Case History for BMD-01 – BMD-06

This bone marrow aspirate smear is from a 55-year-old man who injured his back while lifting heavy weighted objects. Laboratory values: WBC = 3.3 x 10E9/L; RBC = 3.77 x 10E12/L; HGB = 11.3 g/dL; HCT = 32.6%; MCV = 97 fL; and PLT = 234 x 10E9/L. Additional laboratory data: Positive by FISH for *IGH/CCND1* gene rearrangement. Negative by FISH for del(13q) and *TP53* deletion.

(BONE MARROW, WRIGHT-GIEMSA)

Please click on the hyperlink below to view the DigitalScope images for this case. Click on the "i" icon for each region of interest (challenge) to view the text that is found in the Participant Summary Report (PSR).
http://www.digitalscope.org/LinkHandler.axd?LinkId=12064222-d5fa-461a-8748-59ddc7488310

To access the online Hematology Glossary, please click the hyperlink below:
http://www.cap.org/ShowProperty?nodePath=/UCMCon/Contribution%20Folders/WebContent/pdf/hematology-glossary.pdf

Summary of Participant Survey Results

The following is a statistical summary of all results submitted by participating labs. These are provided to allow participants to see their responses in the context of their peers. These results may identify findings or topics for further education or review. Survey results are not intended to represent the correct or desired responses for proficiency testing purposes and the SD and CV should not be interpreted as acceptable reporting limits. Participants are encouraged to review discrepant results with their medical director.

Bone Marrow Differential – %

	NO. LABS	MEAN	S.D.	C.V.*	Median	Low Value	High Value
BMD-01 Blasts	262	0.52	0.63	*	0.3	0.0	2.4
Promyelocytes	270	1.42	1.21	84.6	1.0	0.0	5.4
Myelocytes	274	5.91	2.51	42.4	5.8	0.0	13.5
Metamyelocytes	275	5.13	2.63	51.3	5.0	0.0	13.7
Band/Segmented Neutrophils	276	19.30	5.52	28.6	19.1	3.0	36.0
Eosinophils (all stages)	274	2.60	1.26	48.5	2.5	0.0	6.0
Basophils	245	0.03	0.09	*	0.0	0.0	0.5
Monocytes	257	0.84	0.83	98.7	0.8	0.0	3.2
Lymphocytes	269	7.80	4.81	61.7	7.0	0.0	24.0
Plasma cells (normal and abnormal)	276	14.60	9.33	63.9	13.6	0.0	43.6
Erythroid precursors (all stages)	275	40.19	9.43	23.5	39.0	16.0	65.6
Other	166	0.13	0.50	*	0.0	0.0	3.2
Myeloid : Erythroid ratio	270	0.96	0.30	31.6	0.9	0.0	1.9

* When low results are reported on an analyte, a high coefficient of variation (CV) may result. When the mean value is very low the C.V. may be exaggerated.

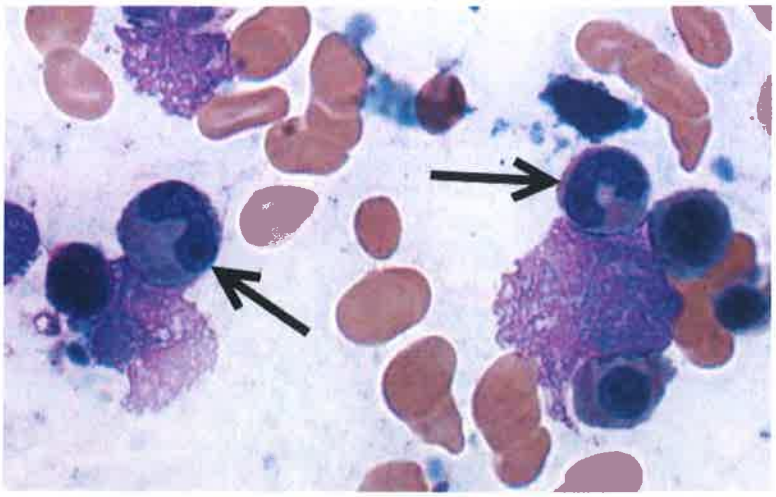
BMD-01 Other cells not listed:	Total (N=13)	%
Histiocytes/macrophages	5	38.5
Atypical mononuclear cells	4	30.7
Pronormoblast with parvovirus infection	1	7.7
Malignant lymphoid cell (other than blast)	1	7.7
Mast Cell	1	7.7
Megakaryocytes	1	7.7

Committee Comments on Bone Marrow Differential and Aspirate

The whole slide image from a bone marrow aspirate smear originates from a 55-year-old man who injured his back while lifting heavy weight. The aspirate is notable for an increased number of plasma cells (62% by 200 cell count). An accompanying increase in marrow lymphocytes is not noted. Hematopoietic elements from the three primary lineages are present, showing full maturation, without morphologic evidence of dysplasia, and without an associated increase in blasts.

