Practical Updates in Primary Care

Multiple Myeloma Across the Care Continuum: The Expanding Role of Primary Care from Early Detection to Long-Term Management

Joseph Mikhael, MD, MEd, FRCPC

Professor, Translational Genomics Research Institute (TGen)
City of Hope Cancer Center
Director of Myeloma Research
HonorHealth Research Institute

Brittany Watson, MD, MPH, FAAFP

Assistant Professor, Department of Family & Community Medicine
Atrium Health Wake Forest Baptist
Wake Forest University School of Medicine

Supported by an educational grant from Johnson & Johnson.

Disclosures

- **Joseph Mikhael, MD, MEd, FRCPC:** Consultant – Bristol Myers Squibb, Janssen Biotech, Menarini, Sanofi

- **Brittany Watson, MD, MPH, FAAFP** has nothing to disclose in relation to this activity

- This presentation will discuss the unapproved use of melphalan flufenamide for the treatment of multiple myeloma

This CME activity includes brand names for participant clarity purposes only.
No product promotion or recommendation should be inferred.

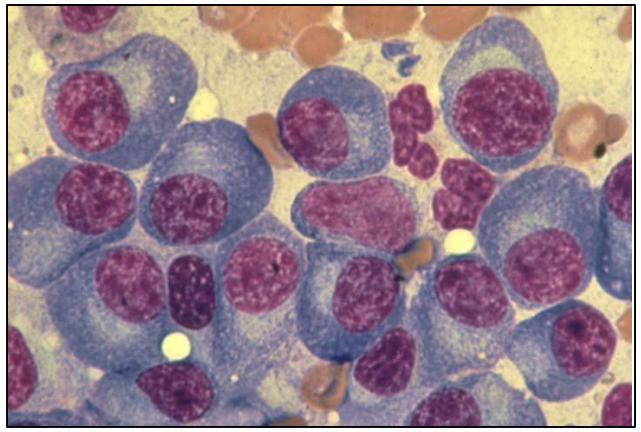
Learning Objectives

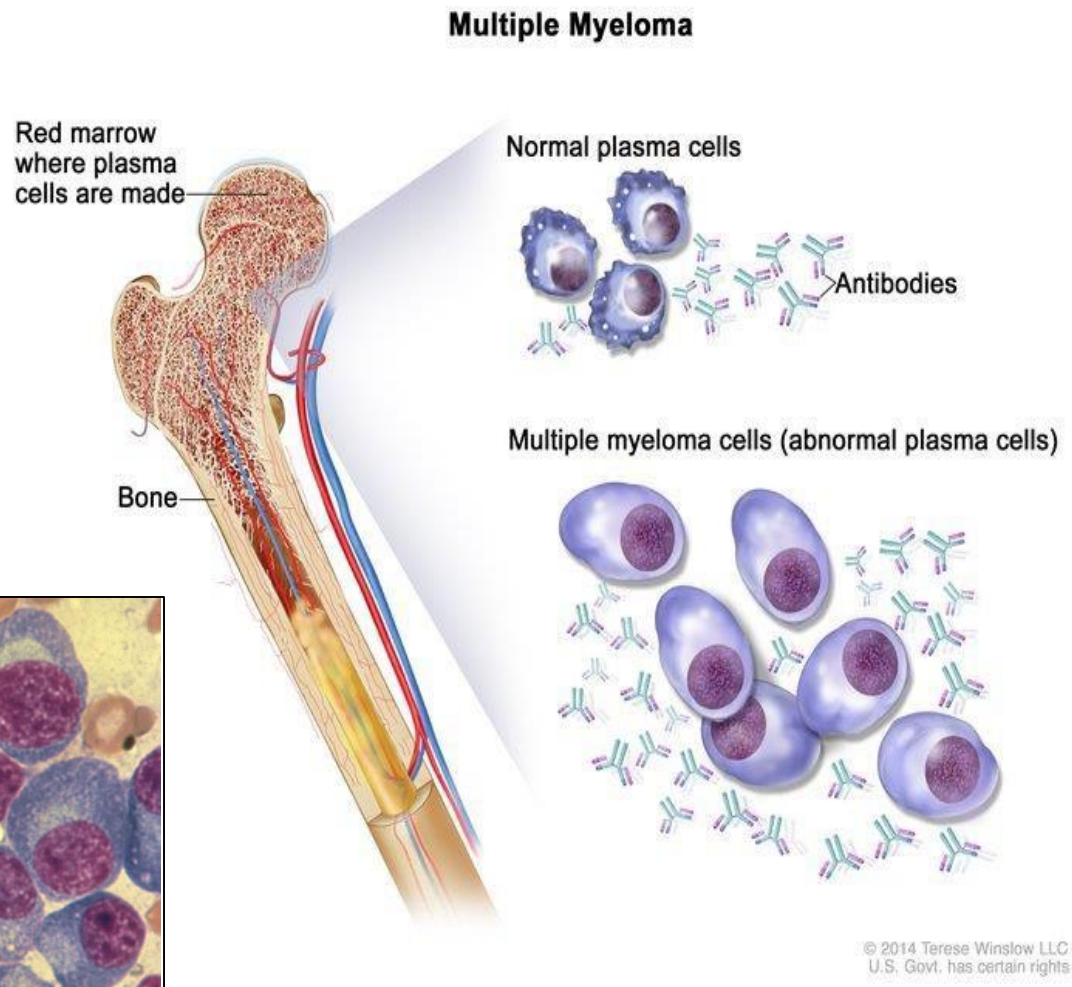
- Assess signs and symptoms of MM in primary care settings to facilitate timely identification and referral
- Differentiate current and emerging therapies and combination regimens for the treatment of MM across the disease continuum
- Apply strategies to manage treatment- and disease-related adverse events to optimize clinical and quality of life outcomes in patients with MM

MM = multiple myeloma.

What Is Multiple Myeloma?

- **Multiple myeloma** is a blood cancer that starts in *plasma cells* in the marrow
- These malignant plasma cells produce monoclonal (or “M”) proteins
- It is characterized by the classic CRAB criteria
  - Calcium elevation
  - Renal insufficiency
  - Anemia
  - Bone disease

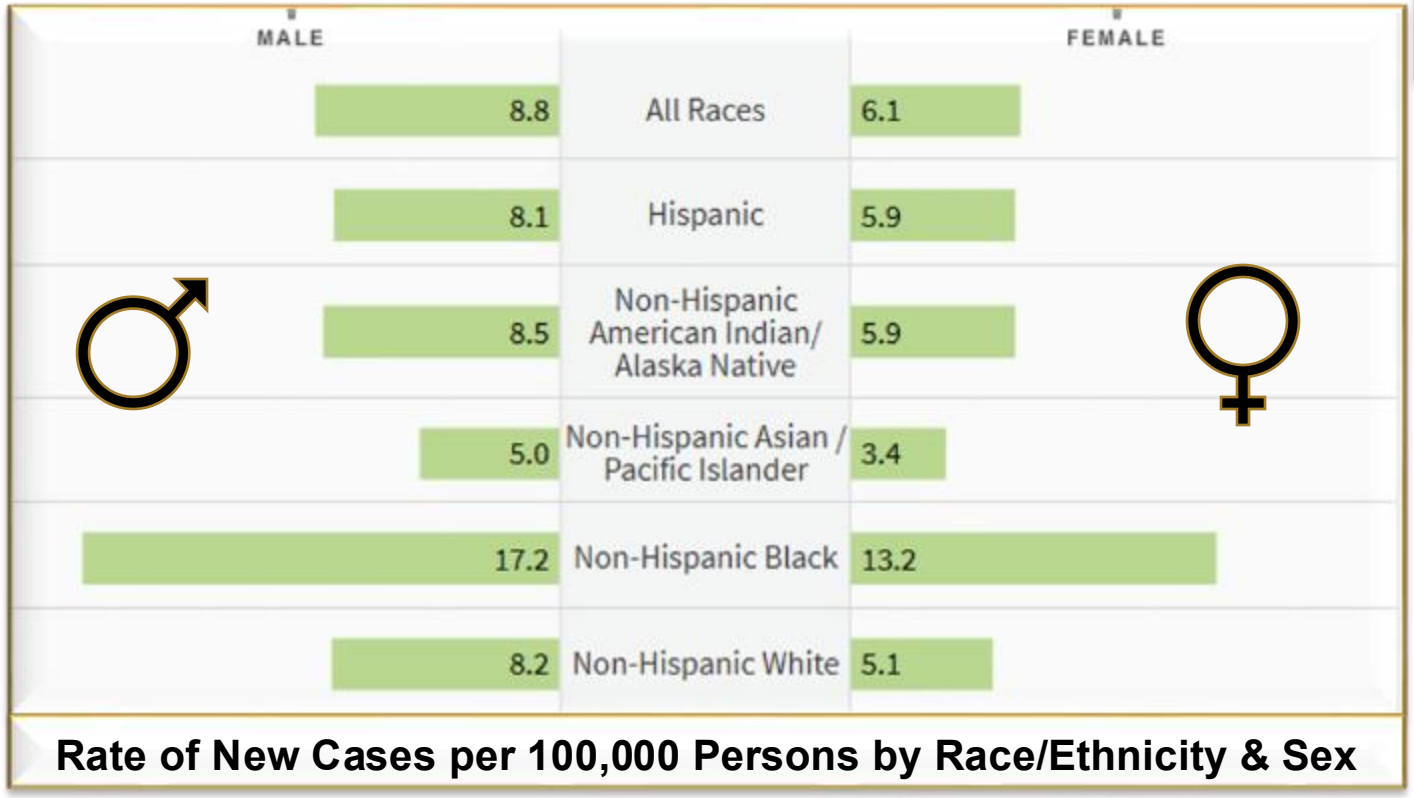




National Cancer Institute. Accessed April 13, 2026. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/myeloma.

How Common Is Myeloma in the US?

Estimated New Cases in 2025	36,110
% of All New Cancer Cases	1.8%
Median Age at Diagnosis	69 years

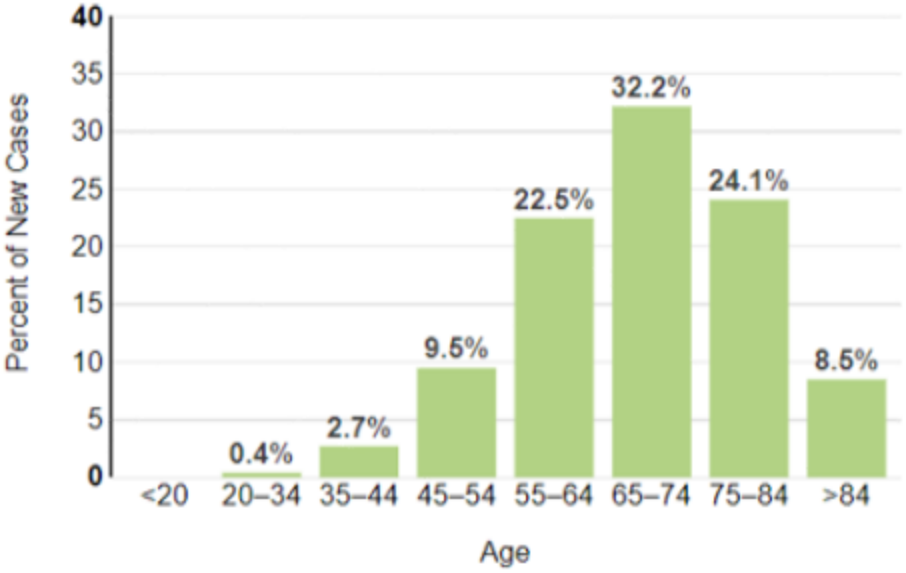


Rate of New Cases per 100,000 Persons by Race/Ethnicity & Sex

How Common Is Myeloma?

1.	Breast Cancer (Female)	316,950	42,170
2.	Prostate Cancer	313,780	35,770
3.	Lung and Bronchus Cancer	226,650	124,730
4.	Colorectal Cancer	154,270	52,900
5.	Melanoma of the Skin	104,960	8,430
	-	-	-
14.	**Myeloma**	**36,110**	**12,030**

