The Good, Bad and Ugly of Reporting Multiple Myeloma Data

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Disclosures

- I have no relevant conflicts of interest to disclose.

Overview

- The Good, Bad & Ugly of Reporting Multiple Myeloma Data
- Multiple Myeloma Basics
- Multiple Myeloma Case Studies

The Good…..

- **Myeloma disease tracker**
  - This is a tool you should use to give you the best chance of reporting myeloma data accurately!
- **Myeloma labs**
  - In general, there are a lot of laboratory values available to determine disease statuses at different time points.
- **Response criteria**
  - Updates to response criteria by myeloma sub-type (e.g., light chain only, measurable & non-measurable, non-measurable myeloma, etc.) have been made to the instruction manual.

The Bad…..

- **Confirmatory assessments**
  - What date to report? Is it the date of the first assessment that documents a new disease status or is it the date of the confirmatory assessment?
  - When documenting a new disease status, it's always the date of the first assessment & not the date of the confirmatory assessment.

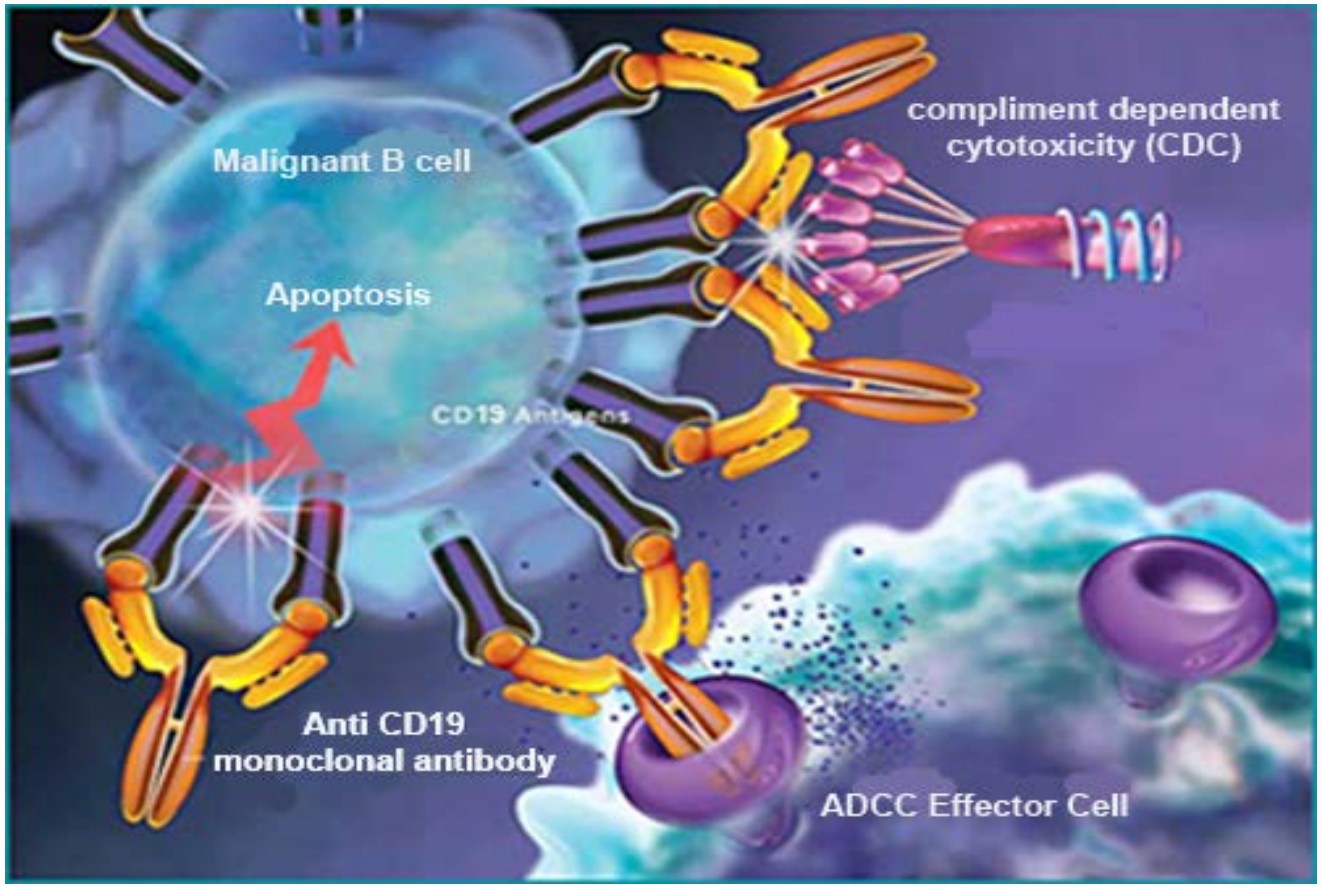
The Ugly…..