Cell Identification

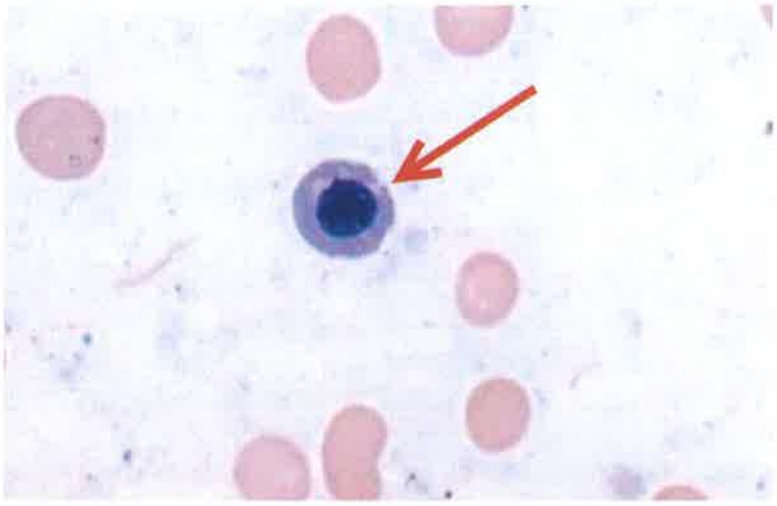
BMD-02



Identification	Participants No.	%	Evaluation
Neutrophil, segmented or band	268	94.7	Educational
Neutrophil, metamyelocyte	11	3.9	Educational
Neutrophil, giant band or giant metamyelocyte	4	1.4	Educational

The arrowed cells are neutrophil, band forms, as correctly identified by 94.7% of participants. Together, band neutrophils and segmented neutrophils constitute 12% to 25% of the nucleated cells in the bone marrow. Both segmented and band neutrophils have specific granules and mature chromatin. Unlike the segmented neutrophil, however, the band neutrophil does not show nuclear condensation to thin filament. Also, unlike the next most immature neutrophil form (the metamyelocyte), the band neutrophil nucleus is indented to *more* than half the distance to the farthest nuclear margin. The nucleus can assume many shapes: it can be band-like; sausage-like; S-, C-, or U-shaped; or twisted and folded on itself.

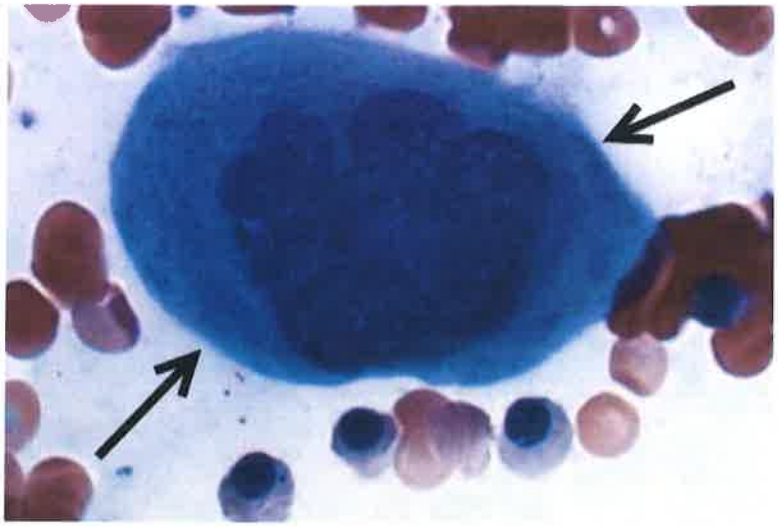
BMD-03



Identification	Participants No.	%	Evaluation
Erythrocyte precursor, normal (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	276	97.3	Educational
Erythrocyte precursor, abnormal/dysplastic nuclear features (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	5	1.8	Educational
Erythrocyte precursor with megaloblastic changes/maturation	1	0.3	Educational
Erythrocyte	1	0.3	Educational
Neutrophil, metamyelocyte	1	0.3	Educational