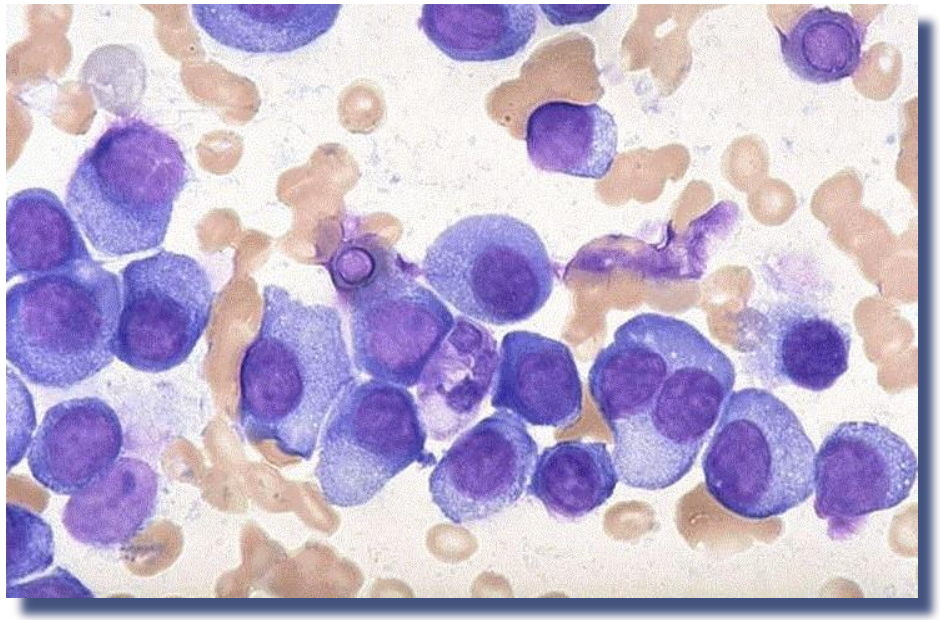
Percent of New Cases by Age

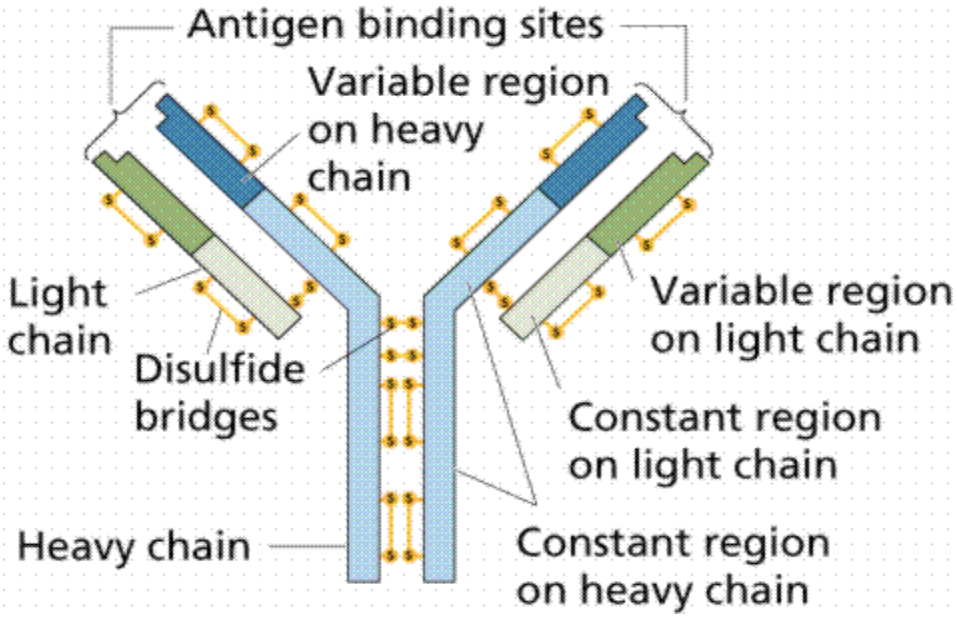


National Cancer Institute. Accessed April 13, 2026. https://seer.cancer.gov/statfacts/html/mulmy.html.

Practical Updates in Primary Care

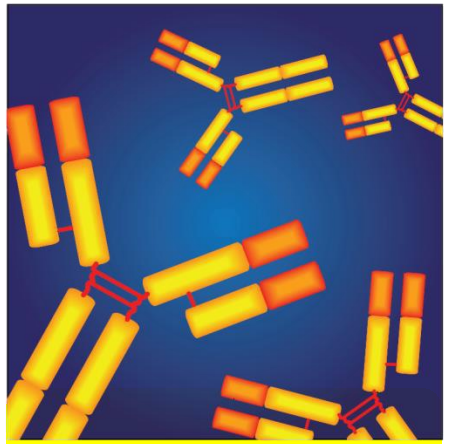
The Plasma Cell and Immunoglobulins





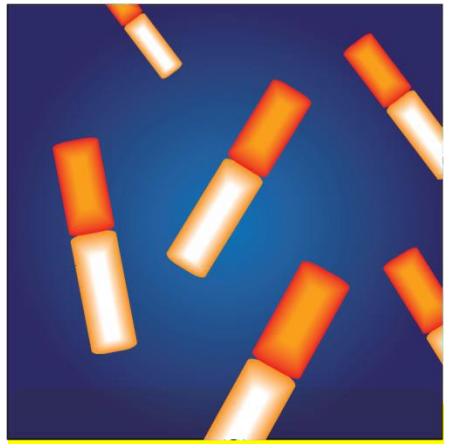
Practical Updates in Primary Care

Types of Monoclonal Protein in Multiple Myeloma



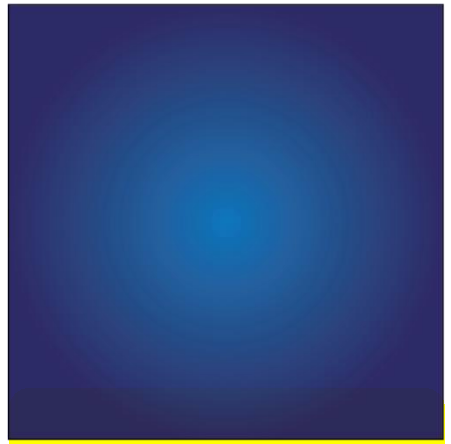
Intact immunoglobulin

- For example
  - IgG + kappa
  - IgG + lambda
  - IgA + kappa
  - IgA + lambda
  - Etc…
- 80% of myeloma cases



Light chain only

- Also known as Bence Jones protein
- 18% of all myeloma cases
- Renal failure more common in light chain multiple myeloma; creatinine >2 mg/dL in 1/3 of cases



Non-secretory

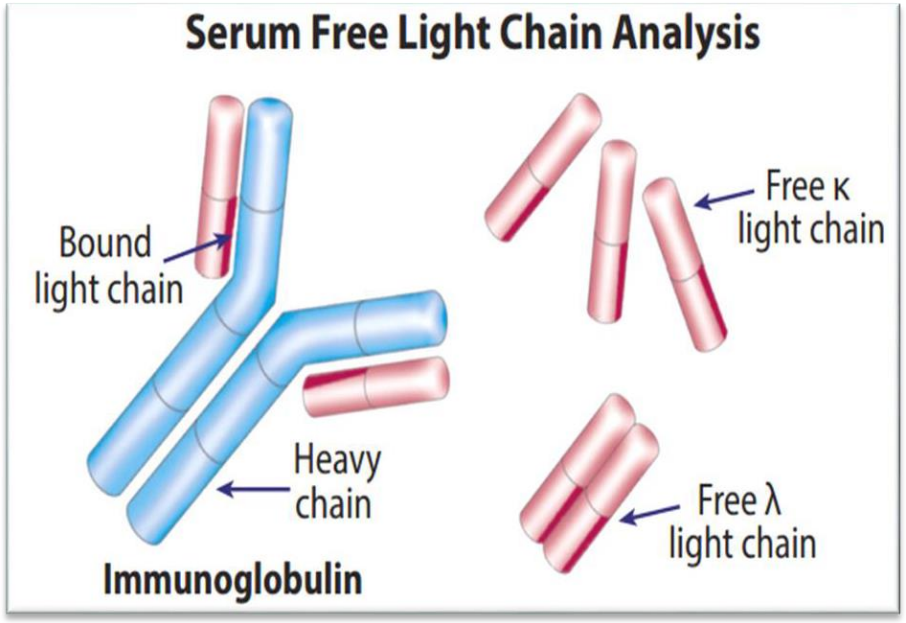
- No monoclonal protein present
- Less than 3% of cases of multiple myeloma

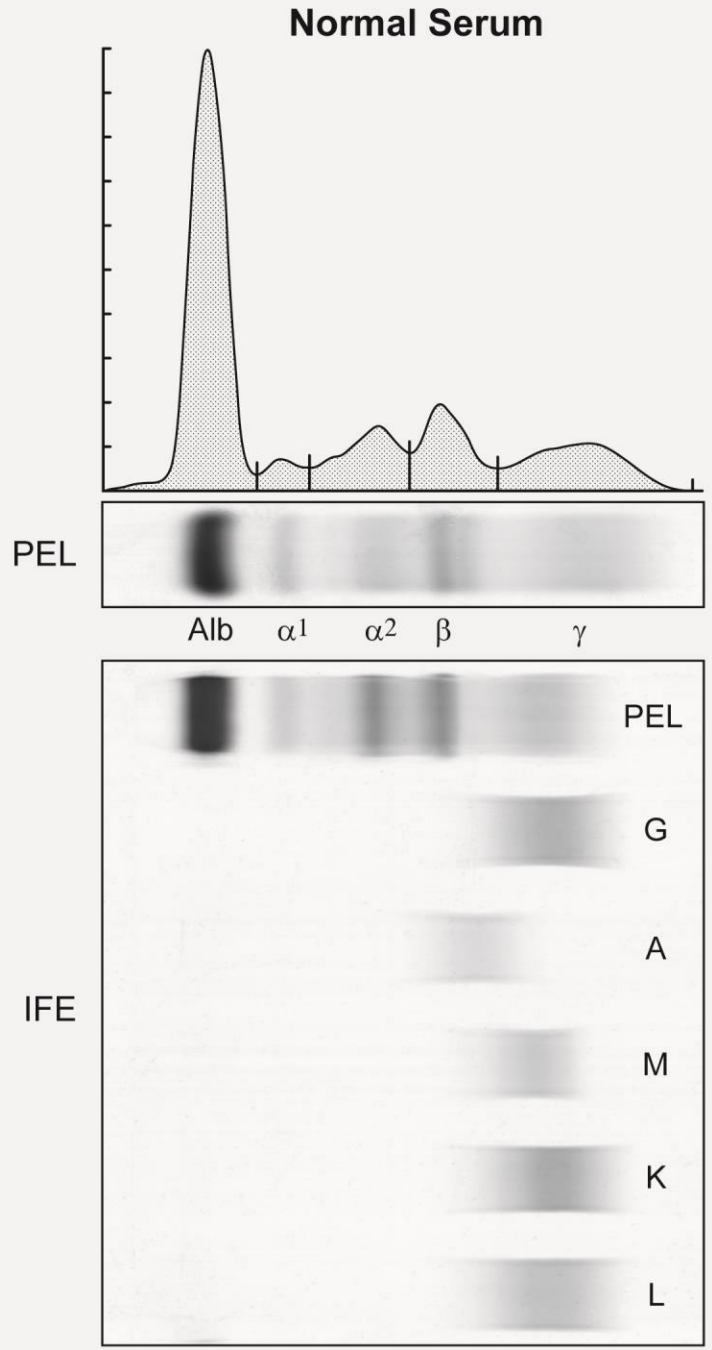
Ig = immunoglobulin.

Yee, et al. Presented at: MM Research Foundation (MMRF) Patient Summit; 2017; West Palm Beach, FL.

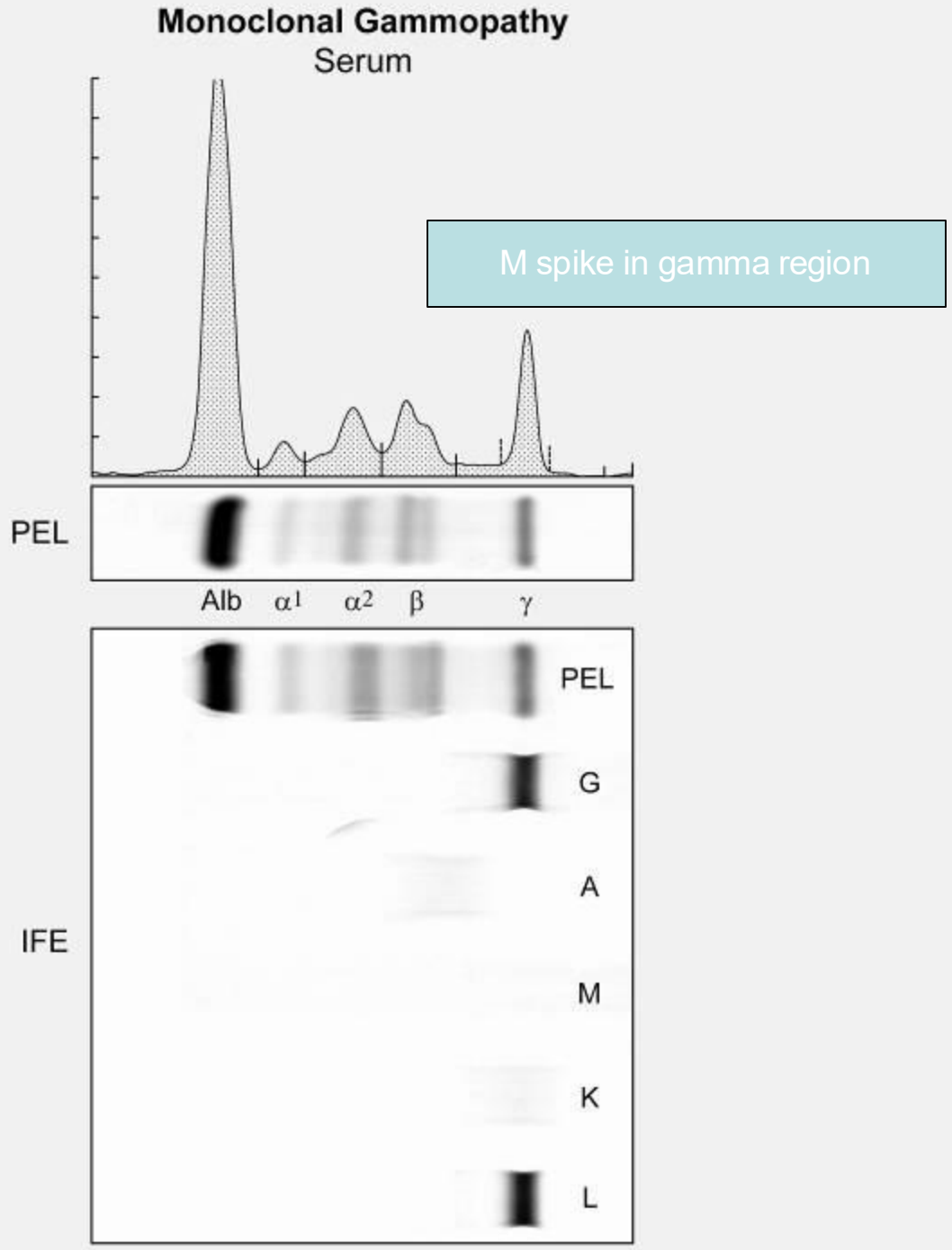
Multiple Myeloma: Types

- Subtypes of MM are determined based on the kind of abnormal protein
  - IgG – 55%
  - IgA – 25%
  - IgD – 1-2%
  - IgM – 1%
  - Light chain disease only – 20%
  - Non-secretors – 1-2%