- **Changing M-protein** (e.g., **IgA** lambda to **IgG** lambda)
  - A new or different M-protein may be detected by SPEP/UPEP or serum/urine immunofixation post-HCT.
  - In most cases this represents immune reconstitution and not the patient's underlying myeloma!
  - Consult with the transplant physician if unsure.

The Ugly…..

- **Different myeloma sub-types**
  - Non-measurable secretory myeloma vs. light chain only myeloma vs. non-secretory myeloma
  - E.g., A patient is diagnosed with IgG kappa myeloma
    - SPEP- 0.25 g/L M-protein detected
    - Serum/urine immunofixation (SIFE/UIFE) shows IgG kappa
    - Free light chain (FLC) ratio is high
    - What is the correct myeloma sub-type?

Multiple Myeloma Reporting Basics



Multiple Myeloma Reporting Basics

- **What is considered measurable disease?**
  - Serum M-protein >/= 1 g/dL and/or
  - Urine M-protein >/= 200 mg/24 hours

Free light chain levels may be used in place of the M-protein, provided the involved chain is >10 mg/dL & the κ/λ ratio is abnormal at diagnosis

Multiple Myeloma Reporting Basics

- **What is Light Chain (LC) only myeloma?**
  - The malignant plasma cells make only the light chain (e.g., kappa or lambda) component of the antibody & not the heavy chain (e.g., IgG). The light chains are often excreted in the urine.
  - LC only myeloma does not include oligo-secretory myeloma.
- **What is non-secretory myeloma?**
  - The malignant plasma cells do not make a heavy or light chain resulting in no measurable protein in the blood or urine. There will be significant plasma cell burden in the bone marrow & evidence of end-organ damage.
  - Non-secretory myeloma does not include oligo-secretory myeloma.

Summary of Which Baseline to Use When** Determining Disease Status Before or After HCT

Has there been a relapse or progression?	Disease Status at Time of HCT	Disease Status in Response to HCT
No R/P	DP at diagnosis	DP at diagnosis
Yes R/P (treated)	DP at R/P	DP at R/P
Yes R/P (untreated)	DP prior to the start of prep	DP prior to the start of prep

R/P = relapse or progression
DP = disease parameters
**Remember the 3 W's- What, When & Where

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Confirmatory Testing Requirements

- Includes SPEP/UPEP, serum/urine immunofixation & κ/λ free light chains
- Confirmatory testing does not apply to BM biopsies, skeletal surveys & other radiographic studies

Confirmatory Testing Requirements

- Every disease response (sCR, CR, VGPR, PR & SD) requires two consecutive assessments (by the same method) made at any time before the initiation of any new therapy.
- Progressive disease (PD) & relapse from CR are a bit different….

  PD & relapse from CR requires two consecutive assessments (by the same method) before classification, **and/or** the start of any new therapy.

Confirmatory Testing Requirements

- To report CR, both the serum & urine immunofixation must be negative as well as confirmed!
- Many institutions don’t obtain urine studies on a regular basis.
- CR may be reported as long as there is at least one negative serum & one negative urine immunofixation and one of them has been confirmed!