The arrowed cell is an erythrocyte precursor, normal (polychromatophilic normoblast), as correctly identified by 97.3% of participants. Polychromatophilic normoblasts are the next most mature of the nucleated erythroid precursors, characterized by well-rounded nuclei with condensed chromatin, producing a checkerboard or cartwheel appearance. In distinction to the more immature basophilic normobolast erythroid precursors, polychromatophilic normoblasts have a far less basophilic cytoplasm, owing to a greater degree of hemoglobinization, producing a gray colored cytoplasm. Orthochromatic normoblasts (the next more mature erythroid precursors), in contrast, have much more prominent hemoglobinization, resulting in a far more characteristic erythroid (ergo orthochromatic) pink-colored cytoplasm.

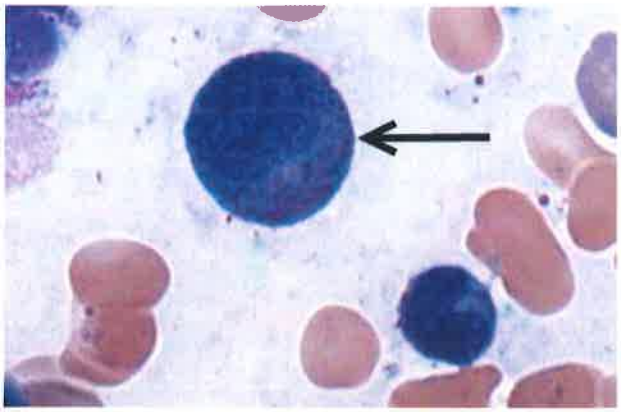
BMD-04



Identification	Participants No.	%	Evaluation
Megakaryocyte or precursor, normal	273	96.1	Educational
Megakaryocyte or precursor, abnormal	6	2.1	Educational
Megakaryocyte nucleus	4	1.4	Educational
Osteoclast	1	0.4	Educational

The arrowed cell is a normal megakaryocyte, as correctly identified by 96.1% of participants. Megakaryocytes are usually easily recognizable as the largest bone marrow hematopoietic cells. During development, the cell does not divide, but instead the nucleus undergoes nuclear replication without cell division giving rise to a convoluted nucleus with several lobes. As producers of platelets by cytoplasmic fragmentation, the megakaryocyte cytoplasm has a characteristic pink or wine-red and contains fine azurophilic granules that may be clustered.

BMD-05



Identification	Participants No.	%	Evaluation
Neutrophil, myelocyte	251	88.4	Educational
Neutrophil, promyelocyte	27	9.5	Educational
Neutrophil, metamyelocyte	5	1.8	Educational
Eosinophil, any stage with atypical/basophilic granulation	1	0.3	Educational

The arrowed cell is this is a very challenging cell and caused controversy among the committee panel as well as participants. This image is an outstanding example of the need for excellent quality staining to be able to confidently distinguish between promyelocytes and myelocytes in the laboratory.

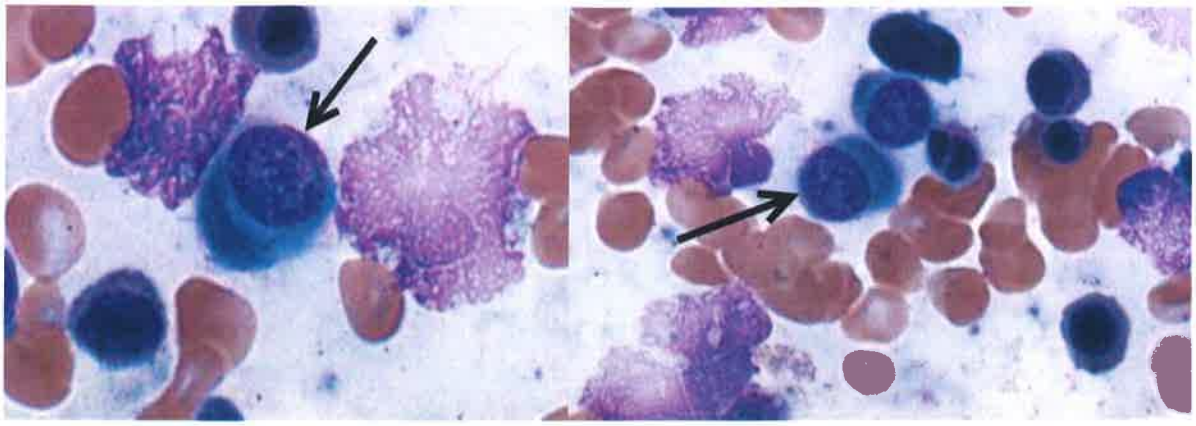
The image was called a neutrophil, myelocyte by 88.4% of participants and a neutrophil, promyelocyte by 9.5% of participants.

