Template for Reporting Results of Biomarker Testing for Myeloproliferative Neoplasms

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For the Members of the Cancer Biomarker Reporting Committee, College of American Pathologists
Myeloproliferative Neoplasms • Biomarkers

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CAP MPN Biomarker Template Revision History

Version Code
The definition of the version code can be found at www.cap.org/cancerprotocols.

Version: MPN_Biomarkers 1.0.0.1

Summary of Changes

RESULTS

The following note was added:
Note: If a marker is tested by more than one method (eg, polymerase chain reaction and immunohistochemistry), please document the additional result(s) and method(s) in the Comments section of the report.

The following data elements were changed to “select all that apply”:
Fluorescence In Situ Hybridization (FISH) Testing
Additional Mutation Testing

Added the following data element and notes:

COMMENT(S)


All reported gene sequence variations should be identified following the recommendations of the Human Genome Variation Society (www.hgvs.org/mutnomen/; accessed February 10, 2015).
MPN Biomarker Reporting Template

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Completion of the template is the responsibility of the laboratory performing the biomarker testing and/or providing the interpretation. When both testing and interpretation are performed elsewhere (eg, a reference laboratory), synoptic reporting of the results by the laboratory submitting the tissue for testing is also encouraged to ensure that all information is included in the patient’s medical record and thus readily available to the treating clinical team.

MYELOPROLIFERATIVE NEOPLASMS (MPNs)

Select a single response unless otherwise indicated.

Note: Use of this template is optional.

+ SPECIMEN TYPE
  + ___ Peripheral blood
  + ___ Bone marrow
  + ___ Isolated granulocytes from peripheral blood
  + ___ Other (specify): __________

+ RESULTS

Note: If a marker is tested by more than one method (eg, polymerase chain reaction and immunohistochemistry), please document the additional result(s) and method(s) in the Comments section of the report.

+ Cytogenetic Testing Results (karyotype)
  + ___ No abnormalities detected
  + ___ Abnormal karyotype detected (specify): ____________________________

+ Fluorescence In Situ Hybridization (FISH) Testing (select all that apply)
  + ___ BCR-ABL1
    + ___ No BCR-ABL1 fusion detected
    + ___ BCR-ABL1 fusion detected (specify percent positive cells): _______%
  + ___ PDGFRα
    + ___ No PDGFRα fusion detected
    + ___ FIP1L1-PDGFRα fusion detected (specify percent positive cells): _______%
    + ___ Other PDGFRα fusion detected (specify percent positive cells): _______%
  + ___ PDGFRβ
    + ___ No PDGFRβ fusion detected
    + ___ ETV6-PDGFRβ fusion detected (specify percent positive cells): _______%
    + ___ Other PDGFRβ fusion detected (specify percent positive cells): _______%
  + ___ FGFR1
    + ___ No FGFR1 rearrangement detected
    + ___ FGFR1 rearrangement detected (specify percent positive cells): _______%

+ Data elements preceded by this symbol are not required.
**BCR-ABL1 Transcript Reverse Transcription Polymerase Chain Reaction (RT-PCR) Testing**

+ ___ No BCR-ABL1 fusions detected
+ ___ BCR-ABL1 fusions detected
  
  If quantitative testing performed:
  + BCR-ABL1 normalized copy number (BCR-ABL1/reference gene): ______________
  + Percent BCR-ABL1 on international scale (e13/14a2 (p210) fusions only): __________ %

**JAK2 p.V617F (c. 1849G>T) Mutation Testing**

+ ___ No mutation detected
+ ___ Mutation detected

  + For JAK2 p.V617F, if test is quantitative, specify quantitative value: ______________
    
    Reported as:
    + ___ Percent mutant allele burden
    + ___ Percent transcript levels
    + ___ Normalized copy number (V617F transcripts/reference gene)

**Additional Mutation Testing (select all that apply)**

+ ___ JAK2 exon 12
  + ___ No JAK2 exon 12 mutation detected
  + ___ JAK2 exon 12 mutation detected (specify mutation): ______________

+ ___ MPL
  + ___ No MPL mutation detected
  + ___ MPL mutation detected (specify mutation): ______________

+ ___ CALR (calreticulin)
  + ___ No CALR mutation detected
  + ___ CALR mutation detected (specify mutation): ______________

+ ___ KIT
  + ___ No KIT mutation detected
  + ___ KIT mutation detected (specify mutation): ______________

+ ___ Other (specify gene): ______________
  + ___ No mutation detected
  + ___ Mutation detected (specify mutation): ______________