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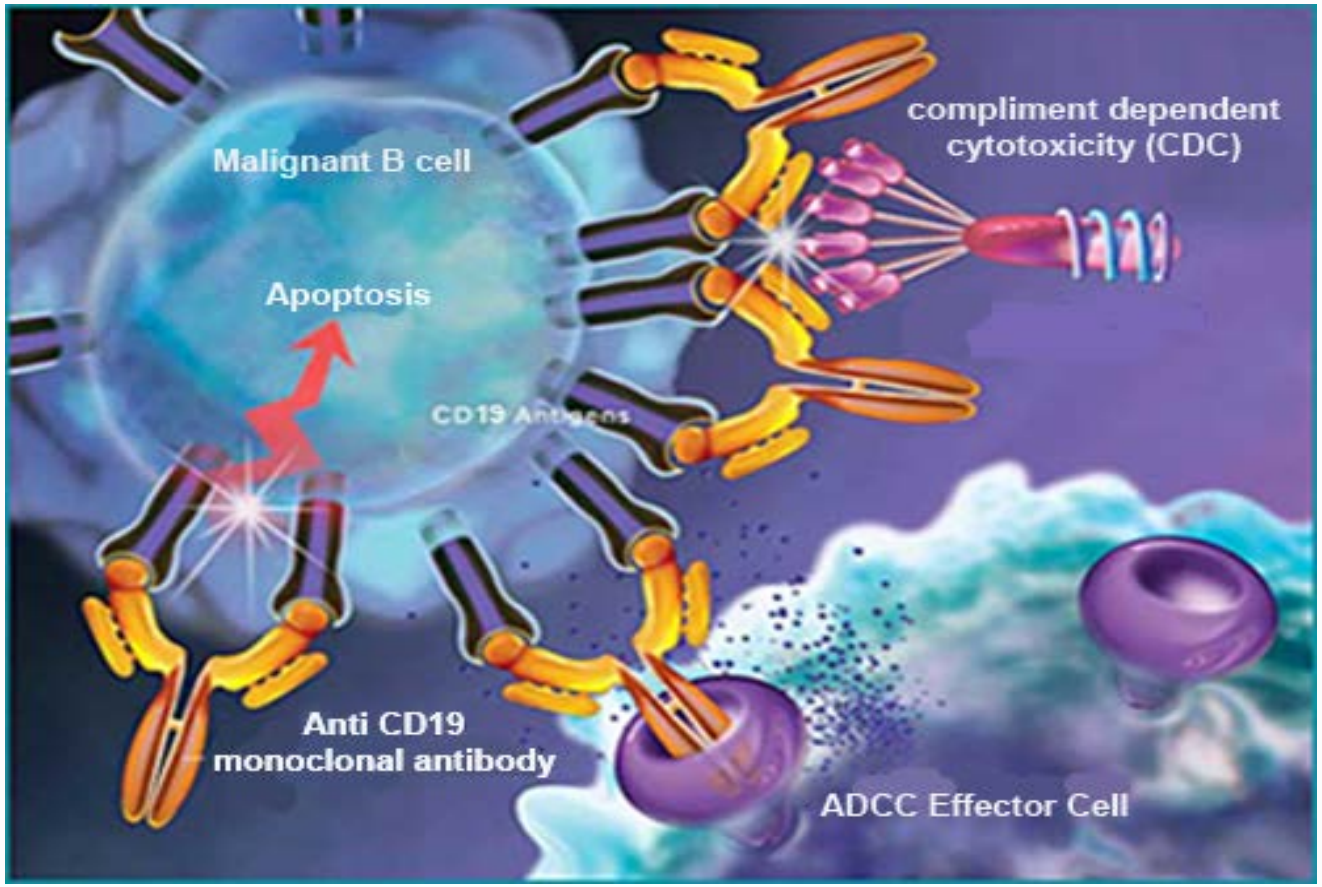
Multiple Myeloma Case Studies



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Myeloma Case Study #1

A 60-yo AA male was diagnosed with **IgG lambda myeloma**. Results of the initial work-up included:

- Serum M-spike = 4 g/dL (or 4000 mg/dL)
- 24-hr urine M-protein = 1000 mg/24 hr
- Bone marrow aspirate = 60% plasma cells

Patient received 2 cycles of bortezomib, lenalidomide & dexamethasone (VRD), then re-evaluated:

- Serum M-spike = 2000 mg/dL
- 24-hr urine M-protein = 195 mg/24 hr

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Myeloma Case Study #1

What was the patient's disease response after two cycles of VRD?

A) Very Good Partial Remission (VGPR)
B) Partial Remission (PR)
C) Stable Disease (SD)

Myeloma Case Study #1

The patient's PR status was confirmed with a 2nd measurement. The patient received two additional cycles of VRD & re-evaluated for disease response.

Labs obtained after 4 cycles of VRD:

- Serum M-spike = 2900 mg/dL
- 24-hr urine M-protein = 600 mg/24 hr
- Bone marrow aspirate = 30% plasma cells

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Myeloma Case Study #1

What was the patient's disease response after a total of four cycles of VRD?

A) Very Good Partial Response (VGPR)
B) Partial Response (PR)
C) Stable Disease (SD)
D) Progressive Disease (PD)

Myeloma Case Study #1

Progressive Disease Criteria

Requires **one or more** of the following-
Increase of ≥ 25% from the lowest response value achieved in:

- Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); *and/or*
- Urine M-component with an absolute increase ≥ 200 mg/24 hours; *and/or*
- For recipients without measurable serum or urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase >10 mg/dL; and/or
- Plasma cell percentage with absolute percentage increase ≥10%; and/or …

Myeloma Case Study #1

Patient is switched to daratumumab, lenalidomide and dexamethasone (DRd) and was re-evaluated after two cycles.