Promyelocytes represent the next recognizable step in myeloid maturation after the myeloblast. Like blasts, promyelocytes are rarely seen outside the marrow and typically are seen therein in rare numbers (< 2% of total marrow nucleated cells). Promyelocytes are round to oval cells that are generally slightly larger than myeloblasts, with a diameter of 12 to 24 µm. They are normally confined to bone marrow, where they constitute less than 2% of nucleated cells. However, like the myeloblast, promyelocytes can be seen in the blood in pathologic states. The nuclear-to-cytoplasmic ratio is high (5:1 to 3:1). The nucleus is round to oval, has fine chromatin, and contains distinct nucleoli. The cytoplasm is basophilic, more plentiful than in a myeloblast, and contains multiple distinct azurophilic (primary) granules. A paranuclear hof or cleared space is typically present.

The transition from promyelocyte to myelocyte occurs with the end of production of azurophilic (primary) granules and the beginning of production of lilac or pale orange/pink (specific) granules. Myelocytes are usually confined to the marrow where they constitute approximately 10% of the nucleated cells. In pathologic states, myelocytes are seen in blood. The myelocyte is smaller than the earlier precursors, usually 10 to 18 µm. The cells are round to oval in shape and have a nuclear-to-cytoplasmic ratio of 2:1 to 1:1. The nucleus is slightly eccentric, lacks a nucleolus, and begins to demonstrate chromatin clumping; one side often shows slight flattening. Sometimes a clear space or hof is seen adjacent to the nucleus, indicating the location of the Golgi apparatus. The cytoplasm is relatively more abundant than in earlier precursors and is amphophilic. Both azurophilic and specific granules are present in the cytoplasm with specific granules coming to predominate as maturation progresses.

In this instance, the committee feels that the distinction between a promyelocyte and myelocyte is challenging, mainly owing to the dark staining in this region. However, the arrowed cell in this image, unlike a typical myelocyte, does have a nucleolus when carefully examined. Also, the perinuclear hof is much more characteristic of a promyelocyte than a myelocyte. In addition, the cytoplasm of the arrowed cells is basophilic, more plentiful than would be expected of a myeloblast, and contains multiple azurophilic (primary) granules. For these reasons, the committee feels that classification as a promyelocyte is more appropriate.

BMD-06



Identification	Participants No.	Participants %	Evaluation
Plasma cell (to include morphologically mature, abnormal, and containing inclusion, eg, Dutcher body, Russell body, etc)	273	96.1	Educational
Malignant lymphoid cell (other than blast)	3	1.1	Educational
Erythrocyte precursor, normal (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	2	0.7	Educational
Erythrocyte precursor, abnormal/dysplastic nuclear features (includes pronormoblast, basophilic, polychromatophilic, and orthochromic normoblasts)	2	0.7	Educational
Megakaryocyte or precursor, abnormal	2	0.7	Educational
Lymphocyte	2	0.7	Educational

The arrowed cells are plasma cells, as correctly identified by 96.1% of participants. Plasma cells represent terminally differentiated B-lymphocytes and are a normal constituent of the bone marrow; of import, however, is that plasma cells comprise less than 5% of total marrow cellularity under normal conditions. Plasma cells are usually easily recognizable by their triad of deeply basophilic cytoplasmic coloration, eccentrically placed nucleus with a paranuclear hof, and coarse, clumped chromatin that is often arranged in a cartwheel-like or clock-face pattern. Morphologic differentiation of malignant from benign plasma cells can be challenging. While not considered morphologically diagnostic, malignant plasma cells are more likely to show multinucleation, more frequent immature nuclear features (ie. less condensed chromatin and nucleoli), abundant and atypical mitotic figures and peripheralization.

Case Presentation:

This bone marrow aspirate smear is from a 55-year-old man who injured his back while lifting heavy weighted objects. Laboratory values: WBC = 3.3 x 10E9/L; RBC = 3.77 x 10E12/L; HGB = 11.3 g/dL; HCT = 32.6%; MCV = 97 fL; and PLT = 234 x 10E9/L. Additional laboratory data: Positive by FISH for *IGH/CCND1* gene rearrangement. Negative by FISH for del(13q) and *TP53* deletion.