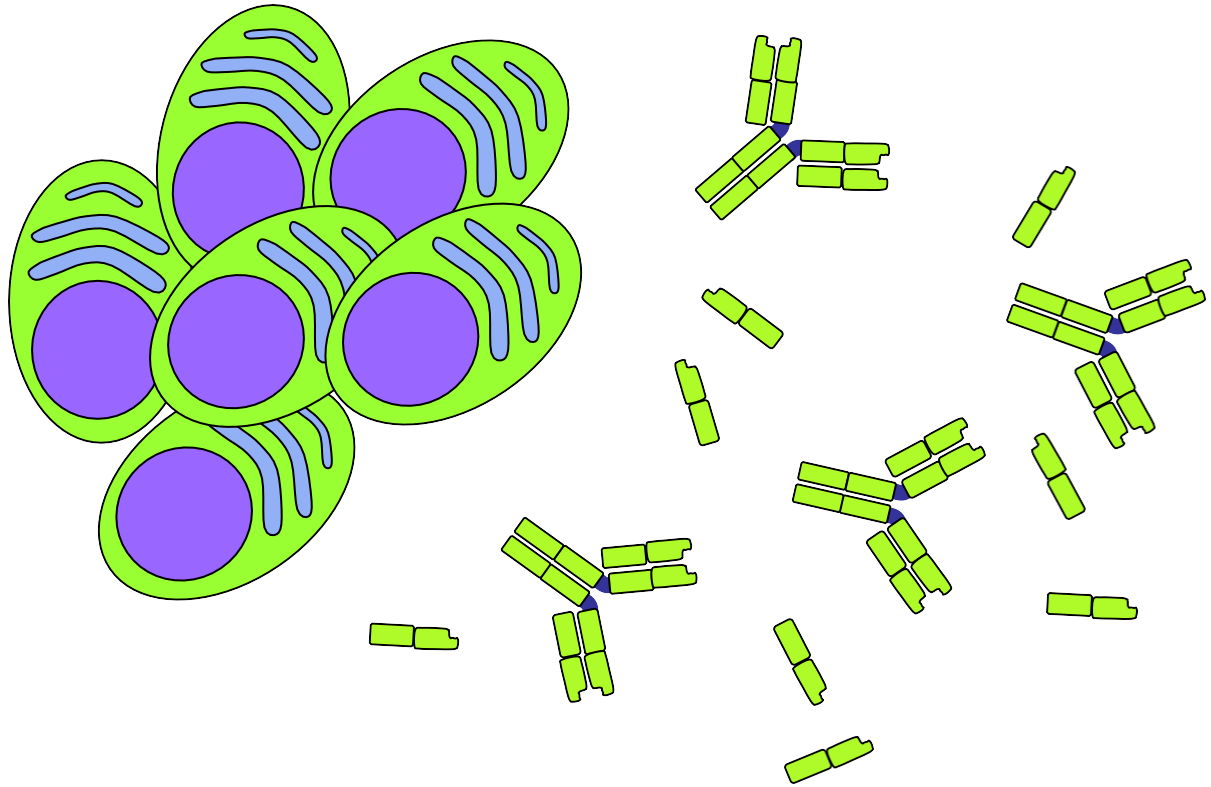




PEL = protein electrophoresis; IFE = immunofixation electrophoresis.



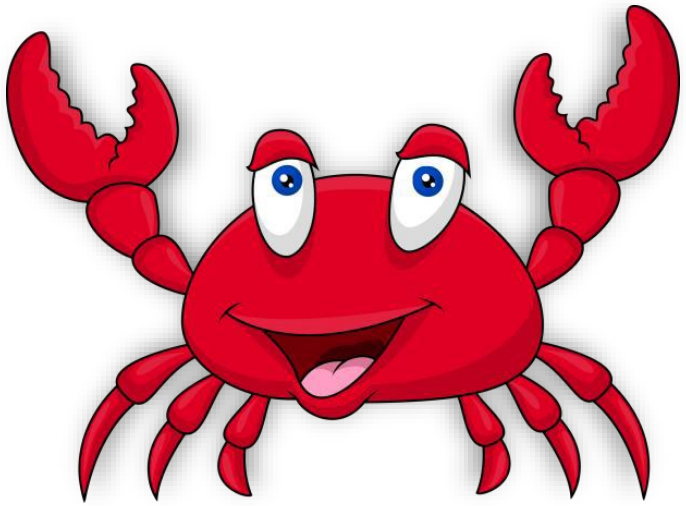
Diagnosis of Multiple Myeloma: Monoclonal Immunoglobulin – Both “Heavy” and “Light” Chains



Practical Updates in Primary Care

The Important Details

- Remember: Myeloma is a unique cancer – defined by the presence of organ damage, not just pathology
- Traditionally, we wait until CRAB
- For good reason!!! Many will smolder for years… and may NEVER progress!
- Hence the phrase “monoclonal gammopathy of undetermined significance”



Practical Updates in Primary Care

Multiple Myeloma Typically Preceded by Premalignant Conditions

	Premalignant		Malignant
Condition	**MGUS (Monoclonal Gammopathy of Undetermined Significance)**	**SMM (Smoldering Multiple Myeloma)**	**Active Multiple Myeloma**
Clonal plasma cells in bone marrow	<10%	10-60%	≥10%
Presence of myeloma-defining events	None	None	Yes
Likelihood of progression	~1% per year	~10% per year	Not applicable
Treatment	No; observation	Possibly for high risk*; no for others	Yes

***Recent FDA approval of daratumumab monotherapy in high-risk SMM.**

Kyle RA, et al. *N Engl J Med*. 2007;356(25):2582-2590. International Myeloma Working Group. *Br J Haematol*. 2003;121(5):749-757. Jagannath S, et al. *Clin Lymphoma Myeloma Leuk*. 2010;10(1):28-43. Kyle RA, et al. *Curr Hematol Malig Rep*. 2010;5(2):62-69. Mateos MV, et al. *Blood*. 2009;114(22):614. Durie BG, Salmon SE. *Cancer*. 1975;36(3):842-854. Durie BGM, et al. *Leukemia*. 2006;20(9):1467-1473. Rajkumar SV, et al. *Lancet Oncol*. 2014;15(12):e538-e548.

Practical Updates in Primary Care

2014 IMWG Active Myeloma Criteria: Myeloma-Defining Events

Clonal bone marrow ≥10% or bony/extramedullary plasmacytoma

AND any one or more **m**yeloma-**d**efining **e**vent

Calcium elevation

Renal complications

Anemia

Bone disease

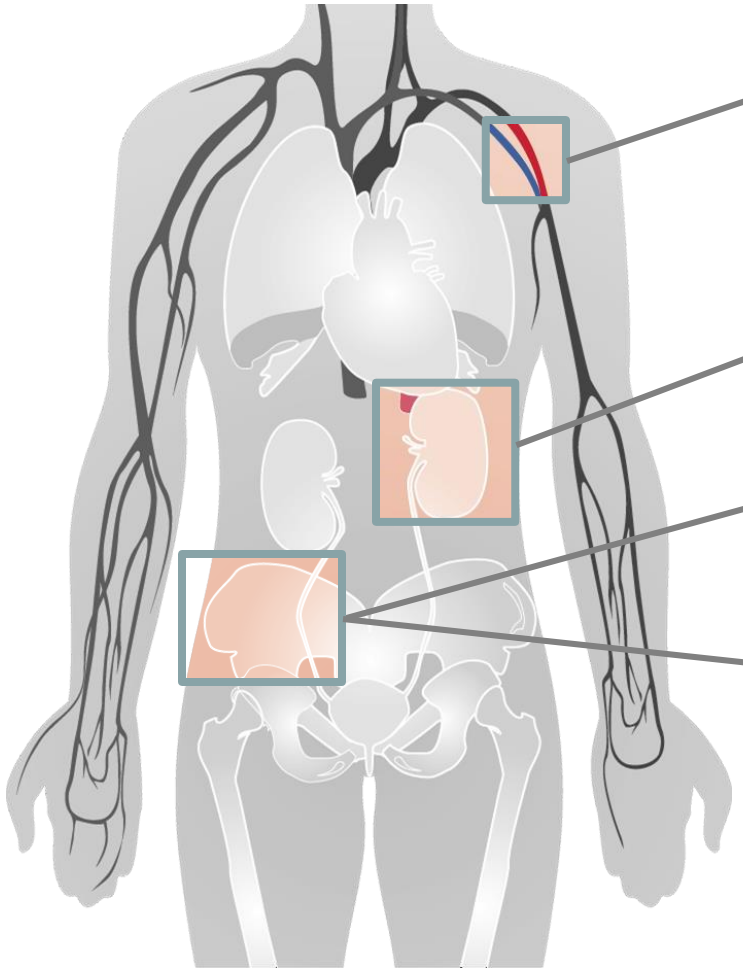
BM	Clonal bone marrow ≥60%
FLC	sFLC ratio >100
MRI	>1 focal lesion by MRI

IMWG = International Myeloma Working Group; BM = bone marrow; FLC = free light chain; sFLC = serum FLC; MRI = magnetic resonance imaging.

Rajkumar SV, et al. *Lancet Oncol*. 2014;15(12):e538-e548. Kyle RA, et al. *Leukemia*. 2010;24(6):1121-1127.

Practical Updates in Primary Care

More about the Common "CRAB" Symptoms



Low Blood Counts
- May lead to **anemia** and infection
- **Anemia** is present in 60% at diagnosis

→ **Weakness Fatigue Infection**

Decreased Kidney Function
- Occurs in over half of patients with myeloma

→ **Weakness**

Bone Damage
- Affects 85% of patients
- Leads to fractures

→ **Bone Pain**

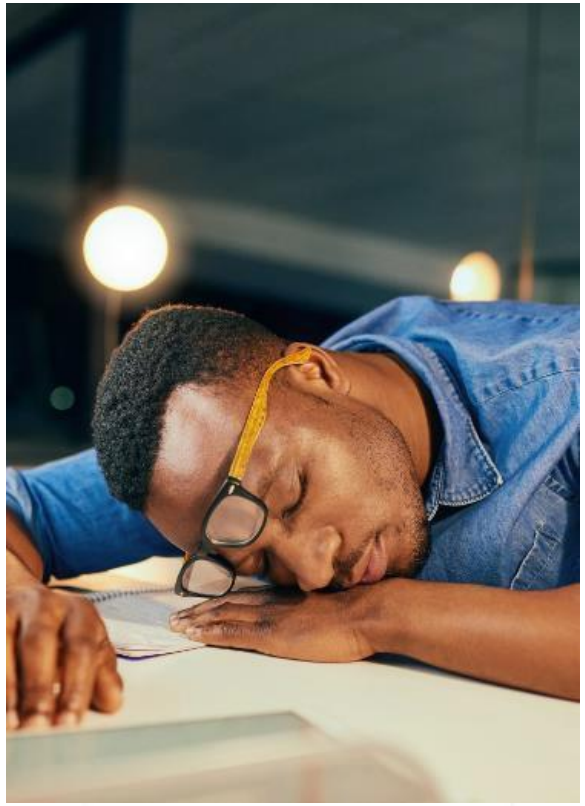
Bone Turnover
- Leads to high levels of **calcium** in blood (hypercalcemia)

→ **Loss of Appetite & Weight Loss**

About 10-20% of patients with newly diagnosed myeloma will not have any symptoms

Campbell K. *Nurs Times*. 2014;110(34-35):12-15.

Multiple Myeloma Diagnosis Can Be Challenging



32%

Fatigue

58%

Bone Pain

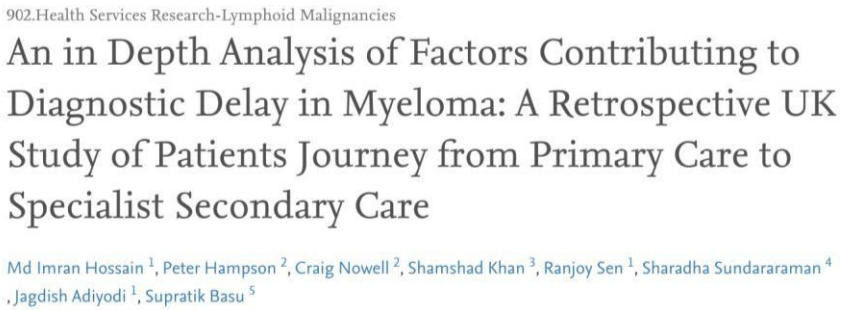
73%

Anemia

Kyle RA, et al. *Mayo Clin Proc*. 2003;78(1):21-33.

Practical Updates in Primary Care

Delayed Diagnosis of Myeloma



902.Health Services Research-Lymphoid Malignancies

An in Depth Analysis of Factors Contributing to Diagnostic Delay in Myeloma: A Retrospective UK Study of Patients Journey from Primary Care to Specialist Secondary Care

Md Imran Hossain [1], Peter Hampson [2], Craig Nowell [2], Shamshad Khan [3], Ranjoy Sen [1], Sharadha Sundararaman [4], Jagdish Adiyodi [1], Supratik Basu [5]

- The average patient with MM sees their primary care physician **THREE** times with signs or symptoms consistent with MM prior to the diagnosis
- Certain populations are at higher risk of delayed diagnosis based on race, ethnicity, socio-economic status, and confounding diagnoses such as **diabetes**
- Recognizing the appropriate signs/symptoms **AND** ordering the right testing is critical to a more timely diagnosis

Hossain MI, et al. *Blood*. 2021;138(Suppl 1):3007.

A Call to Action – Facts about African Americans and Myeloma

1. There is a **longer time from symptoms to diagnosis** among African Americans
2. African Americans are **younger by about 5 years** on average at diagnosis
3. MM and MGUS are **more than 2x as common** in African Americans
4. African Americans are **less likely to receive the four "T"s: Triplets, transplants, trials, and CAR T**
5. African Americans have **biologic differences** with more t(11;14) and less high-risk cytogenetics with deletion 17p
6. Survival outcomes in African Americans are HALF of what is seen in White Americans
7. African Americans can **achieve equal or better outcomes** <u>when</u> they receive therapy

CAR = chimeric antigen receptor.