- Serum M-spike = 1400 mg/dL
- 24-hr urine M-protein = 190 mg/24 hr
- Bone marrow aspirate = 15% plasma cells

The patient achieved a PR after two cycles of DRd. The plan is to give IV Cytoxan mobilization.

Myeloma Case Study #1

What studies were used as a baseline to make that determination?

A) The studies obtained at diagnosis
B) The studies obtained after first two cycles of DRd
C) The studies obtained at time of progression

Myeloma Case Study #1

The patient has undergone their autologous PBSC HCT & has been evaluated monthly for the 1st three months post HSCT.

- **Day +30 evaluation:**
  - Serum M-spike = 1000 mg/dL
  - Serum immunofixation (+) for IgG lambda
  - 24-hr urine M-protein = 190 mg/24 hrs
  - Bone marrow biopsy = 7% plasma cells

Myeloma Case Study #1

Day +60 evaluation:

- SPEP/UPEP- no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 90 mg/24 hrs

Myeloma Case Study #1

Day +100 evaluation:

- SPEP/UPEP- no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 0 mg/24 hrs
- Bone marrow aspirate <5% plasma cells

Myeloma Case Study #1

What is the best disease response to HCT you would report at Day +100 for this patient?

A) Stable Disease (SD)
B) Partial Remission (PR)
C) Very Good Partial Remission (VGPR)
D) Complete Remission (CR)

Myeloma Case Study #2

Light Chain only myeloma

- Malignant plasma cells make only the light chain component of the antibody
- Light chains are most often excreted in the urine
- Lab studies include urine protein electrophoresis (UPEP), urine immunofixation electrophoresis (UIFE) and serum free light chain (FLC)

Myeloma Case Study #2

- John D. was diagnosed with Kappa light chain only myeloma in February 2015. Labs included-
  - SPEP = 0 mg/dL; SIFE (+) kappa light chains
  - UPEP = 750 mg/dL; UIFE (+) kappa light chains
  - SFL Kappa = 200 mg/dL & Lambda = 2.0 mg/dL
  - SFL K/L ratio = 100
  - 24^0 urine M-protein = 600 mg/24 hours
  - BMBx plasma cells = 45%

Myeloma Case Study #2

- Planned treatment included 6 cycles of bortezamid, lenalidomide & dexamethasone (VRD). Labs were obtained prior to start of each cycle.

Labs	2/1 Diagnosis	3/1	4/1	5/1	6/1	7/1
SPEP	0 g/dL			0 g/dL		
SIFE	+ kappa LC			negative		
UPEP	750 mg/dL			50 mg/dL		250 mg/dL
UIFE	+ kappa LC			+ kappa LC		+ kappa LC
24^0 urine	600 mg/24^0			175 mg/24^0		400 mg/24^0
SFL Kappa	200 mg/dL	120	75	30	15	70
SFL Lambda	2 mg/dL	2	1.5	6	8	4
SFL K/L ratio	100	60	50	5	1.88	17.5
**Difference	198	118	73.5	24	7	66
% plasma cells	45%			8%		20%
VRD	Cycle #1	Cycle #2	Cycle #3	Cycle #4	Cycle #5	On hold

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Myeloma Case Study #2

- The patient was re-evaluated on 5/1/15 after 3 cycles of VRD.

What is the disease response at this time point?

A) Partial Response (PR)
B) Very Good Partial Response (VGPR)
C) Stable Disease (SD)

Myeloma Case Study #2

- The patient's disease was re-evaluated on 7/1/15, prior to the start of cycle 6.

What is the disease response at this time point?

A) Partial Response (PR)
B) Stable Disease (SD)
C) Progressive Disease (PD)

Myeloma Case Study #2

- Free Light Chain results & how to use them
  - A PR response requires a ≥50% decrease in the difference between the involved & uninvolved light chains.
  - A VGPR response requires a ≥90% decrease in the difference between the involved & uninvolved light chains.
  - Progressive disease (PD) requires a ≥25% increase from the lowest response value achieved with an absolute increase >10 mg/dL in the difference between the involved & uninvolved light chains.

Myeloma Case Study #2

- Therapy was switched to bortezomib in July.