(BONE MARROW, WRIGHT-GIEMSA)

Case Discussion: Plasma cell myeloma

This bone marrow aspirate smear originates from a 55-year-old man who injured his back while lifting heavy weight. The provided peripheral blood data are notable for normocytic anemia, but with normal leukocyte and platelet counts. The bone marrow aspirate is notable for an increased number of plasma cells (62% of total nucleated marrow cells by 200 cell count). An accompanying increase in marrow lymphocytes is not noted. Hematopoietic elements from the three primary lineages are present, showing full maturation, without morphologic evidence of dysplasia, and without an associated increase in blasts. Ancillary fluorescence in situ hybridization (FISH) data are positive for an *IGH/CCND1* (t(11;14)) translocation, without evidence of del(13q) nor *TP53* (17p) deletion.

The International Myeloma Working Group (IMWG) defines a number of clinically relevant subtypes of plasma cell proliferations; these represent distinct clinicopathologic entities with distinct disease-related risk factors and specific recommendations for medical intervention. As outlined in the IMWG guidelines, diagnosis requires a breadth of data, including chemistry, radiology, pathology and molecular/cytogenetic data for completeness.

The IMWG diagnostic criteria for symptomatic myeloma require a clonal bone marrow plasma cell count of 10% or more, in combination with evidence of end-organ damage: one or more of the extended "CRAB" criteria, namely hyper<u>C</u>alcemia (> 1 mg/dL higher than the upper limit of normal or > 11 mg/dL), <u>R</u>enal insufficiency (creatinine clearance < 40 mL/min or serum creatinine > 2 mg/dL), <u>A</u>nemia (hemoglobin value of > 2 g/dL below the lowest limit of normal, or a hemoglobin value < 10 g/dL) or <u>B</u>one disease (defined as one or more osteolytic lesion on skeletal radiography, CT or PET/CT, or more than one focal lesion on MRI that is at least 5mm or greater in size); or in the presence of extremes of clonal bone marrow plasmacytosis (> 60%); or extremes of free light chain ratio (involved to uninvolved light chain ratio > or = 100).

In the absence of evidence of end-organ damage or biomarkers of malignancy, but in the presence of a sufficiently large M-protein (serum monoclonal protein (IgG or IgA) ≥ 3 g/dL or urinary monoclonal protein ≥ 500 mg/24h), a clonal bone marrow plasma cell count of 10% or more can still be used to establish smoldering myeloma. In contrast, in the absence of at least 10% clonal plasma cells in the bone marrow, without evidence of end-organ damage and in the absence of a significant M-protein, a diagnosis of monoclonal gammopathy of uncertain significance (MGUS) would be favored. Thus, the significance of the marrow plasma cell count (and the establishment of clonality in the plasma cell population) cannot be understated.

Question 1. Assuming an IgG kappa M-protein of 12 g/L; a hemoglobin of 11.3 g/dL (normal range 13.7-18.0 g/dL); an insignificant urine protein electrophoresis result; a normal range glomerular filtration rate; a normal range Calcium level; and an absence of PET/CT and MRI evidence of bone disease, the above case meets the IMWG criteria for:

A. MGUS
B. Smoldering myeloma
C. Symptomatic myeloma
D. Nothing; this case is non-diagnostic

Despite the complexity of diagnostic criteria, there is clinical utility in distinguishing MGUS, from smoldering myeloma to symptomatic myeloma (as well as the other subtypes of plasma cell proliferations). The clinical course for patients with MGUS, for example, is characteristically mild, with a typical risk of progression to myeloma of approximately 1% of cases per year. Likewise, for patients with smoldering myeloma, the risk of progression to symptomatic myeloma is estimated at 10% per year for the first 5 years post-diagnosis. At the extreme, myeloma may present as or evolve into outright plasma cell leukemia, defined by the presence of at least 20% circulating plasma cells; these cases are typically aggressive and portend a poor prognosis.

Akin to many other malignancies, cases of myeloma (and indeed other neoplastic plasma cell proliferations) are far more frequently seen in older populations: 90% of cases occur in patients older than age 50, and incidence increases with age with a median age at diagnosis of 70 years. Myeloma is more frequent in males than females and occurs more frequently in African Americans than Caucasians.