Bhutani M, et al. *Blood Cancer J*. 2023;13(1):189.

Practical Updates in Primary Care

What Are the DRIVERS of Disparities in MM?

1. Systemic racism
2. The healthcare system
3. Social determinants of health
4. Lack of trust in the medical system
5. Biology of the disease and concomitant comorbidities
6. **Delayed diagnosis**
7. Access to care: Triplets, transplants, trials, and CAR T
8. Lack of diversity, cultural sensitivity, and optimal communication

Bhutani M, et al. *Blood Cancer J*. 2023;13(1):189.

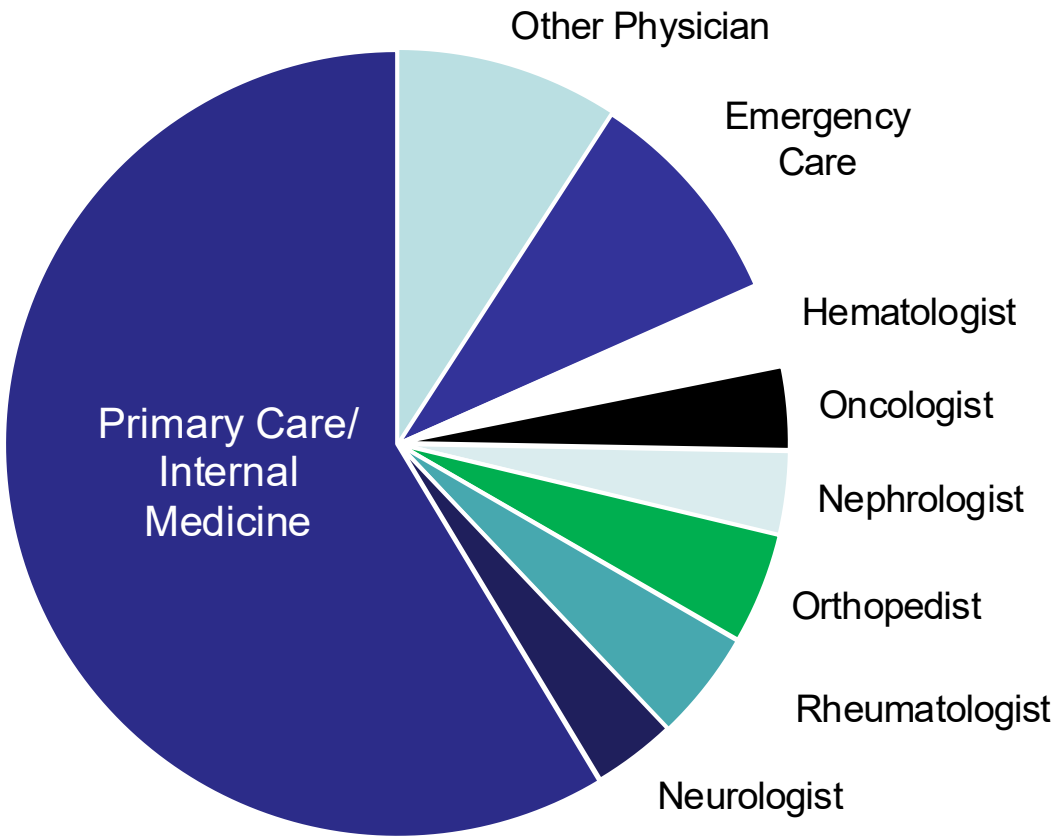
Practical Updates in Primary Care

Access to Care in the US – Health Insurance Status Is a Primary Determinant of Access to Care

- Being uninsured or underinsured affects
  - Time to diagnosis
  - Ability to accept treatment
  - Heath outcomes
- Financial toxicity is associated with
  - Lower rates of treatment acceptance
  - Reduced follow-up care
  - Reduced adherence to medication
  - Difficulty keeping appointments
- African Americans are disproportionately affected by financial toxicity, and are more likely to be uninsured or underinsured

American Association for Cancer Research (AACR). *AACR Cancer Disparities Progress Report 2020*. Accessed April 13, 2026. https://cancerprogressreport.aacr.org/wp-content/uploads/sites/2/2020/09/AACR_CDPR_2020.pdf.

Different Specialists See and Diagnose Patients with Multiple Myeloma



Typical diagnostic intervals

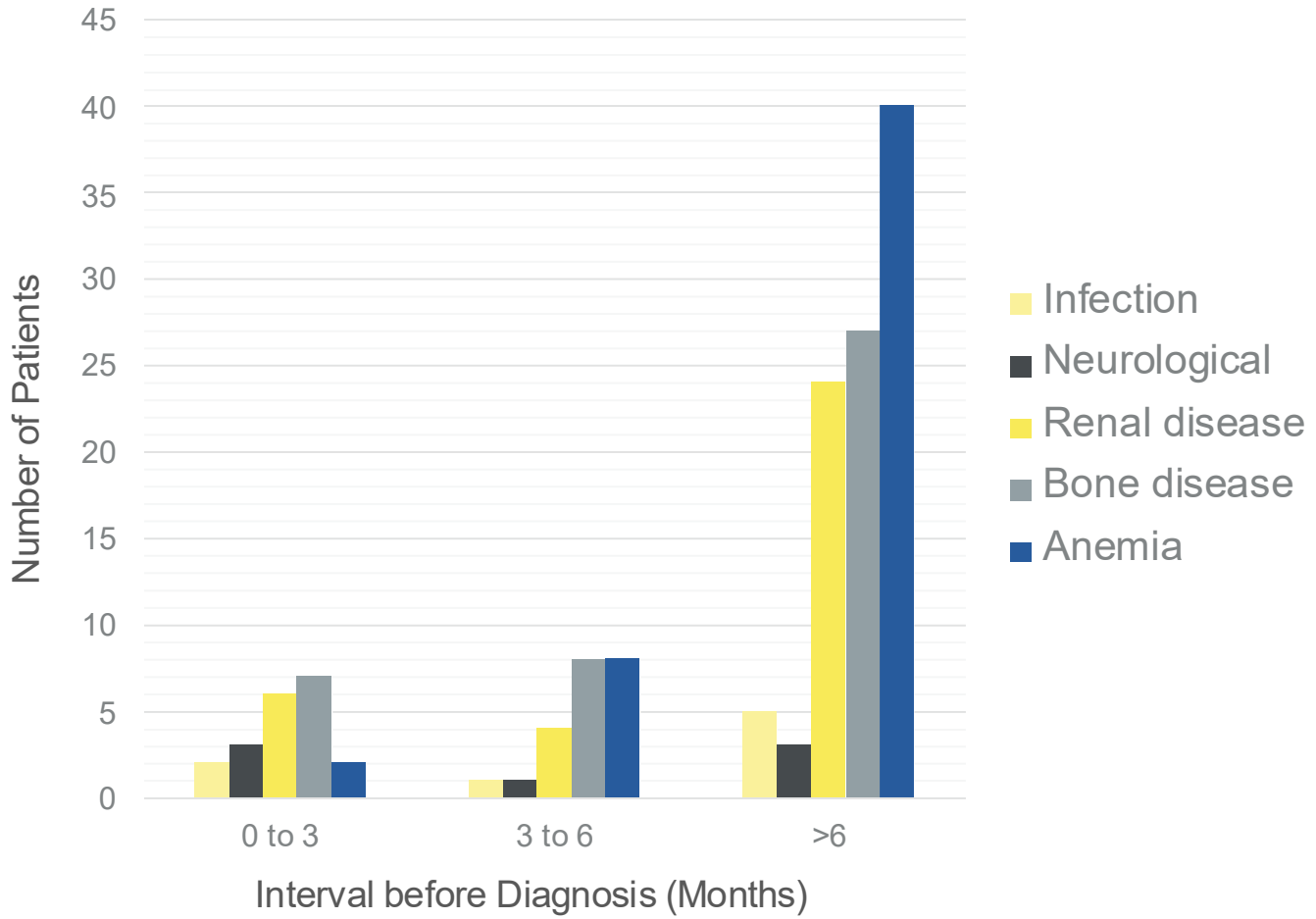
Hematology/oncology: <3 months
Primary care: >6 months

The average patient will see their PCP THREE times with signs and symptoms of MM before the diagnosis is suspected!

Kariyawasan CC, et al. *QJM*. 2007;100(10):635-640. Hossain MI, et al. *Blood*. 2021;138(Suppl 1):3007.

Practical Updates in Primary Care

Diagnosis Delays Lead to Clinical Complications



Adapted from: Kariyawasan CC, et al. *QJM*. 2007;100(10):635-640. Koshiaris C, et al. *BMJ Open*. 2018;8(6):e019758.

Practical Updates in Primary Care

Don’t Delay Testing: Expert Recommendations

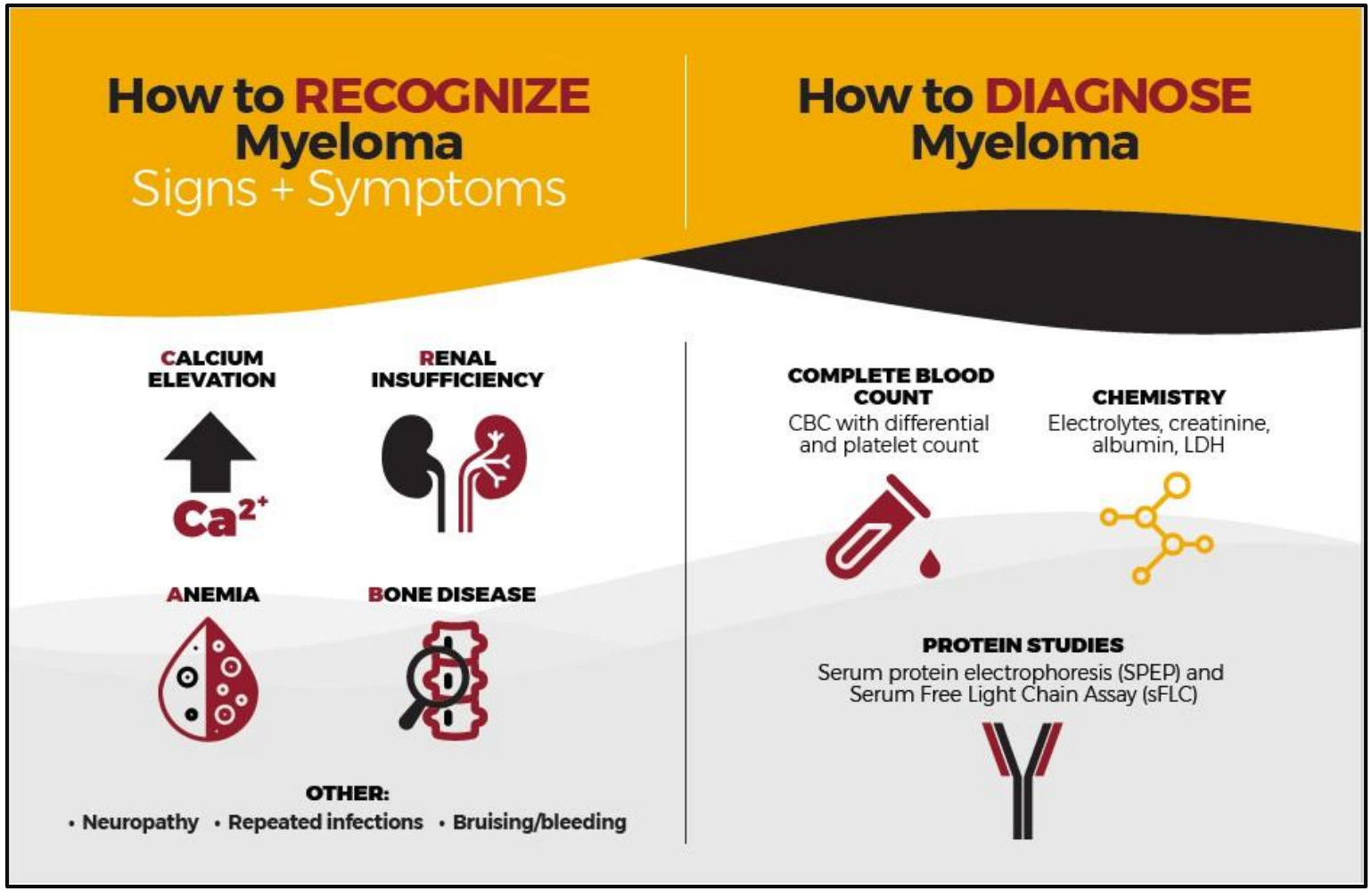
Initiate preliminary lab testing for

- Persistent bone or back pain
- Unexplained fracture
- Incidental findings associated with myeloma
  - Anemia
  - Impaired kidney function
  - Hypercalcemia or leukopenia
  - Bony lesions
  - Neuropathy
  - Osteopenia/osteoporosis atypical of age and/or gender

- ?? Maybe screen high-risk populations someday in the future

Education of PCPs: Don’t Miss the Signs

Our goal is to reduce **DELAYS** in diagnosis among African Americans by educating the primary care community



CBC = complete blood count; LDH = lactate dehydrogenase.

Practical Updates in Primary Care

Making the Diagnosis
Laboratory Testing

Blood counts

CBC with differential and platelet count

- ✓ Anemia
- ✓ Leukopenia
- ✓ Thrombocytopenia
- ✓ Neutropenia

International Myeloma Foundation (IMF). Accessed April 13, 2026. https://www.myeloma.org/resource-library/understanding-your-test-results.

Making the Diagnosis
Laboratory Testing

Blood counts

CBC with differential and platelet count

Kidney function

Chemistry panel, eGFR, electrolytes

- ✓ Decreased creatinine clearance
- ✓ Hypercalcemia
- ✓ Elevated glucose

eGFR = estimated glomerular filtration rate.

