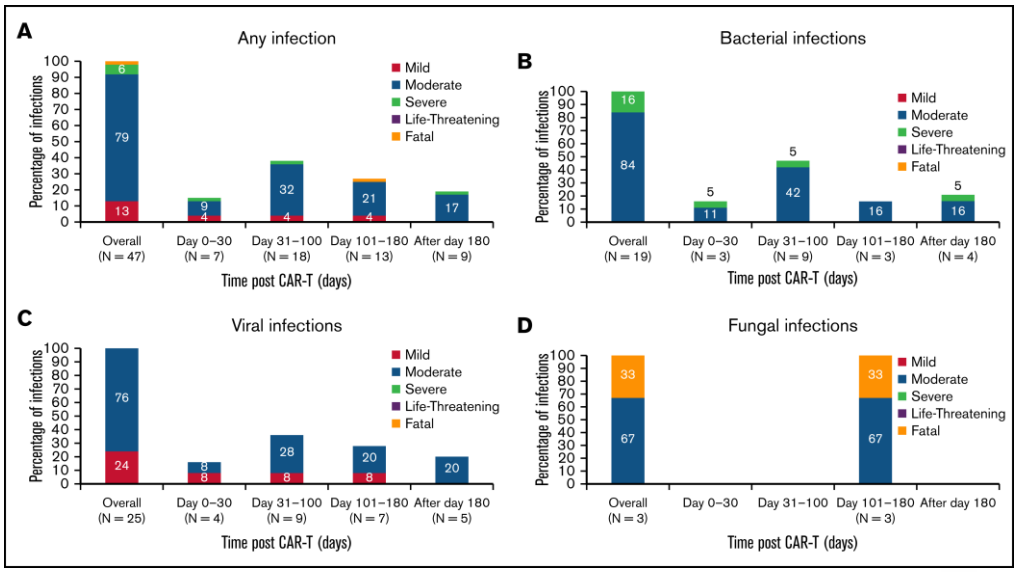
Consequences Of BCMA Targeted Therapies



Kambhampati, et al. Blood Adv 2022

86

ARS Question 7

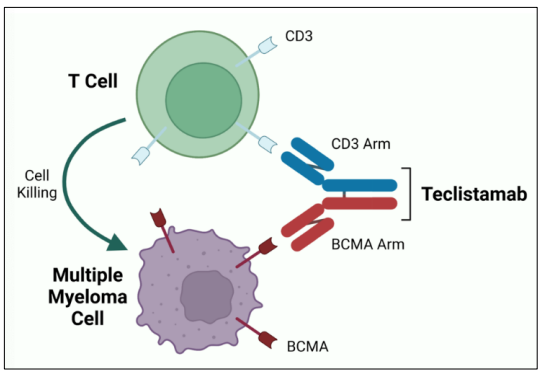
What is the rate of grade 3/4 infections for teclistamab?

A. 10%
B. 20%
C. 40%
D. 60%

87

Bispecific T-Cell Engagers

- Teclistamab
- MOA: Bispecific = 2 arms → binds BCMA on the cell surface of the myeloma cell & CD3 on the T cell. This bridging enables the T cell to recognize the cancer cell & trigger a series of immune reactions which leads to myeloma cell death
- Side effects:
  - CRS
  - Neurotoxicity/ICANS
  - Infections
    (40% grade 3/4)
- Registrational MajesTEC-1 trial:
  - ORR 63%
  - 39% CR or better
  - mDOR 18.4 months
  - mPFS 11.3 months



Moreau P. NEJM 2022; 387:495-505

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ARS Question 7

What is the rate of grade 3/4 infections for teclistamab?

A. 10%
B. 20%
C. 40%
D. 60%

89

Novel Therapies in Clinical Trials

Talquetamab	GPRC5D bispecific
Cevostamab	FCRH5 bispecific
Modakafusp alfa	CD38 fusion protein targeting interferon
Elranatamab	BCMA bispecific
Linvoseltamamb	BCMA bispecific
CC-95266	GPRC5D CAR T

90

ARS Question 8

What antigen below is not being targeted in myeloma with novel therapies?

A. FCRH5
B. SLAMF7
C. KPRH23
D. GPRC5D

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ARS Question 8

What antigen below is not being targeted in myeloma with novel therapies?

A. FCRH5
B. SLAMF7
C. KPRH23
D. GPRC5D

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Patient & Family Resources

- The Leukemia & Lymphoma Society
  www.LLS.org
- American Cancer Society
  www.cancer.org/cancer/multiple-myeloma.html
- Multiple Myeloma Research Foundation
  www.themmrf.org/resources/patient-navigator-center/
- International Myeloma Foundation
  www.myeloma.org/
- My Cancer Haven
  www.mycancerhaven.org/
- HealthTree
  www.healthtree.org/myeloma

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Summary

- Myeloma is a cancer of the plasma cells
- Patients with myeloma are at risk for bone fractures, pain, hypercalcemia, renal failure, anemia, infections, neuropathy
- There is currently no cure for myeloma and patients are living longer due to newer therapies
- Deeper responses lead to longer progression free survival which is associated with better QOL
- Nurses play a critical role in empowering the myeloma patient through education, effective side effect management, setting expectations, learning to live with a chronic illness, and survivorship issues

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ARS QUESTION

What URL can HCPs use to access free CE & CME inline courses, as well as an HCP podcast channel, videos, and fact sheets?

A. www.LLS.org/ContEd
B. www.LLS.org/CE
C. www/LLS.org/HCPEducation

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ARS QUESTION

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MYELOMA: TREATING BLOOD CANCER AS A CHRONIC DISEASE

Thank you for joining us.

Held in conjunction with the
Oncology Nursing Society's 48th Annual Congress

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