Plasma cell neoplasms can show a number of abnormal morphologic and immunophenotypic features, although these features may not be diagnostic unto themselves. Neoplastic plasma cell proliferations are more likely to show plasma cells with multinucleation, pleomorphism, nucleoli and atypical mitotic figures. Collections of over-produced immunoglobulin may also be seen; these may take on the form of grape-like intracellular collections (so-called Mott cells), round often red-colored inclusions (so-called Russel bodies) or even as intra- or extra-cytoplasmic crystalline materials (the latter sometimes phagocytosed by histiocytes). More consistently, neoplastic plasma cell proliferations show abnormal flow cytometric phenotypes such as loss of CD19 and aberrant expression of CD20, CD56, CD117 or Cyclin D1. The latter Cyclin D1 positive cases may show t(11;14) positivity, a rearrangement that (in the absence of other high-risk features) has been shown to confer a good prognosis.

Question 2. Which of the following is CORRECT?

A. Monoclonal gammopathy of uncertain significance is most frequent in age groups under age 50
B. Progression of MGUS to smoldering myeloma is not observed
C. The anticipated clinical course of monoclonal gammopathy of uncertain significance warrants immediate clinical intervention
D. The outcome risk of a patient presenting with plasma cell leukemia with normal plasma cell cytogenetics is expected to be worse than a patient presenting with symptomatic myeloma (but without circulating plasma cells)

Well-established scoring systems exist to better risk-stratify cases of otherwise indistinguishable myeloma. The recently revised International Staging System (R-ISS) incorporates a number of laboratory parameters (including serum albumin, beta-2-microglobulin and lactate dehydrogenase) as well as FISH-defined risk parameters. High-risk FISH features include the presence of one or more of del(17p), t(4;14) or t(14;16); non-high risk FISH findings are otherwise classified as standard risk. With

these details, myeloma patients can be reliably stratified into three disease stages at diagnosis, with progressively worse expected outcomes.

Question 3. Which of the following statements is CORRECT?

A. According to R-ISS, cases of symptomatic myeloma with bone marrow plasma cell counts of 30% and 50%, with otherwise equivalent R-ISS scores, can be expected to have comparable clinical outcomes if treated similarly
B. Cases of myeloma with del(17p) and t(4;14) can be expected to have worse clinical outcomes than cases with either FISH abnormality alone
C. The high-risk t(11;14) translocation, when encountered in myeloma, portends a poor prognosis
D. The R-ISS scoring system incorporates laboratory data, including bone marrow pathology results, as well as cytogenetic data to arrive at a prognostic score

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Treatment options in myeloma are numerous and varied, and depend greatly on risk stratification and transplant eligibility. Recent decades have seen the introduction of numerous biologic and small-molecule based therapies that, while less frequently used in upfront treatments currently, have substantially improved outcomes for refractory and multiply-relapsed patients. Current upfront therapies involve combinations of immunomodulatory drugs (so-called IMiDs, eg. lenalidomide), proteasome inhibitors (eg. bortezomib) and steroids, which have been shown to be most effective in combination rather than as single agents. Treatment responsive patients, deemed to be candidates for additional intensive treatment, will then be encouraged to undergo autologous stem cell transplant. Although relapses are relatively common in myeloma, patients may later undergo additional intensive treatment (including second transplant attempts) and long-term treatments with the above drugs in combination have shown success as well. The recent introduction of anti-CD38 monoclonal antibodies (eg. daratumumab) has led to substantial improvements in disease response in some relapsed and refractory patients.

Recent developments in Next-Generation Sequencing (NGS) have led to the application of highly sensitive minimal (or measurable)-residual disease (MRD) assays to myeloma. While not widely available as yet, these techniques offer a greater degree of sensitivity for the persistent presence of malignant plasma cell clones than current disease response indicators (which, depending on the center, may include high-sensitivity flow cytometry, PET/CT or other imaging techniques, and/or high-sensitivity serum electrophoresis with immunofixation). Based on MRD assessment, additional second line treatments can be considered; studies looking into whether MRD assessment can serve to highlight populations of patients unlikely to require maintenance therapy (due to durable response) are ongoing.

Question 4. Which statement is CORRECT?

A. Allogeneic stem cell transplant is recommended as the first line treatment for symptomatic myeloma
B. MRD assessment can be used to demonstrate primary treatment failure
C. Single agent treatment is always recommended for symptomatic myeloma patients
D. The use of NGS for MRD assessment is not recommended given its lack of sensitivity when compared with other laboratory methods

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Etienne R. Mahe, MD, MSc, FRCPC, FCAP
Hematology and Clinical Microscopy Committee

References:

Swerdlow SH, Campo E, Harris NL, et al. *WHO Classification of Tumours of the Haematopoietic and Lymphoid Tissues.* 4th ed. Lyon, France: IARC Press, 2008.