IMF. Accessed April 13, 2026. https://www.myeloma.org/resource-library/understanding-your-test-results.

Making the Diagnosis
Laboratory Testing

Blood counts

CBC with differential and platelet count

Kidney function

Chemistry panel, eGFR, electrolytes

Serum proteins

Albumin, β-2 microglobulin, LDH, CRP

- ✓ LDH and β-2 microglobulin reflect tumor cell characteristics
- ✓ CRP signals inflammation
- ✓ Elevated total protein indicates additional albumin and globulin testing

CRP = C-reactive protein.

IMF. Accessed April 13, 2026. https://www.myeloma.org/resource-library/understanding-your-test-results.

Making the Diagnosis
Laboratory Testing

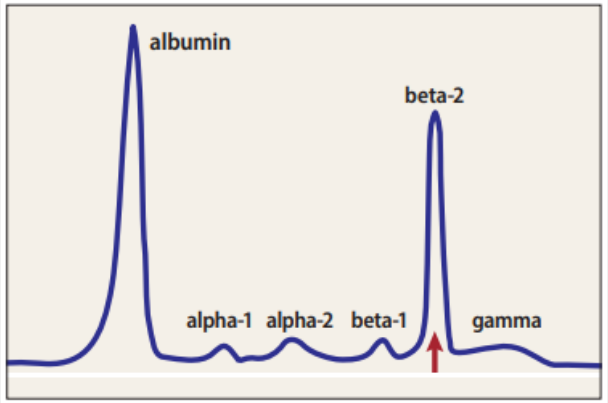
Blood counts
CBC with differential and platelet count

Kidney function
Chemistry panel, eGFR, electrolytes

Serum proteins
Albumin, β-2 microglobulin, LDH, CRP

Monoclonal protein (M protein)
Serum and urine protein electrophoresis, immunofixation electrophoresis, quantitative immunoglobulins, serum FLC assay

- ✓ QIg: Quantifies each isotypes
- ✓ SPEP: Identifies presence of M protein

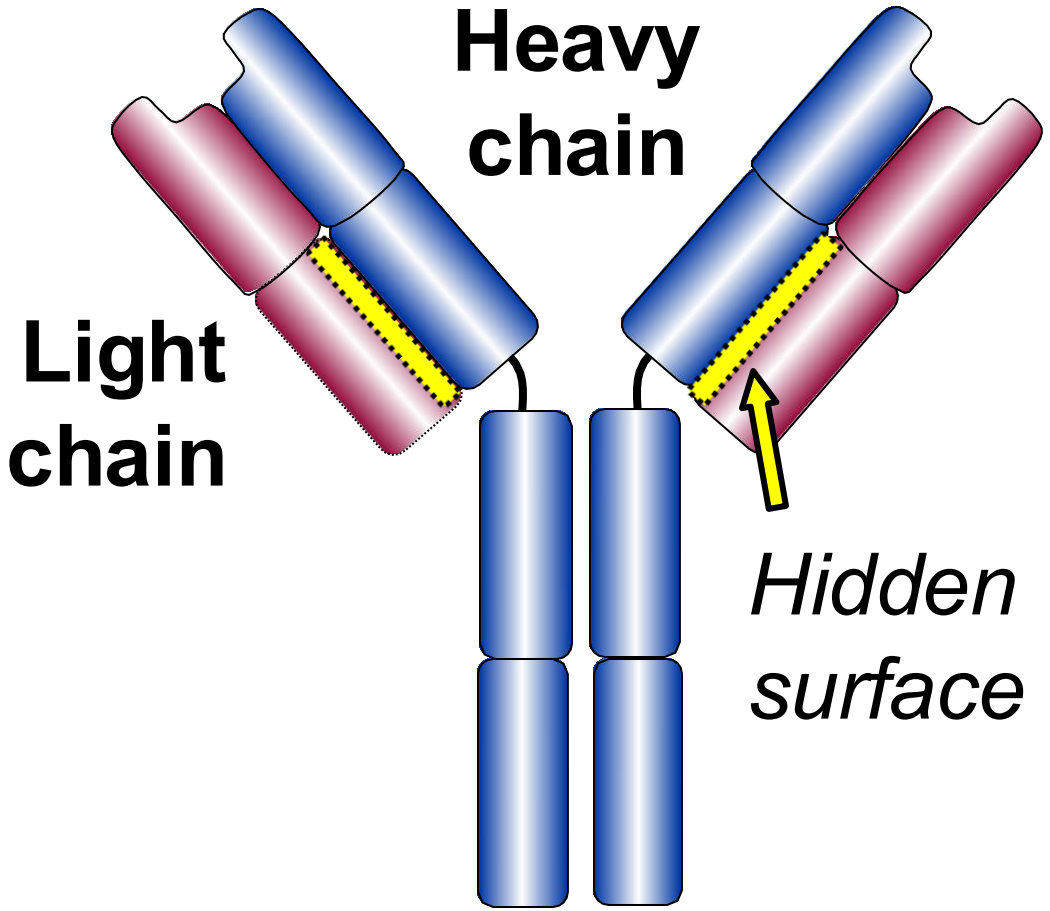


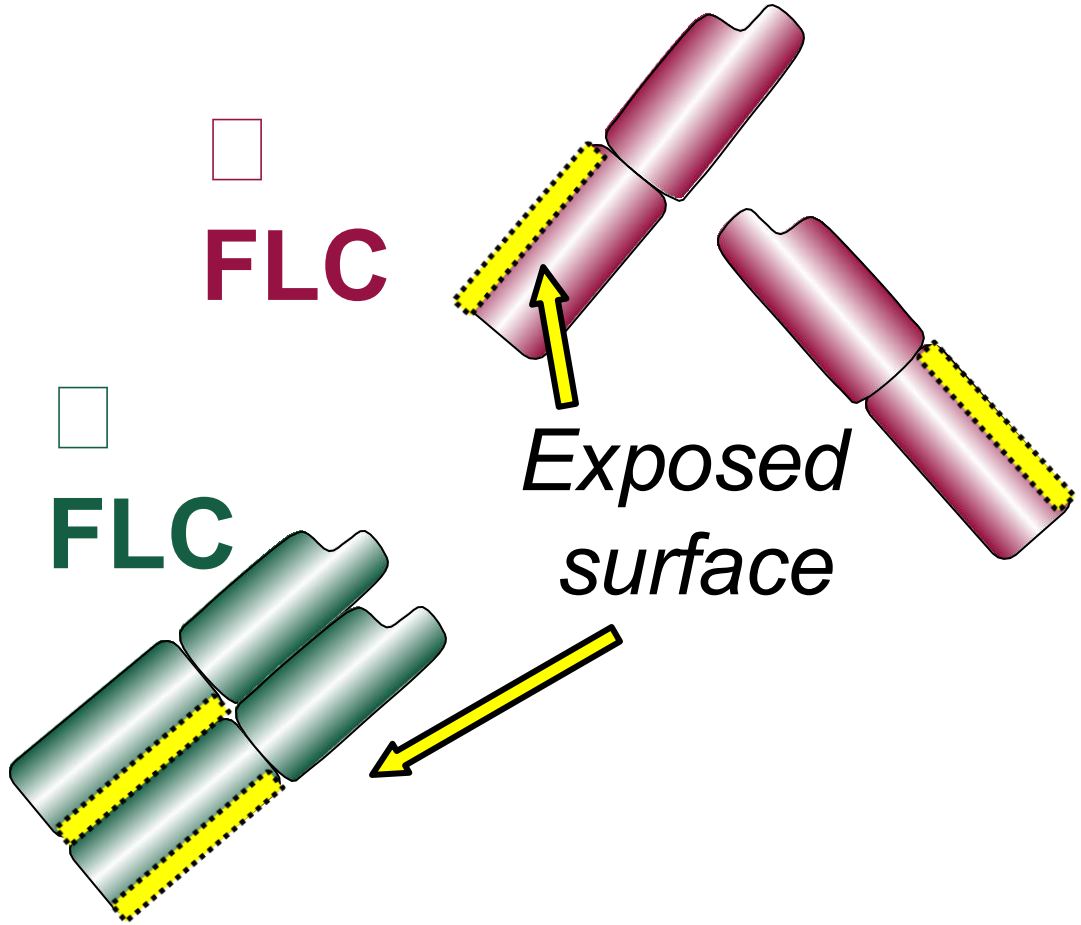
- ✓ UPEP: Quantifies circulating light chains
- ✓ IFE: Identifies type of M protein
- ✓ sFLC assay: Quantifies circulating light chains and specifically measures free light chain proteins

SPEP = serum protein electrophoresis; UPEP = urine protein electrophoresis.

IMF. Accessed April 13, 2026. https://www.myeloma.org/resource-library/understanding-your-test-results.

Serum Free Light Chain Immunoassay





Practical Updates in Primary Care

SPE Alone Is Insensitive at Diagnosis

Screening Algorithm	Diagnostic Sensitivity (%)	
SPE	**MM** **AL**	87.6 65.9
sIFE + uIFE	**MM** **AL**	98.7 94.2
SPE + sFLC	**MM** **AL**	100 96.2

sFLC testing in addition to SPE improves detection rates and eliminates the reliance on urine testing

AL = amyloidosis.

Katzmann JA, et al. *Clin Chem*. 2009;55(8):1517-1522.

CAP Guidelines

Guideline Statement	Strength of Recommendation
1. Clinical care providers should order both SPEP and sFLC for the initial detection of M protein in all patients with suspected MG	Strong
2. Laboratorians should confirm an SPEP abnormality suspicious for a presence of an M protein with additional testing by sIFE or alternative method with similar sensitivity	Strong
3. Laboratorians and/or clinical care providers should follow up an abnormal sFLC ratio for the presence of an M protein with an sIFE or alternative method with similar sensitivity	Conditional
4. Clinical care providers should order SPEP, sFLC, sIFE, and uIFE for the initial detection of M protein in all patients with suspected AL amyloidosis	Strong
5. Clinical care providers should NOT order HLC for initial detection of M protein in patients with suspected MG	Strong
6. Clinical care providers should NOT use total/intact light chains for the quantitation of M proteins in patients with suspected myeloma	Strong
7. In patients with intact M proteins outside the γ region by SPEP, laboratories should use total immunoglobulin (IgA, IgG, or IgM) for the quantitation of the M proteins; quantitation of a band in the β region by SPEP can be performed if the M protein is distinguished from background normal protein bands	Conditional
8. Laboratorians should report both quantitative levels of free κ and free λ and the rFLC when the sFLC assay is performed	Strong
9. Clinical care providers may use rFLC, IgM isotype, M protein >1.5 g/dL, and immunoparesis as risk factors for progression to MM or a B-cell lymphoproliferative disorder	Conditional

Abbreviations: AL, amyloid light chain; HLC, heavy/light-chain isotype assay; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; M protein, monoclonal immunoglobulin protein; MG, monoclonal gammopathy; MM, multiple myeloma; rFLC, ratio of serum free κ to serum free λ; sFLC, serum free light chain; sIFE, serum immunofixation electrophoresis; SPEP, serum protein electrophoresis; uIFE, urine immunofixation electrophoresis.

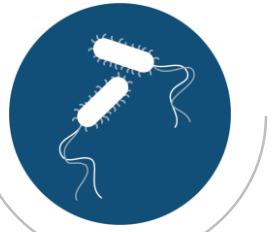
CAP = College of American Pathologists.

Keren DF, et al. *Arch Pathol Lab Med*. 2022;146(5):575-590.

What Does Active Myeloma Look Like?
Signs and Symptoms

Bone Pain

Especially lower back, hips, skull



Signs of Cytopenias

Ongoing fatigue
Infections
Dizziness
Bleeding
Bruising

Signs of Hypercalcemia

Excessive thirst
Excessive urination
Dehydration
Constipation
Loss of appetite
Weakness

Signs of Kidney Disease

Leg swelling
Shortness of breath
Itching

Neurologic Symptoms

Neuropathy

Ischemia-like symptoms

American Cancer Society (ACS). Accessed April 13, 2026. https://www.cancer.org/cancer/types/multiple-myeloma/detection-diagnosis-staging/signs-symptoms.html.

Practical Updates in Primary Care

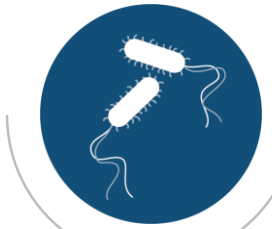
Spotting the Signs

Myeloma or Diabetes?

- Symptoms in common

Bone Pain

Especially lower back, hips, skull



Signs of Cytopenias

Ongoing fatigue
Infections
Dizziness
Bleeding
Bruising

Signs of Hypercalcemia

Excessive thirst
Excessive urination
Dehydration
Constipation
Loss of appetite
Weakness

Signs of Kidney Disease

Leg swelling
Shortness of breath
Itching

Neurologic Symptoms

Neuropathy

Ischemia-like symptoms

ACS. Accessed April 13, 2026. https://www.cancer.org/cancer/types/multiple-myeloma/detection-diagnosis-staging/signs-symptoms.html. American Diabetes Association (ADA). Accessed April 13, 2026. https://diabetes.org/diabetes/type-2/symptoms; https://diabetes.org/about-diabetes/complications.