Labs	2/1 Diagnosis	5/1	6/1	7/1	8/1	9/1	10/1
SPEP	0 g/dL	0 g/dL					
SIFE	+ kappa LC	negative					
UPEP	750 mg/dL	50 mg/dL		250 mg/dL	50 mg/dL	0 mg/dL	0 mg/dL
UIFE	+ kappa LC	+ kappa LC		+ kappa LC	+ kappa LC	+ kappa LC	+ kappa LC
24^0 urine	600 mg/24^0	175 mg/24^0					0 mg/24^0
SFL Kappa	200 mg/dL	30	15	70	20	12	15
SFL Lambda	5 mg/dL	6	8	4	5	6	10
SFL K/L ratio	40	45	1.88	17.5	4	2	1.5
**Difference	195	24	7	66	15	6	5
% plasma cells	45%	8%		20%			4%
Carfilzomib / Dex (Kd)		Cycle #4 VRD	Cycle #5 VRD	Cycle #1 7/15/15	Cycle #2 8/15/15	Cycle #3 9/15/15	Cycle #4 10/15/15

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Myeloma Case Study #2

- PBSCs were collected & patient underwent an Auto HCT on 12/1/15.

Labs	7/1	8/1	9/1	10/1	11/15	1/15/16	3/15/16
SPEP							0 mg/dL
SIFE							negative
UPEP	250 mg/dL	50 mg/dL	0 mg/dL	0 mg/dL	0 mg/dL	0 mg/dL	0 mg/dL
UIFE	+ kappa LC	+ kappa LC	+ kappa LC	+ kappa LC	+ kappa LC	negative	negative
24^0 urine				0 mg/24^0			0 mg/24^0
SFL Kappa	70	20	12	15	12	7.75	10
SFL Lambda	4	5	6	10	10	12	15
SFL K/L ratio	17.5	4	2	1.5	1.2	0.65	0.67
**Difference	66	15	6	5	5	n/a	n/a
% plasma cells	20%			4%			2%**

** Clonal plasma cells absent based on immunohistochemistry

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Myeloma Case Study #2

- What was the patient's disease status prior to the start of conditioning?

A) Complete Remission (CR)

B) Very Good Partial Remission (VGPR)

C) Stable Disease (SD)

Myeloma Case Study #2

- What was the recipient's disease status at the Day +100 evaluation?

A) Very Good Partial Remission (VGPR)

B) Complete Remission (CR)

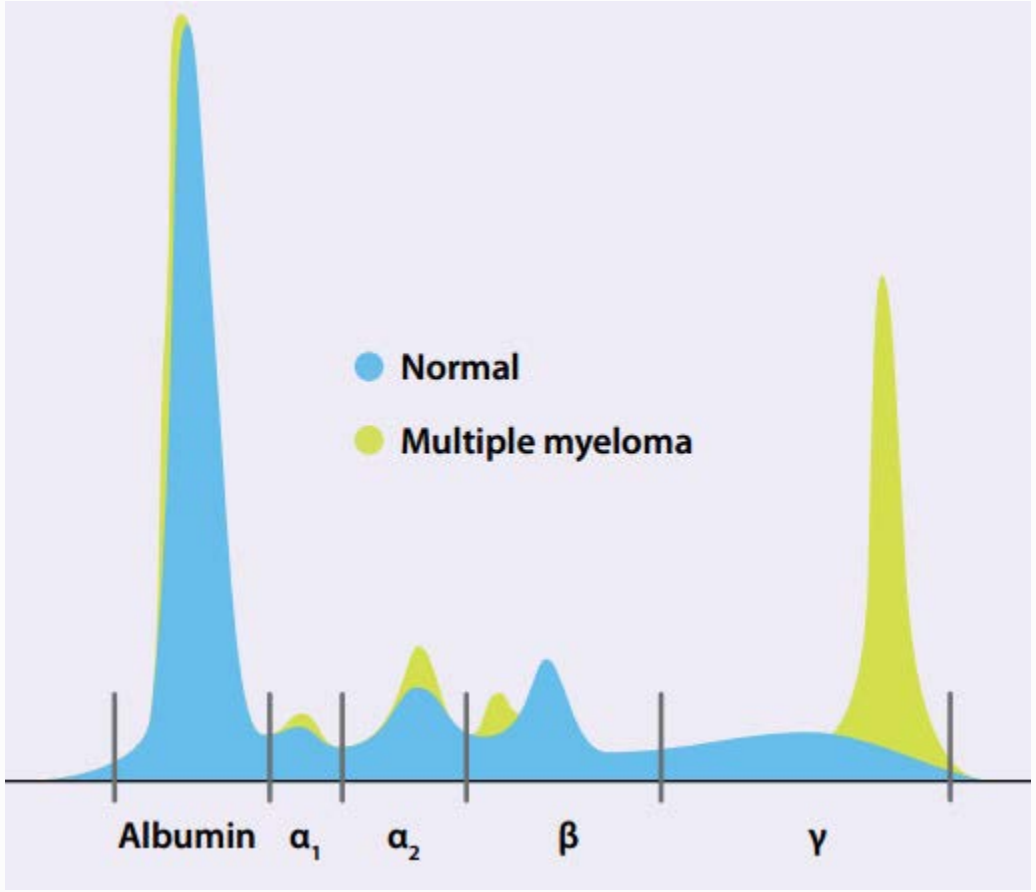
C) Strict CR (sCR)