Rajkumar, S Vincent, et al., International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *The Lancet Oncology.* Volume 15, Issue 12, e538 - e548

Palumbo, A, et al. Revised International Staging System for Multiple Myeloma: A Report from the International Myeloma Working Group. *Journal of Clinical Oncology.* 2015 33:26, 2863-2869

Kumar, SK, et al. *Clinical Practice Guidelines in Oncology: Multiple Myeloma.* National Comprehensive Cancer Network. Version 3.2017, November 28, 2016

Answers to Questions:

Question 1. Assuming an IgG kappa M-protein of 12 g/L, an insignificant urine protein electrophoresis result, a normal range glomerular filtration rate, a normal range Calcium level and an absence of PET/CT and MRI evidence of bone disease, the above case meets the IMWG criteria for:

Answer: C. Symptomatic myeloma

In addition to a clonal plasma cell population identified on bone marrow evaluation numbering greater than 60%, the patient is noted to have anemia, with a level of hemoglobin reduction greater than 2.0 g/dL from normal range of approximately 14-18 g/dL. Thus, the patient meets two of the IMWG extended "CRAB" criteria for the diagnosis of symptomatic myeloma.

Question 2. Which of the following is most CORRECT?

Answer D. The outcome risk of a patient presenting with plasma cell leukemia with normal plasma cell cytogenetics is expected to be worse than a patient presenting with symptomatic myeloma (but without circulating plasma cells)

Patients with a history of plasma cell neoplasia may progress to plasma cell leukemia (defined as having a peripheral blood plasma cell count of at least 20%); likewise, some cases of plasma cell leukemia may present de novo. All other factors equal, (especially cytogenetic risk factors), these patients tend to have poor outcomes relative to non-leukemic symptomatic plasma cell myeloma.

Question 3. Which of the following statements is CORRECT?

Answer: A. According to R-ISS, cases of symptomatic myeloma with bone marrow plasma cell counts of 30% and 70%, with otherwise equivalent R-ISS scores, can be expected to have comparable clinical outcomes if treated similarly

Notably, the R-ISS scoring system does not take bone marrow plasma cell counts into account. Thus, patients meeting the IMWG criteria for symptomatic myeloma with bone marrow plasma cell counts of 30% or 50% should be expected to have comparable outcomes. The t(11;14) is not considered a high-risk cytogenetic feature in myeloma. Based on the R-ISS data, a combination of two or more high-risk FISH features does not confer a statistically worse prognosis than one high-risk FISH feature alone.

Question 4. Which of the following statements is CORRECT?

Answer: B. MRD assessment can be used to demonstrate primary treatment failure

As in many other cancers, MRD assessment can be used to demonstrate treatment failure and serves as an adjunct to other clinical assessment tools. While allogeneic stem cell transplant has been used as a means to treat myeloma, it is in fact autologous stem cell transplant that is recommended in myeloma patients that are candidates for intensive therapy. Multi-agent chemotherapy is the recommended norm in the treatment of myeloma. NGS for MRD assessment is currently not the standard in all centers given its expense and lack of availability; NGS techniques have been shown to be equal or superior to all other MRD assessment tools evaluated thus far.

Actions Laboratories Should Take when a PT Result is Not Graded

The College uses Exception Reason Codes that signify the proficiency testing (PT) for an analyte has not been graded. The Exception Reason Code is located on the evaluation report in brackets to the right of the result. Your laboratory must identify all of the analytes with an Exception Reason Code and investigate the acceptability of performance with the same rigor as if it were an unacceptable performance. The actions accredited laboratories should take include but are not limited to:

Code	*Exception Reason Code Description*	*Action Required*
11	Unable to analyze.	Document why the specimens were not analyzed (eg, instrument not functioning or reagents not available). Perform and document alternative assessment (ie, split samples) for the period that commercial PT was not tested to the same level and extent that would have been tested.
20	No appropriate target/response; cannot be graded.	Document that the laboratory performed a self-evaluation using the data presented in the Participant Summary and compared its results to a similar method, all method, or all participant statistics if provided. If comparison is not available, perform and document alternative assessment (ie, split samples) for the period that commercial PT was not tested to the same level and extent that would have been tested.
21	Specimen problem.	Document that the laboratory has reviewed the proper statistics supplied in the Participant Summary. Perform and document alternative assessment for the period that commercial PT was not tested to the same level and extent that would have been tested. Credit is not awarded in these cases.
22	Result is outside the method/ instrument reportable range.	Document the comparison of results to the proper statistics supplied in the Participant Summary. Verify detection limits.
24	Incorrect response due to failure to provide a valid response code.	Document the laboratory's self-evaluation against the proper statistics and evaluation criteria supplied in the Participant Summary. Perform and document the corrective action of any unacceptable results. Document corrective action to prevent future failures.
25	Inappropriate use of antimicrobial.	Document the investigation of the result as if they were unacceptable and review the proper reference documents to gain knowledge of the reason your response is not appropriate.
26	Educational challenge.	Response to the CAP is not required. Laboratory should document its review.
27,31	Lack of participant or referee consensus.	Document that the laboratory performed a self-evaluation and compared its results to the intended response when provided in the Participant Summary. If comparison is not available, perform and document alternative assessment (ie, split samples) for the period that commercial PT reached non-consensus to the same level and extent that would have been tested.
28	Response qualified with a greater than or less than sign; unable to quantitate.	Document that the laboratory performed a self-evaluation and compared its results to the proper statistics supplied in the Participant Summary. Verify detection limits.
30	Scientific Committee decision.	Document that the laboratory has reviewed the proper statistics supplied in the Participant Summary.
33	Specimen determined to be unsatisfactory after contacting the CAP.	Document that the laboratory has contacted the CAP and no replacements specimens were available. Perform and document alternative assessment (ie, split samples) for the period that commercial PT was not tested to the same level and extent that would have been tested.
40	Results for this kit were not received.	Document why results were not received, corrective action to prevent recurrence and the laboratory's self-evaluation of the results by comparing results to the proper statistics and evaluation criteria supplied in the Participant Summary. If PT specimens were not analyzed, perform and document alternative assessment (ie, split samples) for the period that commercial PT was not tested to the same level and extent that would have been tested.
41	Results for this kit were received past the evaluation cut-off date.	
42	No credit assigned due to absence of response.	The Participant Summary indicates which tests are graded (see evaluation criteria) and which tests are Not Evaluated/Educational. Updates to grading will also be noted. If a test is educational, the laboratory is not penalized for leaving a result(s) blank. The code 42 that appears on the evaluation is **not** a penalty. However, if a test is graded (regulated and non-regulated analytes) and your laboratory performs that test, results cannot be left blank. The laboratory is required to submit results for **all** challenges within that test or use an appropriate exception code or indicate test not performed/not applicable/not indicated. Exceptions may be noted in the Kit Instructions and/or the Result Form. Document corrective actions to prevent future failures.
44	This drug is not included in our test menu. Use of this code counts as a correct response.	Verify that the drug is not tested on patient samples and document to ensure proper future reporting.
45	Antimicrobial agent is likely ineffective for this organism or site of infection.	Document that the laboratory performed a self-evaluation of written protocols and practices for routine reporting of antimicrobial susceptibility reports to patient medical records. Document that routine reporting of this result to clinicians for patient care is compliant with specific recommendations of relevant Medical Staff and Committees (eg, infectious Diseases, Pharmacy and Therapeutics, Infection Control). Response to the CAP is not required.
77	Improper use of the exception code for this mailing.	Document the identification of the correct code to use for future mailings.
91	There was an insufficient number of contributing challenges to establish a composite grade.	Document the investigation of the result as if it were an unacceptable result. Perform and document the corrective action if required.
35, 43, 88, 92	Various codes.	No action required.

COLLEGE of AMERICAN PATHOLOGISTS

Attestation of Participation for Self-Reported Training*

We the participants below have completed the review of the CAP BMD-A, 2017 (Product Mailing, Year) Participant Summary/Final Critique report, and can self report the recommended 0.5 (Education Hours) hours towards fulfilling education and certification of maintenance requirements.

Participant	Date	Participant	Date

Director (or Designee) Signature - I have verified that the individuals listed above have successfully participated in this activity. Date

Retain this page for record-keeping and auditing purposes.
Individuals can also track their participation of educational activities through the CAP Learning Management System (LMS).

1. Log in to www.cap.org, using your User ID and Password. If you don't have an online account, you will need to create one.
2. Click **Learning**, select **Learning Transcript**
3. Click '**Add My Own Activity**'
4. Enter the required information, and click **Save** when complete

For assistance, call our Customer Contact Center at 800-323-4040 or 847-832-7000 option 1.

**CAP Self-Reported Training activities do not offer CE credit, but can be used towards fulfilling requirements for certification of maintenance by agencies such as the American Society of Clinical Pathology (ASCP). Please verify with your certifying agency to determine your education requirements.* 49215