Practical Updates in Primary Care

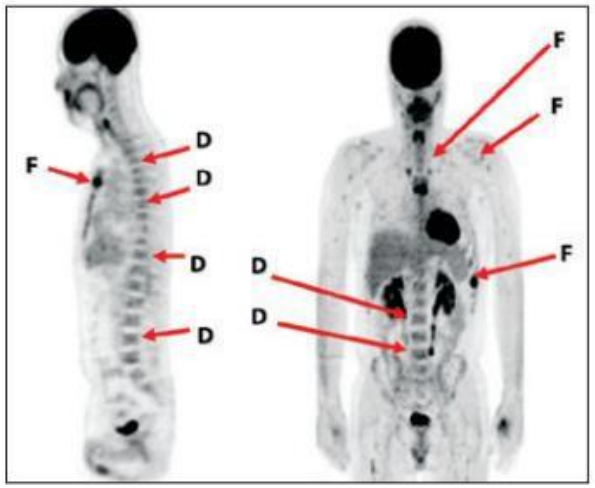
The Essential 5

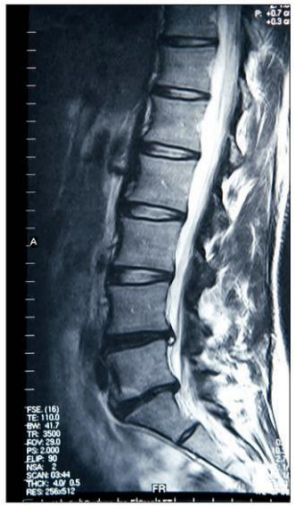
Key blood tests in making the diagnosis of multiple myeloma

CBC
Creatinine
Calcium
Serum protein electrophoresis
Serum free light chain assay

Imaging

70-80% present with bone disease





Whole-body CT is the standard of care for detection of lytic bone lesions

- More sensitive than skeletal survey, detects soft tissue masses, improved assessment of fracture risk

MRI is highly sensitive for focal lesions

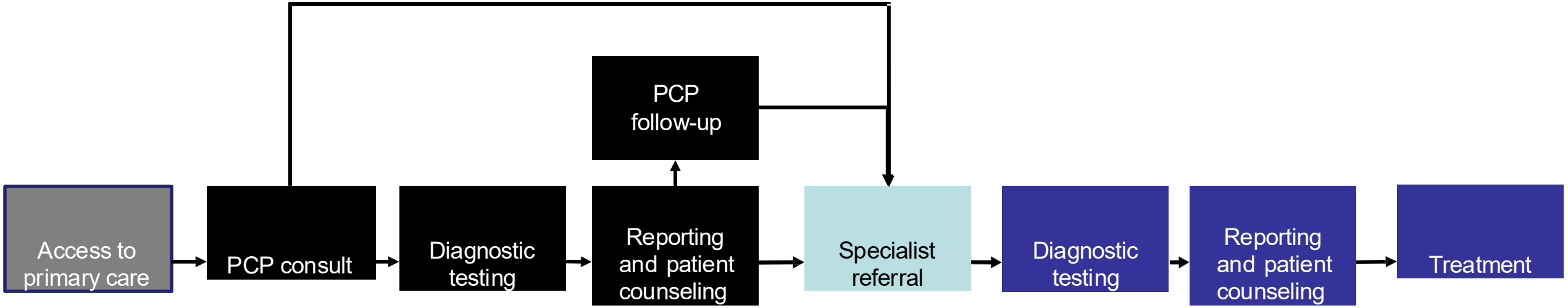
- Best used early in the disease process

CT = computed tomography.

IMF. Accessed April 13, 2026. https://www.myeloma.org/resource-library/understanding-your-test-results.

Pathway to Care

Goal: Minimize Time from Symptoms to Treatment



Success factors:						
	Effective communication Clinician awareness	Test characteristics sufficient for diagnosis Accurate interpretation	Timely reporting Adherence to follow-up	Provider selection Patient access Adherence to consult Effective communication	Test characteristics Accurate interpretation	Timely reporting Adherence to follow-up

Nekhlyudov L, et al. *J Natl Cancer Inst Monogr*. 2010;2010(40):11-17.

Practical Updates in Primary Care

The Evolution of Myeloma Therapy

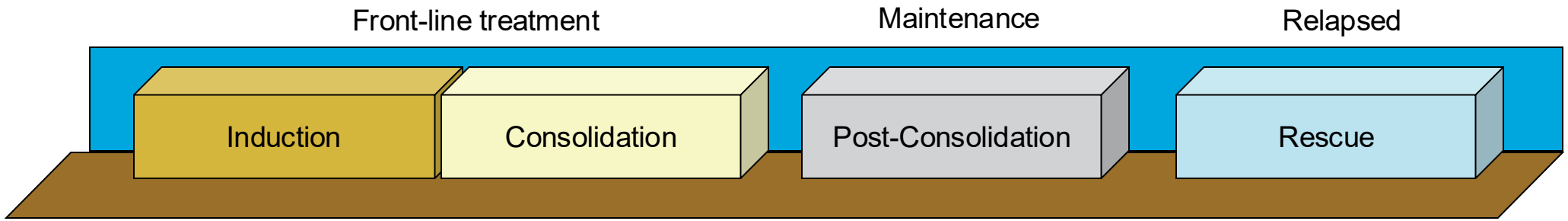
Bortezomib
Lenalidomide
Carfilzomib
Pomalidomide
Selinexor
Panobinostat
Daratumumab
Ixazomib
Elotuzumab
Isatuximab
Belantamab mafodotin
Melphalan flufenamide
Idecabtagene autoleucel
Ciltacabtagene autoleucel
Teclistamab, talquetamab
Elranatamab, Linvoseltamab

Now

VD
Rev/Dex
CyBorD
VTD
VRD
KRD
D-VMP
DRD

ASCT
Tandem ASCT (?)

Nothing
Thalidomide?
Bortezomib
Ixazomib
Lenalidomide
Combinations



New

D-VRD
Isa-VRD
D-KRD
Isa-VRD

"More" induction?

Daratumumab?
Carfilzomib?
Lenalidomide + PI

CAR T-cell therapy
Bispecific/tri-specific antibodies
Cell-modifying agents
Venetoclax
PD/PDL-1 inhibition?
Small molecules

Anito-cel
Cevostomab
Iberdomide, mezigdomide
Sonrotoclax
KLN-1010
AZD0120

ASCT = autologous stem cell transplant; Cy = cyclophosphamide; d = daratumumab; D/dex = dexamethasone; isa = isatuximab; K = carfilzomib; M = melphalan; PD-L1 = programmed death ligand-1; PI = proteasome inhibitor; Rev = lenalidomide; V = bortezomib.
Speaker's own opinions.

Practical Updates in Primary Care

Review Article

Multiple Myeloma for the Primary Care Provider: A Practical Review to Promote Earlier Diagnosis Among Diverse Populations

Joseph Mikhael, MD,[a,b] Manisha Bhutani, MD,[c] Craig E. Cole, MD[d]

[a]Applied Cancer Research and Drug Discovery Division, Translational Genomics Research Institute (TGen), City of Hope Cancer Center, Phoenix, Ariz; [b]International Myeloma Foundation, Studio City, Calif; [c]Department of Hematologic Oncology and Blood Disorders, Division of Plasma Cell Disorders, Atrium Health/Wake Forest Baptist, Levine Cancer Institute, Charlotte, NC; [d]Department of Medicine, Michigan State University-Karmanos Cancer Institute at McLaren Greater Lansing, Lansing.

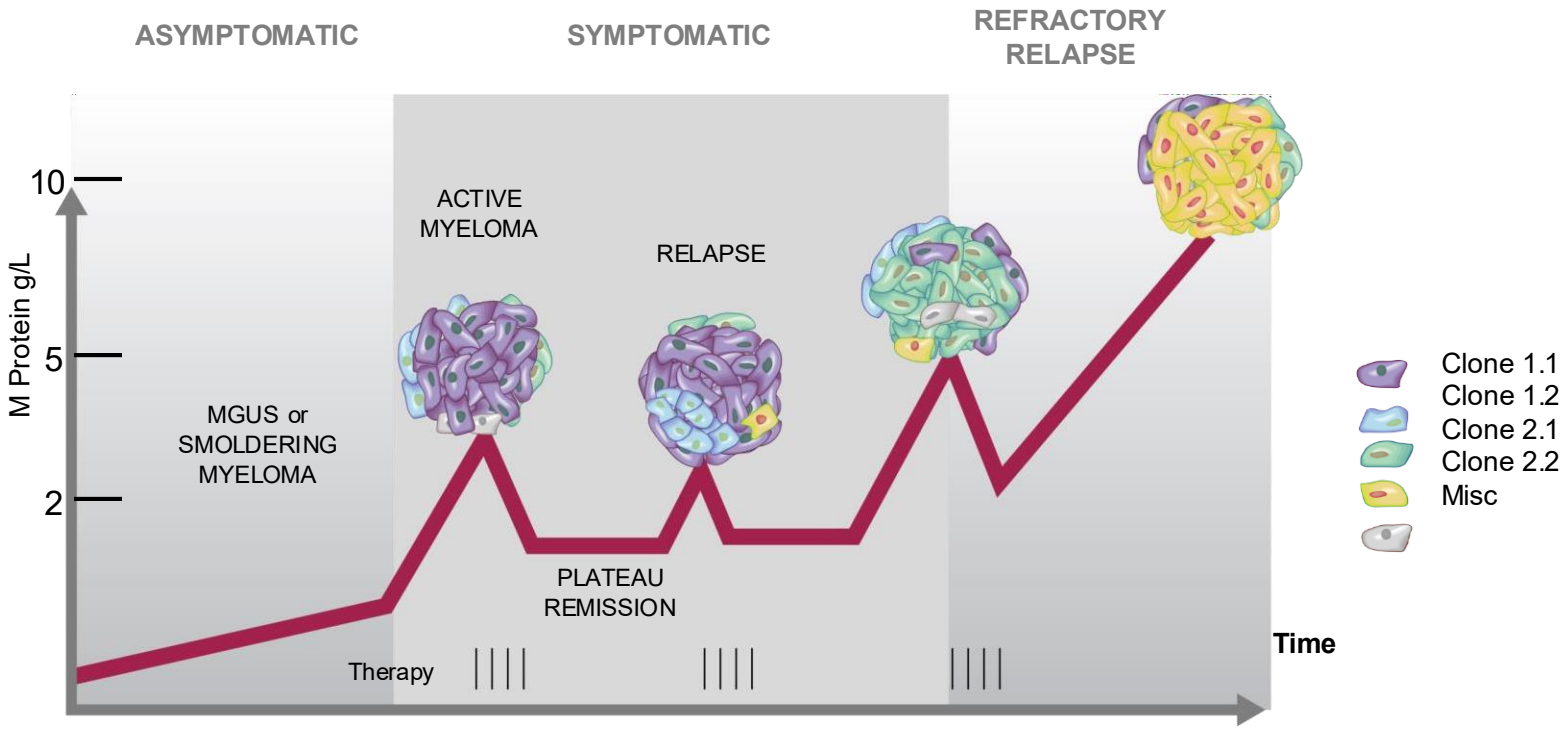
Mikhael J, et al. *Am J Med*. 2023;136(1):33-41.

Practical Updates in Primary Care

An Overview of the Treatment of Multiple Myeloma

- It remains “incurable”, but most patients live more than 10 years now
- Initially patients are divided into transplant-eligible and ineligible
- The first remission is typically the longest, but the disease does recur 3-4 years later, on average
- Subsequent therapies tend to be different classes of novel agents
- More recently, CAR T-cell therapy has revolutionized myeloma with the deepest and most durable responses ever seen
- Bispecific antibodies are the next wave of therapies that can be given “off the shelf”
- But these new therapies come with new risks and require careful management and collaboration with primary care…

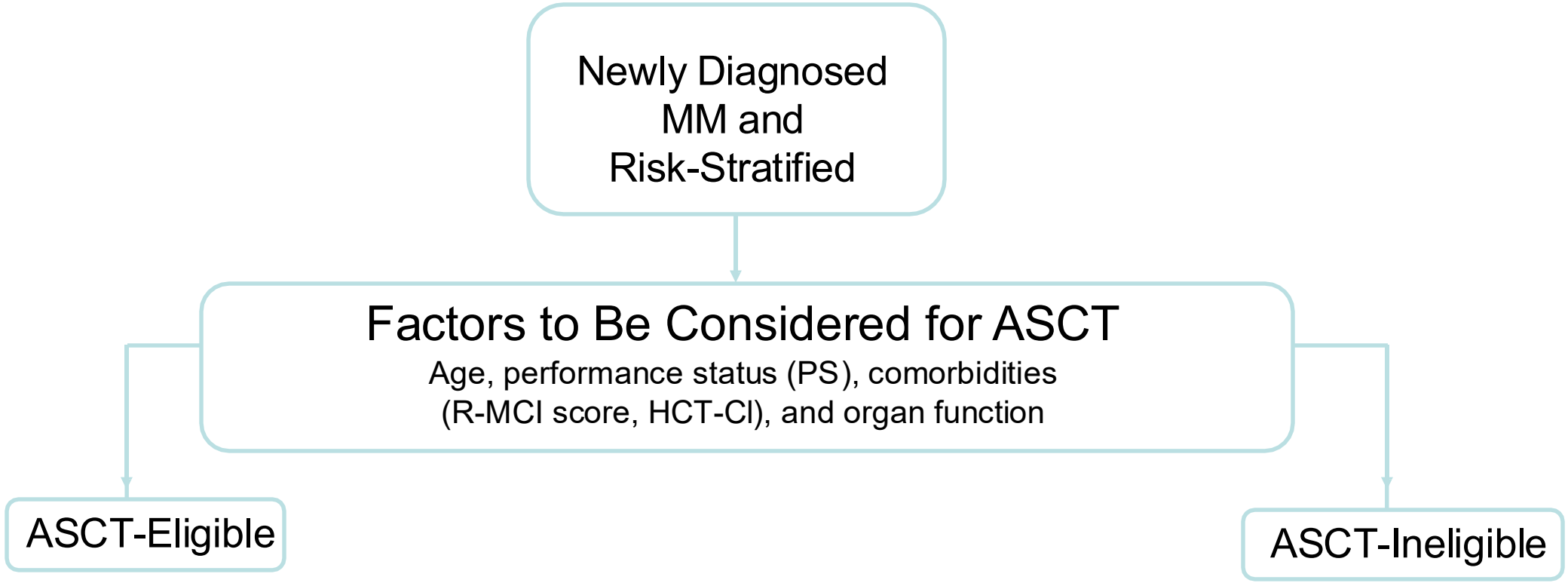
The Nature of Multiple Myeloma: Clones Change over Time



Adapted from: Keats JJ, et al. *Blood*. 2012;120(5):1067-1076.