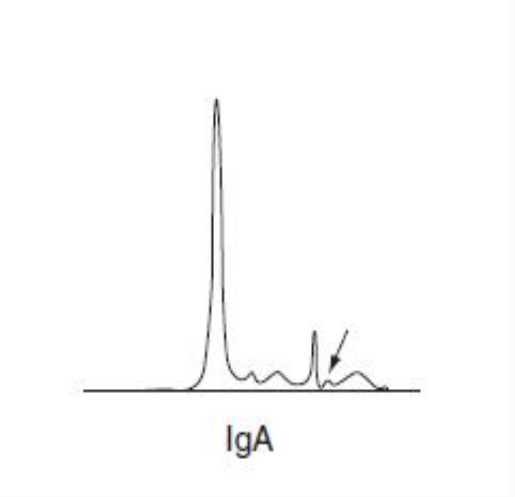
Myeloma Case Study #3

- Jane D. is a 61 yo woman diagnosed with **IgA** kappa myeloma. Results from her diagnostic work-up included-
  - IgG = 361 mg/dL; IgA = **7120 mg/dL***; IgM <25 mg/dL
  - SPEP 4.5 g/dl M-protein (Beta-2)
    1.0 g/dl M-protein (Gamma)
  - SIFE (+) IgA kappa
  - BM plasma cells = 45%

*The IgA normal range in a healthy adult is between 80-350 mg/dL.

Myeloma Case Study #3





Myeloma Case Study #3

- Laboratory tests measuring M-protein
  - In general, serum M-protein is measured using densitometry on SPEP.
  - The SPEP may be unreliable in patients with IgA myeloma, as the monoclonal protein can migrate to the beta region.
  - Quantitative IgA immunoglobulin levels by nephelometry or turbidometry can be used to assess a disease response in place of the SPEP.

Myeloma Case Study #3

- Jane is treated 2 cycles of bortezomib, lenalidomide & dexamethasone (VAD) and repeat labs were obtained-
  - IgA = 2400 mg/dl
  - SPEP 1.75 g/dl M-protein (Beta-2)
    0.25 g/dl M-protein (Gamma)
  - SIFE (+) IgA kappa

Myeloma Case Study #3

- Jane is now s/p 4 cycles of bortezomib, lenalidomide & dexamethasone (VAD). Labs are obtained prior to start of PBSC collection-
  - IgA = 500 mg/dl
  - SPEP 0.5 g/dl M-protein (Beta-2)
    0 g/dl M-protein (Gamma)
  - SIFE (+) IgA kappa
  - BM plasma cells = 7%

Myeloma Case Study #3

- What is Jane's disease response prior to the PBSC collection?

A. PR
B. VGPR
C. nCR
D. CR

Myeloma Case Study #3

- Jane is 3 months post autologous HCT and labs obtained prior to her office visit included-
  - IgA = 340 mg/dL (WNL)
  - SPEP 0 g/dL
  - SIFE (+) IgA kappa
  - UPEP 0 mg/dL; UIFE negative
  - BM plasma cells = 4%

Myeloma Case Study #3

- What is Jane’s disease response at 100 days post auto HCT?

A. PR
B. VGPR
C. CR

Myeloma Case Study #3

- Jane is 6 months post autologous HCT and labs obtained prior to her office visit included-
  - IgA = 300 mg/dL (WNL)
  - SPEP 0 g/dL; SIFE negative
  - UPEP 0 mg/dL; UIFE negative

- All results have been confirmed

Myeloma Case Study #3

- What is Jane’s disease response at 6 months post auto HCT?

A. PR
B. VGPR
C. CR

Questions