**METHODS**

**BCR-ABL1 Transcript RT-PCR Testing**

+ ___ BCR-ABL1 RT-PCR assay sensitivity: ______________

**JAK2 p.V617F (c. 1849G>T) Mutation Testing**

+ ___ Assay sensitivity: ______________
+ Assay method:
  + ___ Allele-specific PCR
  + ___ Sanger sequencing
  + ___ Pyrosequencing
  + ___ Next-generation sequencing
  + ___ Other (specify): ______________

+ Data elements preceded by this symbol are not required.
+ Other Mutation Testing (specify gene): ________________________
  + Assay sensitivity: ________________________
  + Assay method:
    + ___ Allele-specific PCR
    + ___ Sanger sequencing
    + ___ Pyrosequencing
    + ___ Next-generation sequencing
    + ___ Other (specify): ________________________
  + Exon(s)/codon(s) covered: ________________________

+ COMMENT(S)

____________________________________________________________________
____________________________________________________________________


All reported gene sequence variations should be identified following the recommendations of the Human Genome Variation Society (www.hgvs.org/mutnomen/; accessed February 10, 2015).
Explanatory Notes

Myeloproliferative neoplasms (MPNs) are clonal disorders characterized by the expansion of one or more myeloid lineages leading to increased bone marrow cellularity and elevated peripheral blood myeloid cell counts. The latter may manifest as granulocytosis, erythrocytosis, thrombocytosis, or a combination, depending on the disease subtype. The diagnosis and classification of MPNs require synthesis of the clinical, morphologic, immunophenotypic, and molecular genetic findings. Over the course of the last few years, the spectrum of genetic mutations identified in MPNs has expanded, and polymerase chain reaction (PCR) and/or sequence-based mutation testing is now routinely incorporated into the diagnostic workup. However, the diagnosis still relies heavily on the peripheral blood and bone marrow morphologic findings and the clinical features of the disease, particularly for those patients who do not have a disease-defining genetic abnormality.

In the 2008 World Health Organization (WHO) classification system, the category of MPNs includes chronic myelogenous leukemia (CML), chronic neutrophilic leukemia (CNL), polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), chronic eosinophilic leukemia, NOS, mastocytosis, and myeloproliferative neoplasm, unclassifiable (MPN-U), and the clinical and pathologic findings may overlap with the category of myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRα, PDGFRβ, and FGFR1.1 Classical cytogenetic karyotyping and fluorescence in situ hybridization (FISH) testing are often used in the evaluation of patients to test for the presence of t(9;22)(q34;q11.2);BCR-ABL1, particularly for those who present with neutrophilic leukocytosis, and for abnormalities of PDGFRα, PDGFRβ and FGFR1 for those patients who present with eosinophilia. Otherwise, patients with MPNs may have a variety of cytogenetic abnormalities. Various trisomies such as +8 and/or +9 are often identified. Given the degree of standardization and specialization that has occurred in BCR-ABL1 testing, and the repeated nature of the analyses, the College of American Pathologists (CAP) has published a separate CML monitoring template for those patients known to have CML.

When the cytogenetic and/or FISH testing results are nonspecific or negative, it may be necessary to utilize additional molecular genetic tests. The JAK2 p.V617F (c.1849G>T) somatic point mutation is present in almost all patients with PV and in a large proportion (40%-50%) of patients with ET or PMF. Both qualitative and quantitative testing methods are employed, although the utility of quantitation of the mutant JAK2 allele burden remains somewhat controversial. A small percentage of patients with PV who lack evidence of a JAK2 p.V617F mutation may have a mutation in exon 12 of JAK2, and these are often insertions or deletions.2 Different testing methods are often utilized for JAK2 p.V617F and JAK2 exon 12 mutations, and it should be noted that different methods, for example Sanger sequencing and allele-specific PCR, may have markedly different sensitivities. Mutations in the CALR (calreticulin) gene were recently identified in the majority of patients with ET or PMF who lack JAK2 mutations.3,4 Less commonly, mutations in the MPL gene are present in a subset of ET/PMF patients without JAK2 or CALR mutations.3 KIT mutation testing is helpful for the diagnosis and subclassification of mastocytosis and is important for determining the likely response to tyrosine kinase inhibitor (TKI) therapy.5

Given the pace of recent findings, additional pathologically relevant mutations are likely to be identified and/or clinically validated in the near future. With this in mind, the template includes space for reporting other mutation testing, and future template updates will reflect additional molecular genetic findings that may be incorporated into the WHO classification system.

References