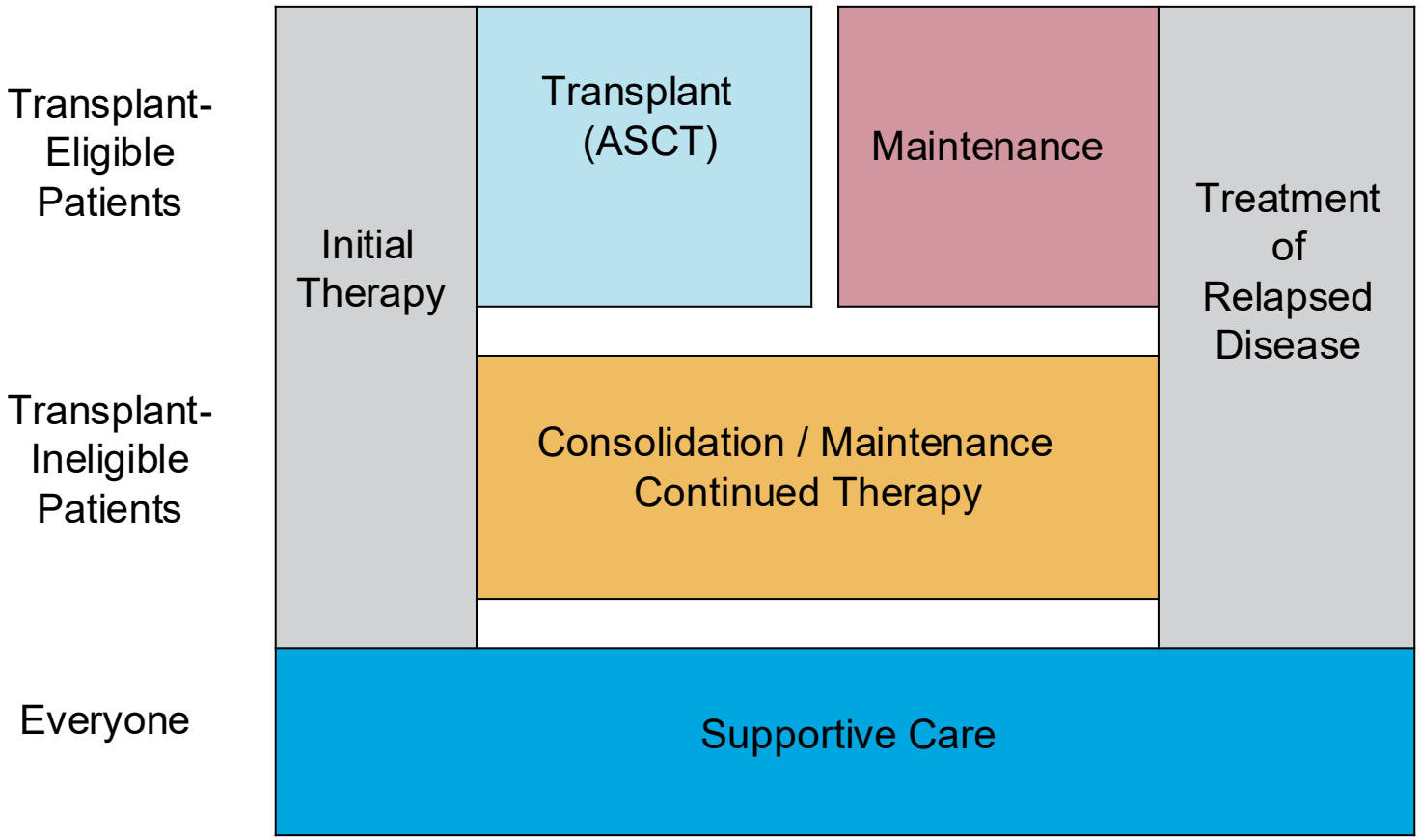
Practical Updates in Primary Care

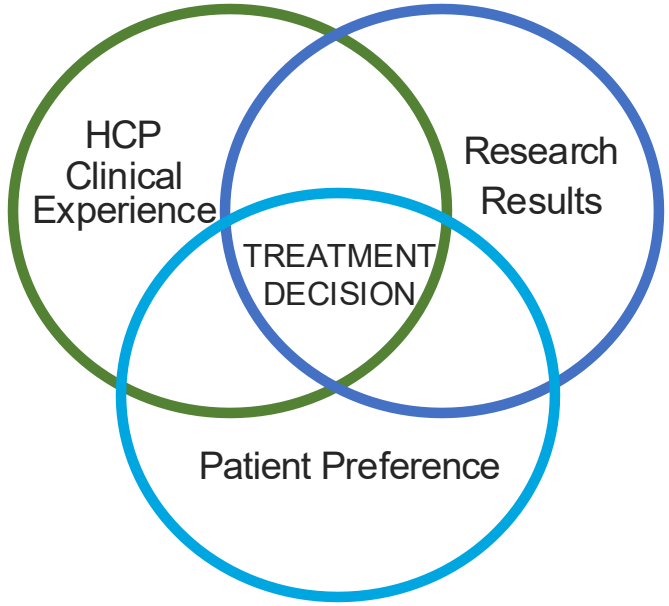
Personalized Approach to Frontline Therapy



R-MCI = revised Myeloma Comorbidity Index; HCT-CI = Hematopoietic Cell Transplant Comorbidity Index.

Myeloma Treatment Schema





HCP = healthcare provider.

Moreau P, et al. *Blood*. 2015;125(20):3076-3084.

Practical Updates in Primary Care

Drug Class Overview

Class	Drug Name	Abbreviation	Administration
IMiD (immunomodulatory drug)	Thalomid® (thalidomide)	T or Thal	Oral (PO)
	Revlimid® (lenalidomide)	R or Rev or Len	
	Pomalyst® (pomalidomide)	P or Pom	
Proteasome inhibitor	Velcade® (bortezomib)	V or Vel or B	SC/SQ or IV
	Kyprolis® (carfilzomib)	C or K or Car	IV
	Ninlaro® (ixazomib)	N or I	Oral
Chemotherapy	Cytoxan® (cyclophosphamide)	C or CTX	Oral IV
	Alkeran® or Evomela® (melphalan)	M or Mel	
Steroids	Decadron® (dexamethasone)	Dex or D or d	Oral IV
	Prednisone	P or Pred	
Monoclonal antibodies	Darzalex® (daratumumab)	Dara	IV or SQ
	Sarclisa® (isatuximab)	Isa	IV
	Empliciti® (elotuzumab)	Elo	IV
XPO1 inhibitors	Xpovio® (selinexor)	X or Sel	Oral

SC/SQ = subcutaneous/under the skin; IV = intravenous.

FDA. Accessed April 13, 2026. https://www.accessdata.fda.gov/scripts/cder/daf/.

Drug Class Overview

Class	Drug Name	Abbreviation	Administration
Peptide drug conjugate*	Pepaxto® (melphalan flufenamide)	Melflufen	IV
BCMA targeted antibody drug conjugate (ADC)	Blenrep® (belantamab mafodotin-blmf)	Bela or Belamaf or B	IV
CAR T-cell therapy	Abecma® (idecabtagene vicleucel)	Ide-cel	IV
	Carvykti® (ciltacabtagene vicleucel)	Cilta-cel	
Bispecific antibodies	Tecvayli® (teclistamab) Talvey® (talquetamab) Elrexfio® (elranatamab) Lynozyfic™ (linvoseltamab)	Tec Talq Elra Linvo	SC/IV
Pipeline	Cevostamab, iberdomide, mezigdomide, anito-cel, venetoclax, AZD0120, etentamig, KLN-1010, trispecifics …… MORE TO COME!		

***This agent is currently off the market in the US, but available through special programs.**
FDA. Accessed April 13, 2026. https://www.accessdata.fda.gov/scripts/cder/daf/.

Targets on the Myeloma Cell Surface and Therapeutic Antibodies

Bispecific antibodies
Talquetamab
CAR T

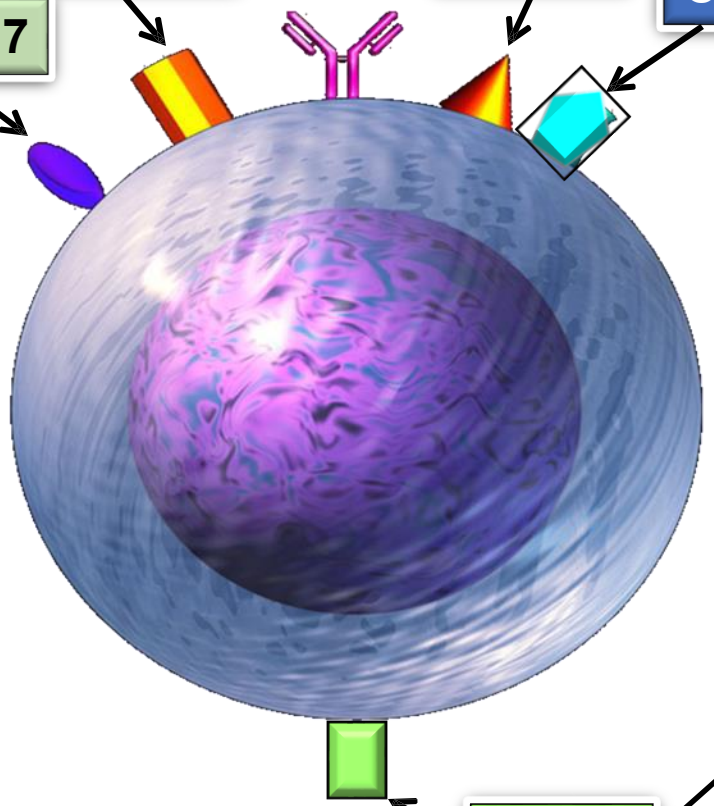
Bispecific antibodies
CAR T

GPRC$_5$D

FcRH5

CD38

SLAMF7



Antibody Drug
Elotuzumab
Bispecific antibodies

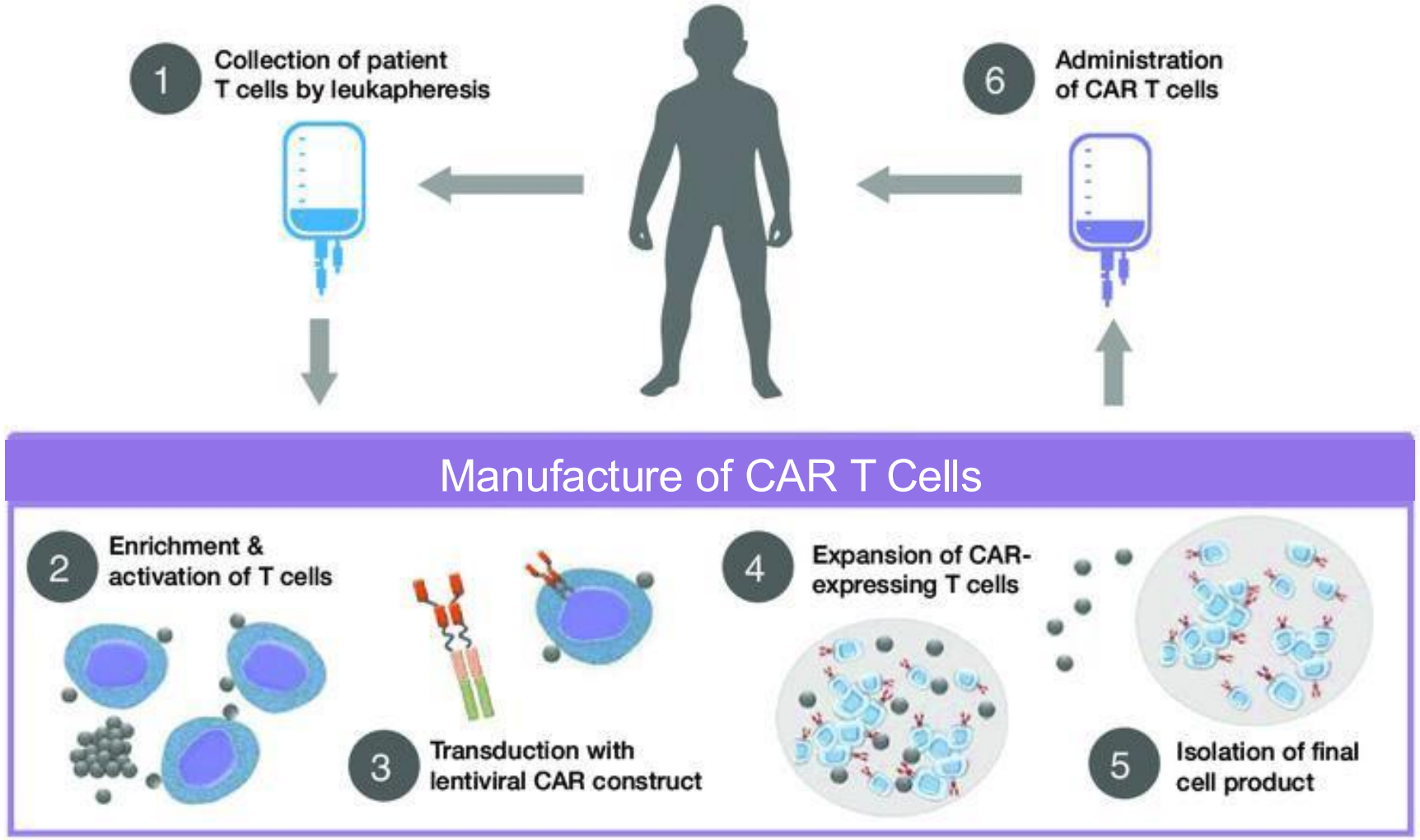
Antibody Drug
Daratumumab and **daratumumab and hyaluronidase fihj**
Isatuximab
TAK-079
MOR202

Immune Therapies
Ide-cel CAR T
Cilta-cel CAR T
Teclistamab
Other bispecific antibodies
Other CAR Ts

BCMA

Practical Updates in Primary Care

The Process of CAR T-Cell Therapy



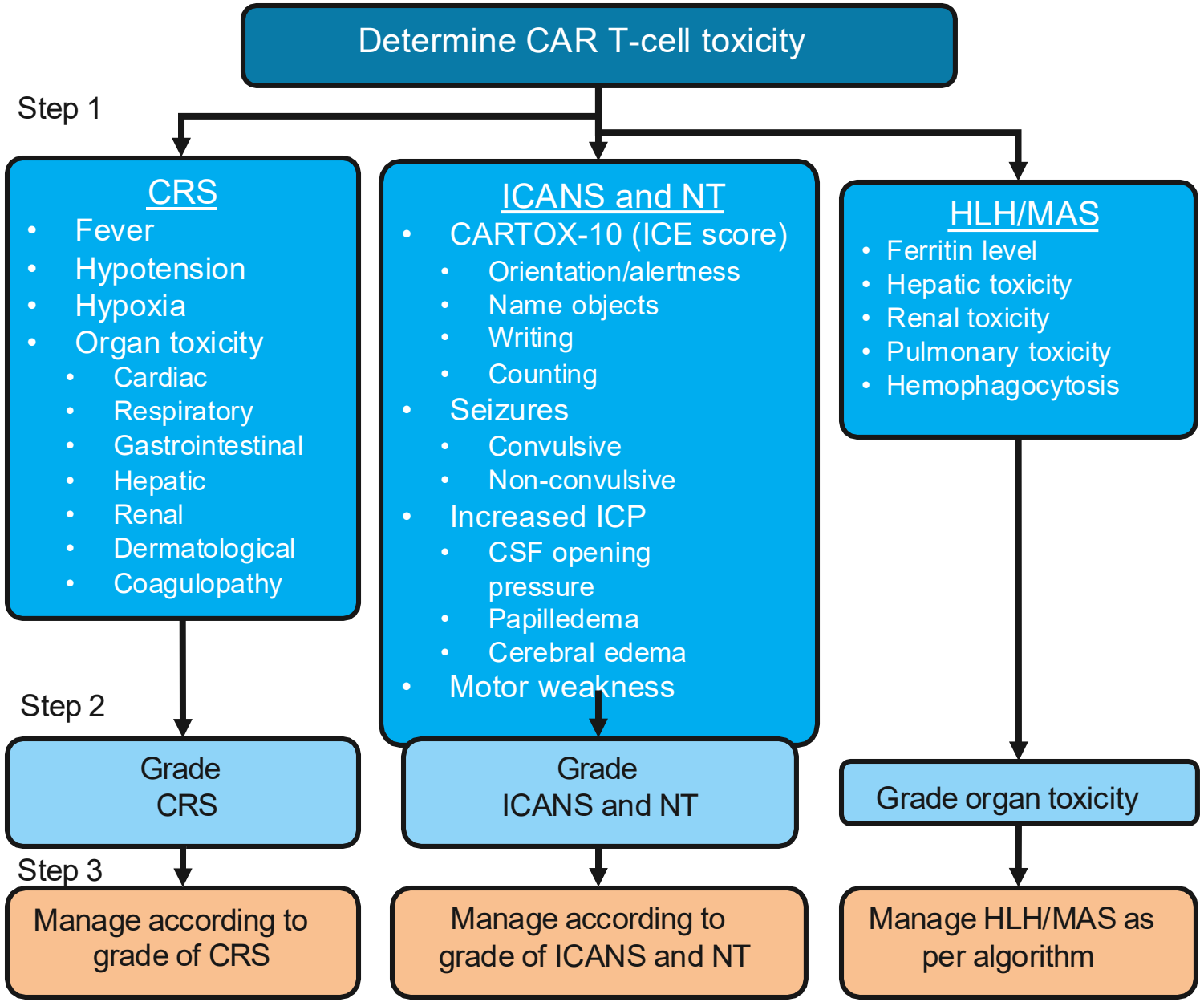
Hucks G, Rheingold SR. *Blood Cancer J.* 2019;9(2):10.

Practical Updates in Primary Care

Adverse Events with CAR T

Three-step approach in management of adverse events (AEs) with CAR T

- Step 1: Determination
- Step 2: Grading
- Step 3: Management



CRS = cytokine release syndrome; CARTOX-10 = CAR T-cell therapy-associated toxicity 10-point neurological assessment; CSF = cerebrospinal fluid; HLH = hemophagocytic lymphohistiocytosis; ICANS = immune effector cell-associated neurotoxicity syndrome; ICE = immune-effector cell-associated encephalopathy; ICP = intracranial pressure; MAS = macrophage-activation syndrome; NT = neurotoxicity.

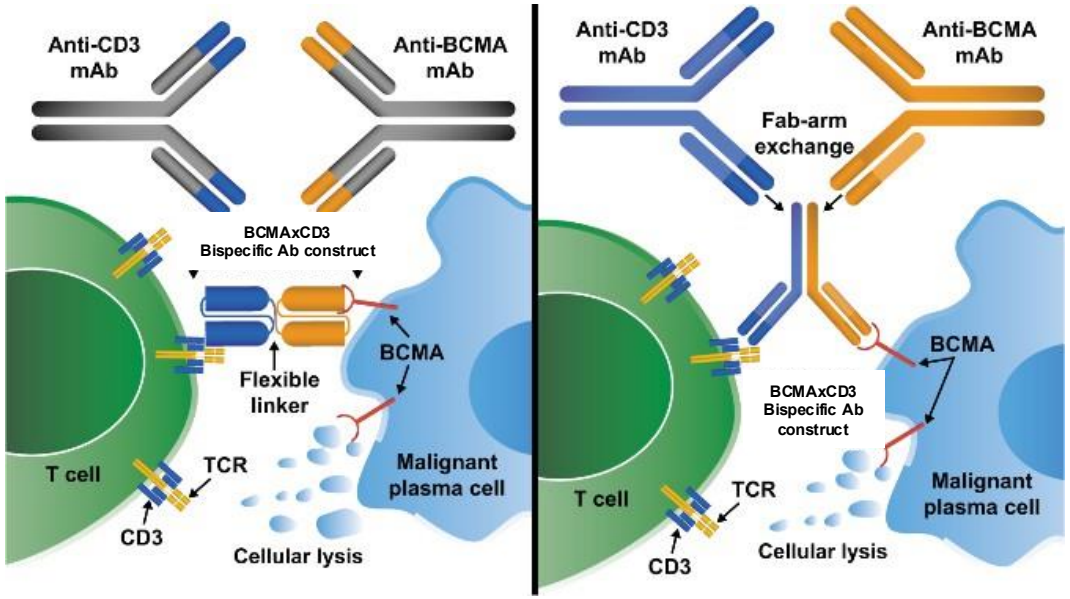
Modified from: Neelapu SS, et al. *Nat Rev Clin Oncol*. 2018;15(1):47-62. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.

Practical Updates in Primary Care

Bispecific Antibodies

Mechanism of Action

- Incorporate two antibody fragments to target and bind both tumor cells and T cells
- Bring target-expressing MM cells and T cells into close proximity, enabling T cells to induce tumor cell death



Bispecific Molecule Targets Vary

Agent	Tumor Cell Target	T-Cell Target
Teclistamab Elranatamab Linvoseltamab	BCMA	CD3
Talquetamab	GPRC5d	CD3
Cevostamab	FcRH5	CD3

"Off-the-Shelf" Advantage

- No manufacturing process, unlike CAR T-cell therapy (but like ADC/belantamab therapy)
- Thus, no delay between decision to treat and administration of drug

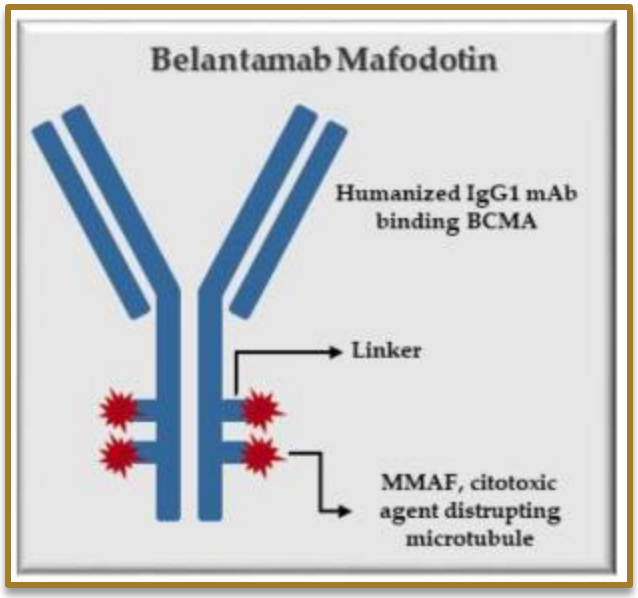
Ab = antibody; BCMA = B-cell maturation antigen; CD3 = cluster of differentiation 3; FcRH5 = Fc receptor-homolog 5; GPRC5D = G-protein coupled receptor family C group 5 member D.

Toxicities of Bispecific Antibodies

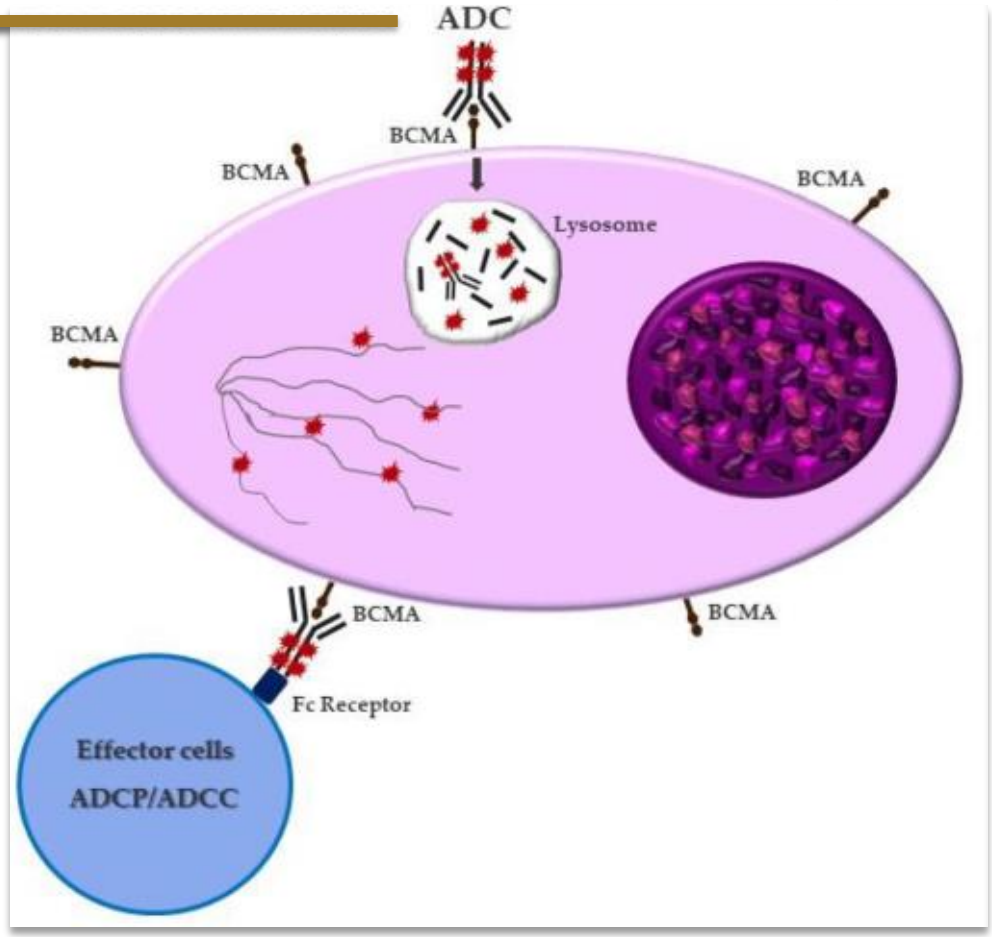
- Lower CRS than CAR T, but still a concern
- All have step-up dosing – mostly inpatient, but some centers now doing as outpatient
- Neurotoxicity less common, but should be monitored
- **Infection** is a real concern – cytopenias and hypogammaglobulinemia
  - May require prophylaxis and IVIG
  - Communication with primary care team to rapidly investigate signs and symptoms of infection
  - Atypical infections can occur, especially PJP and VZV

PJP = pneumocystis jiroveci pneumonia; VZV = varicella-zoster virus.

Antibody Drug Conjugates (Belantamab Recently Approved in MM)



How it works:
An antibody directed at a target (BCMA) combined with a cytotoxic agent (chemotherapy)



- Generally well-tolerated with no CRS, but can have eye-related side effects that require monitoring

ADCC/ADCP = antibody-dependent cellular cytotoxicity/phagocytosis.

Key Learning Points

- MM is typically diagnosed late in the disease course; the average patient sees their PCP THREE times with signs or symptoms consistent with MM prior to the diagnosis
- MM is twice as common in African Americans, with longer delays between symptoms and diagnosis
- Several general signs and symptoms, including fatigue, anemia, and bone pain, can present as myeloma and must be considered, especially in higher-risk populations
- The diagnostic algorithm for MM is not complex, but requires CBC, biochemistry, SPEP, and serum free light chain assessment
- Among various treatment options for MM are the monoclonal antibodies daratumumab, isatuximab, and elotuzumab, and the bispecific antibodies teclistamab, talquetamab, and elranatamab
- Close communication with specialists and other HCPs is critical for best outcomes in patients
- Unique side effects from CAR T-cell therapy, bispecific antibodies (eg, infection), and antibody-drug conjugates require even more careful communication between all providers